UNIVERSITY OF SOUTHAMPTON

FACULTY OF MEDICINE

Human Development and Health

Understanding Change Management in Neonatal Intensive Care

An investigation into the factors affecting the successful integration into routine care of a complex intervention to improve the nutritional support of preterm infants

by

Mark John Johnson

Thesis for the degree of Doctor of Philosophy

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ABSTRACT

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UNDERSTANDING CHANGE MANAGEMENT IN NEONATAL INTENSIVE CARE

AN INVESTIGATION INTO THE FACTORS AFFECTING THE SUCCESSFUL INTEGRATION INTO ROUTINE CARE OF A COMPLEX INTERVENTION TO IMPROVE THE NUTRITIONAL SUPPORT OF PRETERM INFANTS

By Mark John Johnson

It is a consistent finding from clinical and health services research that attempts to translate new research evidence and knowledge into routine clinical practice often fail. This failure often occurs at the point of implementation and integration of new knowledge into everyday practice. Neonatal medicine offers several examples of the challenges associated with effective implementation of practice change to improve care. In particular, the nutritional care of preterm infants is an area where robust evidence for practice is sometimes lacking and clinical practice is variable. However, there is some evidence for potentially better practices in this area, including recommendations for the nutrient intakes for these infants based on research and consensus opinion. There is also evidence that standardising care based on current evidence and consensus 'best practice' can improve outcomes.

This thesis aimed to understand the factors affecting the translation of new practices into a complex health care environment and their integration into routine clinical care, and it used the development, implementation and evaluation of a complex intervention aimed at improving the nutrient intakes and growth of preterm infants in NICU as a framework to do this. The complex intervention consisted of comprehensive nutritional guidelines based on current available evidence or consensus based best-practice, a nutritional screening tool to identify infants at high risk of poor growth, a multidisciplinary nutrition team and a weekly nutrition ward round, and nurse 'champions for nutrition' who helped implement the new practices and

guidelines. Normalization Process Theory (NPT), a novel sociological framework which focusses on embedding new practices into routine care, was used to develop, guide and monitor the implementation of the intervention, and to help understand the factors affecting implementation.

A mixed methods approach was used. Quantitative methods were used to measure infant nutrient intakes and growth, guideline compliance, staff attitudes and intentions towards practice change (using the Theory of Planned Behaviour) and the extent to which the intervention was becoming 'normalised' into routine care (using NPT). Qualitative methods included focus groups to identify barriers prior to implementation and structured staff interviews to assess the factors affecting the normalisation of the new practices following implementation. The intervention was partially implemented during the latter five months of 2011, and then fully implemented during the whole of 2012. Infant outcomes were compared to a pre-implementation period in the first seven months of 2011.

Results demonstrated that both the partial and full implementation of the intervention was associated with modest improvements in daily protein intake and weight gain compared to the pre-implementation period. These were sustained beyond the intervention period into 2013. There was no impact on head growth. Several important processes of nutritional care (such as the timing of commencement of milk feeds and appropriate choice of milk) were not changed by the intervention. Measures of guideline compliance increased during the study period and were related to measures of normalisation using NPT. A theoretical framework outlining the factors affecting implementation was developed from the qualitative interview data, with key elements including an environment ready for change, the distribution of decisions away from doctors and towards nurses, and an emphasis on feedback of the effectiveness of the new practices.

Overall, this thesis allowed insight into the process of practice change in a complex environment. The findings suggest that complex interventions using multiple elements have the potential to change practice and improve patient outcomes. NPT may offer a way of enhancing the implementation process and subsequent integration of new practices into routine care. Understanding and adjusting for the factors that influence this process may lead to improvements in clinical practice and patient outcomes.

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DECLARATION OF AUTHORSHIP

I, Mark John Johnson declare that this thesis and the work presented in it are my own and has been generated by me as the result of my own original research.

Understanding Change Management in Neonatal Intensive Care:

An investigation into the factors affecting the successful integration into routine care of a complex intervention to improve the nutritional support of preterm infants

I confirm that:

1. This work was done wholly or mainly while in candidature for a research degree at this University;
2. Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
3. Where I have consulted the published work of others, this is always clearly attributed;
4. Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
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Johnson MJ et al Developing a new screening tool for nutritional risk in neonatal intensive care. *Acta Paediatr* 2014. DOI: 10.1111/apa.12855

Signed:.....

Date:.....

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Definitions and Abbreviations

AAP	American Academy of Pediatrics
AF	Audit and Feedback
AMSTAR	Assessment of Multiple Systematic Reviews
ANNP	Advanced Neonatal Nurse Practitioner
BAPEN	British Association of Parenteral and Enteral Nutrition
CAN	Clinical Assessment of Nutrition
CDSS	Clinical Decision Support Systems
CLD	Chronic Lung Disease
cm	Centimetre
CME	Continuing Medical Education
CNS	Coagulase Negative Staphylococcus
DBM	Donor Breast Milk
DEM	Dissemination of Educational Materials
DRV	Dietary Reference Value
EAR	Estimated Average Requirement
EDD	Estimated Date of Delivery
ELBW	Extremely Low Birth weight (birth weight less than 1000g)
EOV	Educational Outreach Visits
EPOC	Effective Practice and Organisation of Care
ESPGHAN	European Society for Pediatric Gastroenterology, Hepatology and Nutrition
g	gram
HC	Head Circumference
IGF	Insulin-like Growth Factor
IU	International Unit
IVH	Intraventricular Haemorrhage
Kcal	Kilocalorie
Kg	Kilogram
LBW	Low Birth Weight (birth weight less than 2500g)
LCP	Local Consensus processes
LOL	Local Opinion Leaders
LOS	Late Onset Sepsis
MBM	Maternal Breast Milk
MeSH	Medical Subject Headings
µmol	Micromole
mmol	Millimole
MRC	Medical Research Council
NCEPOD	National Confidential Enquiry into Patient Outcome and death
NEC	Necrotising Enterocolitis
NHS	National Health Service
NICM	Newborn Infant Close Monitoring
NICU	Neonatal Intensive Care Unit
nmol	Nanomole
NPM	Normalization Process Model
NPT	Normalization Process Theory

NST	Nutrition Support Team
OR	Odds Ratio
PBC	Perceived Behavioural Control
PBP	Potentially Better Practices
PCA	Post-conceptional Age
PI	Professional Intervention
PMAC	Proxy Measure of Actual Control
PMI	Patient Mediated Interventions
PN	Parenteral Nutrition
PNRS	Simple Paediatric Nutrition Risk Score
PRISM	Practical, Robust Implementation and Sustainability Model
PYMS	Paediatric Yorkhill Malnutrition Score
RNI	Reasonable Nutrient Intake
ROP	Retinopathy of Prematurity
RRI	Reasonable Range of Intake
SD	Standard Deviation
SDS	Standard Deviation Score
SEND	Standardised Electronic Neonatal Database
SENNAT	Southampton Electronic Neonatal Nutrition Assessment Tool
SN	Subjective Norms
STAMP	Screening Tool for the Assessment of Malnutrition in Paediatrics
STRONGkids	Screening Tool for Risk On Nutritional status and Growth
TPB	Theory of Planned Behaviour
TRA	Theory of Reasoned Action
UK	United Kingdom
US	United States
USA	United States of America
VLBW	Very Low Birth Weight (birth weight less than 1000g)
VON	Vermont Oxford Network
WHO	World Health Organisation

Chapter 1: Improving Clinical Practice by Effective Implementation of Evidence

This thesis aims to understand the factors affecting the translation of new practices into routine clinical care, and will explore strategies for changing practice and potential models for understanding change within complex health care environments. It will use the nutritional care of preterm infants cared for in the Neonatal Intensive Care Unit (NICU) as a vehicle to do this, and in particular, it will present the development, implementation and evaluation of a complex intervention aimed at translating current evidence and consensus best practices into routine care. Nutritional care of preterm infants was chosen as the focus for this thesis because it is an area where practice is varied, with a failure to consistently introduce potentially beneficial practices into care, resulting in suboptimal patient outcomes; nutrient intakes in this population are almost universally below those recommended and growth in the neonatal period is often slow. As there is some evidence that nutrition and growth are associated with developmental outcomes, and as nutritional care can be modified, this is a potentially important area in which to optimise management.

This first chapter will consider the need for effective implementation of new practices in health care and discuss the science of implementation. It will consider the concept of complexity surrounding healthcare interventions, and discuss the nutritional care of preterm infants on NICU as an example of a complex health care situation, in a complex environment. It will then discuss some key issues surrounding the implementation of new practices in this context. It will then briefly discuss models and strategies for implementation, and will conclude by outlining the aims and objective of this thesis.

1.1 The Need for Effective Implementation of Evidence into Practice

Research in the field of health and medicine aims to improve the care and treatments that patients receive, in turn improving both short and long term

outcomes. These improvements may occur through research into new diagnostic tests, treatments or procedures, but may also occur through research into the way in which services are organised and delivered, or through the way in which health care professionals are trained. Whilst large amounts of time, energy and money are invested into all these types of research, it is a consistent finding from both clinical and health services research that attempts to translate new research 'evidence' and knowledge into routine clinical practice or policy often fail.[1] This 'research-practice' gap can mean that patients fail to receive optimal treatments and care, or conversely can mean they receive unnecessary or potentially harmful care. This in turn can lead to provision of healthcare which is unnecessarily inefficient, ineffective or unsafe.

The gap between research evidence and practice is often wide and there are two recognised stages where 'blocks' may occur in the translation of knowledge into practice. The first (often referred to as T1) relates to "the transfer of new understandings of disease mechanisms gained in the laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans", whilst the second (often referred to as T2) is "the translation of results from clinical studies into everyday clinical practice and health decision making".[2] The T2 process relies on the availability of robust evidence, an appropriate method of applying the new evidence in practice and the implementation and dissemination of the new practices into routine care. Referring to both T1 and T2 as translational research is potentially unhelpful and confusing, as they are two very different activities, with T1 focussing on laboratory research and biomedical science, whilst T2 focusses on implementation and practice change at a clinical or organisational level[2].

In particular, it is at the T2 stage that many evidence-based treatments and practices fail to make the transition into routine clinical practice. This translation of research findings into clinical practice represents a significant challenge, and is a growing area of research; 'Implementation science' is the study of "methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and, hence, to improve the quality and effectiveness of health services. It includes the study of influences on healthcare professional and organisational behaviour"[3]. Implementation science seeks to understand the translation of knowledge into

practice and close the 'research-practice' gap. At this point it is prudent to mention Quality Improvement (QI), as QI and implementation science are closely related. One definition of QI is that it is the "improvement of patient experience and outcomes achieved through changing provider behaviour and organisation through using a systematic change method and strategies"[4]. It can be seen that this is very similar to the description of implementation science above, which states that it aims to promote the systematic uptake of research findings and other evidence into routine practice in order to improve the quality and effectiveness of care[3]. However, they are not identical, and perhaps the best way to consider the relationship between the two is that implementation science is about understanding the methods and factors that work best to facilitate QI[5]. Whilst this thesis focusses on implementation, there is clearly overlap with the QI field and some of the literature and models used in QI will be drawn on where relevant.

1.2 The Challenge of Effective Implementation

Whilst the concept of implementing a new practice is simple, in reality it is a complicated and difficult process. The challenge of implementation of evidence into practice is exemplified by hand hygiene and infection prevention. Despite good evidence for hand hygiene in the prevention of hospital acquired infection, combined with wide dissemination of this evidence, performance of hand hygiene behaviours in practice is often poor. There are several reasons for this, including practitioners overestimating the quality of their own practice, diverse clinical settings and environments and competing demands on professionals including time and cost. Several interventions in isolation have demonstrated small but short-lived improvements in practice in this area. It is only by using more comprehensive strategies which combine several interventions and approaches (multifaceted or 'complex' interventions) that significant and sustained improvements are seen[6].

Several steps are required in order for successful implementation; healthcare professionals need to be able to find and review new evidence, there must be an appropriate method and resources available for a change in practice to be developed and there must be a way to implement these changes that is

appropriate for the target environment and the staff involved in the new practices[6 7]. How challenging the implementation process will be depends on a number of factors relating to both the practice itself and the setting where is being implemented. More elaborate practices or treatments will be harder to integrate into routine care, and more complicated clinical environments will be more challenging.

1.3 Neonatal Medicine as an example of the challenges of implementation

Neonatal medicine offers several examples of the issues surrounding the implementation of practice change. As an intensive care unit, the NICU is a good example of a complicated environment; it has patients with multiple medical problems, and a large multidisciplinary healthcare team working variable shift patterns. In addition, staff are required to absorb a constantly changing array of clinical information from a variety of sources, including monitoring equipment, computerised results systems, colleagues and patients themselves. Workload is usually high, with priorities constantly changing across the unit as new patients are admitted or others become clinically unstable due to illness.

Availability of evidence is a particular challenge. This is partly due to the technical difficulties of carrying out adequately powered trials in this relatively small and fragile patient population, which investigate clinically important questions in relation to key outcomes such as necrotising enterocolitis (NEC) or neurodevelopmental impairment, which are also relatively rare. Whilst some practices in neonatal intensive care have a robust evidence base (for example, the use of antenatal steroid therapy for preterm infants, surfactant for respiratory distress syndrome and therapeutic hypothermia for hypoxic ischaemic encephalopathy), many do not. There are several examples in the neonatal medical literature where interventions have become part of routine care in the absence of evidence for their effectiveness, and which have in fact turned out to be detrimental. One example of this is the use of postnatal steroids for the treatment of neonatal chronic lung disease. Initial reports in the 1970s had shown acute improvements in respiratory status of preterm

infants, and several trials went on to demonstrate reduced ventilation requirements in preterm infants who received steroids[8]. The use of postnatal steroids therefore gradually became part of routine practice. However, a systematic review by Barrington in 2001, which combined eight randomised trials looking at neurodevelopmental outcome in relation to steroid therapy, showed that the use of postnatal steroids was associated with a substantial increase in cerebral palsy and neurodevelopmental impairment[9]. The number needed to harm was seven, and the relative risk of neurodevelopmental impairment following postnatal steroid therapy was 1.66[9]. At the same time there was no evidence of any benefit of steroids on mortality. Considering that contemporaneous data at the time suggested that postnatal steroids could be administered to as many as 12000 US infants each year, the number of infants potentially harmed by this therapy was substantial[8]. The review by Barrington[8] pointed out that whilst many neonatal therapies have been subject to large, adequately powered trials which demonstrated their efficacy and long term outcomes, many have not been subject to such evaluation. He warned that the continued uncritical application of treatments with uncertain efficacy and long term effects could lead to similar 'disasters' in the long term[9]. Similar examples of the uncritical introduction of an unproven therapy in neonatal medicine also include the use of 100% oxygen in the resuscitation of newborn infants, which has been shown to increase the risk of mortality or hypoxic ischaemic encephalopathy compared to room air[10 11]. In addition, the use of ranitidine and other H2 receptor blockers for the treatment of gastro-oesophageal reflux or ulcer prophylaxis, have been associated with an increased risk of NEC, infections and mortality[12 13].

1.4 Improving Practice in the Nutritional Care of Preterm Infants

The nutritional care and growth of preterm infants cared for in the NICU is a good example of an area where there is evidence of suboptimal outcomes and a subsequent need for improvements in practice, but where a robust body of evidence on which to base practice is lacking. The 'EPICure studies' are two large epidemiological studies which have investigated the outcomes of extremely preterm infants born between 20 and 26 weeks gestation in the UK

during 1995 and 2006. These studies demonstrated that despite improvements in neonatal intensive care which have seen the survival of preterm infants improve significantly from 39% in 1995 to 52% in 2006, the growth of these infants has not improved. Both the 1995 and 2006 studies showed that whilst preterm infants had weight and head circumferences similar to UK normative data at birth, at their estimated date of delivery (EDD) they were much shorter, lighter and had smaller head circumferences compared to reference data for infants born at term.

However, as mentioned above, establishing robust recommendations for the nutritional care of preterm infants, with the aim of improving their growth, is difficult as the scientific evidence on which to base these is limited, as will be discussed in Chapter 2. Despite this, recommendations for the nutrient intakes of preterm infants have been published[14 15], however there is evidence that these are not achieved in clinical practice[16]. There is also evidence that inconsistent and variable nutritional care may be partly responsible for suboptimal growth. Cooke et al demonstrated that units offering the same level of care had significant variations in rates of postnatal growth restriction and in lengths of stay, with the differences in feeding practices and nutrient intakes felt to be one of the factors responsible for this variation [17].

Variability in neonatal nutritional care has been further demonstrated by a survey of Parenteral Nutrition (PN) provision for preterm infants in neonatal units in the UK, which showed wide variation in prescribing patterns. Only 54% of units initiated PN on day one, and 25% of units did not prescribe maximal nutrition for the first week of life. Protein intakes varied considerably, and only 4% of units even aimed to achieve the recommended targets [18]. Similarly, a report by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) in 2010 on the use of PN in neonatal care identified considerable variability in the practice of both prescription and administration. Only 62 of the 264 cases reviewed (24%) demonstrated what could be considered good practice, and there was a large amount of variability in the prescription of PN in relation to nutritional requirements. This demonstrates not only the variability in practice, but also the need for clearer guidelines based on recommended nutrient intakes[19]. Achieving recommended intakes on enteral feeding is also a major challenge. Whilst breast milk has been shown to reduce the risk of NEC[20] and contains important nutrients such as long chain polyunsaturated fatty

acids, immunoglobulins, growth factors and cytokines, it is inadequate for preterm infants in terms of protein, phosphate, vitamin D and overall energy provision. Human milk fortifiers are available but their use can be variable.

1.5 Variability and the need for standardisation

Variation in practice and outcome is increasingly recognised as one of the major challenges in health care provision, and there is evidence of wide variation between different neonatal units in both nutrient provision and growth, in comparable populations of babies. The Vermont Oxford Network (VON), consisting of over 800 participating neonatal units worldwide, runs a database which aims to provide a bench-marking facility for the care of very low birth weight infants (VLBW, birth weight less than 1501g) and those born below 30 weeks gestation, allowing differences in outcomes between units to be explored[21]. Variation in outcomes between essentially 'similar' neonatal populations and providers is often wide, demonstrating that these variations in clinical care are important. Since variation in the delivery of care is dependent on the clinical staff and service organization, it is possible to see how changes in staff practice and service delivery can make a large impact on care and therefore on outcomes.

Members of the VON demonstrated this concept in the field of nutrition by collaborating to develop guidelines for eight 'potentially better practices' (PBP's) for nutritional care, covering early use of PN, early introduction of feeds, feed advancement and the use of breast milk and breast milk fortifier, as well as introducing regular monitoring of nutrition and growth. The new practices were termed 'potentially better' in recognition of the lack of evidence for some of them. The changes to management were introduced through a number of 'Plan-Do-Study-Act' cycles – a form of rapid-cycle audit that forms the basis of the 'Model for Improvement' originally developed by Associates for Process Improvement (discussed in more detail in chapter 3)[22]. By using before and after assessments, they were able to demonstrate clinically significant reductions in the time to start PN and enteral feeds, length of stay and the number of infants with a discharge weight below the 10th centile for age[23].

Similarly, a systematic review and meta-analysis by Patole and De Klerk demonstrated that standardised feeding regimens significantly reduced the

risk of NEC [24], and there is also evidence that the use of formal nutrition support leads to significantly earlier initiation of both parenteral and enteral feeding, earlier achievement of full enteral feeding, and earlier regaining of birth-weight[25]. Involvement of a dietician in neonatal unit nutrition support has been shown to be associated with an improvement in growth in terms of both weight and head circumference [26], and infants cared for in NICUs with a greater input from a registered dietician were more likely to receive higher and more appropriate nutrient intakes, particularly protein [27].

Outside of neonatal medicine, there are other examples of how the use of guidelines or protocols can be beneficial. This situation is becoming increasingly common, with healthcare providers seeking to implement QI programmes or comprehensive guidelines in order to make an area of care more consistent, efficient and effective. Often guidelines for improving the consistency and quality of care are based on such 'best practice' which may be derived from lower quality evidence or consensus opinion. Some studies have shown that being involved in a research trial can be beneficial to practice and outcomes, regardless of whether participants receive the control or trial treatment, with the benefit felt to be conferred by the use of standardised protocols for treatment for patients in the trial. A review of diabetes trials by Gale et al showed that patients in trials had improved glycaemic control regardless of which treatment arm they were in[28], whilst a similar review looking at multiple myeloma treatment trials by Karjalainen et al found that patients in the trials were more likely to survive regardless of treatment, concluding that treatment protocols improved results compared to free clinician choice of treatment[29]. Braunholtz et al's systematic review of randomised controlled trials found a potentially beneficial effect of trial involvement (a 'trial effect'), though this was felt to be at its greatest in large trials where an effective control treatment already exists and is included in the trial protocol[30]. Interestingly, the authors noted that the 'trial effect' was less apparent in trials where the scope for a 'Hawthorne effect' (when individuals alter their behaviour when they know they are being studied) was limited[30]. However, a Cochrane review by Vist et al in 2009 looking at the effect of trial participation could not detect a difference in outcomes caused by such a 'trial effect[31], although a more recent systematic review by Clarke et al found that this 'trial effect' improved clinician adherence to guidelines and increased use of evidence in practice, but were not clear of its effects on patient outcomes[32].

Thus, whilst the evidence for best practice in neonatal nutritional care is not robust across all areas, there is evidence that standardising care using 'best' or 'potentially better' practices is likely to lead to improved outcomes for preterm infants. However, as discussed above, given the complicated nature of the NICU environment and the preterm infants themselves, coupled with the complexity of nutritional care related to different nutrients and types and methods of feeding, it is unsurprising that a universally accepted model for standardised practice based on the best available evidence, does not yet exist. It is clear therefore that the complex nature of the implementation process in such a situation requires a carefully considered strategy.

1.6 The Challenge of Complexity

The relative complexity of the situation in which implementation will take place will clearly have implications for the implementation process itself. This thesis will repeatedly use the term 'complex' in relation to the implementation of new practices, and so it important to consider what is meant by this. In his book 'Developmental Evaluation', which discusses approaches to the delivery and monitoring of social innovations, Michael Patton provides a framework for recognising when situations into which new innovations are to be deployed are *simple*, *complicated* or *complex*[33]. This framework is also useful for considering the concept of *complexity*, particularly with regard to the implementation of new practices in healthcare.

Patton considers that the degree of complexity can be considered in two dimensions. The first is the degree of certainty there is about how to solve a problem, and the second is the extent to which there is agreement about how to solve a problem. These two dimensions are shown as the two axes of a graph in figure 1.1. It can be seen that situations are *simple* when there is a high level of certainty and agreement about how to solve a problem. Simple situations are more predictable and therefore amenable to detailed planning, controlled execution and precise measurement. Figure 1.1 also shows how some situations may have high agreement but a lack of certainty about how to proceed, or poor levels of agreement but greater certainty; these situations may be considered *complicated*. Situations complicated by a lack of certainty

tend to be those involving a technically challenging the task, which may require experimentation or the coordination of expertise (Patton gives the example of launching rocket into space here). Conversely, situations complicated by a lack of agreement tend to socially complicated, with multiple stakeholders with multiple interactions and conflicts (for this Patton gives human rights campaigns as an example, where there is certainty about what to do, but disagreement about how to do it or the exact nature of the problem). When a situation is complicated by both a lack of agreement and a lack of certainty it becomes *complex*, and this 'zone of complexity' can also be seen in figure 1.1, which also shows how situations where there is extensive disagreement and uncertainty can lead to 'chaos', with people avoiding the situation altogether[33].

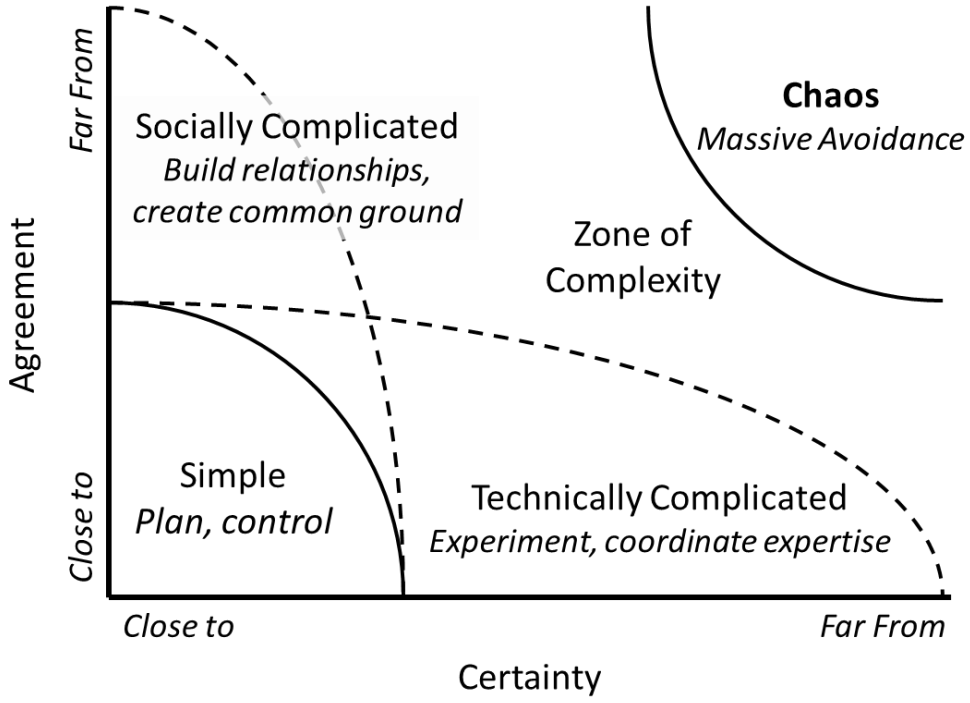


Figure 1.1: A framework for considering complexity (adapted from Patton[33])

When considering the nutritional care of preterm infants using Patton's framework, it can be seen how this is an excellent example of a *complex* situation. As discussed above and in chapter 2, there is uncertainty about the best practices and evidence regarding nutritional care, together with a degree of disagreement regarding the best approach and the most appropriate nutritional and growth outcomes for these infants. In addition, considering figure 1.1, the nature of the evidence around nutritional care makes the situation *technically complicated*, whilst the NICU environment; with

complicated patients and a large multidisciplinary healthcare team working variable shift patterns, is *socially complicated*.

Taking this concept further and looking at figure 1.1, it is possible to appreciate that in a *complex* situation where there is both uncertainty and disagreement, it is not possible to resolve one without dealing with the other. Some of the technical complications regarding the optimal nutrient intakes and patterns of growth for preterm infants will only be able to be resolved when adequate systems exist to deliver consistent and effective nutritional care (i.e. when there are minimal social complications). Similarly, it will not be possible to resolve some of the social complications regarding effective practice and delivery of care until those delivering that care can be certain that they are working with the correct evidence and towards an agreed goal (i.e. when there are minimal technical complications). Therefore, the study described in this thesis will attempt to deal with this complexity by trying to address both the technical complications (by trying to be clear about current evidence and recommendations for practice) and the social complications (by trying to ensure effective implementation and integration into routine care).

1.7 Strategies for effective implementation

There are multiple strategies that can be used to translate research evidence into practice, mostly focussing on changing the behaviour and practice of healthcare providers. Such strategies include the use of practice guidelines, reminder systems, local opinion leaders and audit and feedback, and are discussed in detail in chapter 5. No single intervention appears to be particularly effective in isolation, so using multiple strategies in combination as part of a multifaceted approach in a so-called 'complex intervention' seems to offer the best chances of successful implementation.

The Medical Research Council (MRC) defines a complex intervention as an intervention with several interacting components, and has recently published updated guidance on how such interventions should be developed and evaluated [34]. Complexity can occur at several levels; the number of and interactions of components, the difficulty of behaviours required, the number of groups the intervention targets, and a variety of outcome measures. It can

be seen how such complex interventions might fit with the description of complexity by Patton discussed above, with different components acting to address technical or social complications. The MRC guidance recommends that a good theoretical understanding of how the intervention causes change is needed, together with a measure of the effectiveness of implementation and uptake (a "process evaluation"), and appropriate outcome measures. Tailoring the intervention to the local setting to ensure effective implementation is also recommended, though this additional variability may increase the complexity of the intervention. The use of a model or framework on which to base the intervention is also suggested[34]. A variety of frameworks and theories exist for understanding practice related behaviour, dissemination and implementation, and have been generated across a wide range of disciplines including medicine, public health, sociology, psychology, marketing and the commercial sector. Some of these models are described and discussed in more detail in chapter 3, but the various models have their own advantages and disadvantages, with each lending itself to particular types of practice or setting.

One such model for use in implementation which is particularly appealing in the context of complex interventions is Normalisation Process Theory (NPT), which considers the social processes through which a new practice is implemented, embedded and integrated into normal practice. This sets NPT apart from many other theories as it seeks to move beyond the implementation process to consider the important next step of how newly implemented practices 'stick' within an institution, becoming part of routine practice. This is discussed in more detail in chapter 3.

1.8 Aims and Hypothesis

This thesis focusses on the implementation of a complex intervention aimed at translating current evidence in neonatal nutritional care into practice in order to improve the nutrient intakes and growth of preterm infants. It also seeks to understand the process of implementation of new practices and their subsequent integration into routine care and uses the sociological framework of NPT to do help this, with NPT (and the associated NPT toolkit [35 36]) used to

develop, assess and guide the intervention and its implementation, and subsequent integration into routine care. By utilising this novel approach, this study explores the process of a significant change in practice in a complex care environment, attempting to identify the factors which promote and inhibit its integration into practice, and establish how to embed new ways of working so that they become part of routine care. This is unique in offering the ability to integrate measures of implementation and normalization (provided by the modified NPT toolkit) with detailed clinical data on daily nutritional care, growth and outcomes.

The hypotheses that this study addresses are:

1. *The introduction of a complex intervention for the nutritional care of preterm infants will improve their nutrient intakes and growth*

2. *The use of Normalization Process Theory to both monitor and guide the implementation of a complex intervention will result in improved integration into practice with subsequent improvement in clinical outcome measures*

This research also aims to study the factors that influence the implementation and adoption of a complex intervention into routine care

1.9 Study Objectives

The primary objectives of this study are described in more detail, together with the primary and secondary outcome measures of the study, in chapter 4, but briefly they are to:

1. Develop and implement a complex intervention for the nutritional care of preterm infants (born at less than 30 weeks gestation or with a birth weight less than 1501g). Following implementation of the intervention (for 1 year), assess its effect on improving:
    a. The delivery of Energy (in kcal/kg/day) and Protein (in g/kg/day), compared with recommendations for this group of infants at 1 week of age, 2 weeks of age, 4 weeks of age, 6 weeks of age, 36 weeks post menstrual age and discharge.
    b. Growth (length, weight and head circumference) at 1 week of age, 2 weeks of age, 4 weeks of age, 6 weeks of age, 36 weeks post menstrual age and discharge.

2. Assess the factors which promote or inhibit the implementation, uptake and staff engagement of the complex intervention for the nutritional care of preterm infants. This includes:
    a. The effectiveness of the intervention in terms of changing practice and how successfully components of the complex intervention are embedded and integrated into 'normal' practice ('normalization')
    b. An assessment of the factors which impede or enhance the integration of the new practices into routine normal care ('normalization')
    c. The relationship between the effectiveness of the complex intervention at changing practice and the nutritional and growth outcomes described above.
    d. The effect of NPT to guide and assess the implementation process.

1.10 Summary

Preterm infants often fail to grow adequately and failure in growth may affect their survival and health outcomes in later life. This failure to grow is in part due to their nutritional care, and there is evidence that this care is variable both within and between different neonatal units. It is likely that a more consistent and standardised approach to the nutritional care of preterm infants, based on the best available evidence, will result in improved nutrient delivery and growth.

However, changing practice in order to provide a more evidence based and consistent approach is a difficult process. Whilst there are multiple strategies for approaching practice change (discussed in more detail in chapter 5) there are good reasons to suggest that a multifaceted "complex" intervention is most likely to succeed. In addition, developing an understanding of the context in which a complex intervention is to be implemented is vital to its success. This includes assessment of potential barriers and facilitators to the implementation process, and also the use of an appropriate theory as a framework to understand the implementation process and aid development of the intervention itself.

This thesis will explore strategies for changing practice and models for understanding change within the complex health care environment of NICU, using a complex intervention aimed at improving the nutrition and growth of preterm infants as a vehicle. It can be seen how improving the nutritional care of preterm infants is a complex situation, due to both technical complications related to the uncertainty regarding the best practices in nutritional care, and social complications related to the NICU environment, multiple stakeholders, and lack of agreement regarding best practice. Therefore, being clear about

the current evidence for practice is clearly important, and this discussed in chapter 2. Similarly, gaining an understanding of the social contexts where implementation will take place is key, and the theory chosen to aid the implementation of the intervention in this study is that of NPT. This is discussed in more detail in Chapter 3 together with discussion of other theories, models and frameworks used in this thesis and the reasons for their use. NPT was used to develop, assess and guide the intervention, its implementation, and subsequent integration into routine care[37 38]. A description of the development of the complex intervention, an assessment of potential barriers to change, and the tailoring of the intervention to the clinical setting is presented, followed by the results of the study in terms of both the effect of the intervention on nutrient intakes and growth, and the extent to which the intervention changed practice and became integrated into routine care. An assessment of the factors influencing this process is also presented.

Chapter 2: Nutrient Intakes, Growth and Nutritional Care for Preterm Infants

In order to develop an intervention which would optimise and standardise the nutritional care of preterm infants, with the aim of improving the provision of nutrients and growth during hospital stay, it is important to explore current patterns of growth and their relationship to later outcomes. It also necessary to consider the evidence on which recommended nutrient intakes are defined, together with existing evidence and published guidance for the nutritional management of preterm infants. This chapter will therefore present an overview of the literature in these areas.

2.1 Nutrition, Growth and Outcomes

The inter-relationships between nutrition, growth and the later health and development of preterm infants are complex, and as yet not fully understood. As described briefly in the previous chapter, slow growth is common in infants born extremely preterm, and 'extra uterine growth restriction' is well described in published literature and seen widely in clinical neonatal practice. In addition to the poor growth during NICU stay demonstrated by the EPICure studies, there is good evidence that preterm infants acquire a deficit in weight in the first few weeks of life that is not recovered by term equivalent age, with the majority of preterm infants remaining below the 10th centile for weight at discharge[39]. Furthermore, follow up of infants in the first EPICure study showed that poor growth persisted at 30 months corrected age, although there was a slight improvement in weight [40]. By six years of age, there was moderate 'catch-up' in growth measures, but they still remained well below that of the age-matched term-born controls[41].

While there is evidence of poor growth in the neonatal period, any causal relationship between this and the high risk of adverse neurodevelopmental outcome seen in extremely preterm infants is hard to determine. Ehrenkranz et al explored this relationship in a population of extremely low birth weight infants (ELBW; birth weight less than 1000g), collecting growth data prospectively during their stay on the neonatal unit and then dividing the

cohort into quartiles of growth velocity. This was then paired with data on the infant's development, assessed at 18-22 months of age using the Bayley Scales of Infant Development II-R. The percentage of infants with significant neurodevelopmental impairment increased steadily from the highest to the lowest quartile of neonatal growth and there was also a significant negative correlation between rate of head growth in the neonatal period and incidence of neurodevelopmental impairment [42]. However, the infants with the slowest growth also had higher incidences of sepsis, necrotising enterocolitis, chronic lung disease and postnatal steroid use, and although some of these were included as variables the regression analysis, they are also all risk factors for cerebral palsy and poor neurodevelopmental outcome. The association between growth and neurodevelopmental should therefore be treated with caution. Stephens et al described an association between increased protein and energy intakes during the first four weeks of life and higher Bayley Mental Development Index scores, as well as improved growth[43]. However, whilst this and subsequent observational studies have suggested an association between improved early growth or nutritional care and improved neurodevelopmental outcomes[44 45], there are currently no high quality studies which show this conclusively.

In addition to a quantitative growth failure, there is also evidence that quality of growth may be sub-optimal. A recent systematic review and meta-analysis carried out by myself and colleagues demonstrated that infants born prematurely fail to achieve a similar body composition on reaching term equivalent age compared to those born at full term, with a significant deficit in lean tissue accretion and subsequent relative increase in percentage body fat[46]. This is important, as in addition to the well-established effect of low birth weight increasing the risk of obesity and non-communicable disease in adulthood[47-49], alterations in the relative amounts of fat to lean tissue and the distribution of fat have also been shown to affect metabolic function later in life[48 50]. In particular, the pattern of decreased weight, relatively high adiposity and a deficit in lean tissue, has been observed in full-term Indian babies, where it has been associated with an increased risk of type 2 diabetes and relative adiposity in later life[51].

2.2 Nutrient Intake Recommendations for Preterm Infants

The reasons for the poor growth seen in very preterm infants are complex; they are born prior to the rapid period of growth experienced in utero during the third trimester of pregnancy, and often have multiple concurrent illnesses including respiratory problems and infections. This is further complicated by immature body organs and systems that are insufficiently developed to cope with the assimilation and metabolism of nutrients. However, one factor is that these infants simply do not receive adequate nutrition. Detailed recommendations for the optimal intake of nutrients for very low birth weight and extremely low birth weight infants[14 15] (see below) have been published, but there is evidence that there is often a failure to achieve these in clinical practice. Embleton et al looked at the provision of energy and protein to preterm infants with respect to published recommendations and demonstrated the accumulation of significant deficits early in life that were never recovered[16]. In addition, Martin et al also showed that early provision of nutrients was an important determinant of postnatal growth[52].

Since the 1970's, several different organisations and authors have published recommendations regarding the nutritional needs of preterm or low birth weight infants including the American Academy of Pediatrics (AAP) and the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) [53–55]. However, these were largely superseded and updated following the publication of 'Nutrition of the Preterm Infant: Scientific Basis and Practical Guidelines' edited by Tsang and colleagues in 1993[56], and revised to a second edition in 2005[14]. The original book built on work from an earlier publication 'Vitamin and mineral requirements in preterm infants' also edited by Tsang and colleagues and published in 1985[57]. 'Nutrition of the Preterm Infant' is widely used across the world by those responsible for the nutritional care of preterm infants as a reference for nutrient intakes. Further recommendations were produced in 2010 by ESPGHAN, who published guidance for enteral nutrient requirements for infants up to 1800g in weight[15]. However, Tsang et al's 2005 recommendations were used in this study as they can be applied to both enterally and parenterally fed infants[14]. Since this study has been completed, Tsang et al's text has been revised by Koletzko et al, though recommendations remain similar[58].

Whilst Tsang et al's recommendations for nutrient intakes are widely accepted, it is important to consider how they are defined and derived, as this has implications for any study using them as intake targets. The book gives a 'Reasonable Range of Intake' (RRI) for each specific nutrient, defined as "the range of average intakes derived from observations or evaluated under controlled conditions that appear to sustain adequate nutrition, based on absence of abnormal clinical signs and symptoms, or biochemical/functional normalcy". It is important to point out that the term 'RRI' is unique to Tsang et al's book and should be distinguished from the more commonly used and accepted Dietary Reference Values (DRVs) which include the terms Estimated Average Requirement (EAR) and Reference Nutrient Intake (RNI). EAR is the average requirement value of a specific nutrient for a specific population, based on given criteria (usually related to amounts required to prevent deficiency of the nutrient). RNI (previously referred to as Recommended Daily Amount, RDA) is the amount of a nutrient that is enough (or more than enough) to prevent deficiency for 97% of a population, often corresponding to the EAR plus two standard deviations[14 59]. The problem with the terms EAR and RNI is that they are intended for, and derived from healthy populations, based on data regarding the nutrient intakes required to prevent symptoms and functional and biochemical normality. Preterm infants are not able to be considered 'healthy', and it is difficult to define functional and biochemical normality, partly due to a lack of normative data for this population. The term RRI is used for Tsang et al's recommendations to reflect this, and to recognise limitations in the way in which they are derived.

Tsang et al present RRIs for 42 different nutrients (see Table 2.1 for the recommendations for key nutrients), with separate RRIs for ELBW and VLBW infants, and for both parenteral and enteral administration. The majority of RRIs are based on the goal of achieving growth rates similar to that seen in utero at the equivalent gestation. As discussed below, this may not be an entirely appropriate target, although it has to date been accepted as a reasonable goal[53].

	Extremely Low Birth Weight (<1000g)						Very Low Birth Weight (<1500g)					
	Parenteral			Enteral			Parenteral			Enteral		
	Day 0	Transition	Growing	Day 0	Transition	Growing	Day 0	Transition	Growing	Day 0	Transition	Growing
Energy (kcal)	40 - 50	75 - 85	105 - 115	50 - 60	90 - 100	130 - 150	40 - 50	60 - 70	90 - 100	50 - 60	75 - 90	110 - 130
Protein (g)	2 - 2	3.5 - 3.5	3.5 - 4	2 - 2	3.5 - 3.5	3.8 - 4.4	2 - 2	3.5 - 3.5	3.2 - 3.8	2 - 2	3.5 - 3.5	3.4 - 4.2
Carbohydrate (g)	7 - 7	8 - 15	13 - 17	7 - 7	8 - 15	9 - 20	7 - 7	5 - 12	9.7 - 15	7 - 7	5 - 12	7 - 17
Fat (g)	1 - 1	1 - 3	3 - 4	1 - 1	1 - 3	3.2 - 8.4	1 - 1	1 - 3	3 - 4	1 - 1	1 - 3	5.3 - 7.2
Sodium (mmol)	0 - 1	2 - 5	3 - 5	0 - 1	2 - 5	3 - 5	0 - 1	2 - 5	3 - 5	0 - 1	2 - 5	3 - 5
Potassium (mmol)	0 - 0	0 - 2	2 - 3	0 - 0	0 - 2	2 - 3	0 - 0	0 - 2	2 - 3	0 - 0	0 - 2	2 - 3
Calcium (mmol)	0.5 - 1.5	1.5 - 1.5	1.5 - 2	0.8 - 2.5	2.5 - 2.5	2.5 - 5.5	0.5 - 1.5	1.5 - 1.5	1.5 - 2	0.8 - 2.5	2.5 - 2.5	2.5 - 5.5
Phosphorous (mmol)	0 - 0	1.5 - 1.9	1.5 - 1.9	0.6 - 1.9	1.9 - 4.5	1.9 - 4.5	0 - 0	1.5 - 1.9	1.5 - 1.9	0.6 - 1.9	1.9 - 4.5	1.9 - 4.5
Magnesium (mmol)	0 - 0	0.2 - 0.3	0.2 - 0.3	0.1 - 0.3	0.3 - 0.6	0.3 - 0.6	0 - 0	0.2 - 0.3	0.2 - 0.3	0.1 - 0.3	0.3 - 0.6	0.3 - 0.6
Iron (umol)	0 - 0	0 - 0	1.8 - 3.6	0 - 0	0 - 0	35.8 - 71.6	0 - 0	0 - 0	1.8 - 3.6	0 - 0	0 - 0	35.8 - 71.6
Zinc (umol)	0 - 2.3	2.3 - 2.3	6.1 - 6.1	0 - 15.3	6.1 - 18.3	15.3 - 45.9	0 - 2.3	2.3 - 2.3	6.1 - 6.1	0 - 15.3	6.1 - 18.3	15.3 - 45.9
Copper (umol)	0 - 0	0 - 0.3	0.3 - 0.3	0 - 0	0 - 2.4	1.9 - 2.4	0 - 0	0 - 0.3	0.3 - 0.3	0 - 0	0 - 2.4	1.9 - 2.4
Selenium (nmol)	0 - 0	0 - 16.5	19 - 57	0 - 0	0 - 16.5	16.5 - 57	0 - 0	0 - 16.5	19 - 57	0 - 0	0 - 16.5	16.5 - 57
Iodine (nmol)	0 - 0	0 - 8	7.9 - 7.9	0 - 0	0 - 473	79 - 473	0 - 0	0 - 8	7.9 - 7.9	0 - 0	0 - 473	79 - 473
Manganese (nmol)	0 - 0	0 - 13.7	18.2 - 18.2	0 - 0	0 - 137	13 - 137	0 - 0	0 - 13.7	18.2 - 18.2	0 - 0	0 - 137	13 - 137
Vitamin A (IU)	700 - 1500	700 - 1500	700 - 1500	700 - 1500	700 - 1500	700 - 1500	700 - 1500	700 - 1500	700 - 1500	700 - 1500	700 - 1500	700 - 1500
Vitamin D (IU)	40 - 160	40 - 160	40 - 160	150 - 400	150 - 400	150 - 400	40 - 160	40 - 160	40 - 160	150 - 400	150 - 400	150 - 400
Vitamin E (IU)	2.8 - 3.5	2.8 - 3.5	2.8 - 3.5	6 - 12	6 - 12	6 - 12	2.8 - 3.5	2.8 - 3.5	2.8 - 3.5	6 - 12	6 - 12	6 - 12

Table 2.1: Recommended Range of Intakes of key nutrients, according to Tsang et al

The majority of Tsang et al's RRIs were derived using a combination of several different sources of data including:

1. ***Fetal body composition and corresponding tissue accretion rates***
   In 1976 Zeigler and colleagues used published body composition data from the chemical analysis of several data sets of preterm infants who were stillborn or died within a few hours of birth to compile the body composition of a 'reference fetus' between 24 and 40 weeks gestation[60]. By knowing how the chemical composition changes during this period, it is possible to estimate the nutrient intakes necessary to achieve this reference composition. This approach, whilst logical, has several limitations. Firstly, only a small number of infants were included, which reduces its generalizability. Secondly, the cohort of infants used was mostly born in the early part of the 20th century, so may not represent current trends in birth weight and in-utero growth. Thirdly, this approach assumes that the infant used were representative of the population, when actually they may have been born early or not survived due to a pathological cause, which may also have affected their in utero growth and accretion of tissue. Finally, estimating requirements based on composition relies on assumptions about the way in which nutrient intake relates to the deposition of new tissue[14 60 61].

2. ***Experimental measures of nutrient turnover***
   Several experimental methods exist for estimating the expenditure, turnover or balance of nutrients, particularly for energy and protein. Some studies on preterm infants have been carried out looking at energy expenditure (mainly using 'doubly labelled water' containing isotopes of hydrogen and oxygen) and protein balance, and have been used to inform the development of Tsang et al's RRIs in conjunction with other methods. A limitation of these studies is that the experimental methods are imperfect, as they rely on several assumptions regarding the underlying metabolic pathways. For energy expenditure, these assumptions include a fixed respiratory quotient whilst protein balance studies assume a steady state of protein accretion and require the intake and utilisation of other nutrients (particularly energy which is required in order to use protein for growth) to remain constant[14].

3. ***Results of clinical studies or trials of nutritional interventions in preterm infants***
   Over the past four decades, multiple studies have been carried out looking at the effect of feeds containing known intakes of particular nutrients, sometimes in comparison to feeds containing a different amount of the nutrient in question. Usually growth or nutrient balance is the main outcome measure used. Similarly to the experiments concerned with nutrient turnover described above, the majority of the work has investigated energy and protein intakes. These studies provide evidence of the clinical effect of particular amounts of nutrient and so where available were also used to inform RRIs. They are limited in that they often include only small numbers of infants or are unable to test the amount of nutrient needed to excess (i.e. in some trials a 'ceiling' of a particular nutrient is often not reached in terms of seeing a plateau of the outcome measure or evidence of toxicity). One advantage of these studies however, is that they are on live infants and so provide insight into the relationship

between nutrient intake and the effects of other factors such as concurrent illness. They also allow study of the relationship between nutrient intake and catch up growth, which cannot be adjusted for adequately using body composition based approach described above)[14 61].

4. ***Measures of nutrients in umbilical cord blood or maternal to fetal plasma ratios***
   Analysis of cord blood after preterm delivery, together with data on maternal and fetal plasma levels of nutrients has also been studied. These data allow insight into the amounts of nutrient delivered to the fetus and were taken into account when deriving RRIs for some of nutrients, particularly micronutrients such as vitamins and trace elements[14].

5. ***Data from term infants (including breast milk composition) extrapolated to preterm infants***
   In many cases, the RNI for term infants or the composition of breast milk (taken from reference data) was used as the basis for RRIs, particularly for nutrients where there was little data available in terms of fetal composition or experimental/trial data[14].

6. ***Estimates or experiments on effect of comorbid states in preterm infants***
   Where available, published data regarding the effect of comorbidities (such as chronic lung disease) on energy expenditure and nutrient utilisation were taken into account[14].

The derivation and use of RRIs for preterm infants is in contrast to the way in which the requirements (given as RNIs) for term born infants were derived. In this case breast milk was assumed to be the perfect feed for term infants, and therefore the average composition and volume of breast milk taken by the average term infant who was growing in accordance with accepted growth reference standards was used as the initial basis for term infant requirements. It is not possible to use the same method to derive preterm infant requirements, as it cannot be assumed that breast milk is nutritionally adequate for preterm infants, and also no preterm infant grows to 'ideal' according to reference growth standards (see below)

Given the variety of evidence used to develop the RRIs presented in Tsang et al's 'Nutrition of the Preterm Infant', the intake required for each nutrient was not always clear. Therefore, the recommendations represent a consensus opinion of the authors and editors of the book, based on all the available evidence, hence the development of the term 'RRI', in recognition that these were a 'reasonable' assumption of the required range of intake given the available evidence. Whilst, as outlined above, the evidence base used was subject to several limitations, the use of multiple types of evidence, combined

with consensus among the authors, makes a case for the RRIs as an acceptable standard of nutritional care for preterm infants. Although there is debate about their validity, the Tsang RRIs, together with the similar ESPGHAN recommended nutrient intakes, represent the only current available recommendations for nutrient intakes for preterm infants, and there is some evidence that achieving them can improve growth[62]. The study described in this thesis will therefore aim to try and achieve these RRIs, and assess the subsequent effect on growth in very preterm infants.

2.3 Growth References for Preterm Infants

In 1977, the AAP recommended that the goal of the nutritional care of preterm infants is to achieve rates of growth and body composition similar to that seen in utero at equivalent gestations[55]. ESPGHAN also recommended trying to achieve growth similar to that of fetal growth in their 2010 commentary on the enteral nutrient supply for preterm infants. Whilst this may appear to be a logical goal, there is debate as to whether in-utero growth is an appropriate target for preterm infants. The ex-utero environment is very different to that in-utero, with preterm infants needing to maintain their own body temperature and defend themselves against infections that they would not have encountered in-utero. In addition, the amounts and type of nutrients delivered differ considerably once ex-utero, which in turn will affect growth both directly, and also indirectly via interaction with endocrine influences on growth. Of note, the main factors influencing growth in-utero are insulin and insulin-like growth factor (IGF) I and II, with a shift towards IGF I and II after birth, together with thyroxine. All these factors mean that intrauterine and extrauterine environments differ considerably, such that it may be unreasonable to apply in-utero standards to an ex-utero preterm infant[63]. When considering a more appropriate goal it would be pertinent to consider which pattern of postnatal growth in preterm infants is associated with the best long term outcomes, including neurodevelopmental outcomes and the risk of non-communicable disease, such as heart disease and the metabolic syndrome, in later life. However, whilst evidence regarding preterm birth, growth and outcomes is accumulating, there is currently insufficient evidence on which to base such a growth reference. Therefore, despite the limitations

described above, for the purposes of this study, attempting to achieve an intrauterine growth rate was accepted as the goal for preterm infants in the absence of data regarding a more appropriate target.

When evaluating growth, another important factor is which growth reference is used, together with a consideration of the way in which that reference was constructed and the nature of the source data. Most growth charts for preterm infants use the birth weights of infants born prematurely as a measure of intrauterine growth. This means that such growth charts actually represent a series of cross-sectional data points from infants born at the range of preterm gestations, joined up to make a growth curve which can then be used as a standard for growth in the preterm population. This approach has several limitations. Firstly, the charts will not be a true 'growth chart' as they do not depict longitudinal growth data (i.e. a cohort of infants followed up and repeatedly measured over a period of time, with their patterns of growth used to generate the growth curve). This is understandable for preterm infants, as such a longitudinal chart would look very different, reflecting the 'actual' (often poor) growth of preterm infants, rather than the 'ideal'. Secondly, preterm infants may be born due to many reasons, including a suboptimal intrauterine environment (which will affect growth), infections or other pathological conditions, meaning that such birth weight data may not represent 'normal' intrauterine growth. Finally, plotting birth weight data against gestational age requires accurate assessment of gestational age, which has not always been available, especially during the time many of the datasets used to generate these 'intrauterine growth curves' were collected.

In the United States, one of the most commonly used growth references (particularly in published studies) is the growth curve produced by Fenton in 2003[64]. Similar to other growth references, this was generated by compiling several cross sectional datasets containing the birth weights of live infants born between 22 and 40 weeks for the 'intrauterine' part of the curve, with data from term infants used for the section beyond 40 weeks. Fenton's chart was essentially an updated version of older, similar charts by Babson and Benda in 1976[65], and Lubchenco in 1966[66]. Another chart developed in the US worth mentioning at this point is the one by Dancis et al in 1948[67]. Unlike preterm infant charts developed since, this one was compiled in a longitudinal manner, following up a series of infants born between 1000 and 2500 grams

who received consistent nutrition in line with a local policy. This is interesting, as it represents the actual way in which preterm infants at that time grew, which whilst a fairer reflection on the difficulties in promoting growth, may not represent the optimal possible standard of growth which could be achieved. More recently, Olsen et al produced a new 'intrauterine' growth curve based on a large, contemporaneous US dataset, though again like the Fenton, Babson and Lubchenco charts this used cross sectional birth weight data[68].

Prior to 2009, in the UK the growth chart used for preterm infants was based on the UK 1990 dataset[69]. This was constructed using 12 different datasets, with growth data from over 43000 children. Nearly all of the data were cross-sectional, and spread across different age groups from preterm infants through to adults aged 23 years. The section for preterm infants was compiled from four of the data sets that provided birth weight measures from 23 weeks up 44 weeks gestation. Like the US growth charts, this was again cross sectional birth weight data used to represent intrauterine growth. In late 2009, the UK chart was changed to incorporate new, longitudinal growth data from infants aged 0-4 years from the World Health Organisation (WHO). The WHO data came from a large longitudinal study carried out in 6 countries worldwide (USA, Norway, India, Ghana, Brazil and Oman), and provides a growth standard for term born infants who regardless of ethnicity[70]. To be included in the WHO study, infants had to be breastfed for at least four months and have non-smoking mothers who lived in comfortable economic circumstances, so this needs to be considered when applying the WHO standard to populations who do not fit these criteria[70].

Specific to preterm infants, a new chart was developed based on the WHO data called the Neonatal and Infant Close Monitoring (NICM) chart, designed for use in preterm infants or those who are unwell and require additional growth monitoring. Whilst this chart uses the new WHO data from 42 weeks post-menstrual age to 4 years of age, it still uses the UK 1990 birth weight data (albeit re-analysed) for the preterm section[69]. This means that once they reach post-term, preterm infants are compared to the WHO data for healthy term infants, which may be an unfair comparison.

Unlike the previous UK growth charts, the new WHO charts do not have marked centile lines for the period between birth and two weeks of age. This is to allow for the variable amount of normal weight loss that occurs in term infants in the

period immediately after birth, and it was a criticism of the previous charts that this was not allowed for[71]. This pattern of initial weight loss followed by a regain to birth weight over the first two weeks of life is also seen in preterm infants, yet is not allowed for in the current NICM (or any) preterm growth chart. This is important, as measures of weight, head circumference and length at birth may not necessarily be representative of the growth centile on which the infant is destined to be on. Infants undergo significant shifts in body water after birth, as they move from the 'wet' intrauterine environment to the 'dry' outside world[72 73]. This accounts for the majority of the initial weight loss seen, so it may therefore be more appropriate to consider the centile the infant is on at two weeks of age, after the initial period of weight loss.

Overall, it can be seen that achieving 'intrauterine' growth may not be an appropriate or fair goal for preterm infants, and this is further complicated by the fact that current references for intrauterine growth are subject to several limitations. Whilst term infants now have an 'ideal' standard of growth based on longitudinal WHO data on the growth of a population of healthy term infants receiving an agreed standard of care, no such 'idealised' population of preterm infants currently exist on which to base a growth standard. Therefore, in the absence of such data, using the most contemporaneous and population appropriate current growth standard seems reasonable. The growth reference used in this study was therefore the current UK NICM chart described above.

2.3.1 Standard Deviations Scores

Whilst growth charts give an excellent graphical representation of the pattern of growth of an individual infant in relation to reference standards, they are not useful when trying to compare the growth of populations of infants. A better approach for looking at this is to use standard deviation scores (SDSs, also known as Z-scores). An SDS expresses the anthropometric value as a number of standard deviations below or above the reference population mean value. An infant with an anthropometric value corresponding to the population mean (i.e. on the 50th centile on a growth chart) would have a SDS of zero. Any infant growing along a centile consistently would have a fixed SDS, whilst an infant failing to grow would have a gradually smaller or more negative SDS. An advantage of SDSs for population-based uses is that a group population

summary statistics can be used on a population's SDSs. The formula for calculating a SDS:

$$SDS = \frac{(\text{Observed value} - \text{Mean value of the reference population})}{\text{Standard deviation value of reference population}}$$

Another advantage of SDSs is that, unlike growth chart centile lines, they are linear. They are also sex-independent, thus permitting the evaluation of children's growth status by combining sex and age groups (as sex is accounted for in the reference data from which they are calculated) [74]. This study will therefore use SDS based on the UK NICM growth chart reference data to assess and compare the growth of preterm infants.

2.4 Practice Recommendations for the Nutritional Care for Preterm Infants

2.4.1 Sources of Practice Recommendations

Reviewing in detail the evidence base for the optimum management of all aspects of the nutritional care of the preterm infant is beyond the scope of this thesis, which will focus on the implementation of a standardised approach to nutritional care based on current available evidence or consensus based practice. However, there are several sources which provide guidance or evidence for practice in this area. These include:

- Published recommendations by the ESPGHAN:
    - Enteral nutrient supply for preterm infants: commentary from the ESPGHAN, 2010 [15]
    - Guidelines on Paediatric Parenteral Nutrition of the ESPGHAN and the European Society for Clinical Nutrition and Metabolism, Supported by the European Society of Paediatric Research, 2005 [75]
    - Feeding preterm infants after hospital discharge: a commentary by the ESPGHAN Committee on Nutrition.2006 [76]
- Nutrition of the Preterm Infant: Scientific basis and Practical Guidelines (second edition) by Tsang et al, as described above [14]
- The Vermont Oxford Network's 'Potentially Better Practices (PBPs) for Nutrition'[23]
- WHO and UNICEF publications:
    - Management and support of infant feeding in maternity facilities. Infant and young child feeding : model chapter for textbooks for medical students and allied health professionals, WHO 2009 [77]
    - Optimal feeding of low-birth-weight infants, WHO 2006 [78]

    - UNICEF Baby Friendly Initiative, http://www.unicef.org.uk/babyfriendly
- Guidance by UK national colleges, associations and government bodies
    - Early Breast Feeding-Midwifery Practice Guideline: Royal College of Midwives 2008 [79]
    - Service Standards for Hospitals Providing Neonatal Care (Third Edition): British Association of Perinatal Medicine 2010 [80].
    - Breastfeeding in children's wards and departments: Guidance for good practice: Royal College of Nursing 2009 [81].
    - Toolkit for High-Quality Neonatal Services. NHS Department of Health 2009 [82].
- Cochrane reviews and other published systematic reviews
- Randomised Control Trials and other studies providing evidence for practice where current guidance or Cochrane reviews are not clear.

2.4.2 A set of Practice Recommendations for the Nutritional Care of Preterm Infants

By taking all the above sources together, it is possible to build up a set of recommendations for the nutritional care of preterm infants. These practice recommendations have been collated and summarised in Table 2.2. It can be seen that several of the recommendations are supported by more than one published set of guidelines or commentaries from the organisations listed above, or multiple key references. For each recommendations, the available evidence on which it is based has been assigned a level according to the Oxford Centre for Evidence Based Medicine 2011 Levels of Evidence (shown in Table 2.3)[83]. Also shown is an assessment of the strength of the recommendation using the Grading of Recommendations Assessment, Development and Evaluation (GRADE, see Table 2.4)[84 85]. GRADE is the system currently used by the National Institute for Health and Clinical Excellence (NICE) in the development of national guidelines[86]. It can be seen that the level and strength of the evidence is highly variable, with some recommendations, particularly those relating to parenteral nutrition and the choice and timing of milk feeds, having a more robust evidence base than others.

Practice Area	Recommendations	Source	Other Key References	Level of Evidence	Grade of Evidence
Timing of starting PN	Parenteral Nutrition (carbohydrate/amino acid based solutions) should be commenced in the first 24 hours of life	ESPGHAN Parenteral Nutrition Guidelines 2005 [75], VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23]	87-91	2	B
	Intravenous lipid (as part of Total Parenteral Nutrition) should be commenced in the first 24 hours of life	ESPGHAN Parenteral Nutrition Guidelines 2005 [75], VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23]	44 92	3	C
Timing of starting enteral feeds and rates of increase	Trophic enteral feeds (max 24ml/kg/day) should be started within the first 72 hours of life	VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23]	20 89 93-98	1	B
	Enteral feeds should be increased at 10-20ml/kg/day unless clinically contraindicated.	VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23]	89 99-101	1	B
Dealing with gastric aspirates	There should be a consistent approach to dealing with gastric aspirates, preferably based on a clinical guideline	VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23]	93 102-105	4	D
	Restarting feeds should be reviewed at each subsequent feed time following withholding feeds due to aspirates or clinical concerns	VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23]	102-104	4	D
Optimising use of breast milk (both MBM and DBM)	MBM is the feed of choice for preterm infants	VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23], WHO optimal feeding of LBW infants 2006 [78]	20 106-109	1	A
	There should be clear guidance regarding the use DBM	UKAMB Milk Bank guidelines 3rd edition, 2003 [110]		5	D
Use of fortifier and preterm formula	Breast milk fortifier should be introduced when infants are over 2 weeks old and receiving 150ml/kg/day or greater of MBM/DBM	VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23]	111 112	1	B
	Infants who are not breast fed should receive specialist high calorie and protein preterm infant formula	VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23], WHO optimal feeding of LBW infants 2006 [78], ESPGHAN 2010 Enteral Nutrient Supply for Preterm Infants [15]	113-116	1	B

Practice Area	Recommendations	Source	Other Key References	Level of Evidence	Grade of Evidence
Lactation support and establishing breastfeeding	Mothers should be supported to start and continue breastfeeding, including expressing milk as soon as possible after birth	RCM Early Breast feeding 2008 [79], BAPM 2010 [80], RCN Breastfeeding in children's wards and departments 2009 [81], DOH Toolkit for High-Quality Neonatal Services (2009) [82]		5	D
	Mothers should be helped to initiate breastfeeding within half an hour of birth	WHO Infant and young child feeding : model chapter for textbooks for medical students and allied health professionals 2009 [77]		5	D
	There should be a written breastfeeding policy	RCN Best practice in paediatric services 1998, RCN Breastfeeding in children's wards and departments 2009 [81], DOH Toolkit for High-Quality Neonatal Services (2009) [82]		5	D
Optimising nutrition after discharge	Infants who are not fully breast fed at discharge should be discharged on preterm post-discharge formula	ESPGHAN 2006 Position Paper on Feeding Preterm Infants After Discharge [76]	115 117-119	1	C
Targets for micro- and macronutrient delivery	The nutritional targets for preterm infants should be those laid out in 'Nutrition of the Preterm Infant' by Tsang et al	Nutrition of the Preterm Infant 2005, Tsang et al [14], ESPGHAN 2010 Enteral Nutrient Supply for Preterm Infants [15]		3	C
Monitoring growth and nutrition	All preterm infants should be weighed weekly as a minimum	WHO optimal feeding of LBW infants 2006 [78], RCN Position statement on Malnutrition 2006		4	D
	All preterm infants should have their head circumference and length measured weekly	VON "Got Milk" focus group Potentially Better Practices for Nutrition Support 2003 [23]		4	D
Use of vitamin and mineral supplements	Appropriate mineral supplements should be started in response to abnormal blood results	Nutrition of the Preterm Infant 2005, Tsang et al [14], ESPGHAN 2010 Enteral Nutrient Supply for Preterm Infants [15]		2	B
	Preterm infants should be started on appropriate Iron and vitamin supplements before discharge unless contraindicated	Nutrition of the Preterm Infant 2005, Tsang et al, [14] WHO optimal feeding of LBW infants 2006 [78], ESPGHAN 2010 Enteral Nutrient Supply for Preterm Infants [15]		2	B

Practice Area	Recommendations	Source	Other Key References	Level of Evidence	Grade of Evidence
Staffing for the delivery of a parenteral nutrition service	There should be a pharmacist with neonatal expertise available for the prescription of PN (ideally a multidisciplinary nutrition support team)	BAPM 2010 [80],ESPGHAN Parenteral Nutrition Guidelines 2005 [75], DOH Toolkit for High-Quality Neonatal Services (2009) [82]		5	D
Staffing for the delivery of an enteral nutrition service	There should be a dietician with neonatal expertise available to help guide the prescription of enteral nutrition	BAPM 2010 [80], DOH Toolkit for High-Quality Neonatal Services (2009) [82]		5	D
Staffing for the delivery of a lactation support service	There should be breast feeding support staff available to support mothers	BAPM 2010 [80], RCN Best practice in paediatric services 1998[120], RCN Breastfeeding in children's wards and departments 2009 [81]		4	D
Facilities for provision of PN	There should be access to a computerised system to prescribe PN	ESPGHAN Parenteral Nutrition Guidelines 2005 [75]		2	B
	There should be a guideline for the use of PN	ESPGHAN Parenteral Nutrition Guidelines 2005 [75]		4	D
Facilities for provision of enteral feeds	Expressed maternal and donor milk should be handled appropriately	UKAMB Milk Bank guidelines 3rd edition, 2003 [110]		5	D
Facilities for provision of lactation support	Breast pumps and appropriate facilities for mothers to express should be available	BAPM 2010 [80], RCN Best practice in paediatric services 1998 [120], RCN Breastfeeding in children's wards and departments 2009 [81]		5	D

Table 2.2: Current guidelines and recommendations for the nutritional care of preterm infants

Level	Definition
1	Systematic review of randomized trials or n-of-1 trials
2	Randomized trial or observational study with dramatic effect
3	Non-randomized controlled cohort/follow-up study
4	Case-series, case-control studies, or historically controlled studies
5	Mechanism-based reasoning

Table 2.3: Oxford Centre for Evidence Based Medicine 2011 Levels of Evidence for Treatments (adapted from full Levels of Evidence 2011 table[83]). Note that level may be graded down on the basis of study quality, imprecision, indirectness, because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.

Code	Quality of Evidence	Definition
A	High	Further research is very unlikely to change our confidence in the estimate of effect. • Several high-quality studies with consistent results • In special cases: one large, high-quality multi-centre trial
B	Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. • One high-quality study • Several studies with some limitations
C	Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. • One or more studies with severe limitations
D	Very Low	Any estimate of effect is very uncertain. • Expert opinion • No direct research evidence • One or more studies with very severe limitations

Table 2.4: Grading of Recommendations Assessment, Development and Evaluation (GRADE). Adapted from Guyatt et al[85]

2.5 Summary

This chapter has discussed the various reference sources available regarding the nutrient intakes and growth of preterm infants, and has described the body of literature regarding best practices in nutritional care. In the context of Patton's framework for complexity[33] (Figure 1.1 in Chapter 1), it can be seen that the nutritional care of preterm infants is *technically complicated*, with a degree of uncertainty about what constitutes best practice in this area and a

lack robust evidence regarding how to measure outcomes or assess practice. However, there are some areas of practice such as the timing of commencement and general composition of parenteral and enteral feeds which have a more robust evidence base, while others relating to the finer details of how to deliver nutrition and supplements and how to monitor growth and outcomes, have a less robust evidence base. Importantly, whilst some of the evidence for benefit for some recommendations is weak, there is no evidence for harm. The recommendations laid out above were thus accepted as the basis for this study, while accepting that there were some flaws and limitations of some of these sources, which would be taken into account when interpreting the findings. Importantly, knowledge of the quality of the available evidence means that the effect of any intervention should be carefully monitored to ensure that potentially detrimental practices are not translated into routine care.

The set of recommendations and the published guideline and references on which they are based, were used to form guidelines, which acted as the central element of the intervention used in this study to standardise nutritional care. More details on how the practice recommendations described above were used to develop guidelines, and the guidelines themselves can be found in Chapter 7 and Appendix 1 respectively. The guidelines contain supporting information explaining the evidence behind the practices they advocate. Other elements of the multifaceted 'complex' intervention used in this study included a multidisciplinary nutrition team and a weekly nutrition ward round, and nurse 'champions for nutrition' who helped implement the new practices and guidelines. These elements, described in more detail in Chapter 7, aimed to both try and achieve the practice recommendations described in this chapter, and also to ensure they were taken up by staff and integrated into routine care, which is the focus of this thesis. Key concepts and theories in understanding practice change and the translation and integration of new practices into routine care are therefore discussed in the next chapter.

Chapter 3: Understanding the Process of Practice Change

MRC guidance regarding the development and implementation of complex interventions suggests that intervention selection and implementation should be based on a clear theoretical understanding of the way in which the intervention causes change [34], together with an understanding of the local setting and any potential barriers to implementation (including how ready an organisation is to change). Theories can provide explanations of the mechanism by which change occurs in a particular setting, and therefore help select an intervention which is most likely to succeed. In line with these MRC recommendations, and in order to explain the theoretical basis for this thesis, this chapter will consider the barriers and facilitators to change as perceived by clinical researchers, and go on to discuss the concepts of theories, models and strategies for implementation. The 'Model for Improvement', is then discussed, as this is the most commonly used model and strategy for QI programmes in healthcare, particularly in neonatal care, and so is potentially relevant to this thesis. However, as mentioned briefly in chapter 1, QI work and particularly the Model for Improvement, does not always consider in full the theoretical basis of behaviour change. Therefore, this chapter goes on to discuss the two theories that were used in this study; the Theory of Planned Behaviour [121], which was used to measure organisational readiness for change and inform the development of the intervention, and Normalization Process theory [37 38], which was used to explain and inform the process of implementation of the intervention.

3.1 Barriers and Facilitators to Change

Barriers to a change in practice come in many forms, and are likely to be specific to the combination of the behaviours required by the new practices and the setting in which it is to be performed (including staff and available resources). A barrier to practice change is any factor which could potentially impair its effectiveness in improving practice, while facilitators are factors that enhance or assist the process of behaviour change. Both will clearly be

important to consider when developing an intervention aimed at changing practice[6 7]. The Cochrane Effective Practice and Organisation of Care (EPOC) review group have identified an agreed set of barriers to change which can be identified prior to a behaviour change intervention (table 3.1)[122]. Whilst this standardised terminology is useful for research purposes, it is of note that adding rigid labels to variable phenomena such as these can potentially cause problems.

1	Information management
2	Clinical uncertainty
3	Sense of competence
4	Perceptions of liability
5	Patient expectations
6	Standards of practice
7	Financial disincentives
8	Administrative constraints
9	Other (specify)

Table 3.1: Prospective Identification by Investigators of Barriers to Change according to the Cochrane EPOC group

Several systematic reviews and studies have considered barriers and facilitators and are discussed here in the context of understanding practice change. A Cochrane review carried out in 2010 by Baker et al[123] demonstrated that tailoring implementation strategies to prospectively identified barriers were more likely to be successful in changing practice than untailored interventions or passive guideline dissemination. Interestingly, whilst the review found tailoring to be effective, it was unable to find evidence for the best method for identifying barriers, although common approaches included interviews (42%), focus groups (38%) and questionnaires (23%), with half of all included studies using multiple methods. Similarly, Chaillet et al reviewed effective strategies for implementing guidelines in obstetric care and found that studies which prospectively identified specific barriers and facilitators for behaviour change were more likely to be successful[124], leading the authors to conclude that prospective identification of barriers was necessary to achieve better implementation. Cabana et al, recognising that guidelines have a limited effect on practice despite wide usage, systematically reviewed the barriers to physician adherence to practice guidelines [125]. They included 76 studies and were able to group the barriers identified across studies into seven general categories, which they incorporated into a model shown in figure 3.1. The

effect of different barriers was variable and dependent on the setting[125]. Cabana et al's model is interesting, as whilst it provides a framework for considering the different barriers and a way of grouping them together, there is no underlying theoretical explanation as to why the barriers have been linked together as depicted in the model. This is very different to more theoretical models such as those described below, which allow some understanding of causation.

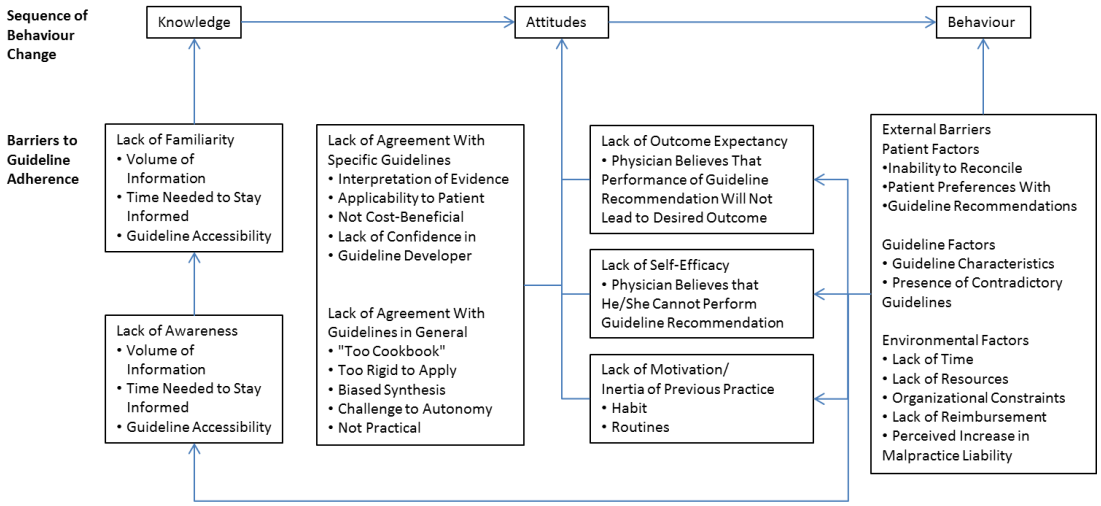


Figure 3.1: The Cabana et al Model for Barriers to Physician Adherence to Practice Guidelines in Relation to Behaviour Change (adapted from Cabana et al [125])

3.2 Theories, Models and Strategies for Dissemination and Implementation

In their paper on using theory to implement evidence-based findings into health care practices, Sales et al define a *theory* as "A set of logical constructs that jointly offer answers to the questions 'why' and 'how'". In the context of practice change, a theory seeks to explain why people or organisations behave as they do and, given the way they behave, what would motivate them to change their behaviour. Sales et al propose that theory provides the clues to the mechanisms by which a practice change intervention is successful, an idea which is further developed in the MRC guidance discussed earlier[34]. Sales et al, in the same paper, define a *model* as "A heuristic framework that joins theory to some specific state or action that is desired or is to be taken". Sales et al consider models to be more specific and concrete than theory, although believe models should contain specific elements derived from theory that

either predict action or outcome, or contribute in some way to achieving the desired change. Leading on from theories and models, a *strategy* is defined by Sales et al as the articulation of how to go from the basic idea of practice change, through to actually making change occur, usually via one or more interventions. Strategies provide overall direction for planning, including plans for addressing prospectively identified barriers or facilitators to change. For interventions aimed across several levels of a social system, these barriers, and facilitators can be identified as part of an overall assessment of organizational readiness to change during implementation strategy development. Sales et al also state that the choice of interventions to be used as part of an implementation strategy should be based on the selected theory and how it explains the most likely approach that will evoke change.

Several theoretical and conceptual models exist for understanding practice related behaviour. A systematic review recently carried out by Tabak et al reviewed all models for dissemination and implementation, identifying as many as 61 different models, theories and frameworks [126]. Tabak et al defined *dissemination* as "the active approach of spreading evidence based interventions to the target audience using a planned strategy", while *implementation* was defined as "the process of putting to use or integrating evidence-based interventions within a setting". In reality, dissemination and implementation represent two points along the same spectrum, and are closely related, if not identical activities. In their detailed review, Tabak et al provide an extensive list of dissemination and implementation models together with a framework to aid researchers in selecting an appropriate model for their study based on how adaptable or rigid they are, whether they focussed more on dissemination or implementation, and at what sociological level they act (i.e. individual, organisational, local governmental or national governmental levels). The authors also advocate using a selected model as part of the study planning and design, and adapting models for use if necessary[126]. It is clear that a model must be chosen which suits both the environment and the new practice being implemented. The models and theories described in Tabak et al's review all approach the implementation process in a different way, and whilst there is some overlapping of the various approaches, there are also gaps, with few theories able to explain the dissemination and implementation process in its entirety. This is further complicated by the fact that certain models fit particular types of interventions or settings better than others. Any model is

only as useful as the extent to which it explains the processes in question, and choosing the right model to understand a specific intervention is therefore an important step in the implementation process.

One model missing from Tabak et al's review is the Model for Improvement (MFI). This is a reasonable omission as the MFI comes from the field of QI, so does not incorporate theory or consideration of barriers and facilitators to change, focussing more on the process of change and the measurement if its effect. However, given that the MFI has been used extensively in healthcare and neonatal care in particular, it is discussed below, partly to demonstrate how using strategy to change practice can be effective but mainly to illustrate how such QI theories differ from those used in implementation science.

3.2.1 The Model for Improvement

The MFI was formally developed by Associates in Process Improvement, a professional collaborative which aims to develop and apply methods for the improvement of quality, and is described in detail in their book "The Improvement Guide" by Langley et al[22]. Whilst the guide is aimed at any organisation wishing to improve its performance, it is noteworthy that Langley himself is a Senior Fellow of the Institute for Healthcare Improvement (IHI). Whilst Langley et al were the first to outline the MFI as a scientific system for improvement, and propose its use in healthcare; it is based on the work of W Edwards Deming in the industrial sector, who developed the idea of the 'Plan-Do-Study-Act' (PDSA) cycle which forms the basis of the model[127]. These PDSA cycles aim to improve process and in turn outcomes, and work by identifying areas for improvement and strategies to address them, implementing change and measuring its impact. The MFI is shown in figure 3.2, and it can be seen the PDSA cycle is preceded by three key questions. Similar to the guidance by the MRC mentioned earlier[34], the model for improvement focuses on being clear about outcome measures and methods to measure them effectively. The 'Plan-Do-Study-Act' cycle then tests the change in the work setting, with a plan made, carried out, the effect studied and then the results acted on. Repeated PDSA cycles over time can lead to gradual and incremental improvements, and it can be seen from figure 3.3 how the MFI can form the basis for a continuous improvement approach. The MFI is designed to be a simple, yet powerful tool for accelerating improvement, though it is meant to

accelerate the improvement process through rapid change cycles rather than replace change models that organizations may already be using. Over time the MFI has developed into an approach which can act as overall framework for change, rather than a specific tool in itself.

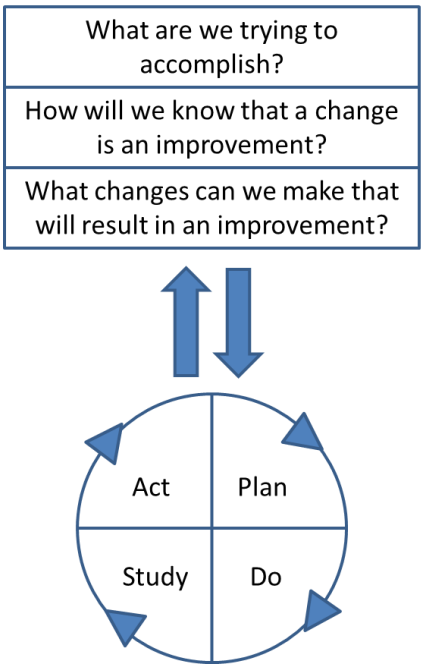


Figure 3.2: The Model for Improvement [22]

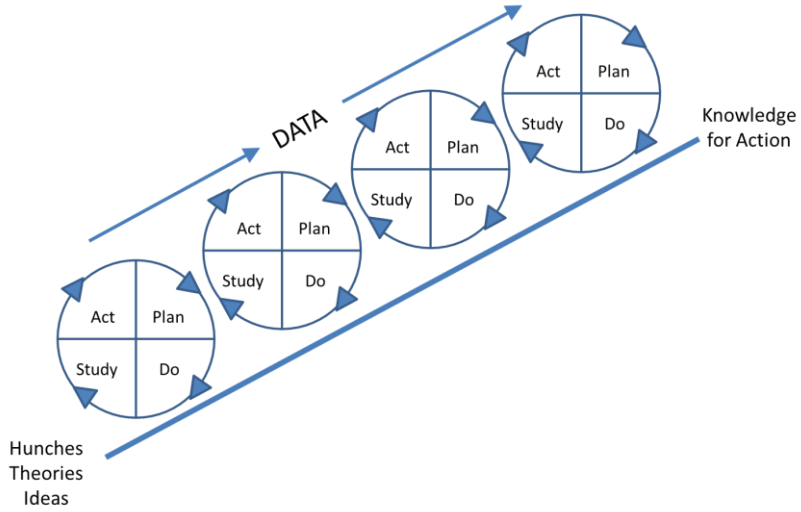


Figure 3.3: The Model for Improvement over time (PDSA Cycles)

However, it can be seen from both figures 3.2 and 3.3 that whilst the MFI offers a useful framework to effect change, these changes need to be focussed and related to a specific goal. The MFI does not incorporate a 'systems' approach, failing to consider the environment and context in which the desired change needs to be effected, or the need for training, adequate staffing and

provision of resources. Similarly, there is no part of the MFI directed towards changing behaviour of staff, which is important as these are the people needed to make the changes. Figure 3.3 also demonstrates how continuous reassessment and re-intervention are required in order to sustain and build on the changes that are made. Again, this is in part due to the fact the MFI does not address underlying factors that will affect the uptake of changes in practice or their impact on other areas of service.

Nonetheless, the MFI has been used effectively in many areas of healthcare, particularly neonatal medicine. The MFI is the model used in much of the work by the Vermont Oxford Network (VON) described in chapter 1. In particular, Horbar et al described a collaborative quality improvement approach aimed at improving care in NICU, specifically infection rates and incidence of chronic lung disease[128]. Based on the MFI, participating NICUs within the VON formed multidisciplinary teams led by a trained facilitator and were able to significantly reduce rates of nosocomial infection, coagulase negative staphylococcal infection, and the number of infants receiving oxygen at 36 weeks post-conceptual age when compared to similar VON NICUs who were not participating in the study[128]. Following on from this, 114 VON NICUs participated in a cluster randomised trial to test a multifaceted collaborative quality improvement intervention designed to promote evidence based surfactant treatment for preterm infants. This intervention included audit and feedback, education and training. Compared to control units, those which participated in the collaborative quality improvement intervention were significantly more likely to administer surfactant in the delivery room, with infants receiving their initial dose significantly sooner[129].

Overall, it can be seen that the MFI offers a simple and focused strategy for changing and improving practice. It is useful for specific changes to practice but may struggle when faced with more complex environments or complex practices, as it does not consider all aspects of the change process. This is in contrast to the theories used in implementation science such as the Theory of Planned Behaviour (TPB) and Normalization Process Theory (NPT), which are used in the study described in this thesis used to understand the effect of staff attitudes and beliefs on their intentions and behaviour (TPB) and to inform the implementation process (NPT). Both theories are discussed in the subsequent sections below, together with the reasons for their use in this thesis.

3.2.2 The Theory of Planned Behaviour

Ajzen's Theory of Planned Behaviour[130] is a well-used and validated theory that aims to predict an individual's behaviour based on their attitudes and beliefs regarding that behaviour. The TPB is an extension of an earlier theory by Ajzen and Fishbein, the Theory of Reasoned Action (TRA). The TRA was born out of the recognition that general attitudes fail to predict specific behaviours, because behaviours tend to be specific in terms of their target, context and time of performance, while attitudes tend to be more general, concerned only with the target of the behaviour. General attitudes can however predict broad patterns of behaviour, and by considering different behaviours towards a particular target together it is possible to generalise across actions, contexts and time and allow compatibility with broad attitudes to the target in question. While these things alone have poor predictive validity on specific behaviours, by considering a particular behaviour across a variety of occasions and situations and therefore accounting for the influence of these conditions on that behaviour, it is possible to use attitudes and traits to have a more valid prediction measure of how likely an individual is to perform that behaviour in any given situation (referred to by Azjen and Fishbein as the 'principle of aggregation')[131]. Early work in this field showed this to be the case, thought essentially demonstrated that while attitudes and personality traits are implicated in human behaviour, other factors also influence it. The TRA was developed to try and address this issue and account for attitude, personality traits and other factors, to allow prediction of human behaviour in specific contexts[121].

The TRA is based on the concept that an individual's *intention* to perform a behaviour could be predicted by a combination of their *attitude* towards that behaviour, and their *subjective norms* (how they perceived expectations from other relevant people together with how they valued the opinions of those people)[121]. Subjective norms are independent of attitudes, as in principle it is possible for people to hold favourable attitudes towards a behaviour but feel social pressure not to perform it[131]. The TRA aimed to measure the strength of an individual's intention to perform a given behaviour, assuming that a stronger intention leads to increased likelihood of performing that behaviour. Importantly, the TRA is only applicable to behaviours that a person is able to decide to do (i.e. are under volitional control). In reality, the performance of

the desired behaviour will also depend in part on the presence of non-motivational factors including opportunities to perform the behaviour and resources such as money, time, skills and the cooperation of others, which may be beyond the individual's control. Collectively these factors determine the extent of a person's actual control over the behaviour in question, and in turn the likelihood of them performing it[121]. When control is high such that anyone is able to perform the target behaviour, intentions alone should predict behaviour [131]. However, more importantly, what matters in terms of a person's intention to perform a behaviour is their *perception* of their level of control over performing it. It is of little consequence how easy it is for a person to perform a specific behaviour in practice if, from the outset they believe they lack the necessary ability or opportunity to do it. This concept of perceived behavioural control (PBC) is therefore important in predicting an individual's intentions to perform a behaviour, so was added to the TRA to produce the TPB, shown in Figure 3.4. Therefore the TPB considers that an individual's behaviour can be determined by their intention to perform that action, which is in turn influenced by three determinants; their own *attitudes* concerning the action in question, their beliefs regarding what their peers and other groups have regarding the action ('*subjective norms*'), and finally, their perceptions regarding what factors may impede or facilitate their ability to perform the action (termed '*perceived behavioural control'*). By including PBC, TPB was able to allow prediction of behaviours where there was limited volitional control[121].

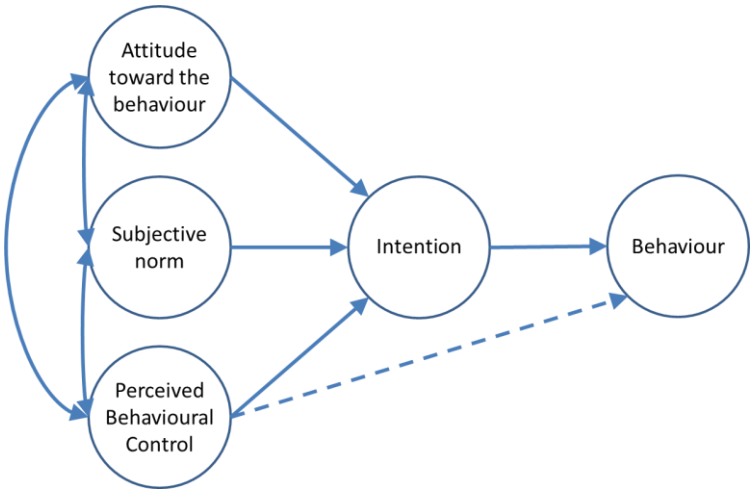


Figure 3.4: The Theory of Planned Behaviour

It can be seen from the model of the TPB in figure 3.2 that whilst the three elements of attitude, subjective norms and PBC together can predict intention and then behaviour, perceived behavioural control can directly interact with and predict behaviour itself. One explanation for this direct link between PBC and behaviour is that PBC can be taken as a surrogate marker for actual control (depending on the accuracy of the individual's perceptions of their control). Another explanation for this direct link is that if two people have the same level of intent about performing a behaviour, then the one who has the greatest belief of success is more likely to succeed[121]. This in part will be due to the effect of PBC on an individual's perseverance, as the more a person believes they have the ability to perform an intended behaviour, the more likely they are to persevere and therefore succeed[131].

3.2.2.1 Using TPB to predict intentions and behaviour

In order to use the TPB to predict behavioural intentions, the measures of attitudes, subjective norms and PBC and intentions must be specific for the behaviour in question. The TPB also requires that these measures remain relatively constant over the period of assessment. Any event which might change an individual's attitudes, subjective norms or PBC may also alter their intent. The relative weight of both intention and PBC in predicting intentions will vary depending on the situation, and it stands to reason that behaviours for which there is less volitional control, PBC will be more influential, as the individual will feel that their performance is more out of their control. In general the more favourable the attitude and subjective norm, and the greater the PBC in respect of the behaviour in question, the stronger the intention to perform it should be. It is important to point out that whilst intentions are used as a proxy for behaviour, they are not the same, and high intention does not guarantee behaviour. The TPB has been used in many studies to predict and understand people's intentions to perform certain behaviours or engage in particular activities, demonstrating that a considerable amount of variation in intentions can be accounted for by the three predictors. Attitudes and PBC are often significant predictors of intention, with variability in the contribution of subjective norms suggesting that personal considerations tend to be more important than the influence of perceived social pressure.

At a more detailed level, the TPB considers the importance of people's underlying beliefs, with their behavioural beliefs influencing their attitudes,

their normative beliefs determining their subjective norms, and their control beliefs dictating their PBC. The extent to which these three underlying beliefs influence each of attitude, subjective norm and PBC respectively will be related to how important an individual views or weights that belief. For instance, a person's attitude to a behaviour will be a product of a combination of their strength of their beliefs in relation to that particular behaviour and how important that belief is to them. This is illustrated in Equation 1, where *A* is attitude and *b* is the strength of belief relating to attitude and *e* is the individual's subjective evaluation of that importance of that belief. Using the same principle, Equation 2 shows the similar relationship between subjective norms (*SN*), normative beliefs (*n*) and the person's motivation to comply with those beliefs (*m*). Motivation to comply will be related to how important the opinion of a particular person, peer or group is to the individual. Equation 3 illustrates how *PBC* is proportional to the magnitude of the sum of the control beliefs (*c*) and the perceived power (*p*) of the particular control factor to facilitate or prevent the target behaviour.

Equation 1: $$A \propto \sum b_i e_i$$

Equation 2: $$SN \propto \sum n_i m_i$$

Equation 3: $$PBC \propto \sum c_i p_i$$

These three equations form the basis of questionnaires used to measure attitudes, SNs and PBC, and in turn estimate intention as a predictor of behaviour. Given the importance of capturing salient beliefs related to the specific behaviour of interest, such questionnaires must be carefully developed, often using pilot work, to ensure the correct items are included. Ajzen has provided guidance on how to construct such questionnaires, and this has been further detailed by Francis et al[132]. The questionnaires use a seven point scale for assessing the belief and evaluation items. According to Francis et al's method, for some items (behavioural beliefs, motivation to comply, control beliefs and the power of those control beliefs) the scale is used in a unipolar fashion (1 to 7), to indicate strength of belief, while for other items (subjective evaluation and normative beliefs) the scale is used in a bipolar fashion (−3 to +3) to provide a zero midpoint to allow respondents equipoise, but also has sufficient scope either side to indicate the strength of feeling. Scores from the answer of the questionnaire items can then be

multiplied together in accordance with the above formula, and summated, giving a measure for each of the three factors of attitude, subjective norms and PBC. The more positive or negative the score, the more positive or negative the impact of that factor. Such measures are referred to as indirect measures, in view of the composite nature of the questions which assess both belief and relative strength of the belief. It is possible (and recommended) to also use direct measures, where the respondent is asked directly about their attitude, SN or PBC using one simple question[132].

3.2.2.2 The TPB and the Prediction of Behaviour

TPB offers an appealing method for investigating attitudes, intentions and behaviour in the context of practice change, providing a measure of the degree to which attitudes, subjective norms and PBC influence intention. This in turn can indicate current likelihood of a behaviour change and highlight important influencing factors. Importantly, the TPB has been used and validated in many studies. A systematic review and meta-analysis by McEachan et al in 2011 looked at 237 prospective tests of TPB in the prediction of behaviours[133]. Attitude and PBC significantly predicted behaviour with a correlation coefficient (*r*) of 0.31. For intentions correlations were stronger, with direct measures of attitude, PBC and SN generating overall *r* values of 0.57, 0.54 and 0.4 respectively (all statistically significant). Correlations were weaker (though remained statistically significant) for indirect measures of attitude, PBC and SN, giving *r* values of 0.42, 0.44 and 0.37 respectively. Overall, the TPB explained 19.3% of variance in behaviour and 44.3% of the variance in intention. Efficacy varied depending on behaviour type, age of sample and length of follow up (shorter follow up meant better prediction). Taking past behaviour into account added 10.9% to variance for behaviour and 5% to intention, suggesting this is a potentially important factor currently not included in the TPB model[133]. Of note, Ajzen himself has given this issue some thought, stating that past behaviour itself cannot directly cause current behaviour, though may perhaps be a proxy for strength of habit in performing that behaviour[134]. It is also noteworthy that all the *r* values above are generally low, with a relatively small amount of variance in behaviour accounted for by TPB predictions. This shows that many other factors impact on people's behaviour in addition to those considered by TPB, and also demonstrates how difficult it is to try and model human behaviour accurately.

Another TPB based meta-analysis carried out by Armitage and Conner in 2001 aimed to test overall efficacy of the TPB and assess its predictive validity in relation to self-reported behaviour[135]. One-hundred and eighty-five independent empirical tests of the TPB were included in the analysis, with the TPB able to predict both self-reported and observed behaviour with reasonable accuracy (correlation coefficients of 0.55 and 0.44 respectively, $p<0.001$ for both). For intentions as opposed to behaviour, TPB correlated more strongly with an *r* value of 0.63. Overall in the meta-analysis, the TPB was capable of explaining 20% of the observed behaviour[135]. Armitage and Connor's meta-analysis therefore provides evidence for the use of TPB for predicting intention and behaviour.

3.2.2.3 Criticisms and Limitations of the TPB

One common criticism of the TPB is that it is insufficient to explain human social behaviour. Several meta-analyses have been carried out on the accuracy of the TPB to predict intention, with variable correlation coefficients of around 0.5 to 0.6, accounting for a corresponding 25-40% of the variance in intention[134]. This demonstrates a failure of the TPB to account for much of the variance seen in intention, although it is unlikely that any theory would be able to account for a high level of intention given the complex nature of human behaviour, which can be irrational and subject to bias and the effect of changes in thought processes or attitude. Therefore, if the TPB is assumed to be focused on an impassionate, rational and unbiased individual, it stands to reason that it will be insufficient to predict intention accurately. However, whilst the TPB considers the three elements of attitude, SN and PBC, there is actually no assumption that these elements are formed in a rational, unbiased way or that they accurately represent reality. The theory in its simplest form merely proposes that these three elements (however they are formed) work together to determine intention, meaning that it is useful in predicting intention[134].

Another criticism is that the TPB fails to account for the emotional state of individuals[134]. Indeed, measuring attitudes, SN and PBC does not account for the current emotional state of an individual at any time and its acute effect on these elements. Considering that humans can be quite emotionally labile, it is perhaps unlikely that any theory would be able to adequately account for emotional state. Several studies have incorporated measures of affect together

with the TPB in studies of behaviour, with most finding that such measures had little impact on the ability of TPB to predict behaviour. Furthermore, due to the way in which the TPB is constructed as described above, measures of attitude, SN and PBC will account for the effect of emotion at the time of measurement[134].

A core part of the TPB is the prediction of intentions (as a proxy for behaviour), and this is a potential issue. The extent to which intentions predict behaviour depends partly on factors beyond an individual's control. Sheeran carried out a meta-analysis of meta-analyses of TPB studies to look at the potential 'gap' between intention and behaviour[136]. Of the ten meta-analyses included, Sheeran found that correlation between intention and behaviour was surprisingly low at 0.53, meaning that intention only accounted for 28% of the variance seen in behaviour. Sheeran also looked at 'implementation intentions', where individuals specify intentions to carry out a behaviour in a particular situation (i.e. "I intend to do X in situation Y" as opposed to the more simple "I intend to do X"). He found that these had a stronger correlation with behaviour, with a correlation coefficient of 0.7. Implementation intentions increased the likelihood of performing a behaviour and the speed of action, perhaps due to the effect of specifying where and when one will perform a behaviour in creating environmental cues and prompts to remind them to do it[136]. Since Sheeran's review, Ajzen himself has carried out a study to investigate the mechanisms behind the effectiveness of implementation intentions, postulating that an additional mechanism by which they act is to increase an individual's commitment to the behaviour[137].

3.2.2.4 The TPB and Practice Change

In the context of changing the behaviour of healthcare professionals, the TPB can be used to develop questionnaires designed to provide valuable insight into the attitudinal, normative and control factors that determine intentions and behaviour. The factors or beliefs which distinguish those who intend to carry out the behaviour and those who do not will be of particular interest, and furthermore by carrying out regression analysis of these data, information about the relative contributions of attitude, SN and PBC to the prediction of intentions can be obtained. These findings can then be used to direct behavioural interventions aimed at changing these beliefs, increasing the chance of successful implementation[138].

Several studies have been interested in the use of the TPB in relation to translational research and the implementation of practice change. Côté et al used the TPB to identify factors that influence nurse's intentions to integrate research evidence into their clinical decision making[139]. They extended the TPB model by including the additional variables of moral norm (attempting to account for a person's feeling of moral obligation towards performing a given behaviour) and past behaviour. These two new factors were considered to directly influence intention without interacting with each other or the existing TPB model. In their study of 336 nurses in a university hospital, their extended model was able to explain 70% of the variance in nurses intentions to integrate evidence into practice[139]. Also in relation to practice change, in their study of 155 physicians, Rashidian et al found that TPB was able to explain 48% of the variation in their intentions to follow prescribing guidelines[140]. Attitude and PBC, but not SN, were predictors of intention and beliefs in isolation were better predictors of behaviour than the composite indirect scores. Effective prescribing was used a proxy for behaviour, though interestingly it did not have a significant relationship with the TPB variables[140].

Whilst the TPB is able to provide insight into the determinants of a behaviour and provide general guidance for behaviour change strategies, it is not able to specifically dictate the nature of any intervention to change behaviour. It is important to target beliefs where there is scope for change and which are shown to contribute significantly to intention in regression modelling. The target of interventions can be either the strength of the belief (i.e. how likely something is) or their scale values (i.e. whether it is desirable or undesirable). It is often easier to produce change by forming new beliefs rather than changing existing ones. Behavioural intervention must *motivate* individuals to perform the behaviour and then ensure *implement* it. TPB based interventions can target beliefs to produce positive intentions in those who would not have performed or did not contemplate performing the target behaviour, or can focus on control issues to aid implementation. Two separate interventions may be required to address both intention and implementation, ensuring intentions translate into changes in behaviour[138]. In 2002 Hardeman et al systematically reviewed the application of the TPB in behaviour change interventions[141], identifying 30 papers which described 24 distinct interventions. The TPB was mainly used to measure process and outcome variables to predict intention and behaviour, and less commonly to develop the intervention. Where

reported, only half the interventions were effective in changing intention, and two thirds effective in changing behaviour, with small effect sizes[141]. Webb et al also systematically reviewed the relationship between behavioural intentions and behaviour change, finding that a medium to large increase in intentions lead to a small to medium change in behaviour[142].

3.2.2.5 The TPB and this study

Whilst subject to some limitations and criticisms, TPB offers a robust and well validated way of measuring attitudes, beliefs, perceived control and intentions. It is of note that its ability to predict intentions and behaviour is strongest in highly experimental situations, with less accuracy in more 'real life' situations. Regardless of its ability to predict behaviour, the TPB also provides a way of measuring attitudes and intentions, allowing a way to assess and understand the setting into which a new behaviour or practice is being introduced. It will therefore be used in this study to provide a baseline assessment of these factors, giving a measure of the 'readiness for change' in the NICU prior to implementation. Importantly, it will also provide insight into any attitudes and beliefs which may impact on implementation, highlighting potentially important strategies to enhance uptake and therefore inform the development of the intervention itself. One area where the TPB provides little insight is the process of implementation itself, with the meta-analyses described above suggesting the TPB alone can only account for 30% of the variability in behaviour seen. Therefore, another theory concerned with the complex social processes of implementation, NPT, is also used in this study.

3.2.3 Normalization Process Theory

Normalization Process Theory (NPT), developed by May et al[37 38], originated in health care and medicine and focusses on the processes that lead to a new practice becoming embedded and integrated into what is considered 'normal' practice after it is implemented. The idea of 'institutionalising' new practices such that they become part of the normal routine is not a new concept in this field, and has formed part of several earlier models and theories. NPT seeks to understand the overall implementation process, and in this context considers 'implementation' to be all activities that take place when an innovation or new

practice is first introduced until it becomes part of routine practice, whilst 'normalization' refers to work people do to engage with new practices or activities which lead to the routine embedding and integration of these new practices or innovations into existing practices, knowledge and social contexts. In contrast to the TPB, which focusses on behaviour as an *outcome*, NPT focusses on *processes*. As described by May and Finch in the original NPT paper, "NPT is concerned with the social organization of the work (implementation), of making practices routine elements of everyday life (embedding), and of sustaining embedded practices in their social contexts (integration)".

NPT evolved from the earlier Normalization Process Model (NPM), which sought to explain the factors that promoted or inhibited the collective action that led to the routine embedding of complex interventions in healthcare settings. Collective action is the work that people do to enact a set of practices, and NPM considered it to be made up of four constructs: *Interactional Workability* (the interactional work people do with each other, objects/equipment or other practices, when they try to operationalize the new practices), *Relational Integration* (the knowledge that people establish in order to understand and maintain confidence in the new practices and how they use them), *Skill Set Workability* (the allocation of work to people with appropriate skills) and *Contextual Integration* (managing the new practices through allocation of resources, including the use of protocols and policies). Whilst NPM was able to explain the factors which promoted and inhibited collective action (and has been shown to be of utility in this respect) it was not able to explain other elements of the implementation process such as how people were enrolled into the new practices or how the new practices were appraised; NPT sought to build on NPM and offer a more comprehensive explanation of the implementation of complex interventions.

NPT proposes that practices become 'normalized' as a result of people working individually or collectively to enact them. In turn, the work of people enacting a practice can be inhibited or promoted by their understanding of the practice itself (*coherence*), their degree of participation, engagement and commitment to it (*cognitive participation*), their ability to enact it and invest effort in it (*collective action*, as described in NPM) and their own assessment and appraisal of the practice (*reflexive monitoring*). These four constructs of coherence,

cognitive participation, collective action and reflexive monitoring underpin the process of normalisation, and the way in which they relate to each other is shown in Figure 3.5. *Coherence* requires that users recognise and differentiate the new practice as different to the previous one, understanding its components and how to operationalize it. *Cognitive participation* describes the way in which users initiate, enrol themselves in and legitimise the new practices, 'buying in' to them. *Collective action* refers to the way in which users invest effort in the new practices and regularly carry them out. Finally, *Reflexive monitoring* describes the way users access and evaluate information on the effects of the new practices and in doing so gain feedback regarding their worth[37]. In addition, NPT also proposes that the continued success of new practices once embedded depends on continuous investment by staff [37 38].

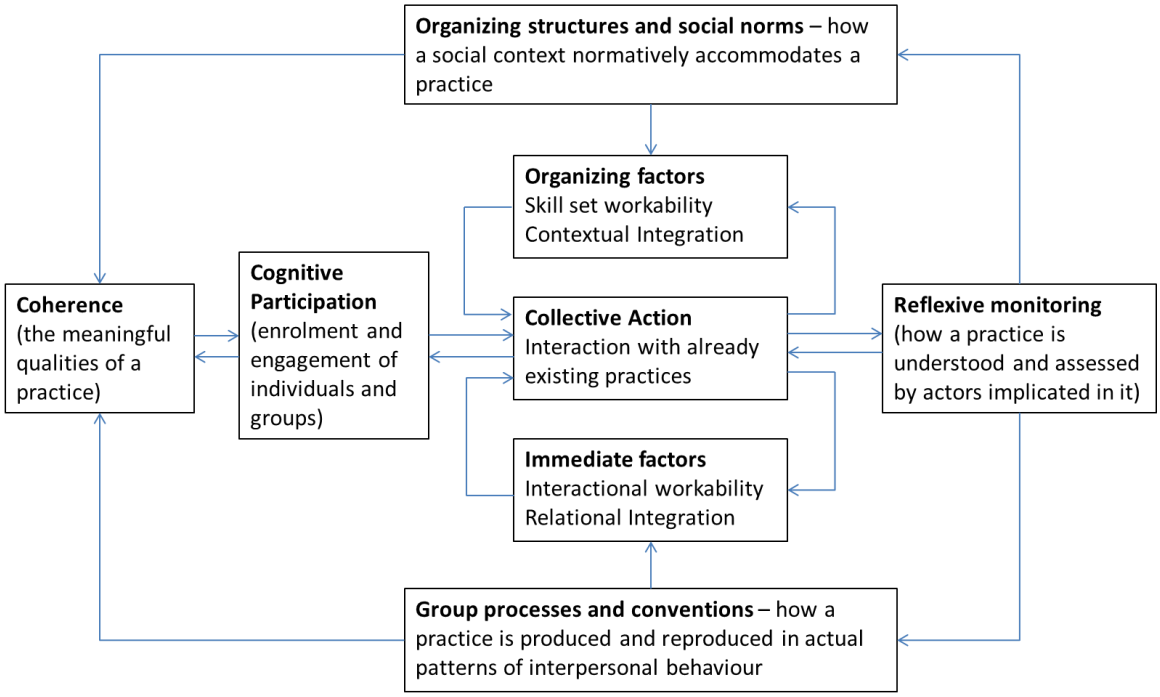


Figure 3.5: The Model of Normalization Process Theory [37]

3.2.3.1 NPT and Complex Interventions

According to Tabak et al's systematic review and appraisal of theories described above, NPT works at multiple sociological levels of system, community, organisation and individual, and is relatively adaptable, making it appealing for use with complex interventions and/or complex healthcare settings[126]. The potential for NPT to provide a framework for developing, evaluating and implementing complex interventions has been discussed and described in detail by Murray et al[143]. They highlight how NPT can be used to

understand the theoretical basis of how an intervention causes change, particularly the mechanisms by which the intervention becomes embedded and normalised, which fits well with the MRC guidance for complex interventions. Murray et al also clarify the need to distinguish between the intervention and its evaluation, which can both be considered using NPT. Careful development of the intervention itself is crucial to its success; an intervention shown to be efficacious in an experimental setting will not work in clinical practice unless it can be implemented successfully and fit with established practices in an existing setting. According to Murray et al's, NPT can assist with:

- Developing the intervention itself- by providing a framework for understanding the context and setting in which it is to be deployed and defining the intervention to ensure it is distinguished from existing practice
- Optimising the evaluation of the intervention – by ensuring the trial parameters and outcome measures will work in the clinical setting and are acceptable to staff
- Implementing the intervention – by providing a framework to identify areas where the implementation may potentially fail and highlighting possible solutions, such as training or the need for additional resources.

Murray et al suggest that by considering each of the four components of NPT at each stage of intervention development, evaluation, optimisation and implementation, areas needing additional attention can be highlighted. They suggest a series of questions that can be used for this purpose, which are shown in table 3.2. Using NPT in this fashion allows the development, implementation and evaluation of a complex intervention to be a methodical and iterative process, making it more likely to succeed[143]. It also follows that asking similar structured questions using the framework of NPT during the implementation process can provide valuable feedback on how well the intervention is being normalised. This would allow changes to be made during implementation to further enhance the uptake of the interventions, making it a dynamic process. To this end, May et al developed a toolkit based on NPT to help evaluate complex interventions[35 36]. This web-based toolkit (www.normalizationprocess.org) consists of 16 questions (four for each of the components of coherence, cognitive participation, collective action and reflexive monitoring) that were developed using a rigorous and iterative process. Each of the questions can be scored from one to ten by respondents (who may be those developing, implementing or evaluating the intervention) with results summarised using radar plots to show graphically how well the intervention is being normalised in each of the four components of NPT (the

fuller the plot, the more normalised the intervention, see figure 3.6 for an example of the plots and the toolkit questions). This provides a measure of the extent to which an intervention is becoming normalised and identifies areas needing more work to enhance normalisation.

Coherence	Is the intervention easy to describe? Is it clearly distinct from other interventions? Does it have a clear purpose for all relevant participants? Do participants have a shared sense of its purpose? What benefits will the intervention bring and to whom? Are these benefits likely to be valued by potential participants? Will it fit with the overall goals and activity of the organisation?
Cognitive Participation	Are target user groups likely to think the intervention is a good idea? Will they see the point easily? Will they be prepared to invest time, energy and work in it?
Collective Action	How will the intervention affect the work of user groups? Will it promote or impede their work? What effect will it have on consultations? Will staff require extensive training before they can use it? How compatible is it with existing work practices? What impact will it have on division of labour, resources, power, and responsibility between different professional groups? Will it fit with the overall goals and activity of the organisation?
Reflexive Monitoring	How are users likely to perceive the intervention once it has been in use for a while? Is it likely to be perceived as advantageous for patients or staff? Will it be clear what effects the intervention has had? Can users/staff contribute feedback about the intervention once it is in use? Can the intervention be adapted/improved on the basis of experience?

Table 3.2: Questions to consider when developing, evaluating and implementing complex interventions (adapted from Murray et al)[143]

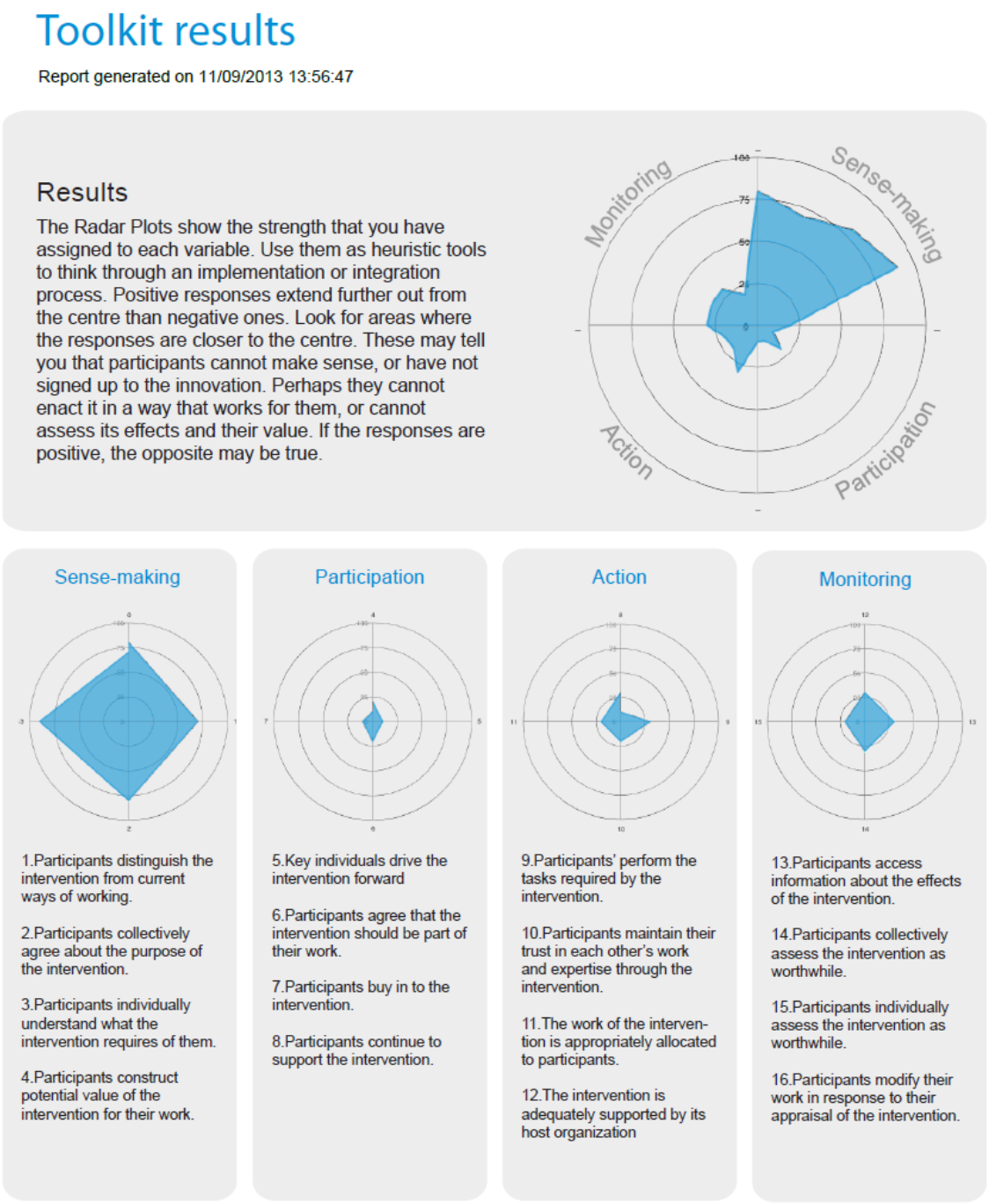


Figure 3.6: An example of an NPT Toolkit Radar Plot, together with the 16 questions included in the Toolkit. This particular example shows that whilst participants understood the intervention and distinguished it from current practice (high coherence) there was a failure buy into and support the intervention, carry it out and an inability to see the effect on practice

3.2.3.2 Use of NPT in current literature

To date the majority of studies using NPT have used it to provide a framework for the analysis of qualitative data in order to understand the normalisation process[144–148]. Such studies have included a process evaluation of the implementation of nutritional guidelines in the setting of elderly care[148], where

NPT was shown to be useful in identifying facilitators and barriers to implementation. NPT has also been used as a coding framework for two systematic reviews of qualitative studies, one focusing on the factors promoting or inhibiting the implementation of e-health services [149] and another which sought to understand patient experience of stroke[150]. The structured nature of NPT lends itself to such applications, where it can act as a framework for analysing qualitative data. One current qualitative study is using NPT to understand the factors affecting guideline implementation in primary care across different cultures[151], and another is using NPT to develop simple tools to improve the implementation of complex interventions[152]. None of these studies however, use NPT to develop or guide the implementation process itself.

3.2.3.3 Extension of NPT towards a General Theory of Implementation

Recently, NPT has been extended to produce a more general theory of implementation. This extension by May occurred during the lifetime of the study described in this thesis and the process of development of this general theory (hereafter referred to as 'Extended NPT') was influenced by some of the work described in this thesis. Extended NPT links the core constructs of NPT to those of other theories and ideas in an attempt to explain the implementation and embedding of new practices, particularly in the context of complex interventions [153]. It is based on four key constructs:

1. *Capability: The capability of agents to employ a complex intervention depends on its workability and integration within a social system. Obviously, capability will be affected by both the workability and integration of the complex intervention itself.*
2. *Capacity: The incorporation of a complex intervention within a social system depends on structural effects on agents' capacity to co-operate and co-ordinate their actions. This will be affected by material resources, social roles, social norms and cognitive resources.*
3. *Potential: The translation of capability into collective action depends on agents' potential to enact the complex intervention. This includes both individual intentions and shared commitment to the intervention.*
4. *Contribution: The implementation of a complex intervention depends on agents' continuous investments that carry forward in time and space. This construct is based on the original NPT, so is made up of coherence, cognitive participation, collective action and reflexive monitoring.*

Extended NPT is particularly aimed at complex interventions, and acknowledges that when a complex intervention is put into practice, users engage with it in multiple ways, both due to the selection of components it will

comprise of, but also due to the variety of levels at which it will act. Considering all of an organisation's *capability, capacity, potential* and *contribution*, provides a framework which attempts to consider these complexities and how they affect implementation. Extended NPT offers a way of considering many aspects of the implementation process, including the characteristics of the agents (staff enacting the intervention), the system (setting where the intervention is to be implemented) and the intervention itself. In addition, Extended NPT considers the on-going processes that occur after implementation, as the new intervention becomes more embedded into routine practice. In reality, all new interventions successfully adopted into practice will evolve over time, with staff gradually changing or adapting them with use in practice to make them more workable and allow them to fit better with existing practices and the current setting. Figure 3.7 shows how the four constructs of Extended NPT fit together with each other, but also how they are part of an on-going feedback process, with restructuring occurring, together with the mobilisation of the resources required to allow the new practice to continue. This restructuring can occur at several levels, including the way in which the intervention is used and how people work together to use it.

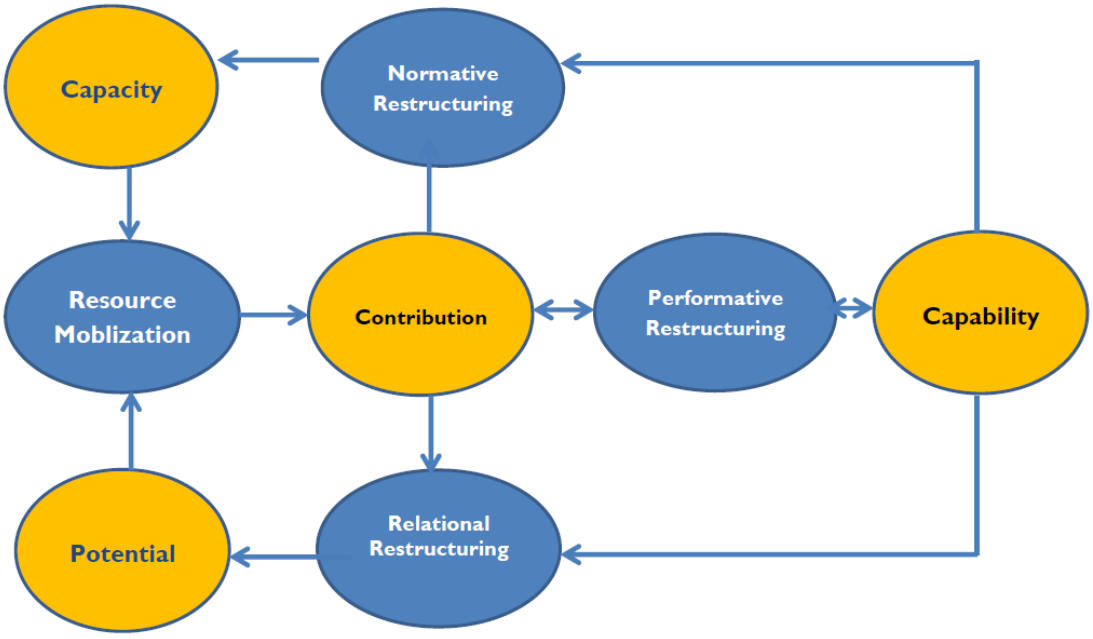


Figure 3.7: Extended NPT as a general theory of implementation

3.2.3.4 NPT and this study

In the context of a complex intervention to improve the nutritional care of preterm infants in a complex healthcare environment like NICU, NPT offers a robust framework to both develop, evaluate and guide implementation that reaches across the entire process at all system levels, making it an appropriate choice for this study. In addition, given the relative lack of measures available to assess the validity of various models, as noted by Tabak et al[126], it is important when applying models to attempt to integrate aspects of the model with measures of the implementation process or outcomes, as this will help further the understanding of the implementation process and offer evidence regarding the validity of a particular model. However, few studies have related measures of the constructs of a model to process or clinical outcomes. NPT and the associated toolkit offer an opportunity to formally assess the implementation process by relating the four constructs of coherence, collective action, cognitive participation and reflexive monitoring to measures of the implementation process itself and clinical outcomes. This thesis focusses mainly on NPT rather than the general theory of implementation (extended NPT), as the latter was not developed during the formative and implementation phases of the study. However, extended NPT was used to provide a structure to the qualitative staff interviews used to retrospectively assess the implementation process (see Chapter 4).

3.3 Conclusions

This chapter has discussed the concept of barriers and facilitators to change, suggesting that understanding them and identifying them prospectively can significantly enhance implementation and increase the likelihood of successful integration of an intervention into routine practice. The EPOC framework is a useful way of categorising barriers, whilst the model by Cabana et al provides a way of thinking about their impact on clinical practice. There is a need to formally assess barriers to practice change prior to any intervention, and this will therefore be carried out in this study, using focus groups and process mapping (described in chapter 4).

This chapter also discussed how TPB provides a way of assessing people's attitudes and intentions regarding new practices in a way which can be used to inform the development of an intervention to change practice. TPB also offers insight into readiness for change and intention to comply. At the same time, NPT provides a framework for understanding the social processes which underlie implementation and is an excellent model to understand, develop and guide the implementation process. It can therefore be seen how the two theories are complementary, and how using them together will provide valuable information in this study. Referring back to Patton's complexity framework discussed in chapter 1[33], using TPB and NPT offers a way to assess and deal with any *social complications* associated with implementation. The MFI was also discussed in order to put implementation into context with quality improvement, demonstrating that while the MFI offers a way to direct targeted improvements in care, it does not allow a theoretical understanding of how to change behaviour or embed practices into normal care in the way that theories used in implementation such as TPB and NPT do.

In line with the MRC's recommendations of using theory to guide the implementation of a complex intervention, NPT was used for this study as it is concerned with how new practices become embedded into routine care. As well as offering a way to guide the development and implementation of an intervention, NPT, through its associated toolkit, also offers a way of measuring the process of normalisation. This thesis therefore offers a unique opportunity to study the relationship between the constructs of NPT and measures of practice change and outcomes in a clinical setting. A 'mixed methods' approach has been chosen for this study in order to fully answer the research questions and to attempt to understand the complexities of changing practice. The next chapter will go on to look at the methods used in this study, including a discussion of the mixed methods approach, including its advantages and disadvantages, together with a justification of how using such an approach is useful in this study.

Chapter 4: Methods used in this thesis

Combining theories such as those described in the previous chapter, together with objective measures of change and outcome requires the use of both qualitative and quantitative research methods. Therefore, a 'mixed methods' approach was chosen for this study in order to fully answer the research questions and attempt to understand the complexities of changing practice. This chapter will discuss advantages and disadvantages of the 'mixed methods' approach that was used in this study. The main objectives and outcome measures of the study are then presented, together with the overall plan of investigation, and a detailed description of the individual quantitative and qualitative methods used.

4.1 The Theory Behind the Mixed Methods Approach

Mixed methods is an emerging research paradigm in health care, with a 2007 review demonstrating that 30% of research commissioned by the UK Health Research and Development Programme from 2000 to 2004 used this approach[154]. It may be defined as "research in which the investigator collects and analyses data, integrates the findings and draws inferences using both qualitative and quantitative approaches or methods in a single study", and it offers several advantages[155]. Firstly, it allows triangulation of results, with the possibility of corroboration between qualitative and quantitative data. Secondly, mixed methods offers the potential of building up a more comprehensive picture of the study phenomena by using a combination of research approaches. Thirdly, mixed methods allows more complex research questions to be addressed that might not be answered by a single method alone[155]. In the context of healthcare, which is increasingly interdisciplinary, complex and dynamic, there is a need to use methods which complement one another in order to fully answer research questions. This becomes paramount in the study of complex interventions in order to provide an understanding of both the effectiveness of the intervention and the way in which it acts [155 156]. Finally, both quantitative and qualitative methods have their own strengths and weaknesses, and by combining them it is possible to draw on the strengths of both and minimise or offset their weaknesses.

The relative strengths and weaknesses of quantitative and qualitative research are shown in table 4.1, which demonstrates that the two different approaches have complementary strengths, which make up for their respective weaknesses.

	Quantitative research	Qualitative research
Strengths	○ Ability to test theories and hypothesis ○ Potential for generalizability ○ The possibility of eliminating confounding factors ○ Relatively quick data collection and analysis ○ Potential for the researcher to remain independent of results ○ Generally higher credibility with administrators and commissioners ○ Potential for use in studying large numbers of people	○ Potential to gain detailed data specific to participants ○ Ability to describe complex phenomena in specific contexts ○ Ability to study dynamic processes and document change ○ Potential to produce explanatory theories ○ Ability to respond to the needs of local situations or stakeholders
Weaknesses	○ Inability to use categories or outcomes that reflect the local setting ○ The production of knowledge that is too abstract and general for application to specific situations, contexts and individuals.	○ Lack of generalizability ○ Inability to make predictions or test hypothesis or theories ○ Time consuming data collection and analyses ○ Lower credibility with administrators and commissioners ○ Increased susceptibility to researcher bias and lack of objectivity

Table 4.1: Strengths and Weaknesses of Quantitative and Qualitative Research Methods

One challenge in using a mixed methods approach is the tension between the values and processes of quantitative and qualitative methods, with qualitative research tending to emphasize an inductive, subjective and contextual approach, whilst quantitative research emphasises a deductive, objective and generalizable approach (though neither are absolute or mutually exclusive) [157]. Whilst some critics consider qualitative and quantitative methods to be incompatible based on these differences, others believe the two approaches lie on extreme ends of the same continuum, with a mixed methods approach lying in the middle ground [155]. Common to both qualitative and quantitative methodologies is that they use empirical observations to answer research questions, with both describing data, constructing explanations and speculating about the meaning of their results. While quantitative methods offer more objectivity, they themselves are subject to human decisions and behaviour, making qualitative methods seem an appropriate accompaniment [156]. Another challenge to a mixed methods approach is that it may be difficult for a single researcher to employ both methods [155].

4.1.1 Mixed Methods approach used in this study

There are several ways in which qualitative and quantitate methods can be combined in a single study, and decisions need to be made regarding how they are combined, the sequence in which they are used, whether one methodology takes precedence over the other and the way in which their results are analysed and integrated. Creswell and Plano Clark produced a typology of mixed method research in 2007, outlining the various study designs which result from these decisions [158]. The study described in this thesis essentially uses an embedded experimental design, with qualitative methods embedded within the quantitative experimental design to both guide the implementation of the intervention and to help understand and explain how it has been effective. Integration of the quantitative and qualitative results will help understand the change process. It can be seen how a mixed methods approach is advantageous for an implementation study such as is described in this thesis, as it provides a way of establishing whether a complex intervention can improve patient and process outcomes using quantitative methods, but also offers the opportunity to understand why and how the intervention has or has not been successful, together with the factors that influenced that degree of success or failure. With reference back to Patton's complexity framework in chapter 1[33], using a mixed methods approach allows an assessment of how well the complex intervention addressed both the *technical* and *social complications* associated with implementation. It is only by resolving both that change can be driven forward and embedded in such a complex situation.

4.2 Study Objectives and Outcome Measures

4.2.1 Study Hypotheses and Objectives

Referring back to chapter 1, the hypotheses that this study addresses are:

1. *The introduction of a complex intervention for the nutritional care of preterm infants will improve their nutrient intakes and growth*

2. *The use of Normalization Process Theory to both monitor and guide the implementation of a complex intervention will result in improved integration into practice with subsequent improvement in clinical outcome measures*

The primary objectives of this study were to:

1. Develop and implement a complex intervention for the nutritional care of preterm infants (born at less than 30 weeks gestation or with a birth weight less than 1501g). Following implementation of the intervention (for 1 year), assess its effect on improving:

    a. The delivery of Energy (in kcal/kg/day) and Protein (in g/kg/day) at 1 week of age, 2 weeks of age, 4 weeks of age, 6 weeks of age, 36 weeks post menstrual age and discharge compared with recommendations for this group of infants.

    b. Growth (length, weight and head circumference) at 1 week of age, 2 weeks of age, 4 weeks of age, 6 weeks of age, 36 weeks post menstrual age and discharge.

2. Assess the factors which promote or inhibit the implementation, uptake and staff engagement of the complex intervention for the nutritional care of preterm infants. This includes:

    a. The effectiveness of the intervention in terms of changing practice and how successfully components of the complex intervention are embedded and integrated into 'normal' practice ('normalization')

    b. An assessment of the factors which impede or enhance the integration of the new practices into routine normal care ('normalization')

    c. The relationship between the effectiveness of the complex intervention at changing practice and the nutritional and growth outcomes described above.

    d. The effect of NPT to guide and assess the implementation process.

4.2.2 Outcome Measures

Infant outcomes

Primary outcome measures

1. Differences in mean daily energy and protein intakes during stay on NICU between pre-implementation and intervention periods
2. Differences in the change in weight and head circumference standard deviation scores between birth and discharge between pre-implementation and intervention periods

Secondary outcomes

1. Differences in mean daily energy and protein intakes during stay on NICU during the following time periods between pre-implementation and intervention periods
    a. First week of life
    b. Second week of life
    c. Fourth week of life
    d. Sixth week of life
    e. Week of 36 weeks corrected gestational age
2. Differences in the change in weight and head circumference standard deviation scores between birth and the following time points between pre-implementation and intervention periods:
    a. End of the first week of life
    b. End of the second week of life
    c. End of the fourth week of life
    d. End of the sixth week of life
    e. Week of 36 weeks corrected gestational age
3. Differences in mortality and morbidity between pre-implementation and intervention periods
    a. Mortality
    b. Numbers of infants with Necrotising Enterocolitis (NEC)
    c. Numbers of infants with Chronic Lung Disease (CLD)
    d. Numbers of infants with Retinopathy of Prematurity (ROP)
    e. Numbers of infants with severe Intraventricular Haemorrhage (IVH)
    f. Numbers of infants with Late Onset Sepsis (LOS)
    g. Numbers of infants with Infection with Coagulase Negative Staphylococcus
    h. Length of stay

Process and Practice Change Outcomes

Process Outcome Measures

The following measures of nutritional processes will be compared across study periods:

a. *Continuous outcome measures*
    i. Time of starting enteral feeds
    ii. Time of starting PN
    iii. Time of starting breast milk fortifier
b. *Dichotomous outcome measures*
    iv. Numbers of breast fed infants that received breast milk fortifier
    v. Numbers of infants discharged on breast milk, preterm formula and term formula

Practice Change Outcome Measures

The following measures will be used to assess and understand the changes in clinical practice over time

1. The change in percentage audit compliance over the intervention and normalisation periods
2. The change in the mean Normalisation Process Theory (NPT) toolkit questionnaires score over the intervention and normalisation periods
3. The relationship between percentage audit compliance and mean NPT toolkit scores over the intervention and normalisation periods
4. The relationship between percentage audit compliance and mean NPT toolkit scores over the intervention and normalisation periods and the primary infant outcome measures described above

4.3 Patients and Participants

This prospective interventional cohort study used several comparative groups to assess the effect of the intervention in improving nutritional care and outcomes:

A) Retrospective pre-implementation period (1st January 2011 and 31st July 2011). Data on infants born during this period were collected retrospectively after the study had finished in order to provide a more contemporaneous 'control' group.

B) Partial implementation period (August 1st – December 31st 2011). Data were collected prospectively during this period, during which some elements of the intervention (including improved nutritional solutions) were introduced, and staff were made aware of and consulted about the main intervention. In addition, the work with staff carried out during this period to develop the intervention would also be likely to begin to affect practice.

C) Main Intervention Period (January 1st- December 31st 2012) during which the full complex intervention was implemented.

D) Post-implementation period (January 1st- June 30th 2013). This was used to assess the degree to which the new practices remained in place after the main intervention period.

In addition, data were collected on a retrospective cohort of infants born during 2009, in order to inform the development of the intervention by assessing nutrient intakes and growth outcomes, and identifying areas where practice could be improved. These data from the 2009 infants will be summarised as described below, but will not be used as a comparator to assess the effectiveness of the intervention. Whilst it had originally been planned to use this retrospective 2009 period as a comparison for the main intervention period, this was not done in the final analysis in view of the amount of time that has passed between 2009 and 2012 (group A above, the

pre-implementation cohort from early 2011 was used instead). However, a comparison between the 2009 period and the new 2011 pre-implementation period (A) will be carried out in order to establish any 'drift' in practice that occurred between periods without any specific intervention, as this will be of interest.

Members of Southampton NICU staff in employment during the study period were recruited to participate in focus groups, staff surveys and interviews.

4.3.1.1 Inclusion and Exclusion Criteria

To be included infants had to have been born at less than 30 weeks gestation or with a birth weight of less than 1501g. They also had to have been born in the study hospital and not transferred in from elsewhere after birth. Infants were automatically included from birth to receive the newly implemented service for the provision and monitoring of nutrition for preterm and VLBW infants (see below regarding the research approvals process).

All NICU staff were eligible for inclusion in the TPB questionnaire and the regular assessment of normalisation using the NPT Toolkit questionnaire, and were recruited during November 2012. For interviews carried out after the intervention period, only staff who had been employed on the NICU prior to the intervention were eligible to take part.

4.4 Project Structure and Plan of Investigation

This study was essentially a before and after study, involving the development, introduction and assessment of a complex intervention to standardise the nutritional care of preterm infants. It consisted of a series of smaller phases as detailed in the subsequent sections. Figure 4.1 shows a detailed plan of the study, and a brief description of each phase is given below. The subsequent section describes in detail the qualitative and quantitative methods used in each phase

4.4.1 Phases of Investigation

1. Development Phase (April 1st – December 31st 2011)

This initial, iterative phase of the study consisted of the gathering of information to inform the development of the guideline and further refine and tailor the intervention itself and the plan for implementation.

An overview of published systematic reviews was carried out to establish the most effective methods and interventions for changing practice (described in Chapter 5). Data on nutrient intakes and growth were collected from the retrospective cohort of infants born during 2009 using a specifically designed electronic tool (the Southampton Electronic Neonatal Nutrition Assessment Tool, SENNAT- see below) and process mapping of current nutritional care practices and processes was carried out (described below).

A complex intervention to improve the nutritional care and growth of preterm infants was then developed based on current evidence and recommendations for practice (described in Chapter 2) and the findings of the above (see chapter 6 for details). The TPB questionnaire and staff focus groups were then carried out during November 2011 and the results used to tailor the intervention. From August 31st 2011, some elements of the intervention were implemented (including improved nutritional products and some staff education-see Chapter 8) and prospective data collection of baseline nutrient intakes and growth of infants born during the 5 month partial implementation period was carried out using SENNAT.

2. Implementation Phase (January 1st- December 31st 2012)

The complex intervention was fully implemented on January 1st 2012 and the prospective data collection of nutrient intakes and growth using SENNAT that began in August 2011 was continued. The new practices were reinforced by the research team during this period.

The staff NPT toolkit based questionnaire was administered at two monthly intervals, generating scores in each of the four domains of coherence, cognitive participation, collective action and reflexive monitoring. This both measured the normalisation process and also identified which domains required additional input to achieve full staff engagement. In addition, rapid cycle audits[159] of adherence to the new guidelines were carried out at two monthly intervals during the intervention period, providing another measure of

practice change. Areas of weakness identified by the NPT questionnaires and audits were acted upon during the implementation period to enhance the uptake of the intervention.

3. Withdrawal and Normalisation Phase (January 1st–June 30th 2013)

One year after implementation, the research team ceased reinforcement and withdrew, leaving the guidelines, multidisciplinary nutrition team and nurse expertise in place.

Structured staff interviews were carried out to measure the effect of the intervention in changing practice and attitudes, and to identify which elements of the intervention were felt to be useful and which were not and why. At the end of the 6 month period the NPT toolkit based questionnaire and rapid cycle audit of adherence to the guidelines were repeated to measure whether the effects of the intervention in changing practice and attitudes had been sustained. Prospective data collection of nutrient intakes and growth using SENNAT was continued until the end of this period, to determine how well changes in practice had been maintained.

4. Integrative Analysis Phase (July 1st 2013 –March 31st 2014)

All data collected during the study were analysed both at the end of the 'Normalization' phase (see below and the formal Statistical Analysis Protocol, Appendix 2 for details). During this time the data for the pre-implementation cohort born in early 2011 were also retrospectively collected.

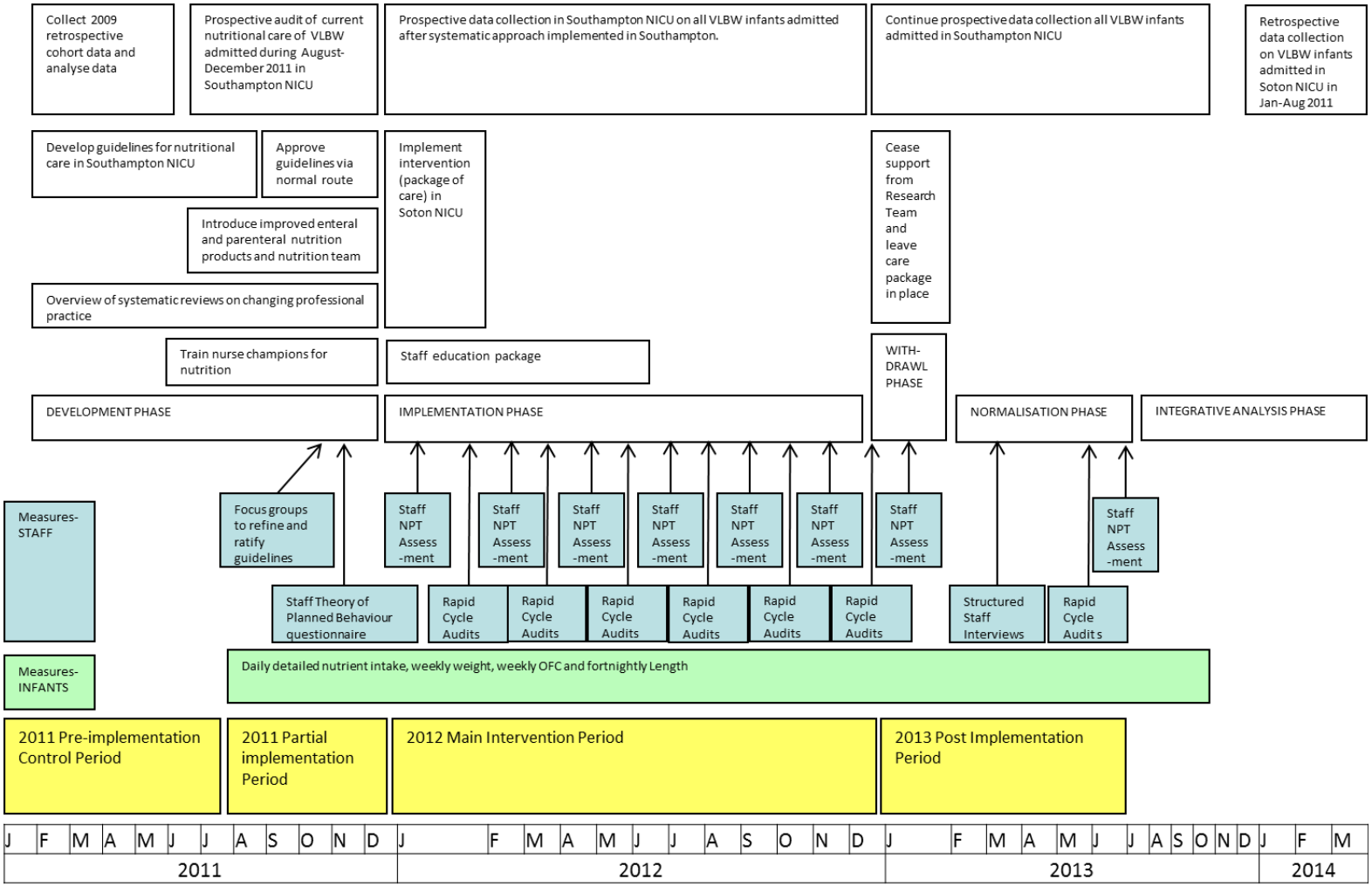


Figure 4.1: Study Flow Chart and Timeline

4.5 Methods used

4.5.1 Systematic review methodology

In order to successfully develop and implement an intervention to improve the nutritional care of preterm infants by translating evidence into routine care, a systematic review of published systematic reviews (an 'overview of systematic reviews') was carried out in order to establish the most effective professional interventions or strategies for implementing evidence based practice changes and improving quality of care and patient outcomes. This followed a standard systematic review methodology, which is described in detail together with inclusion/exclusion criteria, search strategies and results in Chapter 5. A theory led analysis using NPT was also carried out in order to identify the characteristics of interventions that made them more or less successful, and the methods used for this are also described in detail in Chapter 5. Whilst this review was initially carried out in early 2011, it was updated in November 2014 prior being included in this thesis.

4.5.2 Qualitative Methods

4.5.2.1 Process mapping and observation

A process mapping exercise was carried out during late 2010 by myself and Joanne Schofield (Senior Research Nurse) to summarise the processes surrounding nutritional assessment, decision making and the provision of nutrition to infants. This was performed using several approaches:

1. Gathering the information necessary to perform a nutritional assessment on an infant and identifying where relevant information could be found. This included consulting growth charts, current weights, fluid intakes and prescriptions, composition of feeds and fluids and current clinical issues. This was timed to see how long it would take on several occasions.
2. Examining clinical notes to determine how and where nutritional decisions were being made.
3. Direct observation of the nutritional decision making and the delivery of nutritional care to infants.

Notes were made regarding the above, and then processes were mapped to a flow chart.

4.5.2.2 Focus groups

Two, one hour focus groups were carried out on 17th and 18th November 2011, with nursing and medical staff from Southampton NICU participating. The focus groups had two main aims:

1. *Establish potential barriers and facilitators to the implementation of the new guidelines and working practice.*
2. *Promote awareness amongst staff of the new guidelines and practices.*

Staff were recruited using posters in communal NICU staff areas, and by email inviting NICU staff (of all professions) to attend one of the focus groups on the above dates. Focus groups were held over lunchtime with lunch provided to enable staff to attend during their breaks to maximise attendance. The focus groups were facilitated by Dr Wendy Lawrence, with myself as an observer. The question outline used to guide the focus groups is shown in Appendix 3. Focus groups were recorded using a digital audio recorder, then transcribed anonymously by an independent professional transcriber.

4.5.2.3 Structured Interviews

Semi-structured interviews were carried out to establish which elements of the intervention and implementation strategy had been successful and to ascertain how staff had perceived the intervention and implementation. Participants were recruited purposively with an aim of obtaining a heterogeneous sample reflective of the variety of professions, experience and seniority within the NICU staff. Staff members who had not signed up to the initial questionnaire elements of the study were also approached in order to try and ensure that there was a breadth of opinion in the sample. Given that the experience of the implementation and the perception of the new practices was the focus, staff members who had not been part of the NICU staff prior to the intervention were not approached. It is important to remember at this point that small samples are often used in qualitative research as incidence and prevalence are not its primary concern, but rather an understanding of the processes and issues. Qualitative data are relatively rich, containing a large amount of descriptive data, and it is often the case that even a relatively small sample will be likely to lead to a point where no new information is provided by the addition of more participants. It was planned that a sample of 20 to 30 staff

members would be adequate to obtain a sample that represented the full range of opinions across the entire NICU staff (approximately 120 in total).

Generally in qualitative interviewing it is recommended that interviews should be relatively unstructured in order to allow increased flow of information from participants and to allow them freedom to discuss relevant related issues. However, given that the specific nature of the research questions being asked related to the intervention and its implementation, combined with the very limited time of busy NICU staff, a semi structured interview approach was taken. This allowed the interviewer to gather highly relevant information in a short space of time. The structure of the interview was largely based on the elements of extended NPT discussed earlier, with a question aimed at exploring each construct of the theory. Questions specifically about the intervention and its successes and failure from the staff point of view were also included, and the entire interview guide can be seen in Appendix 3. Open questions were included in order to provide freedom to highlight special issues or other problems. Ethics approval was obtained to recruit and interview staff based on this interview guide. After obtaining written consent by the participants, interviews were conducted by myself, and recorded using a digital recorder. Recordings were the transcribed anonymously by a third party professional transcriber, prior to analysis.

4.5.3 Analysis of Qualitative Data

Once transcribed, both focus group data and interview data were analysed using a combination of the framework method developed by the National Centre for Social Research and described by Ritchie and Spence [160], and thematic analysis. The framework method is a systematic way of organising and managing qualitative data in a coherent manner as a grid ('framework'), with each individual participant or group represented as a row and each column a different category (issue, concept or theme) within the data. This provides a systematic, comprehensive and transparent way of managing and analysing the data in a conceptual framework, and allows the researcher to see how different themes are linked to respondents and their contexts. The text of each transcript is indexed and categorised using the framework, so all the data from the transcript is allocated to appropriate category- this may often require addition of further categories or reworking of existing categories. The next

stage is charting, with each box within the framework summarised into a chart to capture the essence of the text for each participant in each case, meaning that the entire framework chart represents and summarises all the collected data. Ensuring each statement within the framework is referenced to the original part of the transcript means that it is possible to go back to the raw data at any time to clarify any issues that arise, making the framework a robust, systematic and rigorous approach to managing qualitative data. The charts can then be used to define concepts, map the range of descriptions or opinions and find associations between categories and themes. In addition, each category/column can be looked at in more detail and analysed in order to draw out common themes within that category using thematic analysis.

Thematic analysis is an established way of analysing qualitative data, which involves going through the data and assigning blocks of text to various 'codes', which relate to a particular theme based on the essence of what is in the text. The idea is that by going through all the transcribed data and assigning it to different codes, it will be possible to see common codes or themes emerge which can be used to make sense of the data and understand what is happening. Thematic analysis arose out of 'Grounded Theory' by Glaser and Strauss, a systematic methodology emphasising the generation of theory from data in the process of conducting research that explains the findings within the data. The Grounded Theory approach uses an iterative process to draw out relevant themes from the data, allowing an *inductive* approach, generating theories or explanations of why particular things are happening. However, thematic analysis may also be used for *deductive* research, generating a description of what is happening in reality which can be compared to theoretical expectations. When used together with the framework method, thematic analysis is a powerful way of understanding the themes and issues that relate to each category in the framework. As mentioned above, the additional advantage of the framework approach here is that the rigorous, systematic and transparent organisation of data allows the researcher to move back and forth between the data and both induction and deduction as appropriate. The organisation and categorisation of qualitative data, followed by further coding during thematic analysis, is made easier using specially designed computer software. In this study, all qualitative analyses used the computer-assisted qualitative data analysis software NVivo v10 (QSR International Pty Ltd) to manage and analyse the data.

For the focus groups, initial categorisation using framework was based on two existing sets of categories. These were the eight 'barriers to change' as laid out by the Cochrane EPOC group [122] which are shown in Table 4.2, and the four main constructs of NPT (Coherence, Cognitive Participation, Collective Action and Reflexive Monitoring), which were discussed in detail in Chapter 3. Suggestions for helping the implementation process were also coded into the framework. For the interviews, the categories used in the initial framework were those of extended NPT discussed earlier in Chapter 3, which fitted with the structure of the interviews. Thematic analysis was then used to draw out common themes within each category.

1. Administrative Constraints
2. Clinical Uncertainty
3. Information Management
4. Patient Expectations
5. Perceptions of Liability
6. Sense of Competence
7. Standards of Practice
8. Financial Disincentives

Table 4.2: Barriers to Change according to the Cochrane EPOC group

4.5.4 Quantitative Methods

4.5.4.1 Staff Outcome Measures – The theory of planned behaviour questionnaire

Ajzen's Theory of Planned Behaviour (TPB, discussed in the previous chapter) was used to assess attitudes and intentions prior to implementation [121]. It was hoped that this would identify potential barriers or beliefs amongst staff that might hinder the implementation processes, and that could be overcome by adapting the implementation strategy accordingly. The use of TPB to measure attitudes and intentions would also provide a baseline assessment of readiness to change prior to implementation. TPB was chosen due to its established validity and ability to provide measurements of attitude and intentions using questionnaires constructed according to an established method [132]. Whilst the initial development of a TPB questionnaire involves some qualitative work, the final output is a numerical measure of the strength of attitudes, beliefs and intentions. TPB is therefore considered here as a quantitative research method.

Based on the guidance by Francis et al[132], a questionnaire to measure attitudes and intentions toward the new practices and guidelines was developed. An

initial elicitation study was developed and carried out during July 2011 in order to inform the final full TPB questionnaire. The elicitation study questionnaire (see Appendix 3), consisted of open, free text questions to establish which core belief statements should be included in the final TPB questionnaire. This was administered to 26 members of staff on the neonatal unit including a mix of consultants, Advanced Neonatal Nurse Practitioners (ANNPs), junior doctors, senior and junior nurses in order to develop the formal TPB questionnaire for use in the study. The results were independently reviewed by Joanne Schofield (Neonatal nutrition research nurse) and myself, in order to identify common attitudes and beliefs which could be used to build the formal TPB questionnaire. After discussion, a consensus was reached on which beliefs and attitudes to include in the final questionnaire, and a draft circulated amongst the ten members of the nutrition team and an expert in qualitative research (Professor Cathy Pope) for review regarding its wording and ease of completion. The final questionnaire was uploaded on the online survey website www.freeonlinesurveys.com to allow it to be filled out online and data collected electronically, and can be seen in Appendix 3, together with an explanation of what each question in the questionnaire was measuring or assessing.

Ethics approval for the staff TPB questionnaire was gained as part of the overall study approval. Staff were recruited by sending an email to all NICU staff providing information regarding the study, then following this up by directly asking staff on NICU if they would be willing to participate. Staff members who provided consent were emailed a link to the questionnaire on the survey website on at each time point that a questionnaire was due to be completed. The TPB questionnaire was sent out in November 2011 prior to implementation.

4.5.4.2 Infant Outcome Measures – Collection of Infant Nutrient Intakes and Growth Data

In order to collect detailed data on the nutrient intakes and growth of infants in each cohort of patients in the study, an electronic nutritional assessment tool was developed. It was also envisaged that such an electronic tool could potentially form part of the intervention itself, by accurately monitoring individual nutrient intakes on a daily basis and to comparing them to recommended amounts, providing contemporaneous and comprehensive measurements of nutrient intakes and growth to aid nutritional management.

4.5.4.2.1 Development of an Electronic Nutrition Assessment Tool

In conjunction with external software developers (Co.Efficient Consultancy), Dr Freya Pearson and I designed the 'Southampton Electronic Neonatal Nutritional Assessment Tool' (SENNAT). SENNAT was programmed in Microsoft Visual Basic and was pre-loaded with the nutritional composition of milk feeds, nutritional supplements, intravenous fluids and standard parenteral nutrition (PN) solutions. Tailor-made PN solutions manufactured by hospital pharmacy could also be entered manually. By entering the amounts and types of feeds and fluids received each day (taken from the infant's daily fluid charts), the intakes of 33 different nutrients (see table 4.3) could be calculated. Recommended ranges for nutrient intakes (see below) were also incorporated, together with source growth data from the UK-WHO Neonatal and Infant Close Monitoring (NICM) growth chart[69]. This allowed SENNAT to produce a graphical representation of an infant's nutritional status, including growth charts and graphs of energy, protein, carbohydrate and fat intakes in relation to recommended ranges, allowing easy clinical assessment (see Figure 4.2 for an example of a typical infant assessment). In addition, nutrient intakes of the 33 nutrients listed below and growth data (weight, length and head circumference) are stored, allowing analysis both individually and at population level.

Nutrient	Unit	Nutrient	Unit	Nutrient	Unit
Energy	kcal/kg	Zinc	µmol/kg	Vitamin B6	µg/kg
Protein	g/kg	Copper	µmol/kg	Folate	µg/kg
Carbohydrate	g/kg	Selenium	nmol/kg	Vitamin B12	µg/kg
Fat	g/kg	Iodine	nmol/kg	Biotin	µg/kg
Sodium	mmol/kg	Manganese	nmol/kg	Pantothenic Acid	mg/kg
Chloride	mmol/kg	Vitamin A	IU/kg	Niacin	mg/kg
Potassium	mmol/kg	Vitamin D	IU/kg	Vitamin C	mg/kg
Calcium	mmol/kg	Vitamin E	IU/kg	Taurine	mg/kg
Phosphorous	mmol/kg	Vitamin K	µg/kg	Choline	mg/kg
Magnesium	mmol/kg	Thiamin	µg/kg	Carnitine	mg/kg
Iron	µmol/kg	Riboflavin	µg/kg	Inositol	mg/kg

Table 4.3: The 33 different nutrient intakes calculated and collected by SENNAT

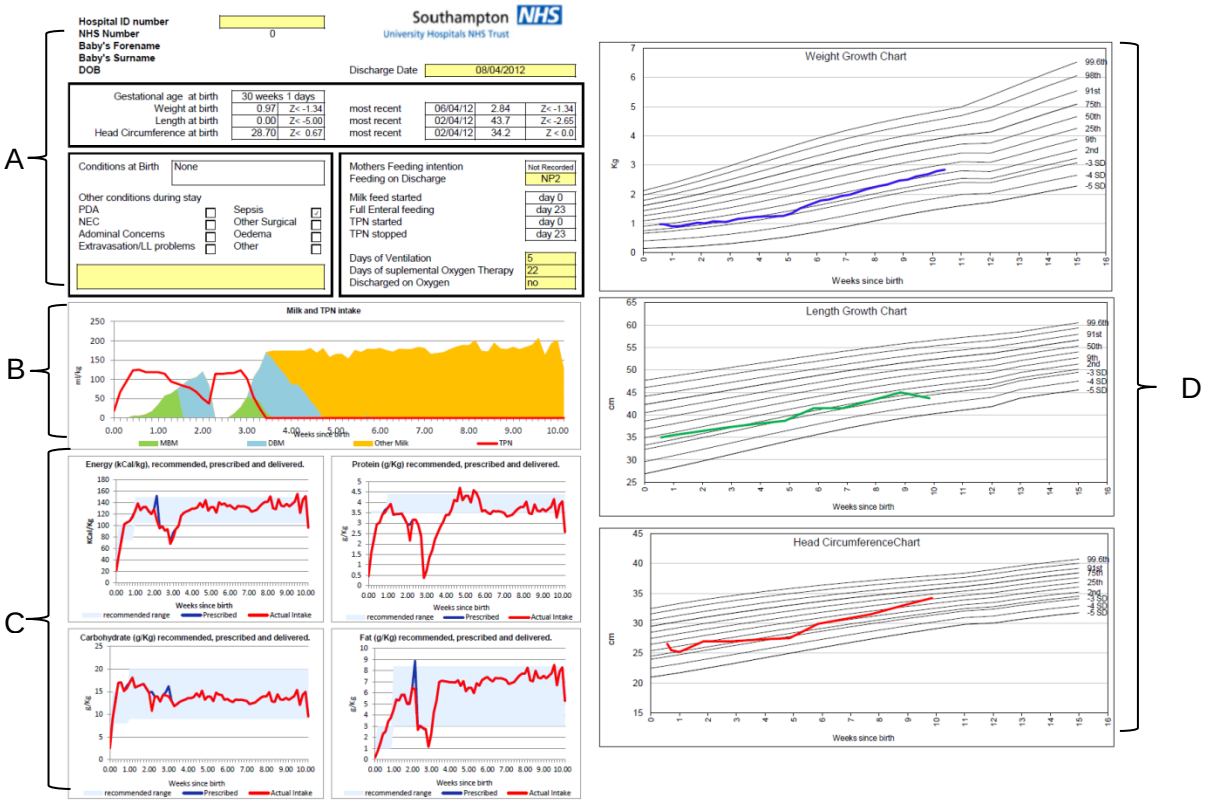


Figure 4.2: SENNAT infant nutritional assessment showing A: Patient details, B: Contributions of parenteral and enteral nutrition (PN ■, MBM■, DBM■, Formula■) C: Intakes of (clockwise from top left) Energy, Protein, Carbohydrate and Fat, (shaded area represents RRI range) and D: Growth charts for weight, length and head circumference.

As discussed earlier in chapter 2, Tsang et al's 'Reasonable Range of Intakes' (RRIs) were chosen as the reference ranges for use in SENNAT as, unlike the more recent ESPGHAN recommendations[15], they offer both enteral and parenteral intakes and so could be used across the whole patient stay[14]. Tsang's RRIs are given for three phases: Day zero, Transition and Growing. For the purposes of analysis, these phases were taken to be day zero, days one to six and day seven onwards respectively. Enteral RRIs were used once an infant was receiving 50% or greater of their total fluids enterally. Infants receiving intakes within the RRI were calculated as receiving 100% of recommendations, with amounts below or above these limits calculated as percentages using the lower and upper limits respectively. Manufacturers' data sheets were used to obtain the nutrient composition of formula milks, nutritional supplements and PN. For vitamins A, D and E, mass units were converted into international units (IU) using the conversion factors of 3.33 IU/µg, 40 IU/µg and 1.49 IU/mg respectively[161]. Maternal breast milk (MBM) and donor breast milk (DBM) were

both considered to have the nutritional composition of mature term breast milk, according to reference data [162 163]. Detailed measures of nutrient intake and growth were extracted from case notes of all infants included in the study, with data entered for each day of each infants stay. The SENNAT tool was used to collect nutrient intake and growth data in all the cohorts used in the study, with the data summarised at the following time points as described above:

- Mean daily nutrient intakes at weeks 1, 2, 4, and 6 of life
- Mean daily nutrient intakes at 36 weeks post-conceptional age (PCA)
- Mean daily nutrient intake across entire stay
- Difference in SDS for weight, length and head circumference between birth and discharge

For the purposes of the overall analysis in this thesis, only energy and protein intakes were analysed, together with growth data.

4.5.4.3 Infant Outcome Measures –Safety data and other sources of data

Data were also collected on the general health of the study population from the BadgerNet Neonatal Data system, clinical patient data management software used to collect data on all admission to NICUs in the UK. Data are entered on this system by medical and nursing staff on and during an infant's admission to NICU as part of routine clinical record keeping, and stored on a central database (part of a national neonatal database) which can be downloaded for analysis later. Data extracted for infants in the study included: mortality, diagnoses of Necrotising Enterocolitis (NEC), Chronic Lung Disease (CLD, according to the VON definition of a need for oxygen at 36 weeks PCA), Severe Intraventricular Haemorrhage (IVH), Retinopathy of Prematurity (ROP), Late-onset sepsis (LOS) and infection with coagulase negative staphylococcus (CNS, an organism associated with infections of central venous lines used for the administration of parenteral nutrition)

4.5.4.4 Process Outcome Measures – Indicators of Nutritional Care

In order to measure changes in some of the processes of nutritional care, the following data were collected from case notes for each patient cohort in the study alongside nutrition and growth data:

- Age in hours at starting PN
- Age in days at starting enteral feeds
- Age in days infants reached full enteral feeds
- Age in days breast milk fortifier commenced
- Type of feed at discharge home

4.5.4.5 Process Outcome Measures – Audit of Guideline Compliance

To provide an additional measure of practice change and another element of process evaluation, regular audits of compliance with the nutrition guideline were carried out throughout the full implementation period. The guideline compliance points are laid out in table 4.4, and included use of the screening tool. Ideal expected compliance with each point was 100% for each area. Audits were carried out as rapid safety audits, a 'snapshot' audit focussing on the all infants on the neonatal unit on one single day [159]. Data were collected using the data collection tool in Appendix 4, then data for each infant reviewed with respect to the guideline compliance point for their given clinical risk category. Audits were carried out on a two monthly basis in conjunction with the NPT questionnaire. In addition to providing a process evaluation, the audits also provided an opportunity to feedback to staff on their compliance with the new practices and highlight areas for improvement.

1	Admission screening tool complete and in folder
2	Correct risk category identified (where screened)
3	Parenteral Nutrition (PN) started in line with guideline
4	Changed to bespoke PN/Preterm+sodium PN as per guideline
5	On appropriate total fluid volume when PN flow rate decreased
6	Lipid halved at correct total PN volume
7	Feeds started in line with guideline
8	Initial feed volume in line with guideline
9	Feed volume increased in line with guideline
10	Appropriate milk chosen
11	Fortifier added/switched from DBM to LBW formula appropriately

Table 4.4: Guideline compliance audit points

4.5.4.6 Normalisation process theory toolkit questionnaire

Although NPT is based on extensive qualitative research, similar to the TPB questionnaire, the NPT toolkit provides quantitative scores of the degree of normalisation, and so is also considered in this section as a quantitative research method. The 16 question web-based NPT toolkit discussed in the chapter 3 [35] was adapted to be more specific to the study, with questions reworded to make them easier for staff to answer in the context of the new nutritional practices in NICU. This customised version was reviewed by Professor Cathy Pope to ensure it would still work within the framework of NPT, and then sent to members of the nutrition team to check that it was easy to understand and answer. The final version was then uploaded onto the online

survey website www.freeonlinesurveys.com to allow it to be filled in online and data collected electronically. A copy of the final version of the questionnaire is included in Appendix 3. For each of the 16 questions, staff were asked to score their level of agreement with each item between one and ten. This provides overall scores for each of the four domains of NPT (coherence, cognitive participation, collective action and reflexive monitoring) and aimed to provide a measure of the degree of normalisation.

The procedure for administering the NPT Toolkit questionnaire was the same as that for the TPB questionnaire described above, with ethics approval gained as part of the overall study approval. The NPT questionnaire was administered at the start of the intervention and then two monthly until the end, plus again six months after the intervention period had ended. Given concerns expressed by staff during the elicitation study regarding their opinions and views regarding practice on the NICU being linked to them, the decision was made to allow staff to answer the questionnaires completely anonymously, with no possibility of their answers being traced back to them. Whilst such a strategy was more acceptable to staff and was likely to improve response rates and the honesty of answers, this did cause some issues during analysis, as described later in this chapter.

4.5.5 Analysis of Quantitative Data – Statistical methods

A full statistical analysis plan for the study can be found in Appendix 2, but methods are covered briefly below. Statistical analyses were carried out using Stata IC v12.3 (Stata Corp) and SAS 9.3 (SAS Institute Inc.).

4.5.5.1 Summary of study data

Descriptive statistics were used to summarise the demographic and outcome variables of the infants in all the study periods. Variables of interest (listed as outcome measures above) were tested for normality using the Kolmogorov-Smirnov test in order to help determine the nature of the analysis methods used, with a cut off value of $p<0.05$ accepted as evidence of a non-normal distribution. For normally distributed continuous variables, the mean and standard deviation were calculated, with the median and interquartile range calculated for non-normally distributed data. Categorical or binary variables, were summarised as frequency and percentage of total.

Measures of attitude and intention using the TPB, and measures of practice change using NPT survey results, were summarised as mean and standard deviation for all staff at each time point (for both the total score and each of the four individual elements of NPT- coherence, cognitive participation, collective action and reflexive monitoring)

4.5.5.2 Analysis of TPB results

The TPB results were analysed in accordance with the method described by Francis et al[132]. Initially correlation analysis of measures of intention (both intention performance and generalised intention), direct attitude, subjective norms and perceived behavioural control and indirect attitude, subjective norms and perceived behavioural control were performed in order to establish which measure of intention worked best within the data. Direct measures of attitude, subjective norms and perceived behavioural control were then entered into a multiple linear regression model as predictor variables with the preferred measure of intention as the dependent variable in order to establish which predictors were most important in the study population. Indirect measures were then calculated using the formulae in Francis et al's method, with each belief statement weighted by the relevant outcome evaluation[132]. Weighted measures were then regressed together with intention in the same way as the direct measures, again to provide insight into the factors significantly affecting intention. In order to determine the difference in beliefs between those with high and low intentions, respondents were split by median intention score into high and low intenders, and an independent samples t-test used to identify the significant differences in beliefs between the two groups.

4.5.5.3 Comparison of Infant outcomes between study periods

Three methods were used to compare the difference in the primary and secondary outcome measures between study periods. These multiple methods were chosen to try and build up a comprehensive picture of the effects of the intervention over time and across study periods.

1. Comparison of non-repeated measures outcomes

   A between study period comparison was made using a single measure for each infant, with repeated measures data reduced to a single outcome measure per infant in each group prior to analysis. For nutrient intakes, these were summarised as the mean nutrient intake during the time period of interest (see

outcome measures above). A two way ANOVA and the Kruskal-wallis test were used to compare groups for normally and non-normally distributed data respectively. Where significant differences were found comparisons between pairs of groups were made using a post hoc analysis according to Tukey's method (normally distributed data) or multiple Mann-Whitney-U tests (non-normally distributed test). Infants were assigned to a study period based on their year of birth. Infants who were born in one period, but were still in hospital during the time of the next study period, had nutrient intake data from the overlapping period excluded from the analysis, whilst for measures of growth all data for such overlapping infants were excluded.

2. Interrupted time series analysis[164]

   This technique provides a useful way of visualising and comparing the effects of the intervention over time and in each time period. Although strictly speaking it should only be used with normally distributed data as it is based on linear regression, in this study it was used for all data given its utility for visualising change over time. Results were interpreted in the context of the non-normal distribution of the data where present. Data were reduced to a single outcome measure per infant per time unit in each group prior to analysis, with nutrient intakes summarised as the mean nutrient intake each week across all study periods, and growth summarised as the mean difference in SDS between birth and each week. The Prais-Winsten method as used to correct for any auto-correlation in the data[165]. Segmented regression was used for estimating intervention effects and comparing study periods. For this analysis, as daily data were used, study periods were assigned based on the date of each measurement, rather than the birth date of the infant.

3. Modelling using mixed effects for repeated measures data

   This statistical technique is advantageous to the standard comparator tests above as it is able to account for repeated measures in the same infant (thus allowing all daily nutrient intake and growth data for each infant to be used). This technique also allows the addition of other potentially confounding variables and subsequent adjustment of the model. All study periods were included in the analysis, with Tukey's method used to adjust significance values in view of multiple comparisons. Sex, gestational age at birth and birth weight were added to the model as covariates. For normally distributed data a general linear model with mixed effects was used, whilst for non-normally distributed data the generalized linear model was used, as by introducing a random effect for the repeated element it is able to account for the non-normal distribution of the data where present. For this analysis, daily infant data were used and study periods assigned based on the date of each measurement, rather than the birth date of the infant.

4.5.5.4 Mortality and Morbidity

These dichotomous outcome measures were compared across study periods using Chi squared test (or Fishers Exact test where numbers were low).

4.5.5.5 Comparison of Process Outcome Measures between study periods

Continuous process outcome measures were compared across study periods using either a two way ANOVA (for normally distributed data) or the Kruskal-Wallis test (for non-normally distributed data). If significant differences were found then comparisons between pairs of groups were made using a post hoc analysis according to Tukey's method (normally distributed data) or multiple Mann-Whitney-U tests (non-normally distributed test). Infants were assigned to a study period based on their year of birth. Infants born in one period, but still in hospital during the time of the next study period had data from the overlapping period excluded from the analysis. Dichotomous outcome measures across study periods were compared using Chi squared test (or Fishers Exact test where numbers were low).

4.5.5.6 Comparison of Practice Change Outcome Measures between study periods

Guideline compliance audit results were summarised as mean percentage compliance across all audit points at each time period, and plotted over time. Linear regression was used to assess the change over time. Measures of the 'normalisation' of practice using scores from the Normalisation Process Theory (NPT) toolkit questionnaires answered by staff at two monthly intervals during the study period were summarised as mean scores (both total score and scores for each of the four domains of coherence, cognitive participation, collective action and reflexive monitoring) and then plotted over time, and linear regression used to establish the nature of the change over time.

In order to relate mean percentage audit compliance to NPT scores, multiple linear regression was used to describe the nature of this relationship over time, with time included as variable to allow adjustment for the effect of time. Ideally, a repeated measures approach would have been used here given that the NPT results are the same group of staff answering the same questions repeatedly over time. However, the decision to use anonymous, untraceable

questionnaires did not allow this. Therefore, standard multiple linear regression with adjustment for time was used, as this is a more conservative approach than repeated measures, so would still give a reasonable measure of effects size with wider confidence intervals. Any statistical significance found using this method would therefore also be found by the less conservative repeated measures approach. A similar approach was then used to relate mean percentage audit compliance and NPT scores to the primary infant outcome measures described above. Plots of mean percentage audit compliance and NPT scores were overlaid with plots of energy intakes, protein intakes and the differences in weight and head circumference SDS between birth and discharge over time during the intervention period.

4.6 Research Approvals Process

This project was complex and consisted of several elements, the majority which did not clearly fit as a group into categorisation as service evaluation, clinical audit or research. Therefore, each element was considered separately and is described below. Despite some elements fitting into the categories of service evaluation or audit, and so not necessarily requiring ethics approval, the entire study protocol was submitted to a NHS research ethics Committee (Oxford B) and received approval (ref 11/sc/0365)

4.6.1 Development, approval and implementation of a package of care for the systematic approach to the nutritional care of preterm infants in Southampton NICU

This followed standard University Hospital Southampton Trust governance procedures as part of a change in service provision and as such did not require ethics approval.

4.6.2 Prospective nutritional and growth data collection in Southampton

Prior to implementation, collection of nutrition and growth data was an audit of the nutritional care of preterm infants in Southampton against the practice recommendations set out in chapter 2, and was registered with Trust Clinical

Effectiveness as per normal audit policy. After implementation, the collection of nutritional data was an evaluation of the new nutritional clinical service so as such did not require ethics approval. All infants born in the Princess Anne Hospital Southampton at less than 30 weeks gestation or with a birth weight less than 1501g were included and data collected prospectively following admission. Consent was not sought for this part of the study as the implemented change in practice in Southampton formed part of standard service provision for these infants, together with an evaluation of that service.

4.6.3 Assessment of staff uptake, staff engagement and 'normalisation' of the new package of care

The assessment of staff using the tools, questionnaires and interviews constitutes research and ethics approval was sought for this aspect of the study. Staff who agreed to take part were asked for their consent before being assessed using any of the tools described above.

4.6.4 Random safety audits to assess adherence to new guidelines.

The series of audits to assess adherence to the new guidelines were clinical audits so did not require ethics approval, but were registered as audits.

4.7 Summary

This chapter has discussed the mixed methods approach and the reasons for its use in this study. The plan of investigation has been outlined, together with details of the specific qualitative and quantitative methods used. A summary of the Statistical Analysis Plan has also been provided. The next chapters will describe how some of these methods were used to develop the complex intervention that was used in this study.

Chapter 5: Promoting professional behaviour change in healthcare – what interventions work, and why? A theory-led overview of systematic reviews

As described in Chapter 1, finding ways to encourage health professionals to routinely incorporate evidence into effective health care practice is important. It is well established that both healthcare delivery and patient outcomes can be improved by such means, but it is also clear that translating evidence into practice is a major challenge [1]. There is a wide ranging research literature in this field, including a large number of randomized controlled trials and systematic reviews. The conceptualization and reporting of behaviour and practice change interventions has been shaped by the application of a robust set of definitions of intervention types (see Table 5.1), a process led by the Cochrane Effective Practice and Organisation of Care (EPOC) Review Group [122]. Although there is now a voluminous literature on professional behaviour change, important questions still remain. The overview of systematic reviews described and reported in this chapter addresses one of these questions: what are the characteristics of relatively successful behaviour change interventions? This is an important question, but one where the literature is often contradictory. It is a difficult question to answer, because interventions themselves are often inadequately described, and because the mechanisms by which they expected to effect change are often poorly understood [166]. Furthermore, even within interventions of the same type, there is considerable heterogeneity. The complexity of these interventions is often recognised, but is less frequently accounted for in reports of their outcomes.

Normalization Process Theory (NPT) [167 168] offers a useful lens through which to explore behaviour change interventions. As described in chapter 3, NPT considers four key elements; coherence (whether users can understand why new practices are needed and different from existing practices), cognitive participation (whether users understand what work is needed and whether they are prepared to do it) collective action (whether users actually carry out the work) and reflexive monitoring (whether users can see the benefit of the work

in their daily practice). These four elements are in turn each further divided into four constructs, which are show in table 5.2.

	Name	Description
A	Distribution of educational materials	Distribution of published or printed recommendations for clinical care, including clinical practice guidelines, audio-visual materials and electronic publications. The materials may have been delivered personally or through mass mailings.
B	Educational meetings	Health care providers who have participated in conferences, lectures, workshops or traineeships
C	Local consensus processes	Inclusion of participating providers in discussion to ensure that they agreed that the chosen clinical problem was important and the approach to managing the problem was appropriate
D	Educational outreach visits	Use of a trained person who met with providers in their practice settings to give information with the intent of changing the provider's practice. The information given may have included feedback on the performance of the provider(s).
E	Local opinion leaders	Use of providers nominated by their colleagues as 'educationally influential'. The investigators must have explicitly stated that their colleagues identified the opinion leaders.
F	Patient mediated interventions	New clinical information (not previously available) collected directly from patients and given to the provider e.g. depression scores from an instrument.
G	Audit and feedback	Any summary of clinical performance of health care over a specified period of time. The summary may also have included recommendations for clinical action. The information may have been obtained from medical records, computerised databases, or observations from patients.
H	Reminders	Patient or provider encounter specific information designed or intended to prompt a health professional to recall information. This would usually be encountered through their general education; in medical records or through interactions with peers, and so remind them to perform or avoid some action to aid individual patient care. Computer aided decision support is included.
I	Marketing	Use of personal interviewing, group discussion ('focus groups'), or a survey of targeted providers to identify barriers to change and subsequent design of an intervention that addresses identified barriers.
J	Mass media	Either 1) Varied use of communication that reached great numbers of people including television, radio, newspapers, posters, leaflets, and booklets, alone or in conjunction with other interventions, or 2) Targeted at the population level.

Table 5.1: Professional Interventions as per Cochrane EPOC Review Group [122]

Group	Construct	Description	Code
Coherence	**Differentiation**	An important element of sense-making work is to understand how a set of practices and their objects are different from each other.	CODI
	Communal specification	Sense-making relies on people working together to build a shared understanding of the aims, objectives, and expected benefits of a set of practices.	COIS
	Individual specification	Sense-making has an individual component too. Here participants in coherence work need to do things that will help them understand their specific tasks and responsibilities around a set of practices.	COCS
	Internalization	Finally, sense-making involves people in work that is about understanding the value, benefits and importance of a set of practices.	COIN
Cognitive Participation	**Initiation**	When a set of practices is new or modified, a core problem is whether or not key participants are working to drive them forward.	CPIN
	Enrolment	Participants may need to organize or reorganize themselves and others in order to collectively contribute to the work involved in new practices. This is complex work that may involve rethinking individual and group relationships between people and things.	CPLE
	Legitimation	An important component of relational work around participation is the work of ensuring that other participants believe it is right for them to be involved, and that they can make a valid contribution to it.	CPEN
	Activation	Once it is underway, participants need to collectively define the actions and procedures needed to sustain a practice and to stay involved.	CPAC
Collective Action	**Interactional Workability**	This refers to the interactional work that people do with each other, with artefacts, and with other elements of a set of practices, when they seek to operationalize them in everyday settings.	CAIW
	Relational Integration	This refers to the knowledge work that people do to build accountability and maintain confidence in a set of practices and in each other as they use them..	CARI
	Skill set Workability	This refers to the allocation work that underpins the division of labour that is built up around a set of practices as they are operationalized in the real world.	CACI
	Contextual Integration	This refers to the resource work - managing a set of practices through the allocation of different kinds of resources and the execution of protocols, policies and procedures.	CASW
Reflexive Monitoring	**Systematization**	Participants in any set of practices may seek to determine how effective and useful it is for them and for others, and this involves the work of collecting information in a variety of ways.	RMSY
	Communal appraisal	Participants work together - sometimes in formal collaboratives, sometimes in informal groups to evaluate the worth of a set of practices. They may use many different means to do this drawing on a variety of experiential and systematized information.	RMIA
	Individual appraisal	Participants in a new set of practices also work experientially as individuals to appraise its effects on them and the contexts in which they are set. From this work stem actions through which individuals express their personal relationships to new technologies or complex interventions.	RMCA
	Reconfiguration	Appraisal work by individuals or groups may lead to attempts to redefine procedures or modify practices - and even to change the shape of a new technology itself.	RMRE

Table 5.2: The Constructs of NPT

As NPT focuses on action – the things that people do when they implement a new way of conceptualizing, enacting, or organizing practice, including the collective action that results from complex patterns of social relations and interactions [169] – rather than on their beliefs, attitudes, and intentions, it facilitates an understanding of the contexts, social structure and processes in which behaviour change interventions take place. Translational frameworks founded on NPT have already been applied to qualitative systematic reviews that have explored the dynamics of organizational behaviour around implementation [170], organizational change in healthcare provision [171], professional behaviour around implementation [172], and patient behaviour [173].

This chapter describes an advance in the use of NPT by applying it to reviews of professional behaviour with the aims of understanding the dynamics of professional behaviour change, and explaining why some interventions appear to be more successful than others. Theory-led reviews offer an opportunity to understand the social mechanisms by which interventions work in addition to whether they work at all. This is an overview of systematic reviews which was led by myself but carried out with assistance from Professor Carl May. This additional input was necessary as a degree of independent input is essential in reviews of this nature. Professor May assisted in the selected of articles, development of the NPT-EPOC coding framework (which was developed by consensus between the two of us) and the coding of intervention type within each review. We aimed to consider all systematic reviews that had looked at the effectiveness of various professional interventions (according to the above EPOC classification) aimed at changing professional behaviour, and then map these interventions to the constructs of NPT in order to establish the characteristics of successful behaviour change interventions in healthcare.

5.1 Methods

The methodology set out by Smith et al for conducting a systematic review of systematic reviews of healthcare interventions was used[174].

5.1.1 Eligibility criteria

Studies were eligible for inclusion if they were systematic reviews, meta-analyses or syntheses of published qualitative or quantitative studies, and if

they examined the effectiveness of interventions intended to lead to the implementation of evidence based practice by healthcare professionals or providers. To be included the interventions used had to be a 'Professional Intervention' as defined by the Cochrane Effective Practice and Organisation of Care (EPOC) review group's (see Table 5.1 [122]). Comparisons of implementation intervention vs. control (no intervention) or another intervention were acceptable. Outcome measures had to include any measures of clinical process change, compliance or patient outcomes. Included studies had to be in the English language. Studies which focused on financial incentives, organisational changes and policy changes were excluded. In addition, studies considering larger public health issues not directly concerned with professional practice changes (e.g. smoking cessation aimed at the general public), together with those concerned with changing patient behaviour rather than practice or professionals behaviour (e.g. promotion of healthy lifestyle changes) were also excluded. Studies which looked at the barriers or factors affecting implementation, rather than the effects of interventions themselves on outcomes were also excluded.

5.1.2 Searches and Information sources

A literature search was carried out using the key words and search strategy detailed in Table 5.3. Montori et al's optimal search strategy for maximum precision for retrieving systematic reviews from Medline was used [175]. Also, given the close relationship between guideline implementation, practice patterns, evidence based medicine and quality improvement, the search was broadened to include these MeSH terms. The electronic databases MEDLINE (1947 to Present), CINAHL (1981 to Present), PsychINFO (1967 to present) were searched using EBSCO. In addition, the Cochrane library (1988 to present) was searched using the same search strategy outlined in Table 5.3, adapted for use in the web interface. Citation and reference searching was performed on articles selected for review. The last search was run in November 2014.

5.1.3 Study selection

Studies were assessed for eligibility by a two reviewers (MJJ and CRM), who were not blinded to the identities of the study authors or institutions.

1	"clinicians"
2	(MH "Nurse Practitioners+") OR (MH "General Practitioners") OR "practitioner"
3	(MH "Nursing Staff+") OR (MH "Medical Staff+") OR (MH "Nursing Staff, Hospital") OR (MH "Medical Staff, Hospital+") OR "staff"
4	"health professional" OR "health professionals"
5	"healthcare teams" OR (MH "Patient Care Team+")
6	(MH "Health Personnel") OR "health personnel" OR (MH "Allied Health Personnel+")
7	(MH "Allied Health Occupations+") OR (MH "Allied Health Personnel") OR "allied health professionals"
8	"occupational therapists"
9	(MH "Pharmacists") OR "pharmacist"
10	(MH "Nutritionists") OR "dietitians"
11	(MH "Physical Therapists") OR "physiotherapist"
12	(MH "Nurses+") OR "nurses"
13	(MH "Physicians") OR "physicians"
14	"doctors"
15	(MH "Algorithms+") OR "algorithm*"
16	(MH "Information Dissemination") OR ""information dissemination""
17	(MH "Clinical Protocols+") OR "protocol"
18	(MH "Mass Media+") OR "mass media"
19	(MH "Medical Audit+") OR (MH "Nursing Audit") OR "audit"
20	(MH "Marketing+") OR "marketing"
21	"opinion leaders"
22	(MH "Reminder Systems") OR "reminder"
23	"academic detailing"
24	"educational outreach"
25	"educational materials"
26	(MH "Guideline+") OR "guideline" OR (MH "Practice Guideline")
27	(MH "Education+") OR "education"
28	"printed"
29	"identify barriers"
30	"reminders"
31	(MH "Process Assessment (Health Care)") OR "process"
32	"outcomes" OR (MH "Outcome Assessment (Health Care)+")
33	(MH "Guideline Adherence")
34	"behaviour"
35	(MH "Behavior+") OR "behavior"
36	(MH "Physician's Practice Patterns") OR (MH "Professional Practice+") OR (MH "Nursing, Practical") OR "practice"
37	"process of care" OR "processes of care" OR "health outcomes" OR "patient outcomes"
38	AB MEDLINE OR TI MEDLINE OR AB systematic review OR TI systematic review OR PT meta-analysis
39	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
40	15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30
41	31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37
42	38 AND 39 AND 40 AND 41

Table 5.3: Search strategy used in overview of systematic reviews (MH= Medical Subject Heading, AB=abstract, TI=title, PT=publication type, '+' indicates an exploded term)

5.1.4 Data collection process

Data extraction was carried out by a single reviewer (MJJ) using a specially designed spread sheet which collected data on the subject of the review, the setting, the participants, the intervention assessed, the outcome measures, the years of literature searched, the main findings and authors conclusions. Studies were coded by MJJ and CRM, as to which single intervention or multiple interventions they were assessing.

5.1.5 Quality assessment of included Systematic Reviews

The quality of included reviews was assessed using the AMSTAR criteria (see Appendix 5) [176]. Studies scored one point for each of the 11 criteria they met.

5.1.6 Synthesis of results

This is an overview of systematic reviews, so vote counting together with a narrative synthesis of included studies was planned to summarise findings. This was because some meta-analysis may have already taken place in the included studies; the likelihood of varying areas of focus between reviews; and anticipated heterogeneity in the reporting of results. Systematic reviews which focussed specifically on guideline implementation as an activity were analysed separately. Where a systematic review had included studies which used more than one kind of intervention it was considered to be assessing multiple strategies. For the purpose of synthesis, systematic reviews considering multiple intervention types were coded to each of the intervention types they assessed, with effectiveness of their component interventions assessed individually. This strategy meant that studies included in several reviews would be counted more than once, but helped gauge the effectiveness of each intervention type when used as part of a multifaceted strategy.

5.1.7 Mapping of EPOC Professional Interventions to NPT

Two authors (MJJ and CRM) mapped each of the ten intervention types (excluding the 'Other' category) defined by EPOC to 14 of the 16 sub-constructs of NPT (see Table 5.2), and developed a coding matrix incorporating both NPT constructs and EPOC intervention types. Two NPT sub-constructs were excluded from coding: differentiation and reconfiguration, because the

first is a precondition for an experimental intervention and the second is a requirement of an intervention study.

5.1.8 Coding of Systematic Reviews to NPT framework

Once included, systematic reviews were assigned to one of three groups; those considering guideline implementation, those considering single interventions, and those which considered studies using multiple interventions. Reviews were coded as using single interventions if they considered only one type of professional intervention exclusively, whilst those that included studies using a variety of interventions or combinations of interventions were coded as using multiple interventions. Each systematic review was then coded as to which interventions it used (based on the studies it had included), and the NPT-EPOC professional intervention coding framework then used to determine which NPT constructs it had covered in its component interventions. This then allowed each review to be given a score for each construct of NPT depending on which EPOC intervention type had been used in the included studies when drawing conclusions about effectiveness. Each systematic review was then also coded as to whether it had concluded that the intervention/interventions it had reviewed had been successful in improving the process of care and/or patient outcomes. For each of these two outcomes, systematic reviews could be coded as 'successful', 'unsuccessful', 'unclear' or 'not assessed'. This was in essence a simple qualitative framework analysis presented using simple counts [177 178]

Once coded, results were then represented as radar plots, with each review overlaid to show how each construct was represented across reviews in each category. This allowed a graphical representation of the number and extent to which each NPT construct was represented in reviews which considered the interventions to be successful in improving practice or outcomes, which could then be compared to those which were less successful. The more complete the area of the radar plot, the more constructs of NPT a review was including, while large peaks in the plot area highlighting NPT constructs that were being most heavily accessed by interventions or groups of interventions. On this basis, we hypothesized that reviews which had found more success in their outcome measures would be associated with fuller radar plots.

5.2 Results

5.2.1 Results of searches

The review process is shown in Figure 5.1. We identified 4350 possible articles, with 4364 left after removal of duplicates; 235/4364 were selected for review of the full text; and 67/235 fully met the criteria for inclusion (reasons for exclusion at this stage are shown in figure 5.1). Of the 67 included, 20 focused on primary, ambulatory or community care; 11 focused on secondary or specialist care, and 36 focused on both primary and secondary care settings. Included reviews fell into three groups: 34/67 reviewed studies of a single type of intervention (see Table 5.4); 33/67 reviewed studies of multiple types of intervention. Of the latter, 21/33 considered interventions themselves (see Table 5.5), and 12/33 examined guideline intervention strategies. These were considered separately (see below and Table 5.6). The findings are considered in more detail below using the EPOC PI classification. Details of all included studies can be found in Appendix 6.

5.2.2 Quality assessment

The quality score was generally lower for studies looking at different guideline implementation strategies (mean score 6.7) than those considering single interventions (see Table 5.4 and 5.5, overall mean scores of 8 and 7.5 for multiple intervention reviews and single PI reviews respectively). Low scores were mainly due to inadequate reporting. Many studies failed to assess publication bias (82%) or include a list of included and excluded publications (69%). The full breakdown of the AMSTAR scores for each review are given in Appendix 7.

5.2.3 Guideline implementation strategies

Twelve systematic reviews specifically considered optimal strategies for guideline implementation. Whilst the use of guidelines can be considered part of the EPOC PI 'Dissemination of Education Materials', reviews specifically dealing with guideline implementation strategies are considered here separately, and are not included in the other sections below focussing on the individual interventions.

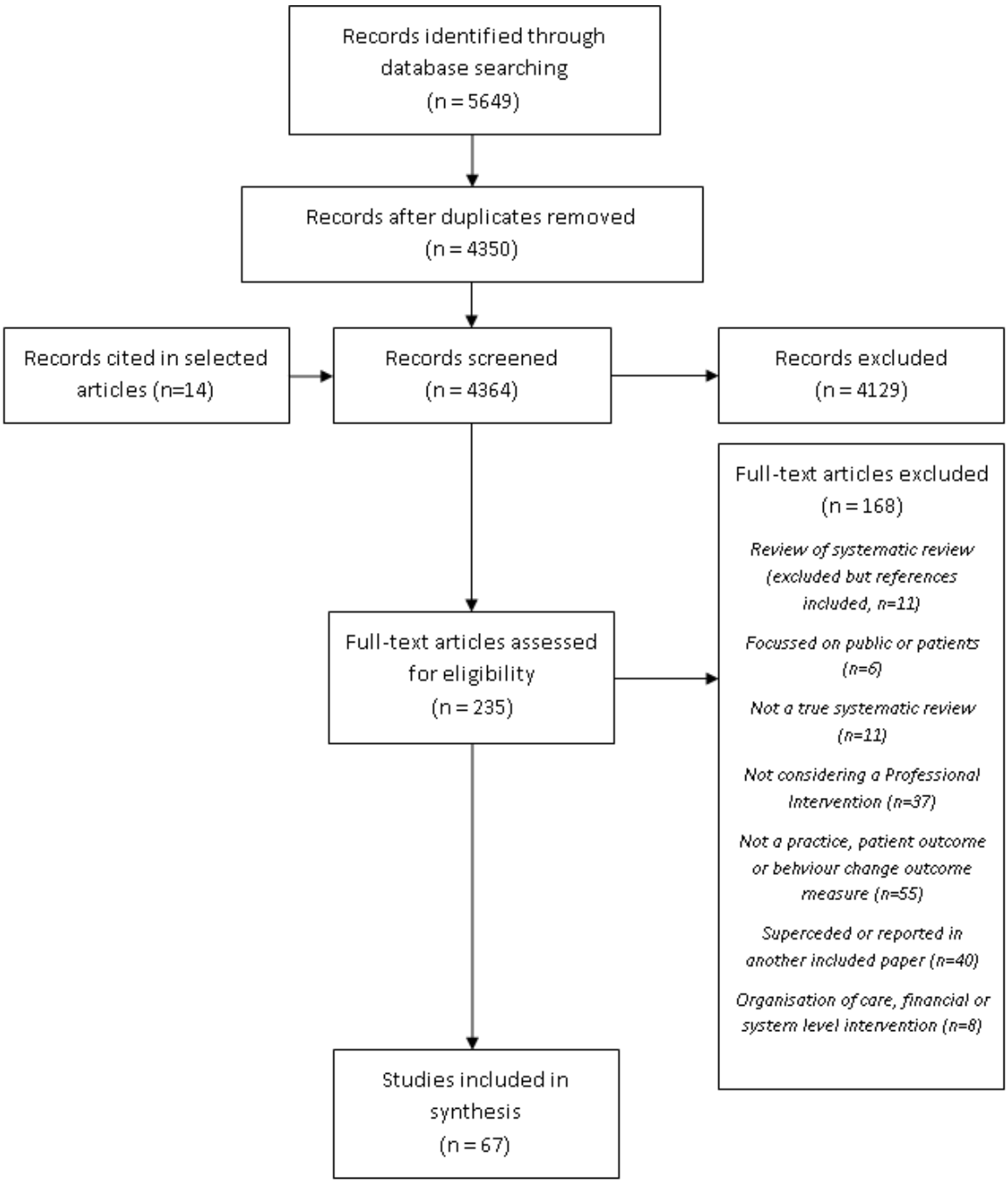


Figure 5.1: Flow Chart of Systematic Review Process

Seven of the reviews that addressed guideline implementation strategies compared in some way various single implementation strategies with more multifaceted approaches which used a combination of interventions, with five (71%) finding that multifaceted implementation strategies were more effective than single ones. Of note, the comprehensive systematic review of guideline

dissemination by Grimshaw et al in 2004 [179] showed no difference between single and multifaceted strategies, a finding also confirmed by Hakkennes et al in 2008 [180]. However, a more recent systematic review by Medves et al in 2010 [181] found a benefit of multifaceted strategies, particularly for more complex healthcare areas. As part of their comprehensive consideration of all professional interventions, they also found that local opinion leaders, audit and feedback and reminders were the most effective strategies, with the proportion of studies with positive results of 81.3%, 82.2% and 85.2% respectively. Chaillet et al also concluded that multifaceted strategies based on audit and feedback, perhaps facilitated by local opinion leaders seemed the most effective in an obstetric setting [182]. However, while Chaillet et al's review was of reasonable quality with an AMSTAR score of seven, the remainder of studies which found multifaceted approaches to be most effective all scored five or less. Conversely, Grimshaw and Hakkennes's reviews which did not find in favour of multifaceted approaches were both of higher quality, with scores of eleven and eight respectively. Table 5.6 shows that while most strategies were effective at improving practice, not all were effective at improving patient outcomes. The most studied interventions were educational meetings, audit and feedback, reminders, educational outreach visits and local opinion leaders, which were also the most effective interventions. Local consensus processes, patient mediated interventions and mass media also appeared to be effective but were under-studied.

Two reviews examined the mode of guideline delivery. Shiffman et al suggested that adherence to guidelines was improved where these were embedded in electronic patient records. Heselmans et al found little evidence for the use of electronic guideline based implementation in ambulatory care [183] [184]. Three reviews examining implementation strategies drew attention to the need to identify barriers to implementation, and to tailor implementation strategies to their settings [124] [180] [185]. In particular, Challiet et al noted that interventions where barrier to change were prospectively identified were more likely to be successful (93.8% vs. 47.1%, p=0.04)[182].

5.2.4 Patient Mediated Interventions

Patient mediated interventions are the provision of new, previously unavailable, clinical information collected directly from the patient, to the provider. No

reviews considered patient mediated interventions in isolation, although four reviews that considered multiple interventions included them, which were all generally of high quality, with AMSTAR scores of seven and above. French et al, in their systematic review looking at interventions to improve the use of imaging for musculoskeletal conditions, found that interventions where they were used had the most potential for benefit [186]. Davis et al and Brennan et al also found benefits to practice in their reviews [187 188]. However, Oxman et al's., review emphasized uncertainty about their effectiveness [189].

5.2.5 Dissemination of Educational Materials

Six reviews focused solely on the dissemination of educational materials – which may take the form of clinical guidelines or similar interventions. Giguère et al concluded that printed materials had a positive effect on professional practice, but an unclear effect on patient outcomes [190]. Thomas and Cullum found positive effects of printed materials (in the form of guidelines) on both professional behaviours and patient outcomes [191]. However, Worrall et al were unable to be clear regarding their effect in primary care[192]. Blackwood et al focussed on the effect of guidelines to improve weaning in ventilated patients in intensive care in their high quality review, finding benefit [193]. Clarke et al found benefits to practice in surgical referral using guidelines, and again their review was of good quality with an AMSTAR score of eight [194]. Wutoh et al found no benefit to practice, but their review was of lower quality with an AMSTAR score of just five [195].

Where educational materials were part of interventions that used multiple behaviour change strategies, 11/15 studies showed benefit to the process of care or practice, of which two 5/11 found a benefit to patient outcomes. Taking all the studies together, it seems that where the 'educational material' consisted of guidelines with a specific purpose or focus, there was more likely to be benefits to practice or outcomes.

5.2.6 Educational Meetings

Systematic reviews by Goodwin et al., and Forsetland et al. [196 197], found evidence of positive effects on professional behaviour. Forestland et al also found a small benefit to patient outcomes, concluding that using multiple and mixed educational strategies was more effective than single media or more

didactic approaches [197]. Brody et al also found benefits to practice in the management of dementia [198]. Whilst there were benefit to practice from educational meetings, the effects on patient outcomes were less clear, with just one study which focused on educational meetings in isolation, Forsetlund et al's review of continuing medical education, finding a positive effect [197]. Educational meetings were considered by 16 reviews looking at multiple interventions in improving professional practice, and were found to be effective in 11/16. Only eight of these reviews also looked at the effect on improving patient outcomes, with just two (25%) finding a benefit.

5.2.7 Educational Outreach Visits

O'Brien et al looked at educational outreach visits (also known as academic detailing) in isolation [199]. They found them to be effective in changing practice, though the effect size varied depending on the clinical domain. Chhina et al looked at the use of academic detailing in modifying prescribing behaviour, finding them to be effective in changing practice [200]. Twelve reviews considering multiple intervention types looked at educational outreach, with 8/12 finding them effective in changing practice, with both Beilby et al and Davis et al specifically highlighting them as superior to other models [187 201]. Gilbody et al concluded that whilst simple guideline and educational strategies are generally ineffective, adding clinician education, an enhanced nursing role and greater integration between primary and secondary care improved effectiveness in primary care [202]. Interestingly, only 1/7 reviews using educational outreach as part of a bundle of interventions found clear benefit for patients.

5.2.8 Local Consensus Processes

Only two of the reviews looking at multiple interventions considered local consensus processes, with neither able to be clear about their usefulness in improving practice or patient outcomes [189 203].

Professional Intervention	Mean Quality Score	Total No. of reviews	Professional Practice				Patient Outcome			
			n	Effective (%)	Ineffective (%)	Unclear (%)	n	Effective (%)	Ineffective (%)	Unclear (%)
Distribution of educational materials	8.3	6	5	3 (60)	1 (20)	1 (20)	5	2 (40)	1 (20)	2 (40)
Educational meetings	8	4	4	3 (75)	0 (0)	1 (25)	2	1 (50)	0 (0)	1 (50)
Local consensus processes	N/A	0	0	-	-	-	0	-	-	-
Educational outreach visits	8.5	2	2	2 (100)	0 (0)	0 (0)	1	0 (0)	0 (0)	1 (100)
Local opinion leaders	10	1	1	1 (100)	0 (0)	0 (0)	0	-	-	-
Patient mediated interventions	N/A	0	0	-	-	-	0	-	-	-
Audit and feedback	10	1	2	1 (100)	0 (0)	0 (0)	1	1 (100)	0 (0)	0 (0)
Reminders	7.6	18	18	14 (78)	2 (11)	2 (11)	11	4 (36)	2 (18)	5 (45)
Marketing	11	1	1	1 (100)	0 (0)	0 (0)	0	-	-	-
Mass media	N/A	0	0	-	-	-	0	-	-	-

Table 5.4: Summary of the effectiveness of single Professional Interventions in changing professional practice and patient outcome in reviews focussing on single interventions

Professional Intervention	Mean Quality Score	Total No. of reviews	Professional Practice				Patient Outcome			
			n	Effective (%)	Ineffective (%)	Unclear (%)	n	Effective (%)	Ineffective (%)	Unclear (%)
Distribution of educational materials	8.3	15	15	11 (73)	1 (7)	3 (20)	11	5 (45)	2 (18)	4 (36)
Educational meetings	7.8	16	16	11 (69)	0 (0)	5 (31)	8	2 (25)	1 (13)	5 (63)
Local consensus processes	7.5	2	2	0 (0)	0 (0)	2 (100)	1	0 (0)	0 (0)	1 (100)
Educational outreach visits	7.6	12	12	8 (67)	1 (8)	3 (25)	7	1 (14)	2 (29)	4 (57)
Local opinion leaders	7	4	4	2 (50)	1 (25)	1 (25)	2	0 (0)	1 (50)	1 (50)
Patient mediated interventions	8.3	4	4	3 (75)	0 (0)	1 (33)	2	1 (50)	0 (0)	1 (50)
Audit and feedback	8	15	15	12 (80)	0 (0)	3 (20)	6	2 (33)	1 (17)	3 (50)
Reminders	7.1	15	15	11 (73))	1 (7)	3 (20)	7	1 (14)	2 (29)	4 (57)
Marketing	8	4	4	2 (50)	0 (0)	2 (50)	2	0 (0)	0 (0)	2 (100)
Mass media	9	2	2	0 (0)	0 (0)	2 (100)	2	0 (0)	0 (0)	2 (100)

Table 5.5: Summary of the effectiveness of Professional Interventions in changing professional practice and patient outcome in reviews focussing on multiple interventions

Professional Intervention	Mean Quality Score	Total No. of reviews	Professional Practice				Patient Outcome			
			n	Effective (%)	Ineffective (%)	Unclear (%)	n	Effective (%)	Ineffective (%)	Unclear (%)
Educational meetings	6.3	8	8	6 (75)	0 (10)	2 (25)	5	4 (80)	0 (0)	1 (20)
Local consensus processes	7.5	2	2	2 (100)	0 (0)	0 (0)	1	1 (100)	0 (0)	0 (0)
Educational outreach visits	6.7	7	7	6 (86)	0 (0)	1 (14)	4	4 (100)	0 (0)	0 (0)
Local opinion leaders	6.2	5	5	5 (100)	0 (0)	0 (0)	2	2 (100)	0 (0)	0 (0)
Patient mediated interventions	7.3	3	3	3 (100)	0 (0)	0 (0)	1	1 (100)	0 (0)	0 (0)
Audit and feedback	6.3	9	9	7 (78)	0 (0)	2 (12)	5	4 (80)	0 (0)	1 (20)
Reminders	6.7	12	12	9 (75)	1 (8)	2 (17)	7	5 (71)	1 (14)	1 (14)
Marketing	6.8	4	4	3 (75)	0 (0))	1 (25)	2	2 (100)	0 (0)	0 (0)
Mass media	7.5	2	2	2 (100)	0 (0)	0 (0)	1	1 (100)	0 (0)	0 (0)

Table 5.6: Summary of reviews that considered multiple Professional Interventions s for the implementation of guidelines. Note that the professional intervention 'Dissemination of Educational Materials' has been omitted as all guidelines themselves are all considered to be educational materials so this was present in all implementation studies, but not used as part of an implementation strategy per se.

5.2.9 Local Opinion Leaders

In their high quality Cochrane review Flodgren et al [204] found that local opinion leaders had a beneficial effect on professional behaviour change, with improvements in risk difference of 0.09 compared to no intervention, 0.14 compared to another single intervention and 0.1 when used as part of a multifaceted intervention compared to no intervention (overall effect was a risk difference of 0.12). However, they noted that as the role of opinion leaders is poorly defined, it is difficult to ascertain the optimal approach to this intervention. The seven systematic reviews that included studies using local opinion leaders as part of multiple interventions had inconsistent findings, though in general while some found benefits to practice, none found benefits to patient outcomes.

5.2.10 Audit and Feedback

In another high quality Cochrane review, Ivers et al [205] found that audit and feedback used in isolation lead to improvements in both professional practice and patient outcomes, though the effect sizes were often small but potentially important. Effectiveness depended on the baseline measure and the method for delivering feedback. 12/15 reviews that reported on multiple interventions found benefits to professional practice from audit and feedback, but only 2/6 reporting patient outcomes found any benefits.

5.2.11 Reminders

Eighteen reviews looked at reminders alone, including the use of computer based clinical decision support systems (CDSS, eight studies), computerised information systems (two studies) and computerised or paper based reminders (eight studies). Fourteen of the eighteen reviews provided evidence suggesting that reminder based systems were beneficial in improving the process of care. Of the four that did not showed clear benefit, three focussed on CDSS rather than specific reminders or prompts. Only four of the eleven which reported the effect on patient outcomes found a positive effect. Fifteen of the studies that reviewed multiple professional interventions considered reminders, with 11/15 finding them to be effective in improving professional practice. The majority of the seven reviews which considered patient outcomes were unclear about their effectiveness, with a benefit seen in just one.

5.2.12 Marketing

Baker et al looked at tailoring interventions to address barriers to change in practice, and was the only review that considered marketing in isolation [123]. Their high quality Cochrane review included 12 studies in the meta-regression analysis, showing that tailoring interventions improved the chances of success with a pooled Odds Ratios (OR) of 1.54 (95% CI 1.16–2.01) or 1.52 (95% CI 1.27–1.82) depending on the analysis method used. The authors concluded that interventions tailored to prospectively identified barriers are more likely to improve professional practice than no intervention or dissemination of guidelines or educational materials alone, though they felt it was not clear which elements of the interventions studied fully explained their effectiveness. Four of the reviews looking at multiple interventions considered marketing,

with two (50%) finding benefits to professional practice, though the effect on patient outcomes was mixed and not widely reported. Oxman et al found that learning experiences based on objective practice-needs assessment had the potential to alter physician performance but felt that whilst marketing was important in targeting interventions, it was not possible to separate its effect from other interventions[189].

5.2.13 Mass Media

Only two of the reviews which considered multiple interventions included mass media, with none of them able to be clear about their effectiveness.

5.2.14 Mapping EPOC to NPT

A coding framework was developed, and is shown in Table 5.7. This mapped NPT constructs against the EPOC intervention taxonomy. Looking across the rows of the Table 5.7 it can be seen that the EPOC intervention types which act across the greatest number of NPT constructs are Audit and Feedback, Reminders, and Educational Outreach. The 12 reviews which focussed on guideline implementation and the 22 reviews which looked at bundled interventions for changing practice and outcomes were then coded using the NPT-EPOC framework. Each review was given a score for each construct of NPT depending on which EPOC intervention type had been used in the included studies when drawing conclusions about effectiveness. Each review was again also coded according to whether it had concluded that the intervention types it had reviewed had been 'successful' or 'unsuccessful' in improving the process of care and/or patient outcomes, or whether findings for each of these two areas was 'unclear'.

These results were then represented as radar plots, with each review overlaid to show how each construct was represented across reviews in each category. Figure 5.2 shows radar plots for studies looking at guideline implementation, whilst figure 5.3 shows those which looked at multiple intervention types for changing practice or outcomes. For guideline implementation studies, figure 5.2 suggests that reviews which had concluded that generally guideline implementation studies using one or more intervention type were successful, had a different, broader coverage pattern of NPT constructs than those which appeared unsuccessful or unclear about their effectiveness. Similarly, for

patient outcomes, a broader and higher scoring pattern of NPT constructs was associated with success. For reviews which looked at changing professional practice and patient outcomes using multiple intervention types, figure 5.3 shows that reviews which concluded that multiple interventions were successful had a broader and higher scoring pattern of NPT construct coverage compared to those which were unsuccessful. Reviews which were unclear also had a broad pattern of coverage, and for some constructs (such as communal specification, legitimation and enrolment) had higher scores than successful studies.

NPT Constructs / **EPOC PI**	Coherence			Cognitive Participation				Collective Action				Reflexive Monitoring			**Total**
	Individual Specification	Communal Specification	Internalization	Initiation	Legitimation	Enrolment	Activation	Interactional Workability	Relational Integration	Contextual Integration	Skill Set Workability	Systematization	Individual Appraisal	Communal Appraisal	
Distribution of educational materials	0	0	1	0	0	0	0	1	1	0	0	0	0	0	**3**
Educational meetings	0	1	0	0	0	1	0	0	0	0	1	0	0	0	**3**
Local consensus processes	0	1	0	0	1	1	0	0	0	0	0	0	0	0	**3**
Educational outreach visits	0	0	0	1	0	0	0	0	0	1	1	0	1	1	**5**
Local opinion leaders	0	0	0	1	0	0	0	0	0	0	0	0	0	0	**1**
Patient mediated interventions	0	0	0	0	0	0	0	1	1	0	0	1	0	0	**3**
Audit and feedback	0	0	1	0	1	1	0	0	0	1	0	1	0	1	**6**
Reminders	0	0	0	0	0	0	0	1	1	1	0	1	1	1	**6**
Marketing	0	1	0	0	0	0	0	0	0	0	0	0	0	0	**1**
Mass media	0	1	0	0	1	0	0	0	0	0	0	0	0	0	**2**
Total	**0**	**4**	**2**	**2**	**3**	**3**	**0**	**3**	**3**	**3**	**2**	**3**	**2**	**3**	

Table 5.7: NPT-EPOC PI coding framework

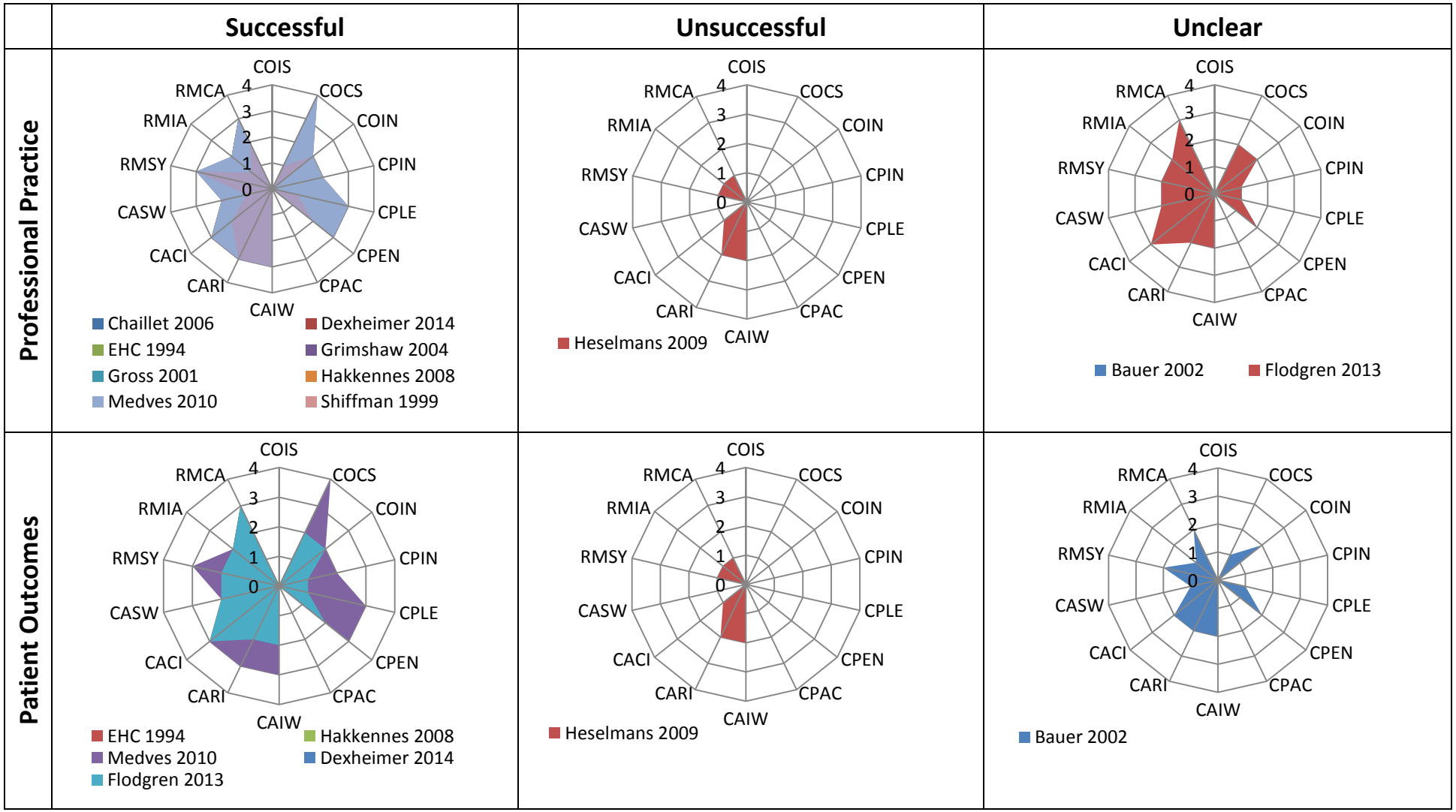


Figure 5.2: Radar Plots for Mapping of Guideline Implementation Reviews to Normalization Process Theory constructs

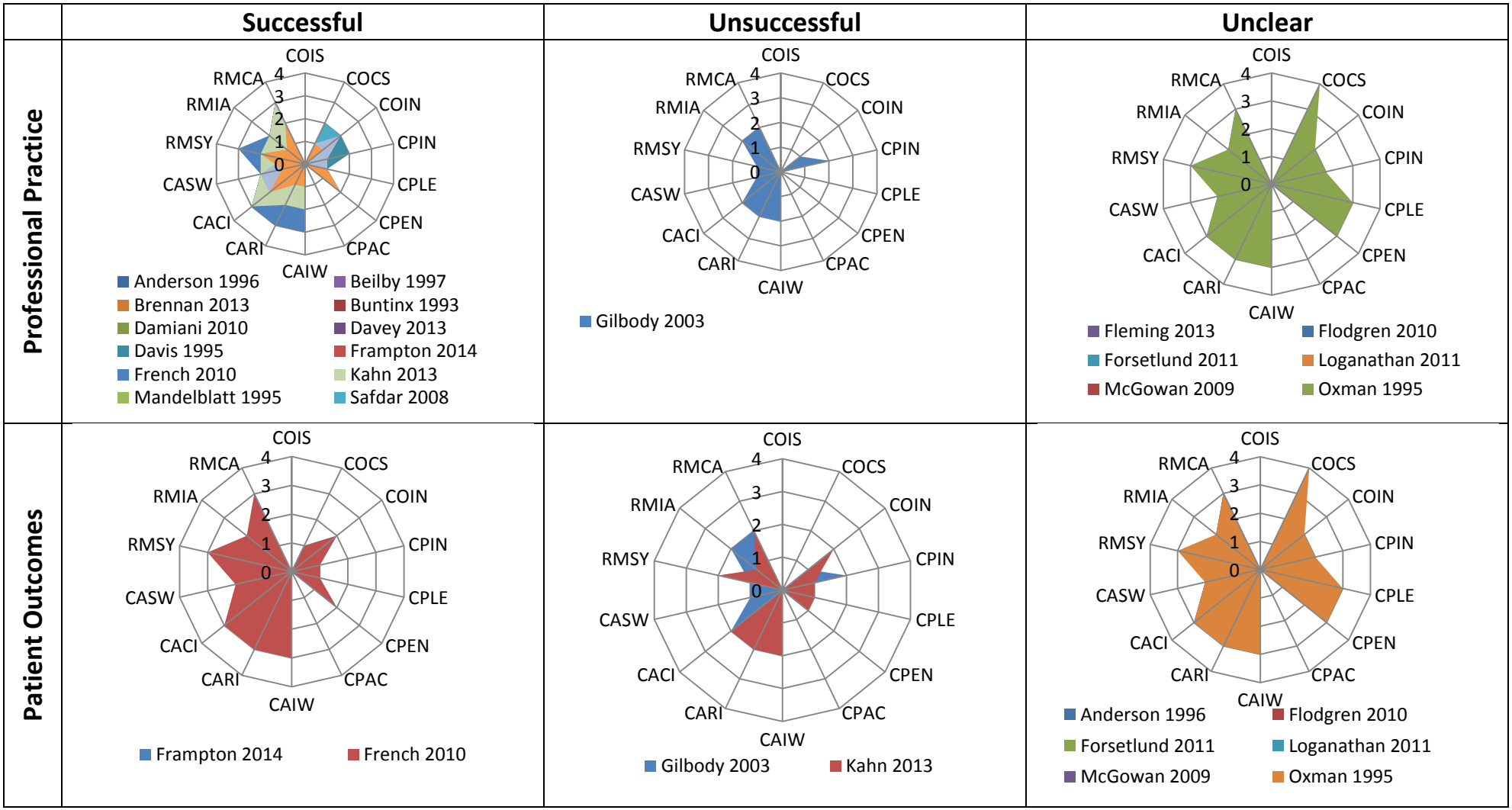


Figure 5.3: Radar Plots for Mapping of Reviews of Multiple Professional Interventions to Normalization Process Theory constructs

5.3 Discussion

By applying NPT it is possible to gain some insight into why some interventions appear more effective than others (see Table 5.7). Those which seem to act across the most constructs of NPT (Audit and Feedback, Reminders and Educational Outreach) also appeared to be the interventions more likely to be effective in changing professional behaviour. This was true for reviews of guidelines implementation interventions, and in reviews of other interventions – both single and bundled. However, amongst those interventions that could be related to just one NPT construct the relationship between was less consistent: opinion leaders, consensus processes and mass media seemed effective in the implementation of guidelines, but were less effective as part of bundled interventions. In all cases there were only a small number of reviews considering each of these. Table 5.7 also suggests that EPOC defined interventions that could be characterized in terms of two or less NPT constructs tended also to be those that reflected individual action rather than peer group and organizational behaviours (these were NPT constructs of individual specification, activation, internalization, initiation, skill set workability and individual appraisal). In addition to being more effective, Audit and Feedback, Reminders and Educational Outreach all act by providing information to help reinforce change in a cyclical manner, making them different from other interventions which tend to act in a linear fashion. They all share the NPT constructs of contextual integration and communal appraisal, which are not addressed by any other interventions. Contextual integration ensures interventions are adapted to work within a setting, whilst communal appraisal means that users collectively evaluate new practices as they use them, setting up a feedback loop of appraisal and adaptation that helps an intervention become part of normal practice. Figures 5.2 and 5.3 suggest that reviews that showed guideline implementation and bundled professional intervention strategies to be successful scored highly on NPT constructs of interactional workability, relational integration, systematization and communal appraisal. In addition, in guideline implementation studies interventions also scored highly on communal specification, legitimation and enrolment (see figure 5.2), with less emphasis on contextual integration, though this was not the case for non-guideline implementation studies, as can be seen in figure 5.3. It is of interest that patient mediated intervention also seemed effective, particularly in implementing guidelines. They also act across the constructs of

interactional workability and relational integration, and are essentially a form of feedback of patient information to professionals, which is potentially a powerful way of driving the behaviour of professionals.

Overviews of systematic reviews are subject to important limitations, especially when they deal with complex, non-standardized interventions which are themselves very heterogeneous. In this overview, there was great variability in the effect size seen within each intervention considered. This was almost certainly further complicated by the changes in study methods in this field over the period of the past 30 years when the included studies were conducted, with an increasing use of newer methodologies such as interrupted time series. This means that while we can describe findings in general terms, definitive conclusions about effectiveness cannot be drawn. Some studies claimed to review single intervention types but actually included studies containing bundles of interventions. This is unsurprising because most attempts to change behaviour involve bundles of interventions. However, it means that the results of these reviews may have been clouded by unconsidered components in the individual studies included. The complex nature of professional interventions is a problem when assessing effectiveness. Several reviews pointed out the difficulties and frustrations associated with trying to 'pick apart' which components of complex interventions were their 'active ingredients', and were forced to conclude that it was not possible to clearly assess the effectiveness of particular components. One of the reasons behind choosing to perform an overview of systematic reviews rather than a standard systematic review was to try to capture an overarching sense of which interventions and combination of interventions seemed to be successful in the context of this complexity. The reviews in this overview were spread across a wide range of settings so again general conclusions should be drawn with caution. Publication bias may therefore be an important problem in this body of literature since it suggests that most intervention types have a positive effect on measures of process or professional behaviour (such as compliance with a guideline or use of a particular resource), but is less certain about effects on patient outcomes.

This review used the Cochrane EPOC taxonomy of behaviour change interventions as a framework to consider the different interventions and strategies. However, whilst it is convenient to classify interventions in this way,

particularly when reviewing groups of interventions, in reality most interventions aimed at individuals or social groups are much more complex, with a single intervention often sharing elements with others in separate classification. Such a broad classification can therefore be quite a blunt instrument when trying to understand interventions in complex healthcare settings. Mazza et al recently attempted to address this issue by developing a more detailed taxonomy of strategies based on the EPOC categories focussing on guideline implementation. This included a specific group of 'Professional Strategies'[206], which potentially offer a way of considering the different aspects of interventions in more detail. This may be of interest to use in future reviews looking at practice change strategies to offer a more detailed description of effective interventions for implementing guidelines.

The limitations of a review like this mean that definitive conclusions about what kinds of interventions are most effective cannot be made. However, by using a theory of practice as the lens through which data are interpreted, this review seeks to suggest explanations for the underlying processes by which interventions have their effects, highlighting key elements which seem to be important in successful professional practice change. This approach also suggests why bundles of interventions packaged together seem more effective than single interventions. This is not because they have an aggregate or cumulative effect, but because they link together to form social systems that facilitate changes in behaviour norms. This means that the collective rather than individual action constructs of NPT explain the key components of effective behaviour change interventions. If this is true, it may explain the preponderance of negative trials of behaviour change interventions founded on models of individual intentions and behaviours. This was an exploratory study in terms of the use of NPT to guide the analysis of the reviews, and the limitations described above mean that empirical claims about the precise degree of effectiveness that is attached to particular intervention types should be made cautiously, but in general terms it is possible to sketch a conceptual model of their actions, and represent these as hypotheses. The first hypothesis is that:

H1. *Interventions that seek to restructure and reinforce practice norms and associate them with peer and reference group behaviours are more likely to lead to behaviour change.*

Two kinds of interventions contribute to the process hypothesised in H1: (i) normative restructuring of practice modifies peer group norms and expectations of practice (e.g. opinion leaders, educational outreach, educational meeting and materials/guidelines); and (ii) relational restructuring reinforces modified peer group norms by emphasising the expectations of an external reference group (e.g. Reminders, Audit and Feedback, Patient Mediated Interventions). Bundled together, such interventions create a coherent and legitimized set of rules about the conduct of practice; where enacting those rules is made to become a normal component of everyday practice; and where individual participants are encouraged to replicate activities common to their peers. The second hypothesis supports this by highlighting outcomes of interventions that have 'soft' attitudinal components:

H2. *Interventions that seek to reshape the attitudinal landscape in which professional behaviours are enacted are less likely to lead to behaviour change.*

Importantly, the kinds of interventions specified by H1 are ones that operationalize clear mechanisms that shape behaviour norms – the rules that give structure to everyday actions. But the interventions that contribute to the process defined in H2 are characterized by more diffuse mechanisms: (i) indirect attempts to redefine behaviours and the scope of practice (e.g. marketing and mass media campaigns); and (ii) local attempts to reformulate ideas about practice (e.g. consensus building exercises).

In general terms, this overview of systematic reviews suggests that successful behaviour change interventions operationalized in complex organizational environments are likely to require intervention types that lead to both normative and relational restructuring (and hence a focus on collective rather than individual action), and the legitimation of new practice norms through experience. The findings of this chapter helped inform the choice of elements which made up the complex intervention used in this study, and provided some theoretical understanding of their mechanisms of action. The next chapter will discuss nutritional care in Southampton prior to the intervention, which was also used to inform the development of the complex intervention..

Chapter 6: Development Phase Results Part 1 – Nutritional care in Southampton Prior to Implementation

In order to both inform the development of the complex intervention to improve nutritional care, and to provide baseline nutrient intakes and growth data in the period prior to the implementation of such an intervention, the nutritional care of preterm infants in Southampton infants was assessed. This was carried out in two ways. Firstly, a process mapping exercise was carried out in order to understand the pathways and processes for delivering nutritional care, using the method described in Chapter 4. Secondly, the nutrient intakes and growth of a cohort of preterm infants born and cared for in Southampton NICU during 2009 were studied retrospectively, using SENNAT. Infants with a birth weight less than 1501g or a gestational age of less than 30 weeks were identified using the clinical admissions database (the Standardised Electronic Neonatal Database, SEND, later replaced by BadgerNet) and data on growth and daily fluid intakes extracted from routine clinical records and entered into SENNAT, with nutrient intakes and growth SDS calculated.

6.1 Results – Process Mapping

In order to assess an infant's nutritional status, including their growth, nutrient intakes and current health, up to 13 different sources of information needed to be consulted, including growth charts, fluid charts, case notes and prescription charts. These were located in variable places around the cot-side or wider unit environment, meaning that gathering all necessary information could take up to 10 minutes. This was prior to using the information to carry out a nutritional assessment. The mapping exercise (see Figure 6.1) demonstrated an incredibly complex relationship between all healthcare professionals and parents in terms of the decision making processes surrounding nutritional care. These decisions, in turn, then interacted with a complicated system of nutritional delivery processes.

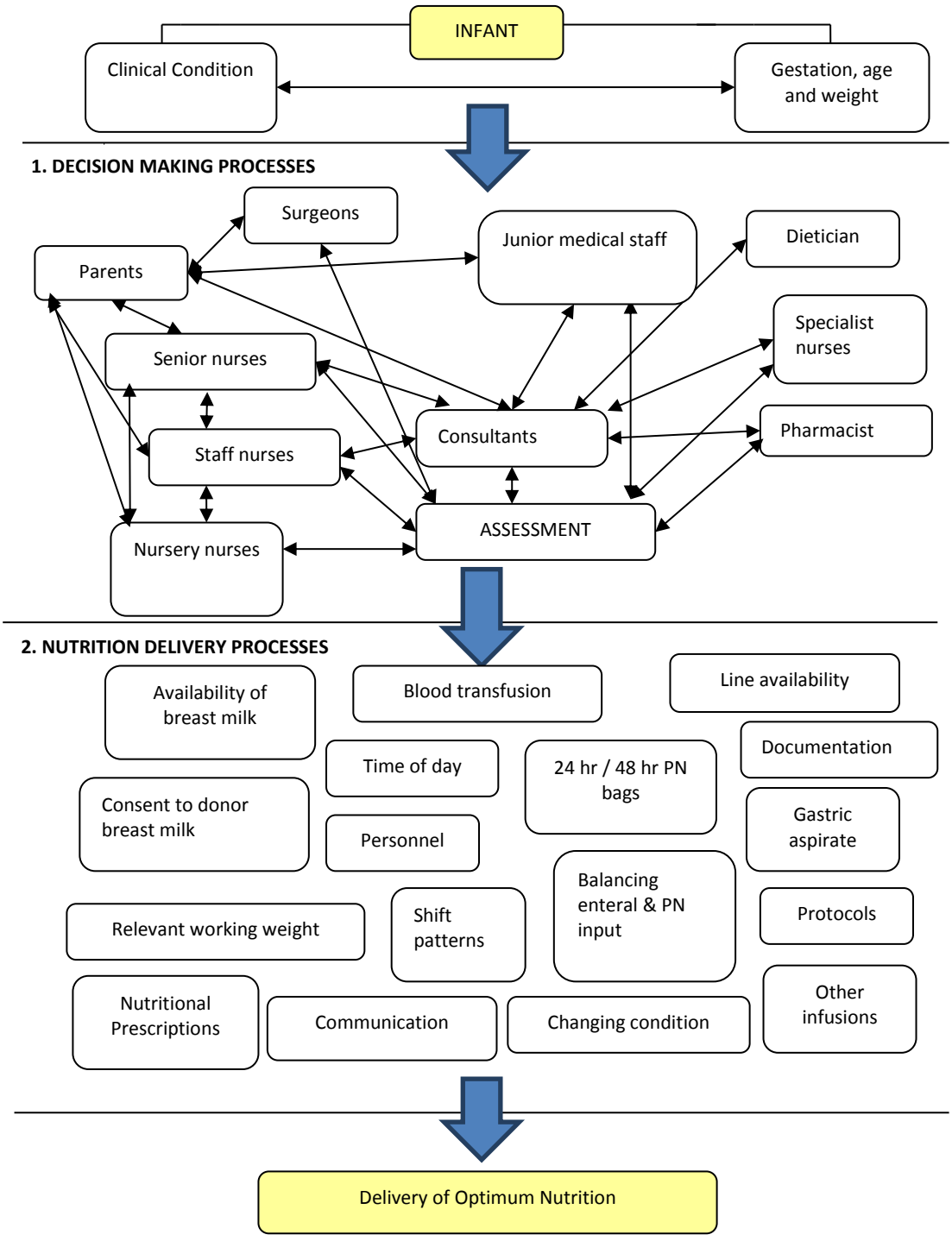


Figure 6.1: Process Map for Nutrition Decision Making and Delivery in Southampton NICU

6.2 Results- Nutrient intakes, growth and nutritional care in 2009

Of 70 eligible infants, 65 had notes available for analysis, representing 3540 infant days. Those 65 infants had a mean GA at birth of 28.5 weeks (SD 2.6), a mean birth weight of 1.07kg (SD 0.29kg). The infants whose notes were unavailable had a mean birth weight of 0.96kg and mean GA at birth of 28.9 weeks.

Tests of normality using the Shapiro Wilk test revealed that the nutrient intake (energy and protein) data were not normally distributed ($p<0.001$ for both), whilst the growth data were ($p=0.56$ and 0.17 for weight and head circumference respectively). Data were summarised across stay using the time points of one, two, four and six weeks of age, plus 36 weeks post-conceptional age (PCA) using medians and interquartile ranges for nutrient intake data, and means and 95% confidence intervals for growth data. Nutrient intakes were also expressed as percentages of the 'Reasonable Range of Intakes' (RRI) according to Tsang et al as described in Chapter 4. Median intakes for the one week period of each time point were calculated for each infant. Analysis was carried out using Stata v12.1 (Stata Corporation).

6.2.1 Nutrient intakes during stay on NICU

Between birth and discharge, median (interquartile range, IQR) daily energy intake was 114.7kcal/kg/day (100.1 to 124.9), which was 96% of Tsang's RRIs (IQR 88.6 to 104.1%). For protein, median (IQR) daily intake between birth and discharge was 2.76g/kg/day (2.26 to 3.11), which represented just 76.3% of Tsang's RRI (IQR 62.6 to 83.2)

Median daily energy intakes across stay (weeks 1, 2 4 and 6 of life, and 36 PCA) are shown in figure 6.2A. Figure 6.2B shows these as a percentage of Tsang's RRI. It can be seen that whilst energy intakes were low in the first week of life, thereafter they were generally at the recommended amount.

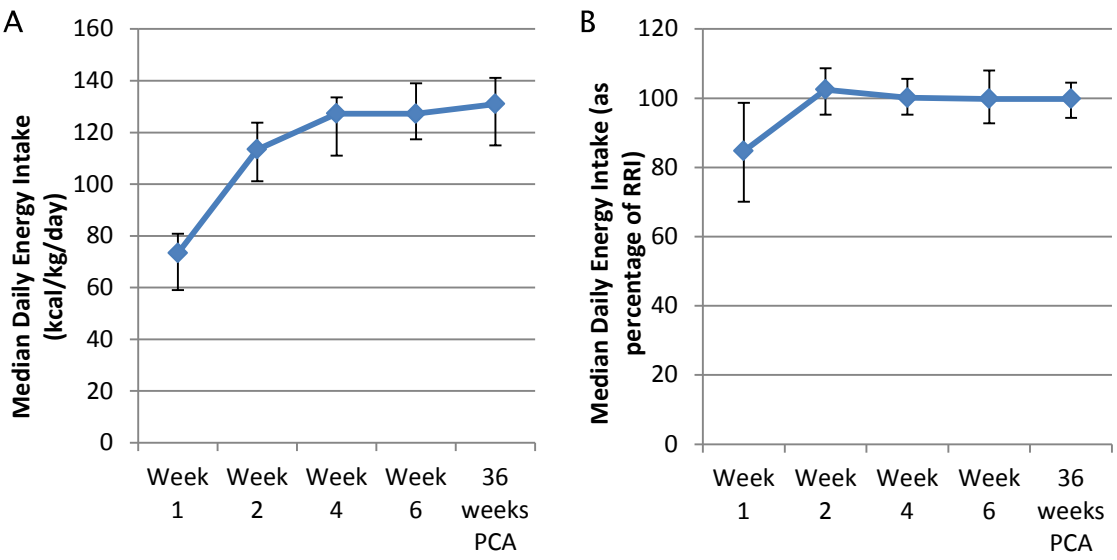


Figure 6.2: Median daily energy delivery across stay in kcal/kg/day (A) and expressed as a percentage of Tsang et al's RRI (B). Error bars represent interquartile range

Figure 6.3A shows protein intakes across stay, with the same data expressed as a percentage of Tsang's RRI in figure 6.3B. Protein intakes were particularly low in the first week of life, at just 54% of RRI, improving to around 80% in weeks two, four and six. By 36 weeks PCA they were 92% of RRI, though still not at the recommended 100%.

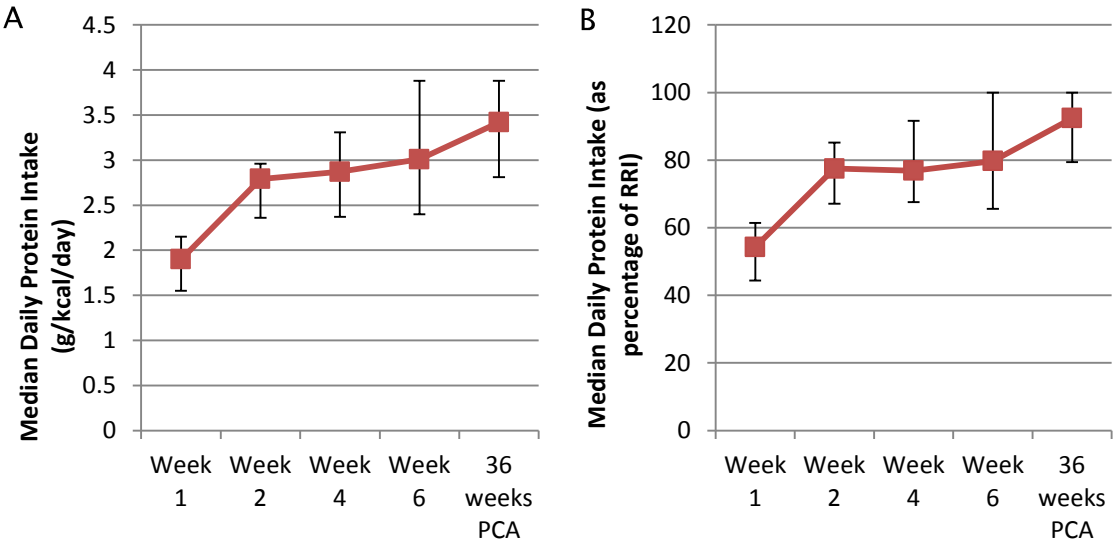


Figure 6.3: Median daily protein delivery across stay in kcal/kg/day (A) and expressed as a percentage of Tsang et al's RRI (B). Error bars represent interquartile range

6.2.2 Growth during stay on NICU

Between birth and discharge, the mean (SD) change in SDS was -1.02 (0.79) for weight and -0.72 (1.60) for head circumference.

Figure 6.4 shows the change in SDS from birth across stay (weeks 1, 2, 4, 6 and 36 weeks PCA). It can be seen that infants fell 0.78 SD for weight in the first week of life, and were 0.92 SD below their birth SDS by week 4, though had recovered to 0.85 standard deviations below birth SDS by 36 weeks PCA. Head circumference SDS in general fell over the first six weeks of life, though again recovered by 36 weeks PCA.

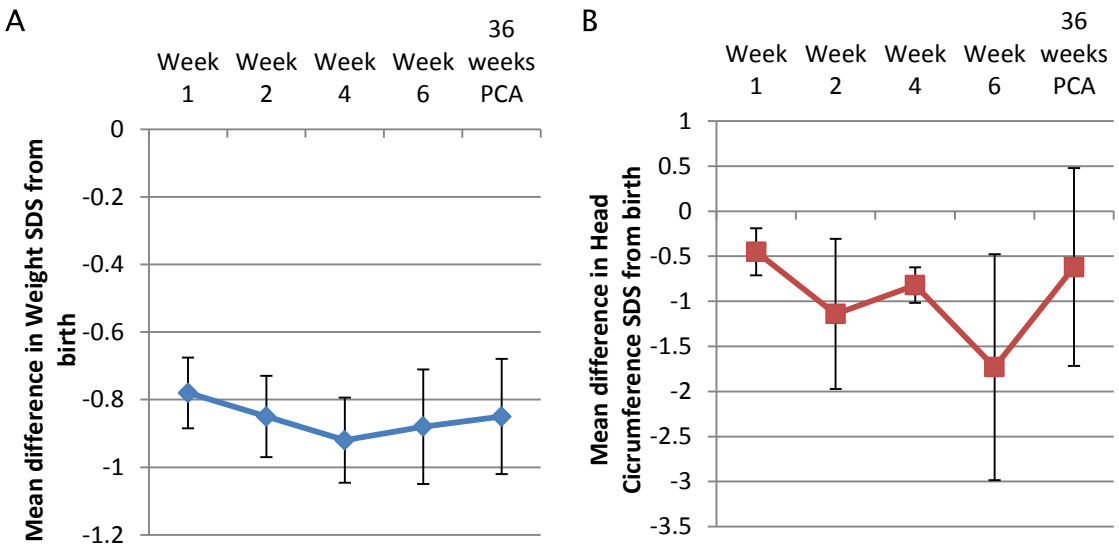


Figure 6.4: Change in SDS for weight (A) and head circumference (B) from birth across stay. Error bars represent 95% confidence intervals.

6.2.3 Measures of the process of care

At the time of SENNAT data entry, information was also collected from the infants' notes on the time that PN and enteral feeds were started. In addition, data from SENNAT were analysed to show when breast milk fortifier was started, and the number of infants who received it, together with the type of feed at discharge (see table 6.1).

Mean Age PN Started (hours, median and IQR)	26.5 (17-35)
Mean Age Enteral feeds started (hours, median and IQR)	48 (31-72)
Mean Age at starting Breast Milk Fortifier (days, median and IQR)	33 (23-46)
Percentage of infants on Breast Milk started on Breast Milk Fortifier (%)	22.4
Percentage of Infants discharged home on Breast Milk (%)	15
Percentage of Infants discharged home on Mixed feeding (%)	22.5
Percentage of Infants discharged home on Preterm Formula (%)	27.5
Percentage of Infants discharged home on Term Formula (%)	35

Table 6.1: Measures of the processes of nutritional care in Southampton in 2009

6.3 Implications of Findings

It is clear from the mapping exercise carried out that the processes for making nutritional assessments and decisions is time consuming and cumbersome due to the number and location of the information sources required. Similarly, the process for delivering nutrition once decisions are made is a complex process, subject to many variables and influenced by multiple actors. This suggests a clear need to consolidate existing documentation regarding nutrition and develop a process for streamlining nutritional assessment and decision making. Whilst the intervention itself will aid this process, as it will provide clear guidelines, physically moving relevant information sources to make them more accessible will clearly also help.

During 2009, preterm infants born and cared for in Southampton were failing to meet recommended intakes for protein and energy during the first weeks of life. Whilst delivery of these nutrients improved over the course of their stay, delivery of protein remained a significant problem right up to 36 weeks PCA, with intakes peaking at 92% of RRI. At the same time, SDSs for weight and head circumference fell between birth and discharge, meaning that infants were discharged on lower centiles than those on which they were born. Measurement of length was very inconsistent during 2009, thus there are no data for length in this section.

Previous studies have demonstrated that the energy and protein intakes of preterm infants fall short of recommended amounts[207]. These findings for Southampton are similar for energy and protein intakes to those described by Embleton et al, suggesting that little has changed between 2001 and 2009[16]. As to the causes of the under-delivery of nutrients seen, they are likely to be multifactorial. In the first two weeks of life, factors affecting adequate

provision of nutrition intravenously may include fluid restriction or concurrent delivery of additional infusions such as inotropes. The latter is a common issue during the first week of life; PN will almost certainly not have been delivered in the prescribed amounts due to other concurrent infusions that infants were receiving. Typically, an extremely premature infant will receive other infusions during the first week or so of life which can include heparinised saline via an arterial catheter, a morphine infusion for sedation whilst ventilated plus other drug infusions such as inotropes. As preterm infants are often managed using a limited or restricted fluid volume, any additional infusions over and above the PN will cause the amount of PN delivered to be decreased such that the infant still receives the same total amount of fluids. This concept is demonstrated in table 6.2, which shows a typical situation for a 500g infant receiving a standard arterial line infusion and morphine.

Total Fluids (ml/kg/day)	60	90	120	150
Infusions (UAC/Morphine, ml/kg/day)	33.6	33.6	33.6	33.6
Actual fluids for PN (ml/kg/day)	26.4	56.4	86.4	116.4

Table 6.2: Fluid delivery volumes for a typical 500g preterm infant

It can be seen that in the first two days of life, the concurrent infusions mean the infant only receives around half the intended volume of PN. Furthermore, measures of nutritional care processes suggest PN was being started on or after the second day of life in many cases, with the mean age at starting outside the 24 hours recommended by ESPGHAN [75]. This may explain the low protein intakes seen in the first week of life, as infants will be receiving 10% dextrose as their main fluid (which contains only glucose and no protein or other nutrients) prior to commencing PN. Measures of process also demonstrate that the majority of infants receiving breast milk did not receive fortifier and that a significant number of infants were discharged on term (rather than preterm) formula milk. This is important, as neither breast milk nor term formula milks are nutritionally adequate for preterm infants, particularly in terms of their protein content, perhaps explaining the consistent under-provision of protein across stay seen in 2009.

The decision to treat all MBM as mature term milk means that SENNAT may have underestimated the nutrient intakes of preterm infants who were receiving preterm MBM, which may have a higher concentration of some

nutrients than mature MBM[208]. The quality of MBM varies both between and within mothers, and over time, as does the timing of transition from preterm to term MBM. In the absence of information on the composition of individual MBM feeds, the decision to treat all milk as term MBM was made in order to simplify the way data items were entered into SENNAT, but also to provide an assessment of the lowest possible intake the infant could have received. Conversely, the decision to treat all DBM the same as MBM may have overestimated nutrient intakes, as there is evidence that the processing of DBM results in it having a lower nutrient content than MBM, particularly for fat and vitamins[209 210]. Whilst SENNAT itself calculated nutrient intakes accurately, these are only as accurate as the quality of the source data so the results should be interpreted with caution given that this was a retrospective case note review.

6.4 Summary

This retrospective analysis of preterm infants born during 2009 demonstrates that growth, protein delivery, and to some extent energy delivery was inadequate. This was a particular issue in the first week of life. Given that PN is the main source of nutrition for the majority of preterm infants during this critical period, and that it was often not commenced until on or after day two of life, the findings of this chapter suggest that there is a need for earlier use of PN and improvements in its formulation, particularly with a view to concentrating the solution so that similar nutrition can be delivered in a smaller volume to allow for concurrent infusions. Furthermore, the finding that protein intakes were consistently low across stay indicates a need for improved provision during this period. Taken together with the findings that fortifier was not used in the majority of infants receiving MBM, and that some infants were receiving term formula at discharge, there is a need to increase the use of breast milk fortifier for preterm infants receiving breast milk and to encourage the use of preterm formulas rather than term formula in those infants whose mothers are not intending to breast feed. In addition, the process mapping exercise highlights a need for clear and efficient pathways for decision making, as well as a need for a way of bringing all nutrition related documents together in one easy to access location. The next chapter will discuss how the findings of this thesis so far were used to develop the complex intervention used in this study.

Chapter 7: Development Phase Results Part 2 - Developing the Intervention

As described in Chapter 5, it appears that a complex intervention with the greatest chance of success at changing practice should be based around guidelines and be implemented using a combination of audit and feedback, reminders and education (in particular educational outreach). Any intervention that will contribute to normative restructuring of practice, modifying peer group norms and expectations (e.g. opinion leaders, educational outreach) and relational restructuring, reinforcing modified peer group norms by emphasising the expectations of an external reference group (e.g. Reminders, Audit and Feedback) will offer the best chances of success. Combining several interventions together which will achieve this, together with the legitimation of new practice through experience is most likely to change behaviour. Chapter 6 demonstrated the complicated nature of delivering nutritional care, but also the current failings in nutrient delivery and growth as they were in 2009, with some suggestions as to the potential causes of the deficits seen.

A complex intervention aimed at translating evidence regarding the nutritional care of preterm infants into practice was developed based on current literature and practice recommendations (Chapter 2) together with the findings of the overview of systematic reviews (Chapter 5) and the results of the process mapping and retrospective review of the nutritional care of preterm infants in Southampton in 2009 (Chapter 6), and is described below. Each component of the intervention also aimed to target core constructs of NPT in order to enhance implementation and uptake.

7.1 Developing the Intervention

7.1.1 Optimising Nutritional Products

7.1.1.1 Parenteral Nutrition

The retrospective analysis of the nutritional care of preterm infants in Southampton in 2009 highlighted that a major issue for these infants was under provision of energy and protein in the first week of life. This was likely due to a combination of inadequate provision in PN, late commencement of PN,

and under-delivery of PN due to concurrent infusions. One way to help address this was to reformulate the PN to increase the nutritional content and concentrate it to deliver nutrition in a smaller volume, allowing for concurrent infusions alongside it.

Therefore, in mid-2011, the 'stock' PN solutions used on Southampton NICU were reformulated. Stock PN solutions are those kept on NICU for use as required, allowing PN to be started at any time without the need for prescription and manufacturing in hospital pharmacy. The reformulation was carried out by Dr Amanda Bevan and Miss Zoe Lansdowne, neonatal pharmacists in Southampton. Previously in Southampton there had been two stock PN solutions for preterm infants; 'Preterm' a sodium free solution for use in preterm infants immediately after birth, and 'Preterm Day 5+', a sodium containing PN solution for use in preterm infants from day five of life onward. These were replaced by a newly formulated 'Preterm' solution, and a 'Preterm plus Sodium' solution respectively. The change in name from 'Preterm Day 5+' to 'Preterm plus Sodium' was deliberate to allow clinicians to feel able to give sodium containing PN (which also contained more protein) sooner than day 5 if appropriate. The nutritional content when given at the maximum volume of the new solutions is shown in Table 7.1, together with the previous formulations for comparison. It can be seen that the new solutions were designed to be given at 130ml/kg/day rather than 150ml/kg/day. Table 7.1 shows that for most nutrients this meant the same amount or greater was delivered in less volume using the new solutions compared to the old.

Of note, only the aqueous phase (containing all water soluble macronutrients, minerals and trace elements) of the PN was reformulated. The lipid component (containing fat and vitamins and given as a separate infusion) remained the same, but recommend infusion rates were altered, meaning that lipid was given as a slightly higher proportion of the overall infusion for the 'Preterm + Sodium' PN, providing greater quantities of fat, energy and vitamins.

	Old Pre-term	New Pre-term	Old Preterm Day 5+	New Preterm + Sodium
Target Maximum Volume/kg (ml)	150.0	130.0	150.0	130.0
Aqueous component volume/kg (ml)	132.5	117.5	140.0	112.5
Lipid component volume/kg (ml)	17.5	12.5	10.0	17.5
Nitrogen (g)	0.4	0.4	0.5	0.5
Protein (g)	2.6	2.8	3.1	3.1
Glucose (g)	14.3	15.7	16.7	13.7
Lipid (g)	0.0	0.0	0.0	0.0
Sodium (mmol)	0.0	0.0	4.2	4.8
Potassium (mmol)	1.9	2.8	2.0	2.0
Magnesium (mmol)	0.1	0.1	0.3	0.1
Calcium (mmol)	1.0	0.9	1.0	1.1
Phosphate (mmol)	1.3	1.2	2.2	2.6
Acetate (mmol)	0.5	1.7	2.0	2.0
Chloride (mmol)	0.5	0.6	2.8	2.9
Zinc (µmol)	3.6	4.5	3.9	3.9
Copper (µmol)	0.3	0.4	0.3	0.3
Selenium (nmol)	23.2	29.4	24.5	25.3
Iodine (nmol)	7.5	9.3	8.0	8.0
Manganese (nmol)	17.2	21.4	18.6	18.4
Lipid (g)	3.0	2.1	1.7	3.0
Vitamin A (IU)	692.1	494.4	395.5	692.1
Vitamin D (IU)	120.4	86.0	68.8	120.4
Vitamin E (IU)	2.1	1.5	1.2	2.1
Vitamin C (mg)	11.9	8.5	6.8	11.9
Total Energy/kg (kcal)	96.7	95.1	95.6	96.3
Total Non Protein Energy/kg (kcal)	86.5	83.9	83.3	83.9
Total Protein/kg (g)	2.6	2.8	3.1	3.1
Non protein energy:protein ratio (kcal/g)	33.6	29.9	27.2	27.1

Table 7.1: Nutritional contents (per 100ml) at maximum volume for the old and revised ('new') PN solutions

7.1.1.2 Enteral Nutrition

Reformulation of the Southampton parenteral nutrition solutions during July 2011 coincided with reformulation of enteral nutritional products for preterm infants by the manufacturers (this was a fortuitous coincidence rather than a deliberate move as part of this study). The preterm infant formula (Aptamil Preterm) and breast milk fortifier (Cow and Gate Nutriprem Breast Milk Fortifier) used in Southampton were both modified by the manufacturers to contain more protein, sodium, zinc, selenium and vitamin A. Table 7.2 shows the nutrient content of the new and old formulations of preterm formula and

fortifier. Using enteral feeding products with higher protein content was also likely to help address the shortfall in protein delivery seen across stay in the 2009 data.

Nutrient per 100ml	Old Preterm Formula	New Preterm Formula	Breast milk fortified with old Fortifier	Breast milk fortified with new Fortifier
Energy (kcal)	80.0	80.0	85.0	85.0
Protein (g)	2.5	2.6	2.1	2.5
Carbohydrate (g)	7.6	8.4	10.2	10.0
Lipid (g)	4.4	3.9	4.1	4.1
Sodium (mmol)	2.2	3.0	1.5	2.2
Chloride (mmol)	1.9	2.1	1.6	1.9
Potassium (mmol)	2.1	2.1	2.5	2.1
Calcium (mmol)	3.0	2.3	2.5	2.5
Phosphate (mmol)	2.1	2.0	2.0	1.7
Magnesium (mmol)	0.3	0.3	0.4	0.3
Iron (µmol)	25.1	28.7	1.3	1.3
Zinc (µmol)	13.8	16.8	10.7	13.8
Copper (µmol)	1.3	1.3	1.1	1.2
Selenium (nmol)	24.1	57.0	12.7	35.5
Iodine (nmol)	197.0	204.9	141.8	141.8
Manganese (nmol)	182.0	182.0	1492.6	1492.6
Vitamin A (IU)	599.4	1202.1	646.0	985.6
Vitamin D (IU)	120.0	120.0	200.0	200.0
Vitamin E (IU)	4.5	5.2	4.4	4.4

Table 7.2: Nutritional content per 100ml of new and old formulations of preterm formula and fortified breast milk

7.1.2 Guidelines

A comprehensive guideline for the nutritional care of infants on the neonatal unit was developed. This was in keeping with the findings of the systematic review in chapter 5 which found that guidelines were an effective way of introducing practice when properly implemented. This would form the centre of the complex intervention, with several other interventions introduced alongside the guidelines to improve implementation.

The guideline was developed by a multidisciplinary team (hereafter referred to as the Nutrition Support Team, NST) consisting of myself, Consultant Neonatologists with an interest in nutrition (Dr Alison Leaf and Dr Freya Pearson), a neonatal dietitian (Anita Emm), a paediatric and neonatal pharmacist (Dr Amanda Bevan), the neonatal research nurses (Joanne Schofield,

Jenny Pond and Jane Rhodes-Kitson) and members of the clinical neonatal nursing team that had shown an interest in nutrition and been seconded to work as 'Champions for Nutrition' (Joanne Armand, Rosemarie Reeve, Linda Anderson and Christina Toy, see below for a description of this role). The team made the decision to create a guideline which covered all infants on the neonatal unit rather than VLBW or preterm infants specifically in order to promote the universal use of the guideline and help it become an established part of practice on the unit.

The guideline was based on the review of current evidence and practice recommendations described in Chapter 2 and can be seen in Appendix 1. It included detailed sections on nutritional risk, growth monitoring, use of PN, starting and increasing enteral feeds, choice of milk and guidance on dealing with special cases or feeding difficulties. Briefly, particular practice points in the guideline that would need to be implemented by staff included:

- Earlier commencement of parenteral nutrition and enteral feeds
- A more structured advancement of milk feeds
- A protocol for dealing with feed intolerance
- Recommendations on the choice of milk for infants
- Use of a protocol for commencing and increasing breast milk fortifier in infants receiving breast milk
- Use of a protocol for reducing PN in response to increasing milk feeds
- Regular (weekly) measurement of weight, length and head circumference, plotting of these on the growth charts, and completion of a nutrition screening tool (see below)

The guideline included easy to follow flow charts which summarised the main content of the guidelines onto four single pages. There was also extensive background literature providing evidence for the content of the guideline. This element was there in order to help users understand the rationale behind the new practices, in line with the NPT construct of *coherence*. The guidelines also supported *cognitive participation*, by providing clear guidance and flow charts on what to do in each situation and why.

7.1.3 Nutrition Support Team and Weekly Ward Round

The multidisciplinary NST described above was also given a clear role in the guideline, providing a specialist nutrition ward round each week on a Tuesday morning. The purpose of this was to review babies at particular risk of poor nutrition and growth, ensure compliance with the clinical guideline, and

provide detailed nutritional advice for special or difficult cases. It also helped to raise the profile of nutrition on the neonatal unit, as well as providing a source of advice and support for clinical staff in the new working practices. This role also incorporated the concepts of both 'local opinion leader' (as many of the team were senior members of neonatal staff) and educational outreach with direct feedback to professionals in their practice, as described in chapter 5, which seem to be particular effective ways of changing behaviour and implementing guidelines. Having a nutrition team composed of staff already working on the unit would help to associate the new practices with reference group behaviours, which the findings of chapter 5 suggest makes them more likely to succeed. The weekly ward round would also help to reinforce the new practices, providing feedback to users on how effective their use of the guideline was as part of the *reflexive monitoring* process described by NPT.

The European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition reviewed the role of NSTs in paediatric units in 2005. They found that current education of paediatricians in clinical nutrition was inadequate to ensure consistent and appropriate nutritional care, and recommended the implementation of specialist paediatric NSTs in hospital in order to address this, stating that such team's roles should include screening for nutritional risk, identification of patients requiring nutritional support and provision of adequate nutritional management[211]. The British Association of Parenteral and Enteral Nutrition (BAPEN) also advocate the use of NSTs as part of good nutritional care in their recent toolkit for healthcare commissioners[212]. There is also a growing body of evidence to support increased nutritional support in the neonatal population; involvement of a dietician in neonatal unit nutrition support has been shown to be associated with improvements in growth [26], and infants cared for in units with a greater input from a registered dietician are more likely to receive appropriate nutrient intakes [27].

7.1.4 Neonatal Nutrition Screening Tool

In recommending the use of NSTs, ESPGHAN clearly state that such teams should carry out patient screening to identify patients in need of increased nutritional support [213]. This is important, as even in hospitals with a relative wealth of specialist staff, the time available for specialised clinical nutrition

support is itself a limited resource, and as such needs to be carefully directed towards those patients with the greatest need. However, there is a lack of appropriate scoring or screening systems for nutritional risk in the neonatal population.

A neonatal nutrition screening tool for use in the NICU was therefore created by myself and colleagues that could be used regularly by nursing staff to identify infants at high risk of poor growth at discharge, and thus be used to direct assessments by the specialist nutrition team. It is noteworthy that whilst nutritional screening makes sense in terms of directing nutritional support, there is no current evidence that screening itself can improve nutrition or growth in preterm infants. However, the weekly completion of such a tool would also act as a reminder regarding growth monitoring and the use of the guidelines, with a specific flow chart for feeding each risk category of infant, and reminders were also shown in chapter 5 to be an effective way of changing professional behaviour. A description of the tool and its development has been published by myself and colleagues in *Acta Paediatrica*[214], and is included in appendix 8.

7.1.5 Nurse 'Champions for Nutrition'

Whilst the NST is able to act as a 'local opinion leader' in promoting and supporting the implementation of the guideline, weekly ward rounds alone may not be sufficient to optimise this process. Therefore, there was a need to develop dedicated members of staff to help champion the new ways of working. Ideally, these staff members would be nurses who worked regularly as part of the clinical team, but had increased knowledge and awareness of the nutrition guideline and the new working practices. Nurses have undertaken the role of 'link advisor' in a number of areas such as infection prevention and palliative care, acting as a link between their clinical area and the specialty, and this has been shown to positively impact on practice [215 216]. The role of such 'link advisors' is to increase awareness of new ways of working and improve practice at clinical level, acting as clinical local opinion leaders [217]. Using this principle, our multidisciplinary group developed the role of 'Champions for Nutrition'. These nurses were full time clinical staff who worked with the nutrition research team one day a week, gaining additional skills in both nutrition and research. This enabled them to both help with the research

aspects of the study, acting as a 'research link advisor', but more importantly, to promote the guideline on the neonatal unit and to provide support for colleagues in the new working practices.

A detailed description of the development of this role by Jan Westbury, myself and colleagues has been published in the *Journal of Neonatal Nursing* [218], and is included in Appendix 9.

7.1.6 SENNAT

The SENNAT tool described in Chapter 4 provides a detailed, clinically useful, graphical summary of an infant's macronutrient intakes and growth. This important visual feedback would be useful in the nutritional care of the infants, helping to facilitate *reflexive monitoring*, a core construct of NPT. It was therefore planned to use this on the nutrition ward round to aid assessment and nutritional planning for individual infants.

7.2 Summary

This chapter has described the components of the multifaceted complex intervention used in this study, together with their development and a justification of their selection for use. NPT was used to try and ensure that each element of the intervention would act together in a way that facilitated its integration into routine care. In summary, the intervention consisted of:

- Improved nutritional products
- Comprehensive nutritional guidelines based on current evidence and consensus best practice (as discussed in chapter 2)
- A multidisciplinary nutrition support team
- A weekly nutrition ward round
- A nutrition screening tool
- Nurse 'Champions for Nutrition'

It was hoped that the introduction of the guidelines, screening tool, nutrition team and nurse champions would lead to a restructuring of practice in relation to nutritional care, again encouraging the new practice to become part of normal care. Taken together, these elements would lead to *collective action*, with staff willing and able to carry out the work required of them by the guideline. The next chapter will describe how the intervention was tailored and adapted to potential barriers to implementation and the local setting.

Chapter 8: Development Phase Results Part 3 – Tailoring the Intervention

As can be seen from Chapter 5, there is good evidence that tailoring an intervention to prospectively identified barriers and the setting in which it is to be deployed increases the chances of successful implementation. In order to help achieve this, focus groups were conducted and the TPB questionnaire administered. These activities and their results are described below, together with a discussion of the implications for implementation.

8.1 Focus Group Results

The focus groups were carried out according to the method described in Chapter 4. All clinical staff were invited to attend, and the first and second focus groups had eight and twelve participants respectively, with a mix of senior and junior nursing staff, plus one Advanced Neonatal Nurse Practitioner in the first group (see table 8.1). These focus groups were carried out after a draft of the guideline had been released, and participants were given access to a copy of the guideline prior to the focus group taking place.

Grade	Number
ANNP	1
Band 7 Senior Sister	4
Band 6 Sister	4
Band 5 Staff nurse	8
Band 3 and 4 (support workers and nursery nurses)	3

Table 8.1: Participants at the Focus Groups

8.1.1 Barriers to implementation drawn out from focus groups

Recordings of the focus groups were transcribed, and the framework method was used to map the content to the eight barriers to change as laid out by the Cochrane EPOC group [122], as detailed in Chapter 4. The framework can be found in Appendix 10, and the findings are summarised below.

1. **Administrative Constraints**
   A commonly identified barrier was that of time to carry out the work of the guideline. The quote

   "and we've all been in the situation where we want to start feeds, and you'll handover at the end of your shift, oh you haven't quite got round to it, you know and haven't had time to go and make the feeds up"

   typified the comments. In addition the administrative burden of more detailed monitoring of growth was mentioned:

   "we're supposed to be doing head circumferences as well aren't we when we weigh them once a week, but that doesn't seem to happen all the time, so I do just wonder whether it will happen or not"

   There was also a recognition that whilst copies of the guideline might be available this may not mean people would read them, with a feeling that everyone would need to be made aware of the changes
   Interestingly, senior nurses were happy to confirm that they felt this was an achievable guideline that was not too onerous for staff. Doing this in front of their junior colleagues meant that they were openly supporting the project and encouraging their colleagues to use the guideline.

2. **Clinical Uncertainty**
   Despite the association of guidelines with loss of individualised care, clinical uncertainty was not particularly identified as barrier during the focus groups. There was recognition however of a need to treat babies as individuals, particularly if they were very unwell, and that guidelines would not replace 'gut feeling' in some cases.

3. **Information Management**
   This was a commonly mentioned group of barriers, with the main emphasis on ensuring that the information in the guideline was readily available in the clinical areas, such as laminated copies of the flow charts in babies' folders. The flow charts were identified as a key

resource for implementing the guideline as they provided an easy to follow summary of the guideline itself, which was seen as a large document that many would not read. Participants also repeatedly highlighted the need for adequate training for staff in the new working practices, suggesting it should be part of induction programmes. As part of this, participants also highlighted the issue of night shifts preventing some staff attending training days. It was felt that nutrition should be highlighted daily at ward rounds, with plans made between nurses and doctors for the coming 24 hours.

Interaction between a member of the medical team (a nurse practitioner) and a senior nurse demonstrated a mutual feeling that sometimes medical feed plans were not carried through, with frustrations on both sides. This was due to breakdown in communication between the two teams, either because the medical team did not tell the nurses the plan (because the nurse was busy with another baby) or because nurse did not read what was written in the notes.

4. **Patient Expectations**

   This was only briefly covered in the focus groups, with issues mentioned including the fixation some parents have on the weight gain of their infant, and the conflicting advice parents receive regarding feeding. It was felt the guideline would help address these issues by focussing on overall growth rather than just weight, whilst providing more consistency in management.

5. **Perceptions of Liability**

   This was a more frequently covered issue, with focus group participants clearly aware of a shift of responsibilities. They recognised a shift towards nurses engaging in feeding decisions, with more shared decisions between medical and nursing staff, away from a previously medical dominated area. One senior nurse summarised the ethos of the guidelines nicely:

   "it's kind of a key thing, because you know when it's two o'clock in the morning on a Saturday night, it's the nurses that are making the nutrition decisions really, as in you know what to do by that team,

because there's no-one else around……people who weren't confident enough to make decisions might wait until the feeding sister (nurse champion) *is in or you know or if it's a Tuesday, people might say well I'm not going to make any decisions, I'll wait for the nutrition round. So there is that element of, I don't know, it's like with any other baby, sometimes we wait for the ward round and leave it for the doctors to decide, but if we think that it's going to be long time before that happens, we have to take it upon ourselves to, but hopefully these guidelines will help us all make the same decision."*

This change in responsibilities (generally perceived as an increase from a nursing perspective) and a need to be clear about who was responsible for what, was mentioned by several individuals. One group discussed how progress had been made when a change in blood transfusion policy had been introduced previously, and that this was because key people were driving it forward. They therefore felt there was no reason why the new nutrition guidelines could not work in the same way. There was also recognition that the guideline has been produced after a lot of work by 'our own team' which was felt to be likely to encourage people to try and follow it. There was some debate about whether it was fair to expect nurses on duty on a Sunday night to be responsible for measurements and plotting, though many felt that having a specific day each week to focus on these things made them more likely to be done.

6. **Sense of Competence**

This was infrequently mentioned, though when it occurred the emphasis was on ensuring staff were aware of the guideline and able to understand and follow it. Both groups discussed the need for training in the new measuring practices. Mention was also made of the large number of junior nursing staff together with a varied mix of skills and education across the unit that meant adequate education would be key.

7. **Standards of Practice**

This was a more common area of discussion, with consensus amongst participants that the guidelines needed to be fully adopted into practice

and become part of 'normal' care. There was general recognition that some of the content represented a significant change in practice, particularly for smaller more vulnerable babies, and that this would be a challenge for implementation. Comments were along the lines of this example by a senior nurse:

"Well this is going break peoples 'norms' for a while and people might get a bit challenged by a new policy and don't like to perhaps be told that that's what you have to do; this is the policy. So I guess people who have kind of done sort of ad hoc behaviour are going to have to realise that actually this is the guideline now and we need to follow that."

Overall both groups felt the new practices should be the norm, with exceptions only with good reason.

8. **Financial Disincentives**
   This topic area was not covered at all.

8.1.2 Mapping of themes identified from focus groups to the Normalization Process Theory

Previous studies have shown benefit from mapping the attitudes of staff towards implementation against the constructs of NPT[148]. Therefore, the responses from participants in the focus groups were also mapped to the constructs of NPT[37 38], according the framework method described in Chapter 4, in order to help understand the relationships within the implementation process. The completed analytical framework can be found in Appendix 11, and the findings summarised below.

- **Coherence (how participants make sense of, and specify, their involvement in a complex intervention)**
  There was recognition that whilst some of the practices introduced by the guideline were similar to current practices, there were some clear differences. One senior nurse commented:

"I think it's something that we have been doing, but it's actually formalising what we've been doing, so that there actually is a structure to when we feed, when we don't we, what we feed with. …. I think it's making it, its structure and it's not ad hoc, and particularly when you're saying it's such a big unit and there's so many different members of staff, it's quite, it would be nice to have the guidelines."

In particular, the structured nature of the guidelines and the reduction in ad hoc practices was acknowledged and seen as beneficial.

"I think these guidelines have pulled together a lot of other guidelines and a lot of other things that have been happening fairly ad hoc, so that people are, well should now be clear as to what the expectations are, and they can, it can help them make decisions about things, you know when maybe there's not someone else to ask."

There was a feeling the guidelines would improve continuity of care and aid decision making. Both groups felt the guidelines served to raise the profile of nutrition on the unit, which they viewed as a good thing.

- **Cognitive Participation (how participants become members of a specific community of practice surrounding the intervention)**
  As mentioned above, staff valued the introduction of standardised practice and less ad hoc decision making. It was suggested it would empower nurses to be more involved in decisions or to prompt doctors where necessary. One senior nurse summarised this:

  "Because you've actually got something there that's actually in black and white, you've actually got a diagram that hopefully everyone's going to agree to, and that will include all the consultants and the medical and the nursing staff. So therefore you've got a common document"

  There was a desire to have a written guideline and a feeling that it would improve practice (especially regarding changes in feed and PN volumes) and outcomes for the babies. The guideline was also valued for teaching junior staff. There was recognition that some of the practices would

represent more work (such as measuring weekly) and also that some people might be resistant to changes, although the general feeling was that everyone would just have get used to it and make the new practices the norm. Staff identified the need for the new practices to be led by someone and 'pushed forward', and recognised that the nutrition team would be able to do this. One group mentioned that the fact the guideline had been produced by the local team gave it 'brownie points' and suggested it would encourage people to use it, as they were confident in the content of the guideline as it had been produced by local experts and was clearly well researched and referenced:

"And also I think people appreciate that a lot of work has gone into this and the work has come from our team as well. It's not people from outside that have inflicted something on us. It's our team that have decided that this needs to be addressed and that you know this is the best way forward, so you know I think, I think that will get it a lot of Brownie points."

Staff felt that the importance of nutrition was clear and were motivated to use the guideline. They felt people would use and refer to it regularly, and senior staff were keen to encourage juniors to familiarise themselves with it. There was an expectation from junior nurses to receive education in the new practices, and they looked to the senior nurses in the room that were part of the education team to help deliver this, with the senior nurses responding by offering to email the guideline and also make it part of orientation programmes.

- **Collective Action (how participants realise and perform the intervention in practice)**
  Staff felt that the guideline made roles and responsibilities clear with the flow charts making it easy to follow. Both groups picked up on the need to have the guideline easily accessible and available to encourage people to use it. It was felt all staff had a responsibility to read and use the guideline. The groups recognised the need for everyone to be seen to be using it, particularly senior staff, who would need to lead by example. Allocating measuring to specific people and shifts (e.g.

measuring on a Sunday night) was felt likely to help it get done. In both groups there was some apprehension about there being sufficient time overnight to carry out the measurements, plot them on a growth chart and complete the nutrition screening tool. However, senior nurses reassured the group that it was possible and achievable:

Senior Nurse 1: "It's just that sometimes the night girls are so busy, they can't do it all can they before they leave. You get a couple that aren't done or something."

Senior Nurse 2: "I don't know, I think you can do it at night"

Junior Nurse: "Because the other thing about the night-staff, that people actually go for an hour break, they don't have a half-hour break. And you know so that makes it, that does impact on the work that if somebody, if somebody's away for an hour, that you know you're one down for that hour, and that, you know if there's three of you, and you're one down for three hours during the night, so.

Senior Nurse 2:"But there's three from twelve hours, then you've got nine hours left to weigh babies and measure them."

A conversation between senior nurses also highlighted that they felt there were no real reasons not to weigh babies at the appropriate time:

Senior Nurse 1:"And a lot of people say their baby's too sick to weigh, but you look, you only have to lift up and down and you change your data."

Senior Nurse 2:"You change your sheets….

Senior Nurse 1:"And you change their sheets, yeah exactly, so I don't think there's any."

Senior Nurse 3:"Any excuse really."

Senior Nurse 1:"Any excuse, unless they're on an overhead (cot), but you know unless they are sick on an overhead and you can't pick them up. But any baby that's in an incubator, you can weigh."

Some of the practices were felt to be just an extension or formalisation of things that were already being done, so some staff felt it would fit with current practices well. Both groups highlighted the need for training in the new measuring equipment and education on the nutritional aspects, which they felt should be incorporated into current rolling study days and inductions. Measuring the length of babies was highlighted as a particular challenge as it was a new thing, though an interesting interaction in one of the groups was a new nursery nurse who had come from another hospital where measuring length was routine, who reassured the rest of the group it was simple and achievable. This prompted the rest of the group to accept that it was possible and they seemed keen to start doing it in practice.

- **Reflexive Monitoring (how participants collect and utilise information about the effects of the intervention)**
  The increased emphasis on growth monitoring and use of growth charts was felt to be positive, and allowed users and parents to see the benefits of improved nutrition on a daily basis. Staff felt that using audit meetings and the unit's audio-visual (AV) system (electronic screens displaying messages for staff) to show the results of better nutrition would be helpful. Both groups felt that the changes would be received positively, especially the increases in consistency of care and growth monitoring, which were things they felt needed improvement. Another common theme was a feeling that seeing the benefits, either in the growth charts of the infants themselves or through departmental audit and the unit AV system, would encourage people to use the guideline. In particular, one nurse identified that seeing pictorial representations of performance or outcomes would aid this:

  "Sometimes I think perhaps some graphs on the wall about this is what happens to a baby fed at this point and this is what, you know you need to do at this point, just so that we can see the massive difference in weights and you know that people think actually it does make a difference if I don't, if I'm, you know I'm busy and haven't started the feed for another twenty-four hours, even after they've told me."

8.2 Theory of Planned Behaviour Questionnaire Results

The final TPB questionnaire was developed and administered according to the method described in Chapter 4. Eighty members of staff were recruited to the survey element of the study from a pool of approximately 120. Sixty responded to the TPB questionnaire (response rate of 75%). The distribution of respondents in terms of their roles and grades is shown in Table 8.2.

Grade	Number
Consultant	5
Specialist Registrar or Specialty Trainee 4 or above	1
ANNP	2
Band 8	1
Band 7 Senior Sister	6
Band 6 Sister	12
Band 5 Staff nurse	26
Band 4 Nursery nurse	4
Band 3 Support workers	3

Table 8.2: Respondents to the TPB questionnaire

Attitudes towards the guidelines were generally very positive, with all scores above 60% of the maximum range (where 50% would represent equipoise between positive and negative attitude, see table 8.3).The mean scores for intention performance and generalised intention were 75.3% and 83.9% respectively.

Correlations between the variables are shown in table 8.4, and it can be seen the 'intention performance' measure correlated better with the belief measures, whereas the 'generalised intention' measure correlation was weak. The composite measures of attitude, subjective norms and perceived behavioural control correlated more strongly ($r=0.65$, 0.27 and 0.31 respectively) with intention performance than the direct measures. Composite attitude and composite perceived behavioural control both had significant correlations with $p<0.001$ and $p=0.022$ respectively, and composite subjective norm approached significance with $p=0.053$. Whilst mean direct attitude correlated significantly with intention ($r=0.47$, $p<0.001$), the composite measure of attitude had a stronger correlation.

	Mean Direct Attitude Score	Mean Direct Subjective Norm Score	Mean Direct Perceived Behavioural Control Score	Composite Attitude	Composite Subjective Norms	Composite Perceived Behavioural Control
Mean Score	6.43	5.75	4.98	88.15	62.80	21.55
Standard Deviation	0.60	1.02	0.89	20.55	30.55	13.76
Mean Score as percentage of max	90.5%	79.2%	66.4%	85.0%	79.9%	62.8%

Table 8.3: Mean Scores from TPB questionnaire

Multiple linear regression analysis using the composite measures of attitude, subjective norms and perceived behavioural control to predict intention (based on intention performance scores) showed that 44% of the variance in intention scores was predicted by the 3 items. Individual coefficients for each of the three items of attitude, subjective norms and perceived behavioural control were 0.700, -0.114 and 0.030 respectively). This demonstrates that the attitude of staff towards the guideline has the strongest influence on their intention to use it.

Splitting respondents into two groups using the median score for intention performance (median=10) allowed comparison of beliefs between those with 'high' intentions (n=35) and those with 'low' intentions (n=25). There was a significant difference in both direct and composite attitude scores ($p<0.01$ and $p<0.001$ respectively). Again, this shows that attitude has the strongest influence on the intentions of staff.

	Intention Performance	Generalised Intention	Mean Direct Attitude Score	Mean Direct Subjective Norm Score	Mean Direct Perceived Behavioural Control Score	Composite Attitude	Composite Subjective Norms
Generalised Intention	r=0.170 p=0.194						
Mean Direct Attitude Score	r=0.420 p<0.001	r=0.253 p=0.051					
Mean Direct Subjective Norm Score	r=0.187 p=0.152	r=0.055 p=0.677	r=0.424 p=0.001				
Mean Direct Perceived Behavioural Control Score	r=0.089 p=0.499	r=0.118 p=0.367	r=0.188 p=0.150	r=0.206 p=0.114			
Composite Attitude	r=0.657 p<0.001	r=0.158 p=0.228	r=0.611 p<0.001	r=0.526 p<0.001	r=0.157 p=0.231		
Composite Subjective Norms	r=0.268 p=0.038	r=0.124 p=0.346	r=0.390 p=0.002	r=0.587 p<0.001	r=0.184 p=0.158	r=0.532 p=0.001	
Composite Perceived Behavioural Control	r=0.337 p=0.009	r=0.074 p=0.575	r=0.474 p<0.001	r=0.372 p=0.003	r=0.304 p=0.018	r=0.524 p<0.001	r=0.538 p<0.001

Table 8.4: Correlations between The Theory of Planned Behaviour variables

8.3 Conclusions from tailoring work

The experience of the focus groups depicts a group of staff aware of a need for change and keen to embrace it. It is important to point out at this stage that attendance at the focus groups was voluntary so it may be that motivated or interested individuals were more likely to attend. It is also noteworthy that no consultants attended, so their views were not taken into account in the tailoring work from the focus groups (though they did provide comments over email regarding the content of the guideline). In both focus groups there was a clear interaction between senior and junior nurses, with the senior ones supporting the introduction of the guideline and encouraging juniors to use it.

The main barriers identified were that of time and increased duties surrounding the screening tool and regular growth measurements. Interestingly, the shift of responsibility for nutritional decisions from mainly medical staff to one that was more shared between medical and nursing staff was not perceived as negative, but rather as a positive change. Nurses identified the change in responsibility and emphasis on decision making laid out in the guideline as a facilitator for change rather than a barrier, highlighting the guideline as something that would empower them to engage with the medical team in nutritional management. Adequate provision of information in terms of availability of the guideline in clinical areas was repeatedly highlighted, and focus group participants suggested ways in which this barrier could be overcome. In fact, several suggestions came out of the focus groups regarding potential ways of overcoming barriers and facilitating implementation. These fitted in with the barriers that had been identified and included:

- Ensuring the guideline was widely distributed and easy to access on the neonatal unit once implemented
- Training and teaching for staff regarding nutrition and the new guidelines
- Producing laminated versions of the use of the nutrition and feeding flow charts (incorporated into the guideline) which could be put in the nursing folder for each infant so they could be seen and used easily
- A 'nutrition folder' in each room containing the nutrition guidelines and related material
- Publicising the new practices and outcomes on the unit's AV system
- Ensure all staff can use the new equipment for measuring infants

Mapping the focus group findings to the constructs of NPT allows a detailed picture of how the complex intervention fits within the setting and with staff members to be built up, making it clear where issues might arise. Staff understood the importance of nutrition and were able to identify how the new practices were different from the old ones, demonstrating *coherence*. Staff were also able to visualise how they would work to enact the new changes, demonstrating clear *cognitive participation*. They felt they would be able to engage with the new guideline, encouraging others to use it. The potential for implementation in the neonatal unit therefore appeared good, with a will for change and potential for *collective action*. Whilst the guidelines proposed a change in social norms and roles in terms of the way nutritional decision and

care were delivered, the focus groups showed that there was clearly a capacity to adopt these changes within the nursing staff. Participants in the focus groups were clear about the resources that the new practices would require, identifying issues surrounding the provision of equipment, training and information surrounding the new practices. More importantly, constraints within the system in terms of adequate staffing levels to perform the work needed, and the complex nature of the patients and environment that would make integrating the changes challenging were identified, together with suggestions by staff on how they might be overcome. These suggestions would clearly need to be included in any implementation plan. Staff identified that growth charts would provide a way of evaluating the effects of the intervention, allowing *reflexive monitoring*, and also identified other strategies that would be beneficial in understanding the effects. There was clearly a desire to be able to see the impact of the new work they would be doing on both practice itself and the patients they cared for, so this would also need to part of the implementation strategy.

The results of the TPB questionnaire demonstrated very positive attitudes amongst staff towards the new guidelines and changes in practice. There was some correlation between composite measures of behaviour and intention, with attitude having the greatest influence on intention, outweighing subjective norms and perceived behavioural control. This suggests that staff on the neonatal unit were most influenced by their own attitudes towards guidelines rather than feelings of pressure from managers or peers, or factors they felt were beyond their control. This is important, as it shows that getting staff to adopt a positive attitude towards the new guideline and working practices was going to be a key factor in improving guideline adherence. This is an interesting finding, as first glance it appears to oppose the findings of chapter 5, which suggested that interventions that seek to change group attitudes are less likely to be effective. However, the sort of processes referred to in chapter 5 which seem less effective are those which try to change general group attitudes through consensus processes and indirect marketing, rather than specific exercises to educate and influence individual attitudes, which the TPB results suggest will be key. Staff training and the role of the NST and nurse champions in promoting the guidelines at ground level will be therefore be important. In addition, whilst the TPB results suggest that peer group and management opinions were less important influences on staff, interactions

within the focus groups demonstrated clear evidence of junior staff being influenced and encouraged to adopt the new practices by their senior colleagues, suggesting that having key senior staff behind the intervention would be vital.

8.4 Summary

This chapter has described the tailoring work carried out prior to implementation, which overall has built up a picture of a neonatal unit ready for and accepting of change. There is a positive attitude amongst staff, and this will clearly be of great help in the implementation process. However, clear barriers to change have been identified, as well as strategies to overcome these barriers and other potential facilitators. In summary, based on the findings of this tailoring work, the implementation process will include:

- Training and teaching for staff regarding nutrition and the new guidelines
- Training for staff in the use of the use of the new measuring equipment (a role for the nurse 'Champions for Nutrition')
- Supporting staff whilst working in the new practices (another role for the nurse 'Champions for Nutrition')
- Producing laminated versions of the use of the nutrition and feeding flow charts and placing these in each infants nursing folder
- Putting a 'nutrition folder' containing the nutrition guidelines and related material into each clinical area, ensuring that the guideline is easy to access
- Publicising information on the new practices on the unit's AV system
- Displaying any relevant outcome or audit data on the unit's AV system during the implementation period
- Introducing the new changes in a staged manner in view of concerns over the scale of the changes by some staff

It is again worth pointing out that these results should be interpreted with caution as it is likely that more positive staff members would have participated in this element of the study. Nonetheless, the information gathered is important, and the very process of these exercises themselves will have served to raise awareness of the proposed changes and help start the implementation process. The next chapter will describe in detail the implementation process itself.

Chapter 9: Implementing the Intervention

Given the multifaceted nature of the intervention and need for specific associated activities to aid implementation, the implementation process was divided into two stages. These are outlined below, together with a narrative description of the processes and issues encountered.

9.1 Implementation Stage 1 – Partial Implementation of Complex Intervention (1st August 2011 – 31st December 2011)

9.1.1 Improved nutritional products

As described in Chapters 6 and 7, the findings of the analysis of the data from the retrospective cohort of infants born in 2009 led to reformulation of the stock PN solutions used in Southampton. These were introduced to Southampton NICU on the 1st August 2011. The revised and improved preterm infant formulas and breast milk fortifiers were available in Southampton NICU from 1st September 2011.

9.1.2 Awareness and advertising

In addition to the focus groups described in the previous chapter, all staff were made aware of the new guideline via email and posters in the coffee room during November and December, as part of a drive to recruit staff to the TPB and NPT elements of the study.

9.1.3 Nurse 'Champions for Nutrition'

Nurse 'Champions for Nutrition' were recruited from existing NICU staff using the role described in Chapter 7 during August and September 2011. Posters were put up to advertise the role and those interested sent CVs to the research team. Four nurses were identified for the role (two band 5 staff nurses and two band 6 sisters), and from early October 2011 they were released one day a week from clinical duties to work with the nutrition team, train and teach staff about the new practices. They were also able to support colleagues in the new practices whilst working clinically.

9.1.4 Nutrition support team and ward rounds

From August 2011, the nutrition team (described in Chapter 7) began doing weekly ward rounds on a Tuesday morning. At this point (prior to the introduction of the guideline and screening tool), infants were selected to be seen on the basis of being extremely low birth weight (less than 1000g) or less than 28 weeks gestation at birth.

9.2 Implementation Stage 2 – Full Implementation of Complex Intervention (1st January 2012 onward)

9.2.1 Nutrition Guidelines

After development, and as part of the approvals process, the guideline was circulated to senior staff (medical, surgical and nursing) during November 2011 and feedback received. Minor changes were made to some of the finer points regarding the timing of enteral and parenteral feeds, and the use of sodium in the first few days of life. The guideline was approved through normal clinical governance channels. Following this approval, the nutrition guidelines (see Chapter 7 and Appendix 1) were officially brought into place on the 1st January 2012. However, copies of the guideline were available in the staff coffee room from mid-November (prior to the focus groups) and were also available online on the hospital intranet following clinical governance approval in mid-December. Providing copies to staff to enable them to read and understand the guideline was hoped to promote both *coherence* and *cognitive participation* of the intervention, particularly as the guidelines contained additional information regarding the rationale behind the choices of feeds and fluids.

As suggested by the focus groups, new 'Nutrition Folders' were created for each room on the neonatal unit, containing a copy of the new nutrition guideline, the current parenteral nutrition guideline, and blank copies of the nutrition screening tool, to make them easily accessible to staff. Copies of the nutrition flow charts contained in the guideline were made and laminated, and a set of flow charts placed in the nursing folder at each cot side for easy reference. Making the guidelines easy to use and access was not only identified

as important by the focus groups, but was also key to facilitating *collective action* in line with NPT.

Reminders of both the guideline (particularly the flow charts) and nutrition screening tool were posted on the staff AV system (two large 50 inch LCD televisions in the staff coffee room and doctors office which display rolling news and information for neonatal unit staff).

9.2.2 Screening Tool

The nutrition screening tool discussed in Chapter 7 was incorporated into the guidelines as an appendix, so also came into force from the 1st January 2012. When used the first time (Monday 9th January) myself and one of the research nurses assisted staff in using it and filling it out. For the subsequent weeks, staff filled it out during a Sunday night shift, with support from the Nurse Champions for Nutrition.

9.2.3 Unit education

In response to the findings of the focus groups carried out in November, a programme of education for the nurses on NICU was carried out between January and June 2012, with a one hour seminar on neonatal nutrition incorporated into the regular study days for nurses of each band and delivered by myself. A similar session was also given as part of the work based learning for NICU nurses, studying for a post qualification module in neonatal intensive care. The dates of these sessions are shown in Table 9.1 and whilst the teaching material used in the session was adapted to suit the band of nurses receiving it, a copy of the slides reflective of the majority of sessions can be seen in Appendix 12. A similar talk was given to medical staff on 23rd November 2011. Education was clearly going to be key in achieving both an understanding of why nutrition was important and why there was a need for a change in the way nutrition was delivered (*coherence*), but also vital in enabling staff *cognitive participation*, with users able to understand and buy in to the guidelines and new practices.

Session/grade	Date
Work based learning NICU module	06/01/2012
Band 6 Sisters	16/03/2012
Band 7 Senior Sisters	30/03/2012
Band 5 Staff nurses	20/04/2012
Band 4 Nursery nurse	18/05/2012
Band 3 Support workers	15/06/2012

Table 9.1: Dates of neonatal nutrition education for nurses

9.2.4 SENNAT

It had initially been planned to implement SENNAT as a clinical decision support system (CDSS), using the graphical patient nutrient intake and growth summary to aid decisions making, on the 1st January along with the rest of the complex intervention. This would provide immediate visual feedback on how well nutrition was being delivered, the impact on growth and in turn an assessment of how well staff were following the guideline, all facilitating the NPT construct of *reflexive monitoring*. However, the amount of data entry required to ensure that SENNAT was suitably up to date, combined with a lack of a suitable trolley and laptop with which to use SENNAT in the NICU clinical rooms, meant that it was not formally implemented until 1st June 2012. An immediate issue was that only infants in the study (those born in Southampton weighing less than 1500g at birth or with a gestational age less than 30 weeks) had summaries available on SENNAT. Infants meeting the birth weight or gestational age criteria but not born in Southampton, which represented around half of the infants seen by the nutrition team, did not therefore have any data or summaries on SENNAT, so it could not be used for them. Another issue was that even for infants who had data available on SENNAT, it was often not sufficiently up to date to be used for an assessment of current nutritional status. This was due to the nature of the data entry meaning that it tended to be entered in blocks of two the three weeks at a time in data entry sessions, rather than updated daily by the research team. Finally, many of the nurses working in intensive care already found the nutrition ward round a little disruptive due to the number of people in the nutrition team (between four and eight) taking up valuable space. The addition of a laptop on a trolley made this

even more difficult, making it harder for nurses to move about the nursery as they cared for the infants.

The failure of the SENNAT tool can be better understood by the application of NPT. Firstly, there was little *coherence* surrounding the tool particularly as by the time it was finally introduced in June, neither the unit staff nor the nutrition team could envisage any significant benefit of it over the existing 'pen and calculator' approach to calculating nutrient intakes, especially given the time consuming nature of the tool and the fact it was not consistently available for every infant. Next there was no *cognitive participation*, as the nutrition team did not drive SENNAT forward (as they found it rather slow and cumbersome). In addition, staff did not legitimate SENNAT as part of their work, as it did not fit with the way the nutrition round worked at the time, and did not fit with existing structures on NICU, as the laptop trolley was bulky and disruptive in the busy nurseries. There was no *collective action*, as SENNAT was not workable, and in fact often increased workload if nutritional data entry was not up to date such that current nutrient intakes still had to be manually calculated. Finally, as mentioned already, neither the nutrition team nor clinical staff could see any benefit of SENNAT in their work, meaning it did poorly in terms of *reflexive monitoring*. In view of all these issues, the use of SENNAT as a clinical tool was abandoned after three weeks. This was both as it was not proving useful, but also in order for the nutrition team to maintain a good working relationship with their colleagues working in NICU.

9.2.5 Response to feedback and NPT questionnaires

Chapter 11 covers in detail the results of the audits of guideline compliance and NPT questionnaires that were carried out during the 12 month intervention period. However, it is important to note at this stage that the results of these were reviewed contemporaneously during the implementation process, and the implementation approach modified in response to them in a dynamic way.

Whilst the audit results generally showed a trend of increasing compliance over time, the results of the first three audits (carried out over the first seven months of the intervention period) were presented to the staff of the neonatal unit at the biannual departmental audit meeting on 29/08/12. This was done in order to highlight the lack of compliance in certain areas and try to encourage further improvement.

Similarly, although the results of the NPT questionnaires showed a trend of increasing normalisation over time, the areas in which scores seemed consistently lower than others were those relating to the constructs of *collective action* and *reflexive monitorin*g. In particular, compared to the responses to other questions, the questions "Can you rely on your colleagues and other professionals to follow the new guidelines and practices?" and "Do you have sufficient information to judge whether the new nutrition guidelines and practices make a difference to the preterm infants you care for?" scored consistently lower. Whilst these scores had improved over the first six months, they were still below that of other questions after the third questionnaire was administered at the start of July 2012. This indicated a need to improve on *reflexive monitoring*, with a need to try and ensure that staff could see that the intervention was working, as they would then feel both able to trust that their colleagues were following the guidelines. Therefore, a brief interim analysis of the nutrient intake and growth data comparing the first six months of the main intervention period to both the partial implementation period and the 2009 historical cohort was carried out in order to show how things had improved, and the results displayed on the neonatal unit's audio visual system (note that the 2011 pre-implementation group was not included at this time as this was added to the study retrospectively as discussed in chapter 4). A copy of the slide that was shown can be seen in Appendix 13, and this was displayed from 13/08/12 until the end of 2012.

9.3 Summary

This chapter has described the way in which the complex intervention was implemented, including changes in response to issues that were identified. The next two chapters present the results of the intervention in terms of infant outcomes and changes in practice and process, together with an assessment of the extent to which the new practices were normalised into routine care.

Chapter 10: Implementation Phase Results Part 1 – Infant outcomes following Implementation

This chapter discusses the effects of the intervention on nutrient intakes and growth of the infants during the study. As discussed in chapter 4, the study comprised four periods- a pre-implementation period prior to any formal intervention (Period A, January-July 2011), a partial implementation period (Period B, August-December 2011), the main intervention period with full implementation of the complex intervention (Period C, January-December 2012) and a post implementation period (Period D, January-June 2013, included to assess the degree to which any changes were sustained after the implementation phase). In addition, a brief comparison is made between the historical 2009 cohort discussed in chapter 6 and the 2011 pre-intervention group (Period A, January-July 2011). Data from the 2009 cohort were used as the original 'baseline' for the study and to develop the guidelines, and inclusion of this analysis allows an understanding of changes that occurred over time before the start of the study.

The statistical methods described in chapter 4 and appendix 2 were used, with comparison between all four periods carried out and presented. In summary this included three separate analyses: non-repeated measures analysis, interrupted time series analysis and repeated measures analysis. Such detailed analysis using multiple methods was carried out to make the most comprehensive and realistic assessment of the extent to which any clinical improvements seen were the result of the full implementation of the guideline and associated interventions (implemented during period C) or of the improved nutritional products implemented during the partial implementation phase, period B. This chapter will present the results of each of these methods, followed by a summary of all the results together with a brief discussion highlighting some key points that will be discussed in more detail in the concluding chapter.

10.1 Tests for normality

All variables were tested for normality using the Kolmogorov-Smirnov test against a normal distribution, and the results are summarised in Table 10.1.

Variable	Combined Kolmogorov-Smirnov test difference	p value	Normally distributed
Energy (kcal/kg/day)	0.136	<0.001	No
Protein (g/kg/day)	0.093	0.019	No
Energy (as percentage of RRI)	0.096	0.014	No
Protein (as percentage of RRI)	0.129	<0.001	No
Difference in weight SDS	0.044	0.695	Yes
Difference in length SDS	0.287	0.564	Yes
Difference in head circumference SDS	0.085	0.071	Yes
Birth Weight SDS	0.081	0.063	Yes
Birth Length SDS	0.228	0.837	Yes
Birth Head Circumference SDS	0.079	0.152	Yes
Birth Weight	0.048	0.551	Yes
Birth Head Circumference	0.196	1	Yes
Age at starting fortifier	0.155	0.003	No
Age at starting PN	0.335	<0.001	No
Age at starting feeds	0.142	<0.001	No
Length of stay	0.058	0.32	Yes

Table 10.1: Results of tests for normality for all variables used in this study (RRI-reasonable Range of Intake, SDS-Standard Deviation Score)

10.2 Summary of study populations

Table 10.2 shows a summary of the sex, gestational age at birth and birth weight of infants. CRIB II[219] scores are also shown as in indication of illness severity. CRIB II scores were not available for all infants and the numbers available with CRIB scores are also shown in Table 10.2. There were no significant differences in sex, birth weight or gestational age between groups. There was a significant difference in CRIB II scores between groups (p=0.008), with post hoc pairwise testing using Tukey's method revealing that only group D was significantly different (higher) from all the others. This suggests an increased level of illness severity in group D when interpreting results.

Period	n	Male (%)	Mean Birth weight (SD)	Mean Gestational Age (SD)	Mean CRIB II (SD), n
A. Pre-implementation period (Jan 2011 – Jul 2011	52	23 (44.2)	1.084 (0.270)	29.2 (2.6)	7.0 (3.6), 30
B. Partial implementation period (Aug – Dec 2011)	36	18 (50)	1.029 (0.311)	29.2 (2.9)	6.4 (3.9), 20
C. Main Intervention Period (Jan – Dec 2012)	75	37 (49.3)	0.998 (0.269)	28.7 (3.0)	6.9 (2.5), 44
D. Post-implementation period (Jan – Jun 2013)	35	22 (62.9)	0.924 (0.261)	28.1 (2.8)	9.7 (3.2), 18
p value for difference between groups (ANOVA)		0.392*	0.066	0.290	**0.008**

Table 10.2: Infant Characteristics in each study group (SD-Standard Deviation) *p value is for Chi^2

10.3 Comparison of outcomes between study periods

10.3.1 Non-repeated measures outcomes

10.3.1.1 Nutrient Intakes for whole stay

Daily nutrient intakes across the entire stay for each infant were summarised using medians and interquartile ranges, and then compared between study groups using the Kruskal-Wallis test. Figures 10.1A and B show the median daily intakes of Energy (kcal/kg/day) and protein (g/kg/day) respectively, whilst figures 10.1C and D show the median daily intakes of energy and protein respectively as a percentage of Tsang et al's Reasonable Range of Intakes (RRIs). There was a trend of increasing protein intakes across periods, with relatively static energy intakes until the post-implementation period (D), where they appear to fall slightly. These results are detailed in table 10.3, which demonstrates significant differences between study periods for intakes of energy and protein as a percentage of RRI. As per the statistical analysis protocol (Appendix 2), only variables where the Kruskal-Wallis test had demonstrated significant differences between groups were subject to closer inspection using pairwise Mann-Whitney U tests. These were carried out for energy and protein as a percentage of RRI, and are shown in table 10.4. For energy as a percentage of RRI, the post implementation period (D) was significantly lower than all other groups, with no other significant pairwise differences. For protein as a percentage of RRI, period C (the main intervention period) was significantly higher than period A and B (the pre- and partial implementation periods, highlighted in figures 10.1 C and D).

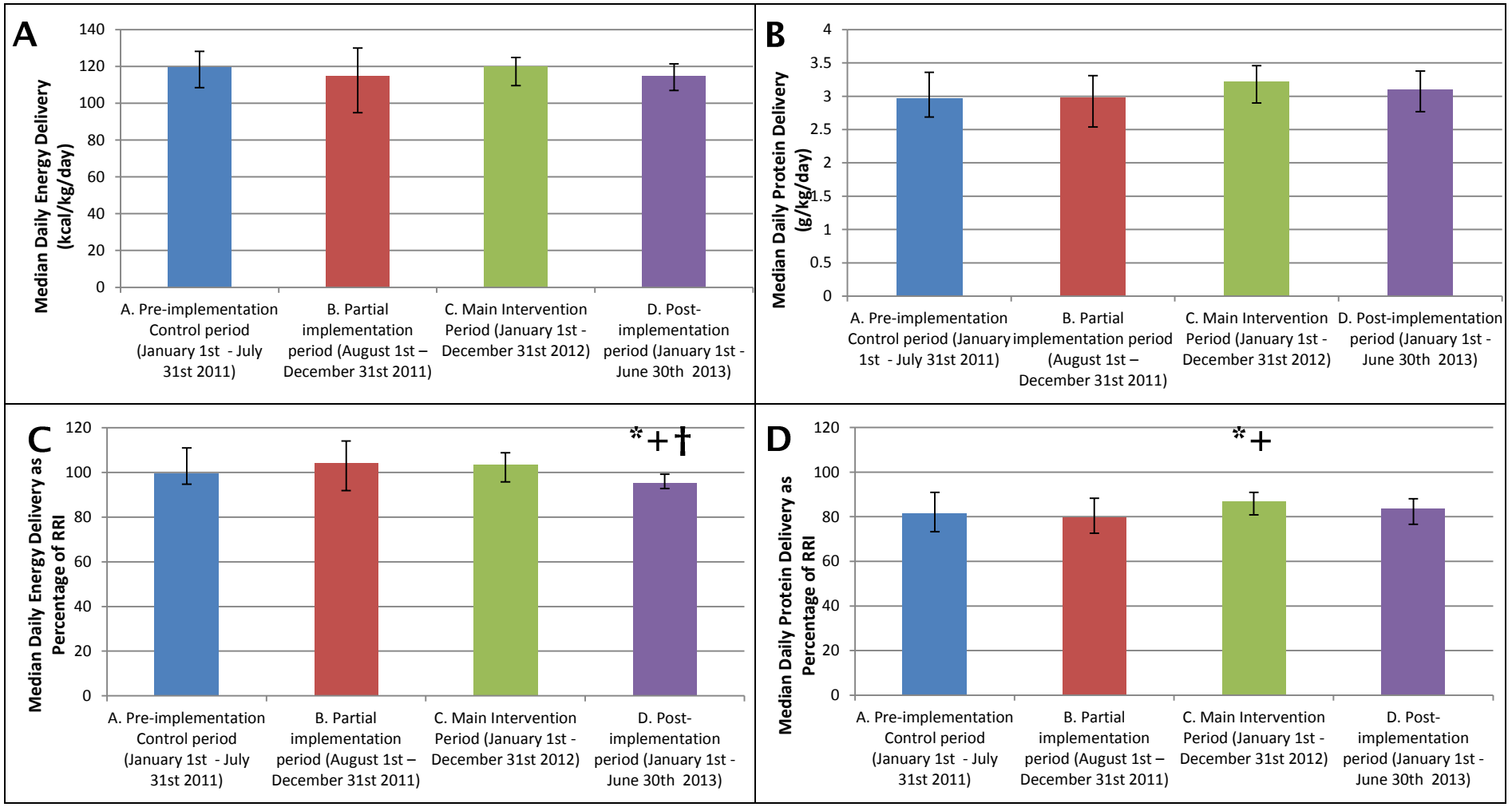


Figure 10.1: Bar graphs showing median nutrient intakes across the four study periods for energy in kcal/kg/day (A), protein in g/kg/day (B), energy as a percentage of RRI (C) and protein as a percentage of RRI (D).Error bars represent interquartile range. * $p<0.05$ for difference vs group A, +$p<0.05$ for differnce vs group B, †$p<0.05$ for difference vs group C (RRI- reasonable range of intake)

Period	n	Median Energy kcal/kg/day (IQR)	Median Protein g/kg/day (IQR)	Median Energy as %RRI per day (IQR)	Median Protein as %RRI per day (IQR)
A. Pre-implementation period (January-July 2011	51	119.4 (108.4-128.2)	2.96 (2.69-3.36)	99.4 (94.7-110.9)	81.4 (73.3-90.9)
B. Partial implementation period (August-December 2011)	35	114.6 (94.9-130)	2.98 (2.54 - 3.31)	104.3 (91.8-114)	79.5 (72.6-88.3)
C. Main Intervention Period (January-December 2012)	73	119.7 (109.6-124.8)	3.22 (2.9 - 3.46)	103.3 (95.7-108.7)	86.8 (80.9-90.9)
D. Post-implementation period (January-June 2013)	34	114.8 (106.9-121.3)	3.1 (2.77 - 3.38)	95.3 (92.8-99.2)	83.6 (76.6-88.1)
Kruskal-Wallis p value		0.303	0.087	**0.010**	**0.044**

Table 10.3: Median nutrient intakes for energy and protein in each study group across entire stay, with comparison across all groups using the Kruskall-Wallis test. P values less than 0.05 are highlighted in bold (IQR- interquartile range, RRI-reasonable range of intake)

10.3.1.2 Growth over whole stay

Growth across stay, expressed as the change in SDS for weight and head circumference between birth and discharge for each infant, was summarised using means and standard deviations, and then compared between study groups using Analysis of Variance (ANOVA). Figures 10.2A and B show the mean difference in SDS between birth and discharge for weight and head circumference respectively. These demonstrate a trend of improving growth in weight gain during stay, with infants being discharged with a SDS closer to that of their birth in later study periods. Head growth appears to be static across study periods. These results are detailed in table 10.5, which demonstrates that there was a significant difference between study periods for weight. This was further explored post hoc by assessing the pairwise differences between each group using Tukey's method, with results shown in table 10.4. The only significant difference was for the change in weight SDS between birth and discharge between groups A and D (the pre-implementation period, January-July 2011 and post implementation period, January-June 2013). This suggests that infants in the post implementation period had significantly increased growth, in terms of weight, compared to those in the pre-implementation period.

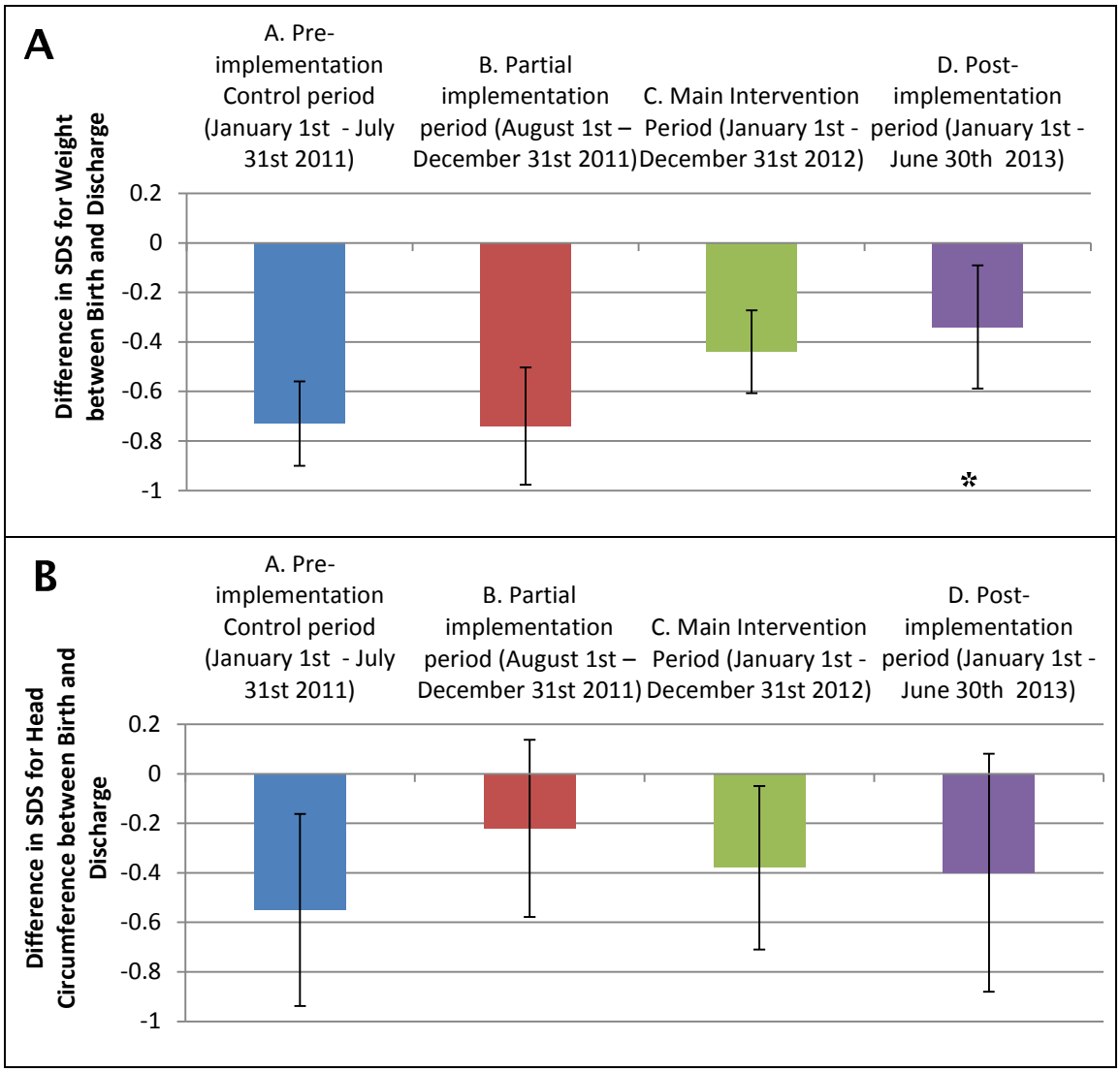


Figure 10.2: Bar charts showing the mean change in SDS for weight (A) and head circumference (B) between birth and discharge across study groups. Error bars represent 95% confidence intervals.* p<0.05 for difference vs group A. (SDS-standard deviation score)

Period	p value for pairwise differences using Mann–Whitney U test		p value for pairwise differences using Tukey's Method
	Median Energy as %RRI per day (IQR)	Median Protein as %RRI per day (IQR)	Difference in SDS for Weight between Birth and Discharge
A vs B	0.595	0.626	1.000
A vs C	0.361	**0.025**	0.117
A vs D	**0.017**	0.365	**0.014**
B vs C	0.905	**0.020**	0.220
B vs D	**0.043**	0.254	0.097
C vs D	**0.004**	0.161	0.891

Table 10.4: Results of statistical comparisons for nutrient intake and weight SDS of paired groups across all study periods. p values <0.05 are highlighted in bold.

Period	Difference in SDS for Weight between Birth and Discharge		Difference in SDS for Head Circumference between Birth and Discharge	
	n	Mean Difference (SD)	n	Mean Difference (SD)
A. Pre-implementation period (January-July 2011	40	-0.73 (0.55)	25	-0.55 (0.99)
B. Partial implementation period (August-December 2011)	23	-0.74 (0.58)	16	-0.22 (0.73)
C. Main Intervention Period (January-December 2012)	60	-0.44 (0.66)	55	-0.38 (1.25)
D. Post-implementation period (January-June 2013)	34	-0.34 (0.74)	29	-0.4 (1.32)
ANOVA p value		**0.016**		0.844

Table 10.5: Mean change in weight and head circumference SDS between birth and discharge, together with results of ANOVA comparing al 4 study groups. p values <0.05 are highlighted in bold. (SDS-standard deviation score)

10.3.1.3 Nutrient intakes by week across stay

Daily nutrient intakes for each infant were summarised for each week of stay (weeks 1, 2, 4 and 6, plus 36 weeks corrected gestational age) using medians and interquartile ranges, and then compared between study periods using the Kruskal-Wallis test for each time point. Figures 10.3A and B show the median daily intakes across stay of energy (kcal/kg/day) and protein (g/kg/day) respectively, whilst figures 10.3C and D show the median daily intakes of energy and protein respectively as a percentage of Tsang et al's Reasonable Range of Intakes (RRI). There was a trend of increasing intakes across time points for energy (kcal/kg/day) and protein (g/kg/day), although when expressed as percentages of RRI, energy intakes appeared static at around 100% across all time points, whilst for protein there was an increase across time points. Comparing the study periods, it can be seen that the most significant differences were seen in the first week of life. Details of these results are shown in tables 10.6 to 10.9 for energy (kcal/kg/day), protein (g/kg/day), energy as a percentage of RRI and protein as a percentage of RRI respectively. This demonstrates that there were significant differences between study groups for all four nutrient variables during week 1 of life, and during week 2 for energy as a percentage of RRI only.

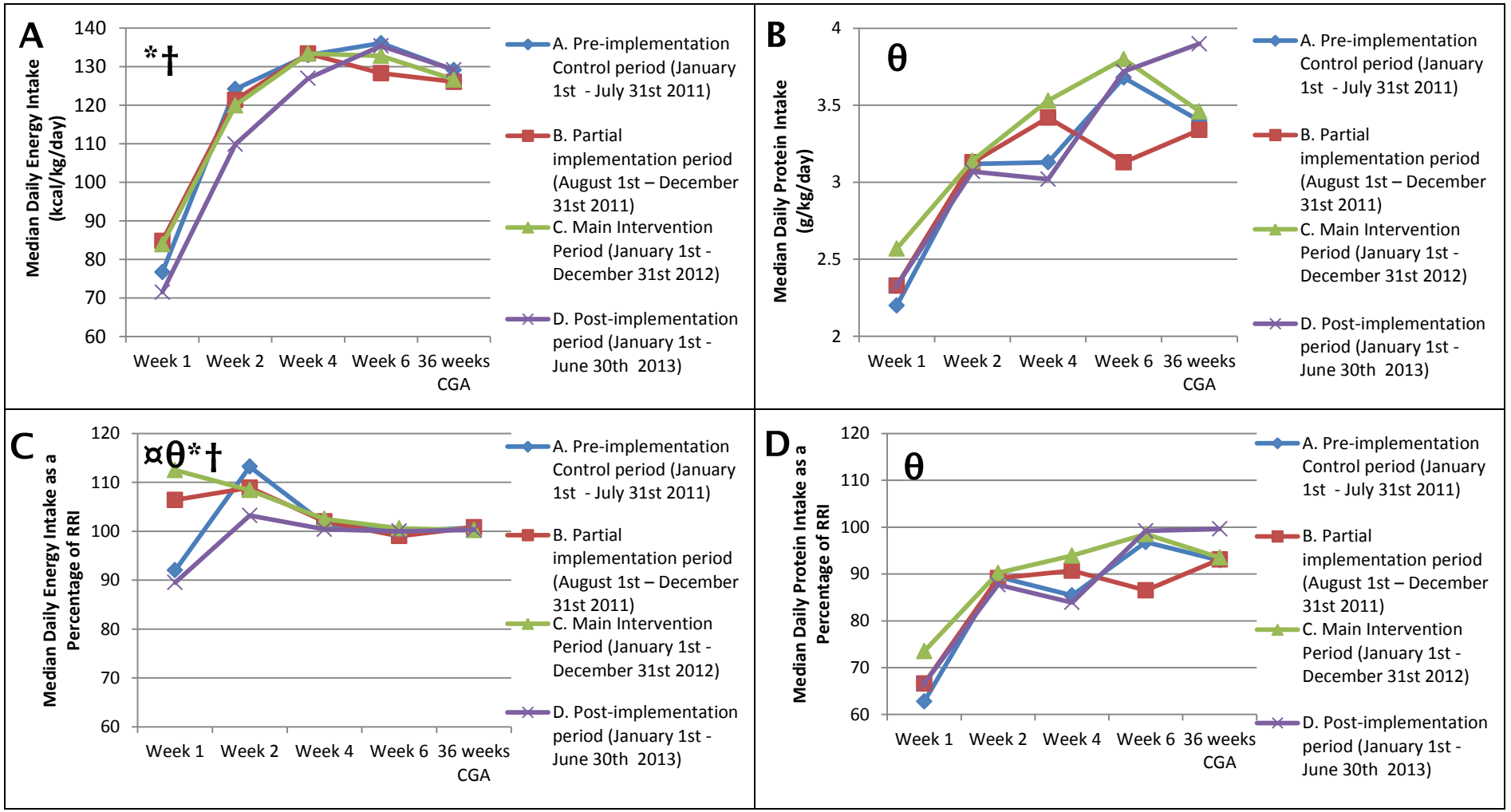


Figure 10.3 Line graphs showing median nutrient intakes over time across stay during the four study periods for energy in kcal/kg/day (A), protein in g/kg/day (B), energy as a percentage of RRI (C) and protein as a percentage of RRI (D).* p<0.05 for difference group B vs D, †p<0.05 for difference group C vs D, +p<0.05 for difference group A vs D, θp<0.05 for difference group A vs C, ¤p<0.05 for difference group A vs B . (RRI- reasonable range of intake)

	Week 1		Week 2		Week 4		Week 6		36 Weeks	
	n	Median Daily Energy kcal/kg/d (IQR)	n	Median Daily Energy kcal/kg/d (IQR)	n	Median Daily Energy kcal/kg/d (IQR)	n	Median Daily Energy kcal/kg/d (IQR)	n	Median Daily Energy kcal/kg/d (IQR)
A. Pre-implementation period (January 1st – July 31st 2011)	51	76.7 (72.2 – 90.2)	46	124.2 (106.6 – 139.3)	41	133 (121 – 141.2)	31	136.1 (129.5 - 145.4)	25	129.1 (120.1 - 143.2)
B. Partial implementation period (August 1st – December 31st 2011)	34	84.8 (71.4 – 95)	30	121.4 (104.4 – 130.4)	26	133.4 (118.2 – 142)	17	128.3 (107.7 - 146.7)	17	126.1 (110.9 - 147)
C. Main Intervention Period (January 1st – December 31st 2012)	72	83.9 (73.2 – 93.4)	67	120 (105.1 – 127.1)	61	133.4 (114.1 – 141.7)	47	132.8 (116.6 - 147)	47	126.7 (115.4 - 143.6)
D. Post-implementation period (January 1st – June 30th 2013)	34	71.5 (62.8 – 83.3)	33	109.9 (98.7 – 121.3)	31	127 (102.9 – 138)	27	135.4 (121.3 - 145.2)	21	129.2 (119.9 - 142)
Kruskal–Wallis p value		**0.0299**		**0.0336**		0.5459		0.5226		0.9671

Table 10.6: Median daily energy intakes in kcal/kg/day over time during stay, across all four study periods. Groups have been compared to each other at each time point using the Kruskal-Wallis test, with p values <0.05 highlighted in bold. (IQR-interquartile range)

	Week 1		Week 2		Week 4		Week 6		36 Weeks	
	n	Median Daily Protein g/kg/d, (IQR)	n	Median Daily Protein g/kg/d, (IQR)	n	Median Daily Protein g/kg/d, (IQR)	n	Median Daily Protein g/kg/d, (IQR)	n	Median Daily Protein g/kg/d, (IQR)
A. Pre-implementation period (January 1st – July 31st 2011)	51	2.2 (1.86 – 2.55)	46	3.12 (2.72 – 3.4)	41	3.13 (2.64 – 3.51)	31	3.68 (3.09 - 3.91)	25	3.4 (2.85 - 3.87)
B. Partial implementation period (August 1st – December 31st 2011)	34	2.33 (1.91 – 2.57)	30	3.13 (2.7 – 3.31)	26	3.42 (2.9 – 3.78)	17	3.13 (2.92 - 4.32)	17	3.34 (2.9 - 4.22)
C. Main Intervention Period (January 1st – December 31st 2012)	72	2.57 (2.16 – 2.73)	67	3.14 (2.82 – 3.35)	61	3.53 (3.03 – 3.82)	47	3.8 (3.18 - 4.3)	47	3.46 (2.83 - 4.19)
D. Post-implementation period (January 1st – June 30th 2013)	34	2.33 (1.8 – 2.6)	33	3.07 (2.52 – 3.28)	31	3.02 (2.73 – 3.69)	27	3.72 (3.45 - 4.27)	21	3.9 (3.29 - 4.27)
Kruskal–Wallis p value		**0.0092**		0.3809		0.0839		0.2334		0.3194

Table 10.7: Median daily protein intakes in g/kg/day over time during stay, across all four study periods. Groups have been compared to each other at each time point using the Kruskal-Wallis test, with p values <0.05 highlighted in bold. (IQR-interquartile range)

	Week 1		Week 2		Week 4		Week 6		36 Weeks	
	n	Median Daily Energy as %RRI/d (IQR)	n	Median Daily Energy as %RRI/d (IQR)	n	Median Daily Energy as %RRI/d (IQR)	n	Median Daily Energy as %RRI/d (IQR)	n	Median Daily Energy as %RRI/d (IQR)
A. Pre-implementation period (January 1st – July 31st 2011)	51	92 (80.4 – 108.2)	46	113.2 (100 – 123)	41	101.5 (100 – 105.2)	31	100 (96.64 - 105.9)	25	100.7 (98.4 - 103.5)
B. Partial implementation period (August 1st – December 31st 2011)	34	106.4 (95.4 – 127.1)	30	108.9 (102.7 – 119.4)	26	102 (102.7 – 108)	17	99 (80.6 - 100.6)	17	100.8 (94.5 - 103.8)
C. Main Intervention Period (January 1st – December 31st 2012)	72	112.5 (94.9 – 127)	67	108.4 (101.6 – 118.7)	61	102.5 (101.6 – 109.1)	47	100.6 (95.9 - 107.8)	47	100.2 (95.6 - 107.9)
D. Post-implementation period (January 1st – June 30th 2013)	34	89.5 (80.1 – 103.9)	33	103.2 (95.3 – 112.7)	31	100.4 (95.3 – 111.2)	27	100 (95.9 - 111.7)	21	100.3 (96.4 - 103.4)
Kruskal–Wallis p value		**0.0001**		0.0584		0.6001		0.2107		0.9746

Table 10.8: Median daily energy intakes as a percentage of reasonable range of intake (RRI) over time during stay. Groups have been compared to each other at each time point using the Kruskal-Wallis test, with p values <0.05 highlighted in bold. (IQR-interquartile range)

	Week 1		Week 2		Week 4		Week 6		36 Weeks	
	n	Median Daily Protein as %RRI/d (IQR)	n	Median Daily Protein as %RRI/d (IQR)	n	Median Daily Protein as %RRI/d (IQR)	n	Median Daily Protein as %RRI/d (IQR)	n	Median Daily Protein as %RRI/d (IQR)
A. Pre-implementation period (January 1st – July 31st 2011)	51	62.8 (53.2 – 72.8)	46	89.4 (96.9 – 96.9)	41	85.4 (71.3 – 98.2)	31	96.8 (81.1 - 100)	25	92.9 (77.7 - 100)
B. Partial implementation period (August 1st – December 31st 2011)	34	66.6 (54.7 – 73.3)	30	89.1 (93.7 – 93.7)	26	90.7 (81.8 – 100)	17	86.5 (78.2 - 100.7)	17	93.1 (85.4 - 100.9)
C. Main Intervention Period (January 1st – December 31st 2012)	72	73.5 (61.8 – 77.9)	67	90.2 (96.4 – 96.4)	61	93.9 (83.1 – 100)	47	98.5 (87.1 - 101.7)	47	93.5 (77.6 - 102.2)
D. Post-implementation period (January 1st – June 30th 2013)	34	66.6 (51.5 – 74.3)	33	87.7 (93.4 – 93.4)	31	83.9 (76.1 – 99.2)	27	99.2 (91.3 - 101.9)	21	99.6 (93.6 - 101.9)
Kruskal–Wallis p value		**0.0092**		0.2485		0.1171		0.2516		0.333

Table 10.9: Median daily protein intakes as a percentage of reasonable range of intake (RRI) over time during stay. Groups have been compared to each other at each time point using the Kruskal-Wallis test, with p values <0.05 highlighted in bold. (IQR-interquartile range)

As per the statistical analysis protocol (Appendix 2), only variables where the Kruskal-Wallis test had demonstrated significant differences between groups were subject to closer inspection using pairwise Mann-Whitney U tests. These were carried out for energy (kcal/kg/day), protein (g/kg/day), energy as a percentage of RRI and protein as a percentage of RRI respectively, and are shown in table 10.10.

	p value for pairwise differences using Mann-Whitney U test				
	Week 1				Week 2
	Median Daily Energy kcal/kg/d (IQR)	Median Daily Protein kcal/kg/d (IQR)	Median Energy as %RRI per day (IQR	Median Protein as %RRI per day (IQR	Median Daily Energy kcal/kg/d (IQR)
A vs B	0.1784	0.3602	**0.0108**	0.3602	0.323
A vs C	0.1048	**0.0011**	**0.0001**	**0.0011**	0.0623
A vs D	0.1295	0.5842	0.713	0.5842	**0.008**
B vs C	0.9514	0.0554	0.6022	0.0554	0.601
B vs D	**0.0443**	0.8157	**0.0191**	0.8157	0.0959
C vs D	**0.0072**	0.0529	**0.001**	0.0529	0.0791

Table 10.10: Results of pairwise comparisons between groups at time points with significant differences between groups according to the Kruskal-Wallis test. p values<0.05 have been highlighted in bold (IQR-interquartile range)

Period C (the main intervention period, January-December 2012) had significantly higher intakes of energy as a percentage of RRI and protein (both when expressed as raw values and as a percentage of RRI) during week 1 when compared to the pre-implementation period (A). Of note, also during week 1, energy intakes (both when expressed as raw values and as a percentage of RRI) were significantly lower in the post implementation period (D) than in the partial implementation period (B) or the main intervention period (C). Energy intakes as a percentage of RRI were also significantly higher in week 1 in the partial implementation period (B) than in the pre-implementation period (A).

10.3.1.4 Growth by week across stay

Growth across stay, expressed as the change in SDS for weight and head circumference during stay for each infant, was summarised using means and

standard deviations at each time point, and then compared between study groups using Analysis of Variance (ANOVA). Figures 10.4A and B show the mean difference in SDS between birth and discharge for weight and head circumference respectively. These show a similar pattern of growth in each study group across time. Further details are provided in tables 10.11 and 10.12 for weight and head circumference respectively, together with the p values of difference across groups for weight and head circumference, demonstrating that there were no significant differences between groups at each time point for both weight and head circumference.

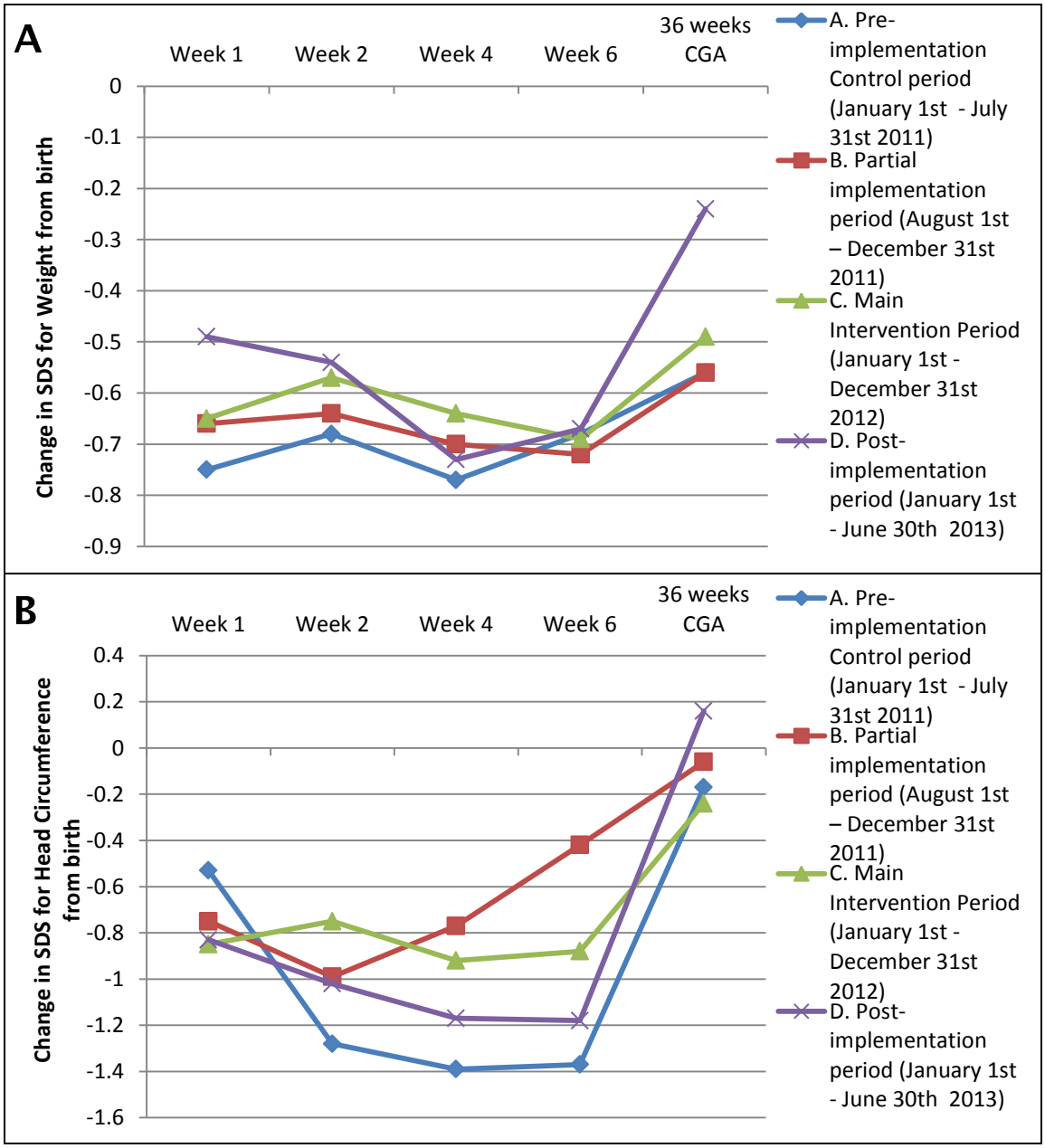


Figure 10.4 Line charts showing the mean change in SDS for weight (A) and head circumference (B) from birth over time during stay, across study groups. (SDS-standard deviation score)

	Week 1		Week 2		Week 4		Week 6		36 Weeks	
	n	Difference in SDS for Weight from Birth (SD)	n	Difference in SDS for Weight from Birth (SD)	n	Difference in SDS for Weight from Birth (SD)	n	Difference in SDS for Weight from Birth (SD)	n	Difference in SDS for Weight from Birth (SD)
A. Pre-implementation period (January 1st – July 31st 2011)	41	−0.75 (0.36)	44	−0.68 (0.35)	40	−0.77 (0.53)	28	-0.68 (0.48)	24	-0.56 (0.64)
B. Partial implementation period (August 1st – December 31st 2011)	27	−0.66 (0.52)	27	−0.64 (0.49)	25	−0.7 (0.42)	27	-0.72 (0.48)	27	-0.64 (0.5)
C. Main Intervention Period (January 1st – December 31st 2012)	64	−0.65 (0.41)	66	−0.57 (0.42)	60	−0.64 (0.54)	64	-0.69 (0.61)	64	-0.49 (0.65)
D. Post-implementation period (January 1st – June 30th 2013)	34	−0.49 (0.38)	32	−0.54 (0.42)	30	−0.73 (0.46)	34	-0.67 (0.59)	34	-0.24 (0.51)
ANOVA p value		0.1765		0.0548		0.7226		0.995		0.161

Table 10.11: Mean change in weight standard deviation score (SDS) from birth over time during stay, across all four study periods. Groups have been compared to each other at each time point using ANOVA, with p values <0.05 highlighted in bold. (SD-standard deviation)

	Week 1		Week 2		Week 4		Week 6		36 Weeks	
	n	Difference in SDS for Head Circum-ference from Birth (SD)	n	Difference in SDS for Head Circum-ference from Birth (SD)	n	Difference in SDS for Head Circum-ference from Birth (SD)	n	Difference in SDS for Head Circum-ference from Birth (SD)	n	Difference in SDS for Head Circum-ference from Birth (SD)
A. Pre-implementation period (January 1st – July 31st 2011)	7	−0.53 (0.36)	16	−1.28 (0.87)	11	−1.39 (0.88)	9	-1.37 (0.79)	6	-0.17 (0.21)
B. Partial implementation period (August 1st – December 31st 2011)	11	−0.75 (0.66)	16	−0.99 (0.67)	13	−0.77 (0.59)	8	-0.42 (0.81)	8	-0.06 (0.42)
C. Main Intervention Period (January 1st – December 31st 2012)	28	−0.85 (0.59)	54	−0.75 (0.72)	43	−0.92 (0.95)	7	-0.88 (0.81)	33	-0.24 (1.06)
D. Post-implementation period (January 1st – June 30th 2013)	15	−0.83 (0.8)	24	−1.02 (0.81)	20	−1.17 (1.13)	18	-1.18 (1.45)	13	0.16 (0.82)
ANOVA p value		0.5486		0.0838		0.3318		0.1997		0.6325

Table 10.12: Mean change in head circumference standard deviation score (SDS) from birth over time during stay, across all four study periods. Groups have been compared to each other at each time point using ANOVA, with p values <0.05 highlighted in bold. (SD-standard deviation)

10.3.1.5 Comparison of infant outcomes between 2009 and 2011

Data were collected on all VLBW infants born in 2009 to provide a baseline for development of the study intervention. Table 10.13 shows a comparison of the primary outcomes between 2009 and the 2011 pre-implementation period (A). There were statistically significant increases in intakes of energy and protein during the intervening interval between the two study periods despite no specific nutritional interventions or changes in practice during that period. No significant improvement was seen in weight gain or head growth.

	Historical 2009 Cohort (1st Jan- 31st Dec 2009)	Pre-implementation period (1st Jan- 31st July 2011)	p value
Number of infants	63	51	N/A
Median Daily Energy Intake kcal/kg/day (IQR)	114.7 (100.1 – 124.9)	119.4 (108.4 – 128.2)	**0.024**
Median Daily Protein Intake g/kg/day (IQR)	2.76 (2.26 – 3.11)	2.96 (2.69 – 3.36)	**0.039**
Median Daily Energy Intake as %RRI per day (IQR)	96 (88.6 – 104.1)	99.4 (94.7 – 110.9)	**0.004**
Median Daily Protein Intake as %RRI per day (IQR)	76.3 (62.6 – 83.2)	81.4 (73.3 – 90.9)	**0.002**
Difference in SDS for Weight between Birth and Discharge (SD)	-1.02 (0.79)	-0.73 (0.55)	0.236
Difference in SDS for Head Circumference between Birth and Discharge (SD)	-0.72 (1.6)	-0.55 (0.99)	0.987

Table 10.13: Median nutrient intakes for energy and protein and mean changes in SDS for weight and head circumference between birth and discharge in 2009 compared to the 2011 pre-implementation period. p values are from Mann-Whitney U tests for nutrient intakes, and t tests for growth. p values less than 0.05 are highlighted in bold (IQR- interquartile range, RRI- reasonable range of intake, SD-Standard deviation).

10.3.1.6 Summary of results for Non-repeated measures outcomes

The above results suggest that during the main intervention period (C) there was an increase in protein intake compared to both the pre-implementation period (A) and the partial implementation period (B). These changes were significant when looking at protein intakes as a percentage of RRI. To a lesser extent, protein intakes were also higher during the post-implementation period (D) than the periods prior to the main implementation period (A and B), although these changes were not statistically significant. Energy intakes were essentially static across the pre and main implementation periods (A to C), but seemed to fall away slightly during the post-implementation period (D). Again this change was statistically significant when looking at energy intakes as a

percentage of RRI. The difference in SDS for weight between birth and discharge appeared to improve across sequential study periods, going from -0.73 in group A, to -0.34 in group D. However, differences between study periods were only statistically significant for group A compared to D. The difference in SDS for head circumference between birth and discharge essentially remained unchanged across study periods.

Looking at nutrient intakes at weekly time points during stay, it appears that the main intervention period (C) was associated with an increase in protein intake across stay, particularly in the first week of life. This difference was significant in the first week of life compared to the pre-implementation period (A). The pattern of intake for energy and protein across stay appears very similar in both the pre-implementation group (A) and the post-implementation group (D), suggesting that the improvements seen in the intervention period were not sustained. Otherwise, energy intakes across stay were essentially similar between study periods beyond the first 2 weeks of life. Whilst there appears to be some improvements in the difference in SDS from birth to 36 weeks CGA in groups D, these differences were not statistically significant, and the pattern of growth for both weight and head circumference across stay was similar in each study period.

Comparing infant outcomes during the 2009 cohort that was studied prior to the development of the intervention to the 2011 pre-implementation period (A) demonstrates significant improvements in protein and energy intake that occurred in the absence of any specific intervention.

10.3.2 Interrupted time series analysis

10.3.2.1 Nutrient Intakes over time

In order to better visualise the changes in energy and protein intakes and growth the data were analysed using interrupted time series analysis (ITS). This technique involves carrying out segmented linear regression across each time period, and then comparing the intercepts (step change) and gradients (rates of change) between time periods. In order to do this, the mean nutrient intakes and change in standard deviation scores for growth were summarised for each week of the study. Initially, this analysis was performed with removal of the days of stay for infants which overlapped into an adjacent (subsequent) study

period, in order to ensure they did not influence the analysis of the later period. Furthermore, the 'interruption points' selected as the cut off between one study period and the next were chosen as the actual dates when each period was deemed to have started from.

However, this approach led to several difficulties. Excluding the days of stay of infants who were born in one study period but still being cared for in the next meant that only recently born infants were being included at the start of each study period. This led to an effect where nutrient intakes and growth appeared to drop suddenly at the start of each study period, as recently born infants receive less nutrition during the first one to two weeks of life (due to both lower RRIs and difficulties in supplying in this early period) and gain weight more slowly during this period[220]. This problem is illustrated in figure 10.5, which shows protein intakes across the study dropping sharply at the start of each period compared to the last.

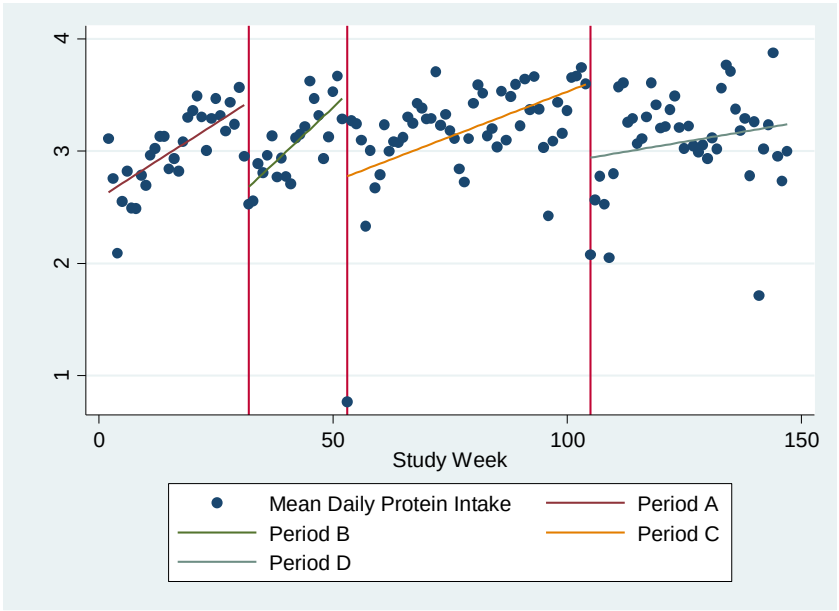


Figure 10.5: Initial erroneous interrupted time series analysis segmented regression plots with removal of days of infants whose care overlapped adjacent study periods, showing mean daily protein intakes across the study periods Red verticle lines separate the study periods, with the red, green, orange and blue regession lines representing study periods A, B, C and D respectively.

Therefore, the days of stay of infants who overlapped study periods were re-included, assigning them to the appropriate study period based on the date of each day of stay, to try and remove this effect. However, the effect still remained for period A, at the start of the study, as all infants initially included were newly born. Figure 10.6 shows a revised plot of protein intakes across the

course of the study, with the originally excluded study days re-included as described above which demonstrates that whilst the drop between study periods has been minimised, there is still a steeply increasing pattern of intake over the first few weeks of period A, partly due to the fact that the initial infants are all newly born.

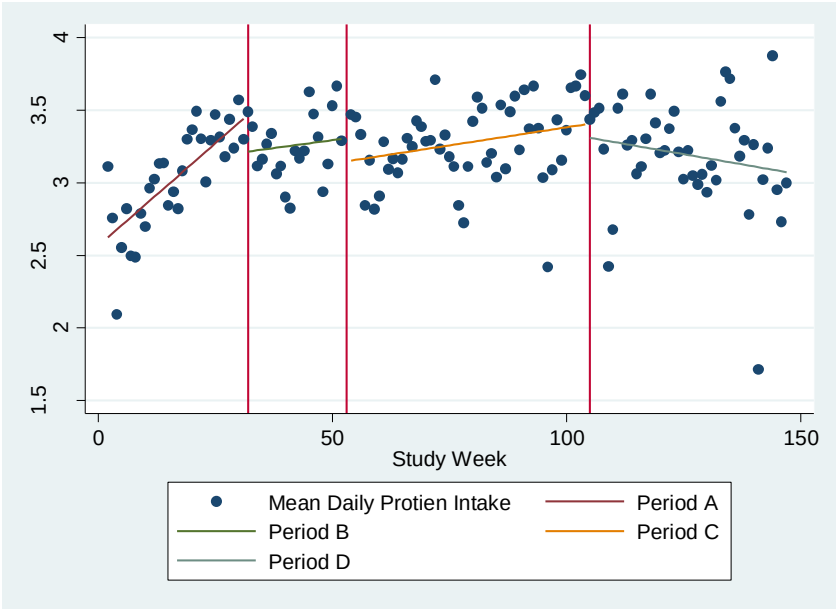


Figure 10.6: Initial erroneous interrupted time series analysis segmented regression plots with inclusion of days for infants whose care overlapped adjacent study periods, showing mean daily protein intakes across the study periods The red verticle lines separate the study periods, with the red, green orange and blue regession lines representing study periods A, B, C and D respectively.

In order to try and minimise this effect of newly born infants, and also to try and build up a more accurate picture of the study changes over time, the following changes were made to the dates which defined each study period, and the corresponding 'interruption points':

- The first two months were removed from period A to reduce effect of newly born infants with increasing intakes without existing infants present (as is the case for other periods).
- The data beyond six months post implementation were also removed, in order to reduce a similar effect of infants at the end of the study, with increasing intakes and growth of infants as they matured, whilst other infants are discharged and no newly born infants are being added to the study group. (approximately two months of data dropped)

- Period B (partial implementation) was given a one month run-in period to allow for the time taken to transition over to the new PN and feed formulations, meaning that the interruption point between periods A and B was moved from 1st August 2011 to 1st September 2011.
- Period C (the main intervention period) was also given a two month run in period to allow new guidelines to be introduced and be used in practice. This meant that the interruption point between periods B and C was moved from 1st January 2012 to 1st March 2012

This meant that for the purposes of ITS analysis, the study periods looked as follows:

- Period A = March to August 2011 inclusive (6 months)
- Period B = September 2011 to February 2012 inclusive (6 months)
- Period C = March 2012 to December 2012 inclusive (10 months)
- Period D = January to June 2013 inclusive (6 months)

With this analysis method, it is not possible to adjust for other factors such as birth weight and gestational age. However, by looking at the intakes as a percentage of RRI, this will allow for some adjustment, as RRIs are different depending on whether infants are less than 1000g at birth or 1001 to 1500g.

Figures 10.7A-D show the segmented regression plots of mean daily intake for each of energy (kcal/kg/day), protein (g/kg/day), energy (a percentage of RRI) and protein (as a percentage of RRI) respectively. For all four outcome variables, period A (the pre-implementation period) appears to be the period where the most substantial rate of change occurred. After this, it can be seen that energy intakes remain relatively static overall across period B and C, with a fall in intake during period D, similar to that seen in the non-repeated measures analysis above. For protein there is a gradual small trend of increasing intakes across periods B and C, particularly when looking at protein intake as a percentage of RRI. Again there is a slight fall in protein intakes during period D, although itappeared to remain higher than at the start of the study during period A. The full models used in this analysis are presented in Appendix 14.

Table 10.14 provides detailed results of the interrupted time series analysis, showing the magnitude of the step change between each time period, together with the difference in the gradients of the regression lines for each adjacent time period. Negative values represent a fall in mean nutrient delivery (step change) from the preceding period, or a fall in the rate of increase in intakes over time (gradient difference). The table also give the Durbin Watson (DW) statistic for each regression line; this is a measure of the degree of autocorrelation, with a value substantially less than 2 suggestive of significant autocorrelation. It can be seen that the majority of the DW values in the table are around 1.5 or less, indicating significant autocorrelation. This has been adjusted for using the Prais-Winsten method, which transforms the data to adjust for and reduce the amount of any autocorrelation present. A transformed DW statistic (TDW) is given for each regression, demonstrating that in most cases new TDW value is much closer to 2, indicating that there has been a degree of compensation for autocorrelation (although it is noteworthy that the DW can be as high as 4, indicating some autocorrelation still exists even after transformation by the Prais-Winsten method). The table demonstrates that the only significant changes in the interrupted time series analysis for nutrient intakes were:

1. A fall in the mean daily energy delivered in kcal/kg/day between time period A and B (indicated by the significant negative difference in step change). Note that this was not apparent when looking at energy as a percentage of RRI
2. A fall in the mean daily protein delivered in g/kg/day between each time period A and B (indicated by the significant negative difference in step change). Note that this was also apparent when looking at protein as a percentage of RRI.

There was also a near significant decrease in the gradient for protein intake (rate of protein intake increase) in both g/kg/day and as a percentage of RRI between periods A and B (i.e. mean protein intakes appear to fall and the increase more slowly in period B compared to A).

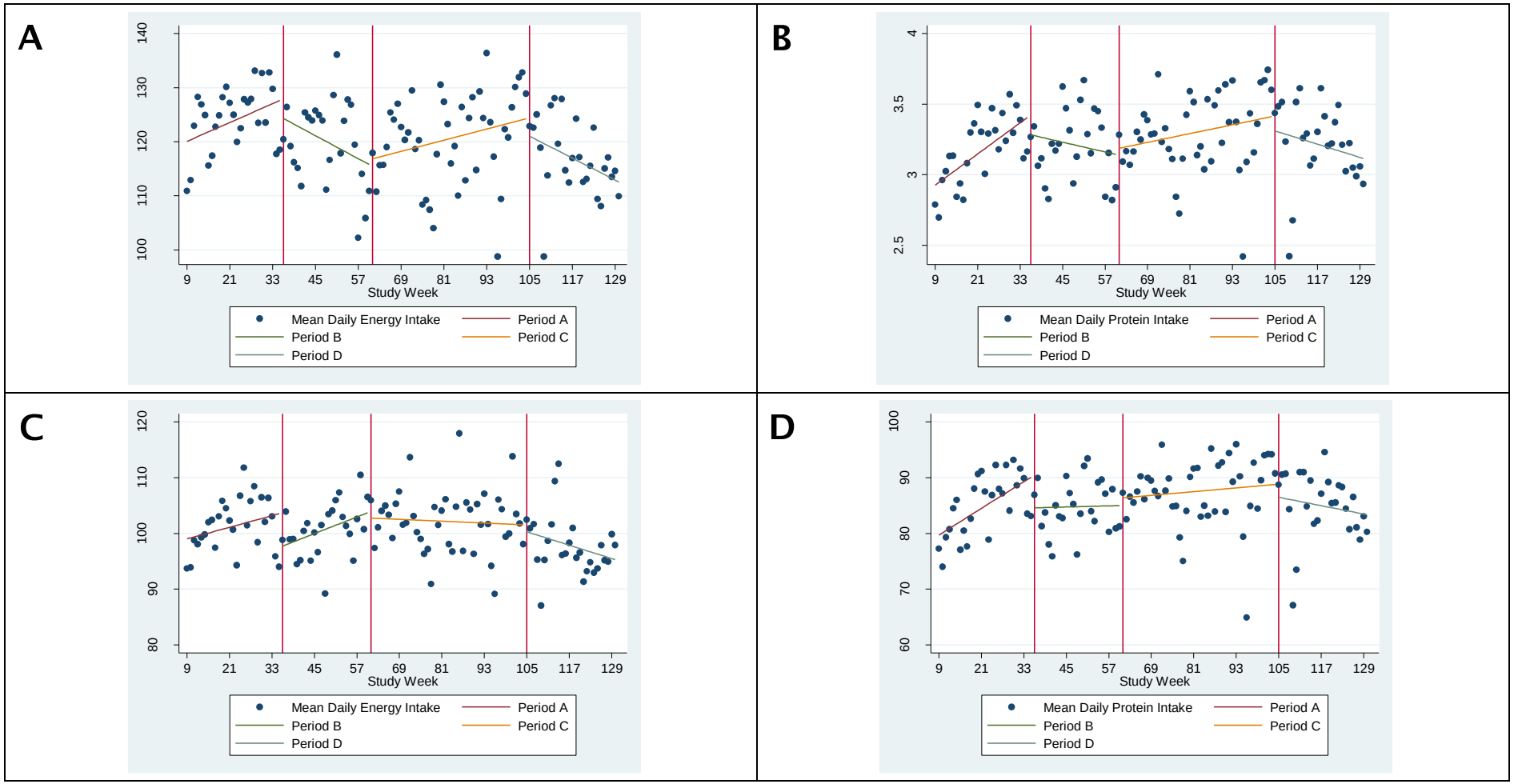


Figure 10.7: Interrupted time series analysis segmented regression plots (after adjustment for autocorrelation using the Prais-Winsten method) showing mean daily nutrient intakes across the entire study for energy in kcal/kg/day (A), protein in g/kg/day (B), energy as a percentage of RRI (C) and protein as a percentage of RRI (D). The red verticle lines separate the study periods, with the red, green orange and blue regession lines representing study periods A, B, C and D respectively. (RRI- reasonable range of intake)

	Comparison	Step Change (95%CI)	p value	Gradient Difference (95%CI)	p value	DW	TDW
Mean Daily Energy Delivered (kcal/kg/day)	A vs B	-3.62 (-13.30 to 6.07)	**0.044**	-0.65 (-1.36 to 0.07)	0.077	1.21	1.86
	B vs C	1.98 (-0.05 to 13.03)	0.884	0.48 (-0.23 to 1.19)	0.185	1.15	1.42
	C vs D	-3.39 (-13.23 to 6.46)	0.323	-0.51 (-1.13 to 0.11)	0.103	1.25	1.93
Mean Daily Energy Delivered (%RRI)	A vs B	-5.98 (-11.53 to -0.43)	0.13	0.08 (-0.30 to 0.45)	0.691	1.74	1.93
	B vs C	-1.38 (-6.78 to 4.03)	0.935	-0.28 (-0.60 to 0.04)	0.085	1.92	1.98
	C vs D	-1.23 (-7.33 to 4.86)	0.33	-0.17 (-0.54 to 0.19)	0.348	1.65	1.94
Mean Daily Protein Delivered (g/kg/day)	A vs B	-0.14 (-0.46 to 0.18)	**0.012**	-0.02 (-0.05 to 0.001)	0.052	1.2	1.86
	B vs C	0.08 (-0.28 to 0.44)	0.413	0.01 (-0.01 to 0.03)	0.409	1.19	1.94
	C vs D	-0.11 (-0.46 to 0.25)	0.376	-0.01 (-0.04 to 0.01)	0.257	1.17	1.8
Mean Daily Protein Delivered (%RRI)	A vs B	-5.88 (-11.97 to 0.20)	**0.043**	-0.38 (-0.81 to 0.04)	0.077	1.56	1.87
	B vs C	1.48 (-5.49 to 8.45)	0.916	0.03 (-0.40 to 0.45)	0.907	1.45	1.92
	C vs D	-2.35 (-9.84 to 5.14)	0.377	-0.18 (-0.64 to 0.28)	0.434	1.34	1.85
Mean Change in Weight SDS from Birth	A vs B	-0.17 (-0.35 to -0.001)	0.192	-0.01 (-0.02 to 0.003)	0.138	1.41	2.02
	B vs C	-0.14 (-0.33 to 0.06)	0.923	-0.01 (-0.03 to 0.001)	0.068	0.86	1.87
	C vs D	0.12 (-0.15 to 0.38)	0.452	0.01 (-0.01 to 0.04)	0.191	0.72	1.98
Mean Change in Head Circumference SDS from Birth	A vs B	-0.29 (-1.36 to 0.78)	0.515	-0.06 (-0.14 to 0.01)	0.142	1.16	1.83
	B vs C	0.02 (-0.52 to 0.57)	0.777	-0.01 (-0.04 to 0.03)	0.601	1.15	2.06
	C vs D	0.02 (-0.74 to 0.79)	0.916	0.03 (-0.02 to 0.09)	0.253	0.7	2

Table 10.14: Detailed results of the interrupted time series analysis (linear regression with Prais-Winsten method) for nutrient intakes and growth over the course of the study, showing the size of the step change between adjacent study periods, and the difference in slope between periods. 'Differences' refer to the later study period minus the preceding one (so a negative value indicates a fall from the previous period). p values <0.05 are highlighted in bold. (RRI-reasonable range of intake, SDS-standard deviation score, DW-Durbin Watson statistic, TDW- transformed Durbin Watson statistic, CI-confidence interval)

10.3.2.2 Growth over time

Figure 10.8 shows the interrupted time series analysis segmented regression plots for growth, in terms of the change in weight (A) and head circumference (B) SDS from birth (A). Each data point is the mean change in SDS from birth for all the infants cared for on the neonatal unit in that particular week in time. It can be seen that the pattern for weight is one of a trend towards a small improvement in weight SDS over the course of the study. The change in head circumference SDS from birth appears to remain static over the entire study, around zero (ie no change from birth). It can be seen there is a negative, downward slope for the change in SDS for both weight and head circumference during the main intervention period C. Table 10.14 shows however that none of these changes (either step changes or gradient changes) are statistically significant between study periods

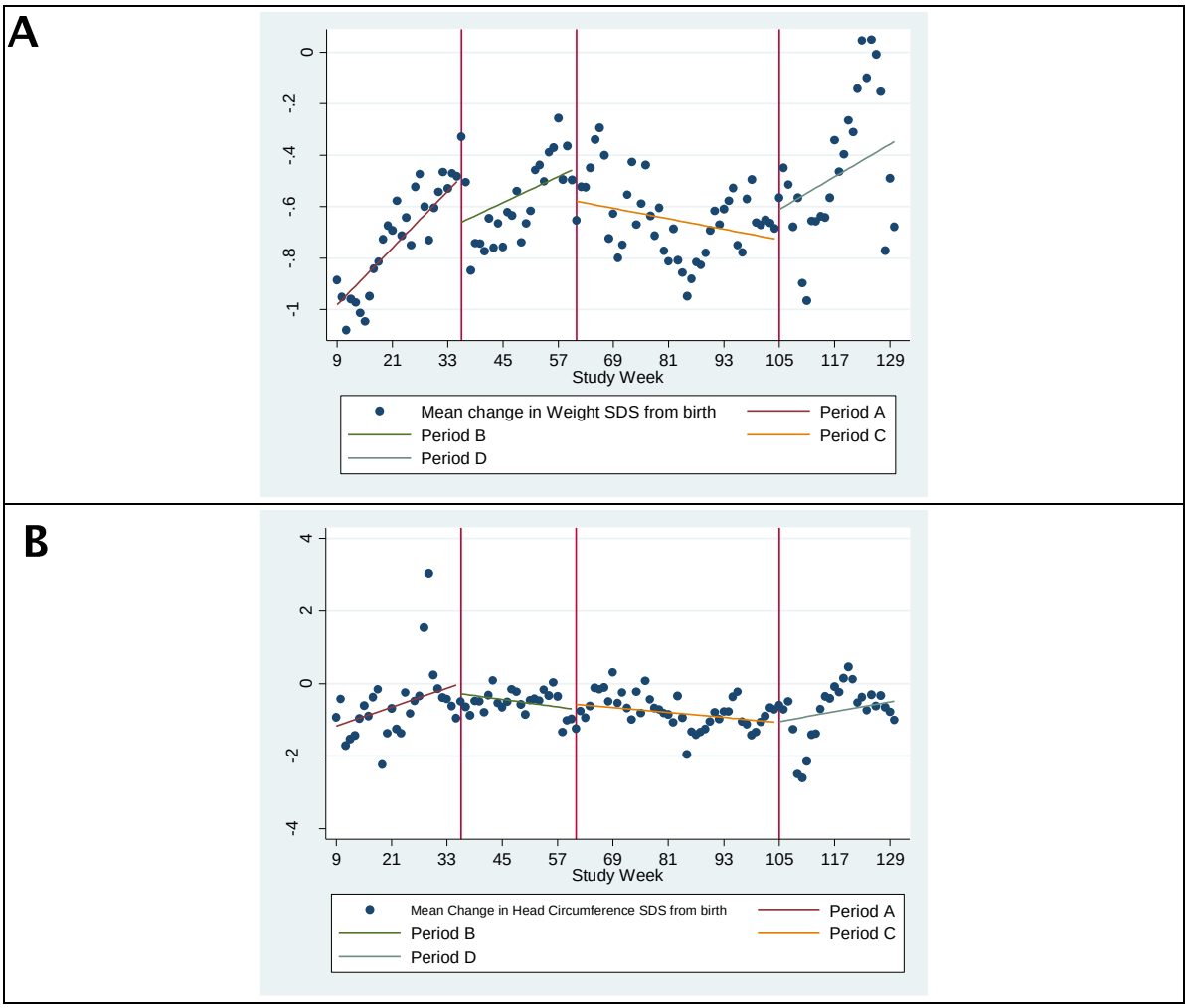


Figure 10.8: Interrupted time series analysis segmented regression plots (after adjustment for autocorrelation using the Prais-Winsten method) showing mean change in standard deviations scores (SDS) from birth across the entire study for weight (A) and head circumference (B). Red vertical lines separate the study periods, with the red, green orange and blue regression lines representing study periods A, B, C and D respectively.

10.3.2.3 Summary of Interrupted Time Series Analysis

While the only statistically significant findings were those suggestive of an initial fall in intake during the partial implementation period (B) compared to the pre-implementation period (A) that preceded it, visually, it can be seen from the figures above that the ITS analysis suggests a trend towards improved protein intakes across the partial implementation period (B), and to a greater extent in the main intervention period (C). At the same time there is a suggestion of a fall in both protein, and to a greater extent, energy intakes during the post-implementation period (D). Whilst there is some fluctuation, there is also a general overall trend towards improved weight gain over the course of the entire study. All these results are in keeping with the non-repeated measures analysis above which looked at the changes across the whole of each study period. It is of interest that even after making allowances during the analysis for the relative proportion of newly born infants early in the study described above, there was still a relatively steep rate of change towards increasing protein intakes and growth during the pre-implementation period. This may be suggestive of an underlying trend towards improved nutritional care prior to the formal implementation of any intervention.

A disadvantage of the method used here means that confounding factors such as sex, gestational age at birth and weight at birth could not be adjusted for, due to the need to aggregate data at each time point. This is important in a non-randomised study such as this one. It may be the case that a more comprehensive model needs to be used, without the need for any data reduction or summary variables, which also allows confounding factors to be accounted for. Such techniques will be used in the next section and the results discussed below.

10.3.3 Modelling using mixed effects for repeated measures data

A disadvantage of the interrupted time series analysis is that it still requires a degree of data aggregation, with infant's data summarised to generate one data point per time unit (in the case of the analysis above this was one week). Using a mixed effects modelling approach allows all data to be utilised, as this takes into account the repeated measures aspect of the data. This allows a

more representative model to be generated. Furthermore, interrupted time series analysis is not ideal for data that is not normally distributed, as is the case for the nutrient intake data, meaning that findings should be interpreted with caution. Whilst the *general* linear modelling approach used for the growth data also requires a normal distribution, using a *generalised* linear model allows an additional random element to be introduced to account for a non-normal distribution, so this approach was used for the nutrient intake data. The full models used in this analysis are presented in Appendix 15.

10.3.3.1 Nutrient Intakes over time

Figures 10.9A-D show the results of the generalised linear modelling analysis for median daily nutrient intakes for each of energy (kcal/kg/day), protein (g/kg/day), energy (as a percentage of RRI) and protein (as a percentage of RRI) respectively. The data for these figures is provided in table 10.15, whilst the differences between study periods are detailed in table 10.16. In all cases the result are provided both with and without adjustment for baseline population sex, gestational age and weight at birth. These results demonstrate that there were progressive increases in protein intake over the course of the study, with periods B, C and D all receiving significantly more protein (both in absolute terms and relative to RRI) compared to the pre-implementation period A. In addition, looking at protein intakes in g/kg/day, figure 10.9B demonstrates a significant increase in period D (the post-implementation period) compared to period B (the partial implementation period). Energy intakes essentially remained unchanged across study periods, though figure 10.9C shows that after adjustment for sex, gestational age and weight at birth, there was a significant fall in energy intakes as a percentage of RRI in period D compared to the pre-implementation period A and the intervention period C.

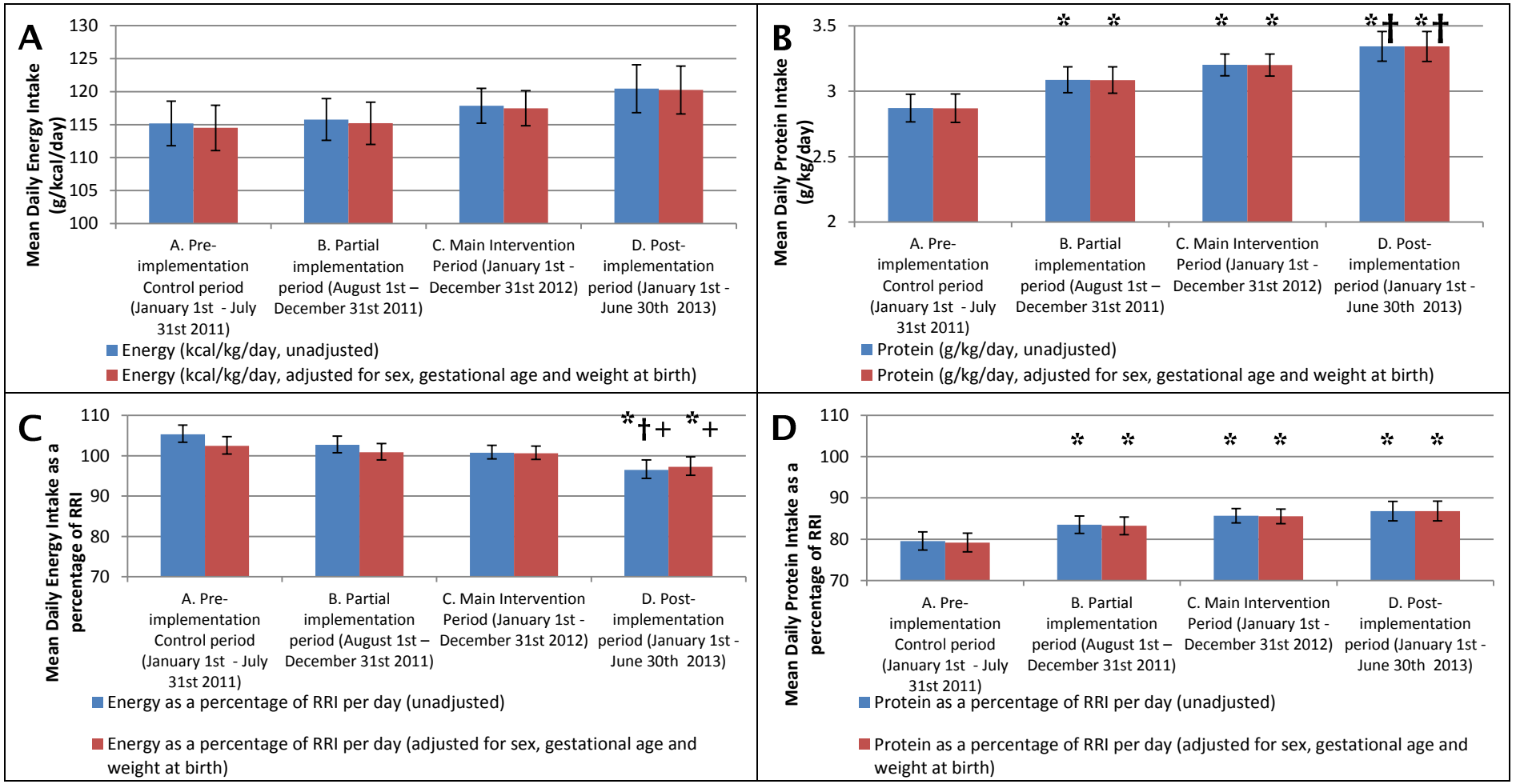


Figure 10.9: Bar graphs showing mean nutrient intakes based on the generalized linear model, across the four study periods for energy in kcal/kg/day (A), protein in g/kg/day (B), energy as a percentage of RRI (C) and protein as a percentage of RRI (D).Error bars represent 95% confidence intervals. Blue bars represent unadjusted data, while red bars are adjusted for sex, gestational age and weight at birth. *p<0.05 for difference vs period A, †p<0.05 for difference vs period B, +p<0.05 for difference vs period C. (RRI- reasonable range of intake)

		Mean Daily Energy Intake in kcal/kg/day (95% CI)		Mean Daily Protein Intake in g/kg/day (95% CI)		Mean Daily Energy Intake as a percentage of RRI (95% CI)		Mean Daily Protein Intake as a percentage of RRI (95% CI)	
Period	Degrees of Freedom	Unadjusted	Adjusted for sex, gestational age and weight at birth	Unadjusted	Adjusted for sex, gestational age and weight at birth	Unadjusted	Adjusted for sex, gestational age and weight at birth	Unadjusted	Adjusted for sex, gestational age and weight at birth
A. Pre-implementation period (January 1st – July 31st 2011)	10190	115.17 (111.79 to 118.54)	114.51 (111.07 to 117.96)	2.88 (2.77 to 2.98)	2.87 (2.76 to 2.98)	105.31 (103.00 to 107.61)	102.42 (100.45 to 104.39)	79.56 (77.35 to 81.77)	79.19 (76.92 to 81.45)
B. Partial implementation period (August 1st – December 31st 2011)	10190	115.77 (112.61 to 118.94)	115.21 (112.00 to 118.42)	3.09 (2.99 to 3.19)	3.09 (2.98 to 3.19)	102.69 (100.50 to 104.88)	100.86 (98.93 to 102.79)	83.53 (81.42 to 85.65)	83.25 (81.10 to 85.40)
C. Main Intervention Period (January 1st – December 31st 2012)	10190	117.87 (115.23 to 120.52)	117.49 (114.82 to 120.16)	3.20 (3.12 to 3.28)	3.20 (3.12 to 3.28)	100.75 (98.95 to 102.54)	100.58 (99.07 to 102.09)	85.70 (83.97 to 87.42)	85.53 (83.78 to 87.28)
D. Post-implementation period (January 1st – June 30th 2013)	10190	120.45 (116.83 to 124.07)	120.25 (116.61 to 123.89)	3.34 (3.23 to 3.46)	3.34 (3.23 to 3.46)	96.50 (94.03 to 98.98)	97.27 (95.18 to 99.36)	86.79 (84.42 to 89.17)	86.82 (84.42 to 89.22)

Table 10.15: Detailed Results of the generalized linear model with mixed effects for nutrient intakes across all 4 study periods. (RRI- reasonable range of intake, CI- confidence interval)

	Mean Difference in Daily Energy Intake kcal/kg/day				Mean Difference in Daily Protein Intake g/kg/day				Mean Difference in Daily Energy Intake as a percentage of RRI				Mean Difference in Daily Protein Intake as a percentage of RRI			
Comparison	Unadjusted	p value	Adjusted for sex, gestational age and weight at birth	p value	Unadjusted	p value	Adjusted for sex, gestational age and weight at birth	p value	Unadjusted	p value	Adjusted for sex, gestational age and weight at birth	p value	Unadjusted	p value	Adjusted for sex, gestational age and weight at birth	p value
A vs B	-0.601	0.986	-0.698	0.979	-0.216	**0.001**	-0.215	**0.001**	2.612	0.162	1.559	0.536	-3.971	**0.006**	-4.066	**0.005**
A vs C	-2.704	0.549	-2.974	0.47	-0.33	**<0.001**	-0.33	**<0.001**	4.559	0.007	1.843	0.431	-6.136	**<0.001**	-6.345	**<0.001**
A vs D	-5.279	0.143	-5.733	0.101	-0.472	**<0.001**	-0.473	**<0.001**	8.802	**<0.001**	5.149	**0.002**	-7.232	**<0.001**	-7.633	**<0.001**
B vs C	-2.103	0.638	-2.276	0.577	-0.114	0.169	-0.115	0.169	1.947	0.409	0.283	0.994	-2.165	0.283	-2.28	0.242
B vs D	-4.678	0.19	-5.035	0.144	-0.256	**0.003**	-0.257	**0.003**	6.19	**0.001**	3.59	0.058	-3.262	0.163	-3.568	0.113
C vs D	-2.575	0.543	-2.759	0.489	-0.142	0.087	-0.143	0.091	4.243	**0.01**	3.306	**0.031**	-1.096	0.837	-1.288	0.766

Table 10.16: Pairwise comparison of all study periods using the generalized linear model with mixed effects approach, showing difference between periods. P values <0.05 are highlighted in bold. Unadjusted differences are given together with differences adjusted for sex, gestational age and weight at birth. Tukey's method was used to adjust for multiple comparisons. (RRI- reasonable range of intake)

10.3.3.2 Growth over time

Figure 10.10 shows the results of the general linear model using mixed effects for the changes in weight and head circumference SDS in each study period (figures 10.10A and B respectively). These data are given in table 10.17, with details of the differences between study periods shown in table 10.18. This demonstrates that there was a sequential improvement in the difference in weight SDS between birth and discharge in each study period during the study, with a significant improvement (demonstrated by a smaller difference in weight SDS between birth and discharge) in periods B, C and D compared to A, and period C and D compared to B, and period D compared to C. With the exception of period D compared to C (p=0.056), these all remained significant after adjustment for sex, gestational age and weight at birth. Whist figure 10.10B suggests a similar trend to weight for head circumference, it can be seen from table 10.18 that there were no significant differences between any of the study periods.

10.3.3.3 Summary of repeated measures analysis

The analysis using linear modelling methods for repeated measures data suggests that the intervention was associated with sequentially improved protein intakes at each stage (partial, full and post-implementation, periods B to D respectively) compared to the pre-implementation period (A). These improvements were statistically significant. However, there were no significant differences between the partial and main intervention periods, raising the possibility that the elements of the intervention that were implemented first (mainly improved nutritional products) may have been solely responsible for the improvements seen across the study. There was a continued statistically significant improvement in protein intakes in period D (the post implementation period) compared to both the pre-implementation period (A) and partial implementation period (B), suggesting that the improvements were sustained beyond the main intervention period. There may also have been an additive effect of the main implementation on the partial implementation of the intervention. Energy intakes in kcal/kg/day seemed to increase sequentially across the study periods (not statistically significant), while energy intake as a percentage of RRI fell sequentially across study periods, with the

reduction becoming statistically significant by period D compared to periods A and C.

For the difference in weight SDS from birth, again there appeared to be a sequential improvement across study periods. All three implementation periods (partial, full and post) were significantly improved compared to the pre-implementation period. In addition the main intervention period had a significant positive change in weight SDS compared to the partial implementation period as did the post-implementation period. This is important as it suggests that whilst the partial implementation of the intervention led to some improvements in growth these were further improved on by the full intervention, and sustained in the post-implementation period.

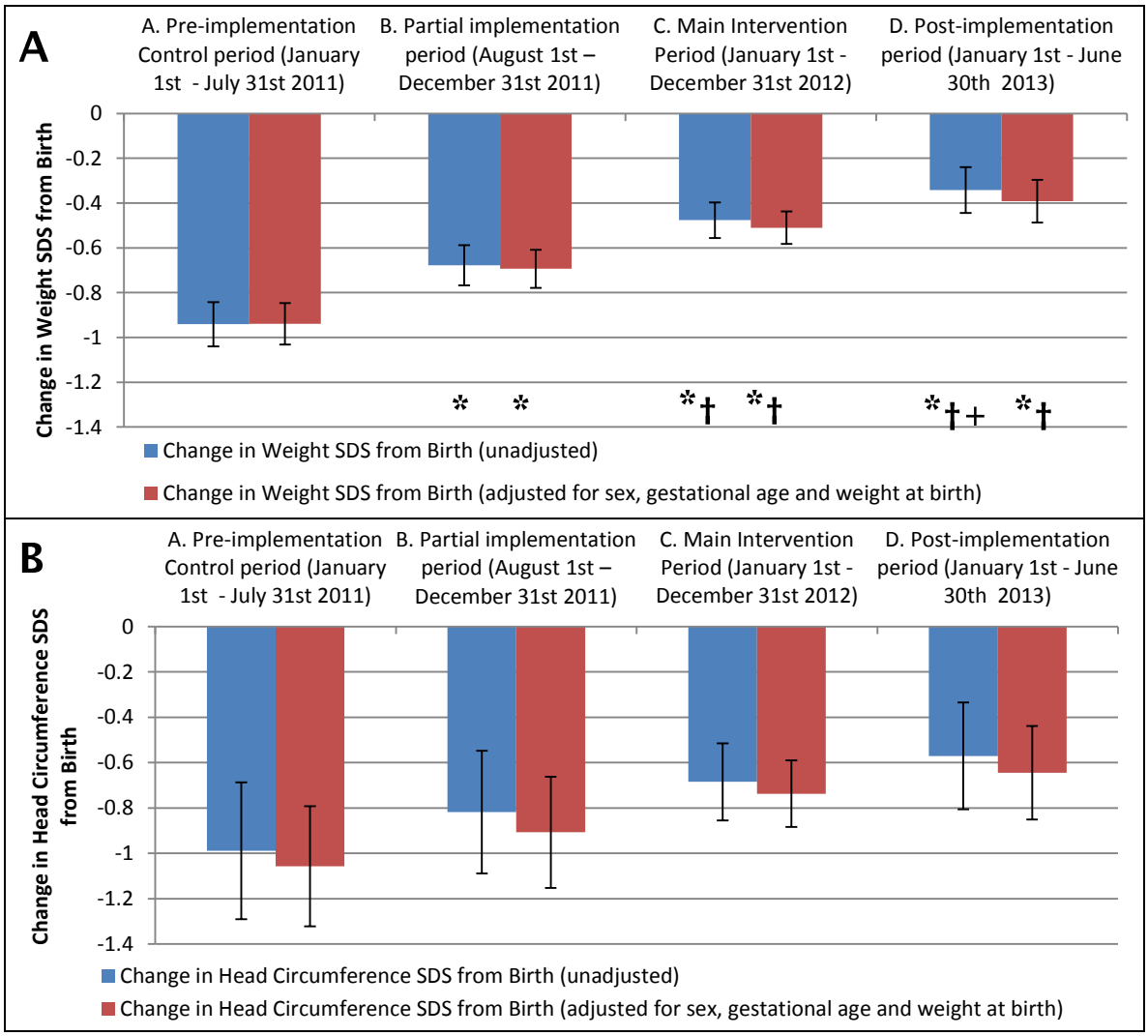


Figure 10.10: Bar graphs showing mean change in standard deviation score (SDS) between from birth based on the general linear model, across the four study periods for weight (A) and head circumference (B). Error bars represent 95% confidence intervals. Blue bars represent unadjusted data, whilst red bars are adjusted for sex, gestational age and weight at birth *p<0.05 for difference vs period A, †p<0.05 for difference vs period B, +p<0.05 for difference vs period C

	Mean Change in Weight SDS from birth (95% Confidence Interval)			Mean Change in Head Circumference from birth (95% Confidence Interval)		
Period	Degrees of Freedom	Unadjusted	Adjusted for sex, gestational age and weight at birth	Degrees of Freedom	Unadjusted	Adjusted for sex, gestational age and weight at birth
A. Pre-implementation period (January 1st – July 31st 2011)	3628	-0.941 (-1.040 to -0.842)	-0.939 (-1.032 to -0.847)	745	-0.989 (-1.290 to -0.687)	-1.0574 (-1.322 to -0.793)
B. Partial implementation period (August 1st – December 31st 2011)	3628	-0.677 (-0.767 to -0.587)	-0.693 (-0.778 to -0.609)	745	-0.819 (-1.089 to -0.548)	-0.908 (-1.153 to -0.662)
C. Main Intervention Period (January 1st – December 31st 2012)	3628	-0.476 (-0.556 to -0.397)	-0.510 (-0.583 to -0.437)	745	-0.685 (-0.855 to -0.515)	-0.738 (-0.884 to -0.591)
D. Post-implementation period (January 1st – June 30th 2013)	3628	-0.342 (-0.445 to -0.239)	-0.3911 (-0.4865 to -0.2957)	745	-0.571 (-0.807 to -0.335)	-0.645 (-0.851 to -0.434)

Table 10.17: Detailed Results of the general linear model with mixed effects for the change in standard deviation scores (SDS) during stay across all 4 study periods.

	Mean Change in Weight SDS from birth				Mean Change in Head Circumference SDS from birth			
Comparison	Unadjusted	p value	Adjusted for sex, gestational age and weight at birth	p value	Unadjusted	p value	Adjusted for sex, gestational age and weight at birth	p value
A vs B	-0.264	**<0.001**	-0.245	**<0.001**	-0.17	0.823	-0.15	0.83
A vs C	-0.465	**<0.001**	-0.429	**<0.001**	-0.304	0.305	-0.32	0.155
A vs D	-0.599	**<0.001**	-0.548	**<0.001**	-0.418	0.14	-0.413	0.077
B vs C	-0.201	**<0.001**	-0.184	**<0.001**	-0.134	0.796	-0.17	0.582
B vs D	-0.335	**<0.001**	-0.302	**<0.001**	-0.248	0.508	-0.263	0.363
C vs D	-0.134	**0.028**	-0.119	0.055	-0.114	0.827	-0.093	0.867

Table 10.18: Pairwise comparison of all study periods using the general linear model with mixed effects approach, showing difference between periods. P values <0.05 are highlighted in bold. Unadjusted differences are given together with differences adjusted for sex, gestational age and weight at birth. Tukey's method was used to adjust for multiple comparisons. (SDS-standard deviation score)

10.3.4 Mortality and Morbidity

Figure 10.11 shows the percentage of infants with each of chronic lung disease, necrotising enterocolitis (NEC), severe intraventricular haemorrhage (IVH), retinopathy of prematurity (ROP), late onset infection and infection with coagulase negative staphylococcus (CoNS). Table 10.19 gives the numbers for these outcomes together with mortality. Whilst the seven month pre-implementation period had no deaths, the mortality rate was around 8% for all other periods. The only statistically significant finding was for CoNS infection, which appeared to increase during the main intervention period (C).

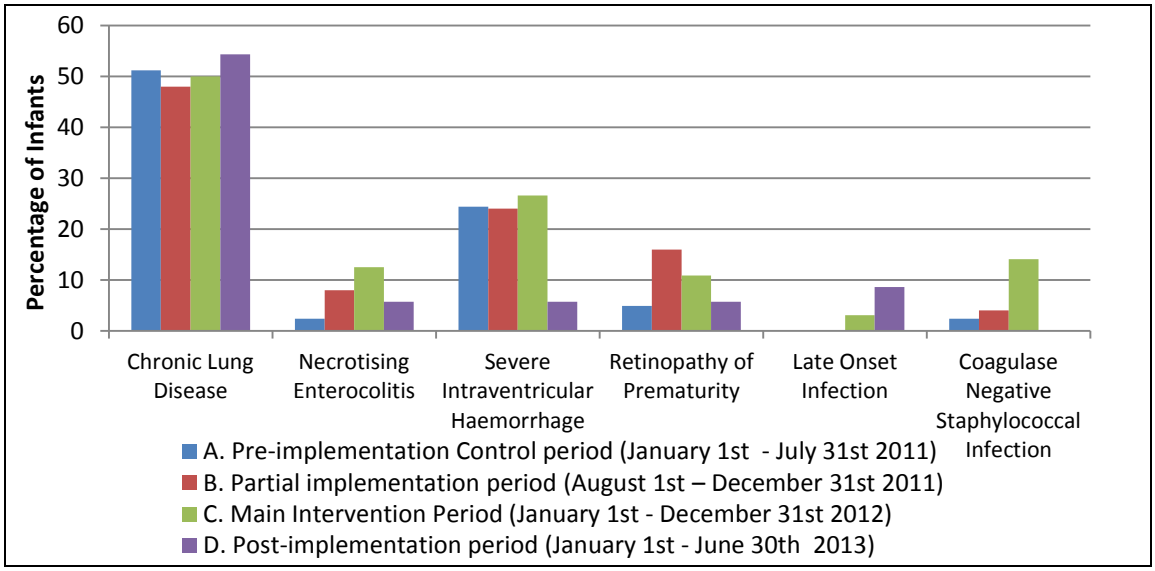


Figure 10.11: Percentage of infants with significant morbidities in each study period.

	Chronic Lung Disease	NEC	Severe IVH	ROP	Late Onset Infection	CoNS Infection	Mortality
A. Pre-implementation period (Jan 1st – Jul 31st 2011)	29 (44.6)	1 (2.4)	10 (24.4)	2 (4.9)	0 (0)	1 (2.4)	0 (0)
B. Partial implementation period (Aug 1st – Dec 31st 2011)	21 (51.2)	2 (8)	6 (24)	4 (16)	0 (0)	1 (4)	3 (8.33)
C. Main Intervention Period (Janu 1st – Dec 31st 2012)	12 (48)	8 (12.5)	17 (26.6)	7 (10.9)	2 (3.1)	9 (14.1)	6 (8%)
D. Post-implementation period (Jan 1st – Jun 30th 2013)	32 (50)	2 (5.7)	2 (5.7)	2 (5.7)	3 (8.6)	0 (0)	3 (8.57)
p value	0.966*	0.302	0.06	0.414	0.168	0.026	0.107

Table 10.19: Number (percent) of infants with major morbidities and mortality in each study period. Periods have been compared using Fisher's exact test, with the p value given in the table (expect *, which used Chi squared). (NEC- Necrotising Enterocolitis, IVH-Intraventricular Haemorrhage, ROP-Retinopathy of Prematurity, CoNS-Coagulase Negative Staphylococcus)

10.4 Overall Summary

This chapter has presented the results of the statistical analysis of the impact of the intervention on infant nutrient intakes and growth. Analysing such detailed individual infant level time series data has proved a challenge, but by using a series of increasingly complex methods it has been possible to try and build up a comprehensive picture of the changes in these outcomes over the course of the study. It has also allowed insight into which analytical method allows the most appropriate interpretation of the data. Non-repeated measures analysis is perhaps too crude, and over-simplifies the complex nature of the data. While ITS has theoretical advantages, it appears that in practice the analytical framework used for ITS analysis was not well suited to this kind of complex individual infant time series data. Figures 10.5 and 10.6 illustrate some of the issues with ITS with this data, and there are perhaps still some issues related to the effects demonstrated in these figures in the current analysis despite measures taken to account for them.

Overall, it seems that the repeated measures analysis accommodates the data here best, allowing for individual level infant analysis without the need for data reduction or summaries of infants, as was the case for the other two methods. It is reassuring that the findings from both the repeated and non-repeated measures analysis are fairly consistent. Table 10.20 gives a summary of these results, which will be discussed in detail in chapter 13, but in summary, while there are some differences in the results of the different analysis methods used, the intervention was associated with:

- **Improvements in protein intake**
  Protein intakes increased in an incremental fashion across the partial and full implementation periods and appear to have been sustained to a degree in the post-implementation period. Non-repeated measures analysis demonstrated significant improvements in protein intake in main intervention period compared to both the pre- and partial implementation periods. Similarly, repeated measures analysis demonstrated statistically significant improvements in protein intakes in all implementation periods compared to the pre-implementation period. ITS analysis appears to suggest a slight trend overall of increasing intake across study period over time, with some drop off in the post-implementation period.

- **Improvements in weight gain**
  There appears to be a reduction in the fall in SDSs for weight between birth and discharge incrementally across all study periods. Non-repeated measures analysis demonstrated a pattern of improved weight gain in the main and post-implementation periods, with a statistically significant change in the post implementation period compare to the pre-implementation period. ITS analysis also showed a similar trend over the course of the study overall. Repeated measures analysis demonstrated statistically significant reductions in the negative change in weight SDS in all implementation periods compared to the pre-implementation period, and also in the main and post implementation periods compared to the partial implementation period.

- **No significant improvements in head growth**
  No analysis methods found any significant benefits of the intervention on head growth, although repeated measures analysis shows a trend towards improvements over the course of the study

- **A reduction in energy intakes in the post implementation period**
  Non-repeated measures analysis demonstrated a significant fall in energy intake as a percentage of RRI during the post implementation period compared to the pre-implementation periods. A similar trend of gradually decreasing energy intake across the study periods in also seen in the ITS analysis. Repeated measures analysis also shows a significant reduction in energy intakes as a percentage of RRI in the post implementation period compared to both the pre- and main intervention periods.

The incremental nature of the changes suggest that partial implementation led to some of these improvements in isolation, raising the possibility that the partial implementation, which included improved nutritional products, may have been responsible for much of the improvements seen. However, the results also show that this was built on by the full implementation of the intervention, with the repeated measures analysis showing almost a 'dose–response' effect to the graded introduction of the intervention, suggesting than the guidelines and associated changes in practice were as important, if not more important that the improvements in nutritional products alone.

		A. Pre-implementation period (January 1st – July 31st 2011)	B. Partial implementation period (August 1st – December 31st 2011)	C. Main Intervention Period (January 1st – December 31st 2012)	D. Post-implementation period (January 1st – June 30th 2013)
Daily Energy Intake in kcal/kg/day	Non-repeated measures analysis	119.4	114.6	119.7	114.8
	Repeated measures analysis	115.2	115.8	117.9	120.5
Daily Energy Intake as a percentage of RRI	Non-repeated measures analysis	99.4	104.3	103.3	95.3
	Repeated measures analysis	105.3	102.7	100.8	96.5
Daily Protein Intake in g/kg/day	Non-repeated measures analysis	2.96	2.98	3.22	3.1
	Repeated measures analysis	2.87	3.09	3.2	3.34
Daily Protein Intake as a percentage of RRI	Non-repeated measures analysis	81.4	79.5	86.8	83.6
	Repeated measures analysis	79.6	83.5	85.7	86.8
Mean Change in Weight SDS between birth and discharge	Non-repeated measures analysis	-0.73	-0.74	-0.44	-0.34
	Repeated measures analysis	-0.94	-0.68	-0.48	-0.34
Mean Change in Head Circumference between birth and discharge	Non-repeated measures analysis	-0.55	-0.22	-0.38	-0.4
	Repeated measures analysis	-0.99	-0.82	-0.69	-0.57

Table 10.20: Summary of main results from non-repeated and repeated measures analysis (SDS-standard deviation score, RRI-Reasonable range of intake)

In relation to the reduction in energy intake as a percentage of RRI seen during the post-implementation period (D), one change of note during this period was the introduction of an new stock PN solution, 'Babiven start up', on 16th March 2013, as a replacement for the existing 'Preterm' stock PN. This change was made by our pharmacy to reduce wastage, as Babiven has a shelf life of 120 days compared to the 30 day expiry of the existing Preterm PN. Of note, Babvien contains less energy at 51kcal/100ml, compared to 63kcal/100ml of the existing stock preterm PN, This represents a reduction in energy content of 19%, which may be in part responsible for the reduced energy intake seen during 2013.This would also fit with the non-repeated measures analysis across each week of life (figure 10.3 and tables 10.6-9), which showed that

that the most significant fall in energy intake occurred during the first two weeks of life, where PN would be the main source of nutrition. It is also important to consider differences in case mix,; table 10.2 demonstrates that period D had higher CRIB II scores (indicating greater severity of illness) and a greater proportion of smaller infants (not statistically significant, p=0.066). This may also explain why there is reduction in energy intakes as a percentage of RRI despite an apparent increase in intakes in terms of kcal/kg/day. RRIs are higher for infants less than 1000g so therefore a group with a higher proportion of such infants will have higher mean energy needs as a group. Data for morbidity and mortality showed variation across the study periods, but numbers were small and only statistically significant finding was for CoNS infection. However, it is important to note that this study was not, and is not, powered to detect differences in these outcomes.

Taking the comparison of the 2009-born infants to the 2011 pre-implementation period (table 10.13 above) together with pattern of intakes seen during the 2011 pre-implementation period in the ITS analysis, suggests that there may have been an underlying trend towards improved nutritional care during prior to any formal implementation of the intervention. This may be a genuine finding, perhaps because of an increasing awareness of nutrition on the unit due to the development of the present study during this period, or perhaps the result of other factors unrelated to this study, such as a changing national perspective (note the ESPGHAN guidance regarding nutrient intakes was published in late 2010). Comparing the incremental increases in protein and energy intakes across all five study periods (Tables 10.3 and 10.13), it can be seen that the increase in protein intake that occurred in the one year period between the 2011 pre-implementation period (A) and the main 2012 intervention period (C) are similar to those seen over the two year period between 2009 and 2011 (0.26 or 5.4% RRI vs 0.2g/kg/day or 5.1% RRI respectively. This suggests that whilst some improvements occurred in the absence of any intervention, they may have been enhanced by the intervention.

These results and related issues will be discussed further in chapter 13. The next chapter will look at the impact of the intervention on the processes of nutritional care, including the extent to which staff complied with the guidelines, and how well the new practices became embedded into routine care.

Chapter 11: Implementation Phase Results Part 2 – Process and Practice Outcomes Following Implementation

The previous chapter discussed the effect of the intervention on infant outcomes of nutrient intakes and growth. This chapter moves away from infant outcomes and focusses on the impact of the intervention on the processes of care and introduction of practices. This includes compliance with the guideline used in the study and markers of nutritional care processes such as the time of starting feeds and PN, and the choice and use of different types of feed. This chapter also focusses on the degree to which the new practices have become embedded in routine care, using measures obtained by the NPT toolkit based questionnaire. Finally this chapter will look at the relationship between measures of normalisation using NPT and the measures of clinical practice, particularly compliance with the nutrition guideline.

11.1 Changes in the Process of Care

As described in chapter 4, data on the time that PN, enteral feeds and breast milk fortifier (for infants receiving breast milk) were commenced were collected from clinical notes for all infants in the study. Figure 11.1 shows that the partial and full implementation periods (B and C) led to a reduction in the time to start PN compared to the pre-implementation period (A), with a slight increase again during the post-implementation period (D). Table 11.1 shows that there was a significant difference between study periods for this process measure using the Kruskal-Wallis test, and closer inspection of these results using pairwise Mann-Whitney U tests reveals that the significant differences appear to be between period C (the main intervention period) and the pre-implementation period A ($p=0.0276$), and between the main intervention period C and the post-implementation period D ($p=0.0362$). Interestingly, figure 11.1 also suggests a serial increase in the time to start feeds, though there appear to be no significant differences between study periods (table 11.1).. Similarly, there were no significant differences in the timing of introduction of breast milk fortifier between periods (figure 11.1 and table 11.1), suggesting that the intervention did not lead to earlier fortification.

Figure 11.2 shows the type of milk feed at discharge to any destination (A) and home (B). Use of breast milk and mixed feeds appears relatively stable across study periods, with a slight increase in the use of breast milk on discharge home in period D. There is a trend towards increased use of term formula with a corresponding reduction in the use of preterm formula. Tables 11.2 and 11.3 detail the numbers for feeding at discharge to any destination and home respectively, and show that there was no significant difference between study periods using Fisher's exact test.

Figure 11.3 and table 11.4 show that there was an increase in the use of fortifier in infants receiving breast milk in periods B–D compared to the pre-implementation period A, though comparison across study periods using Chi squared test showed that these differences did not reach significance (p=0.142).

Table 11.5 shows that length of stay sequentially reduced at each period from A to C, though increased again during period D. Comparison across periods using ANOVA showed that these differences did not reach significance (p=0.056).

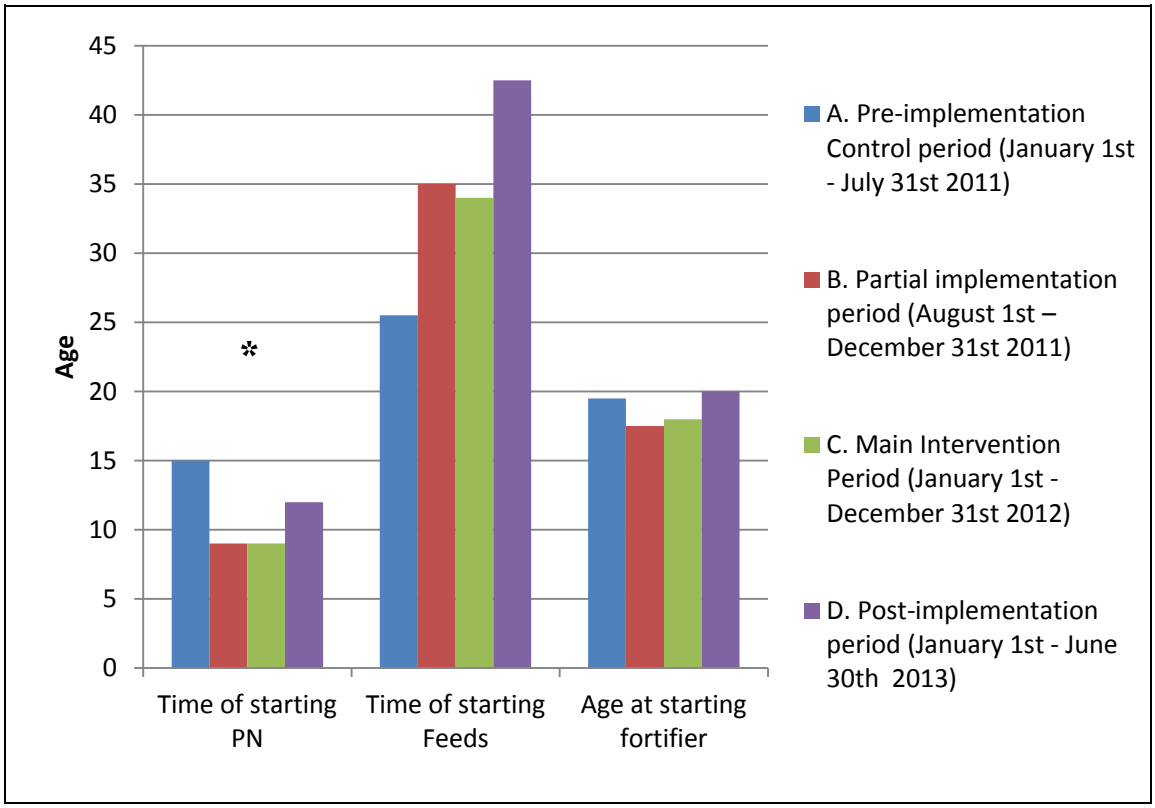


Figure 11.1: Median age at starting parenteral nutrition (PN), enteral feeds (in hours), and fortifier (days).*p<0.05 for difference between periods using Kruskal-Wallis test.

	Time of starting PN		Time of starting Feeds		Age at starting fortifier	
	Number of Infants	Median Age in Hours (IQR)	Number of Infants	Median Age in Hours (IQR)	Number of Infants	Median Age in Days (IQR)
A. Pre-implementation period (Jan 1st – Jul 31st 2011)	35	15 (8–30)	39	25.5 (19–74)	18	19.5 (18–28)
B. Partial implementation period (Aug 1st – Dec 31st 2011)	19	9 (6–23)	11	35 (26–56)	14	17.5 (12–26)
C. Main Intervention Period (Jan 1st – Dec 31st 2012)	63	9 (6–15)	63	34 (22–59)	39	18 (13–25)
D. Post-implementation period (Jan 1st – Jun 30th 2013)	33	12 (8–20)	34	42.5 (30–87)	22	20 (13–29)
Kruskal Wallis p value	**0.0131**		0.1877		0.6229	

Table 11.1: Median age in hours at starting parenteral nutrition (PN), enteral feeds, and fortifier. (IQR-interquartile range). P values<0.05 are highlighted in bold

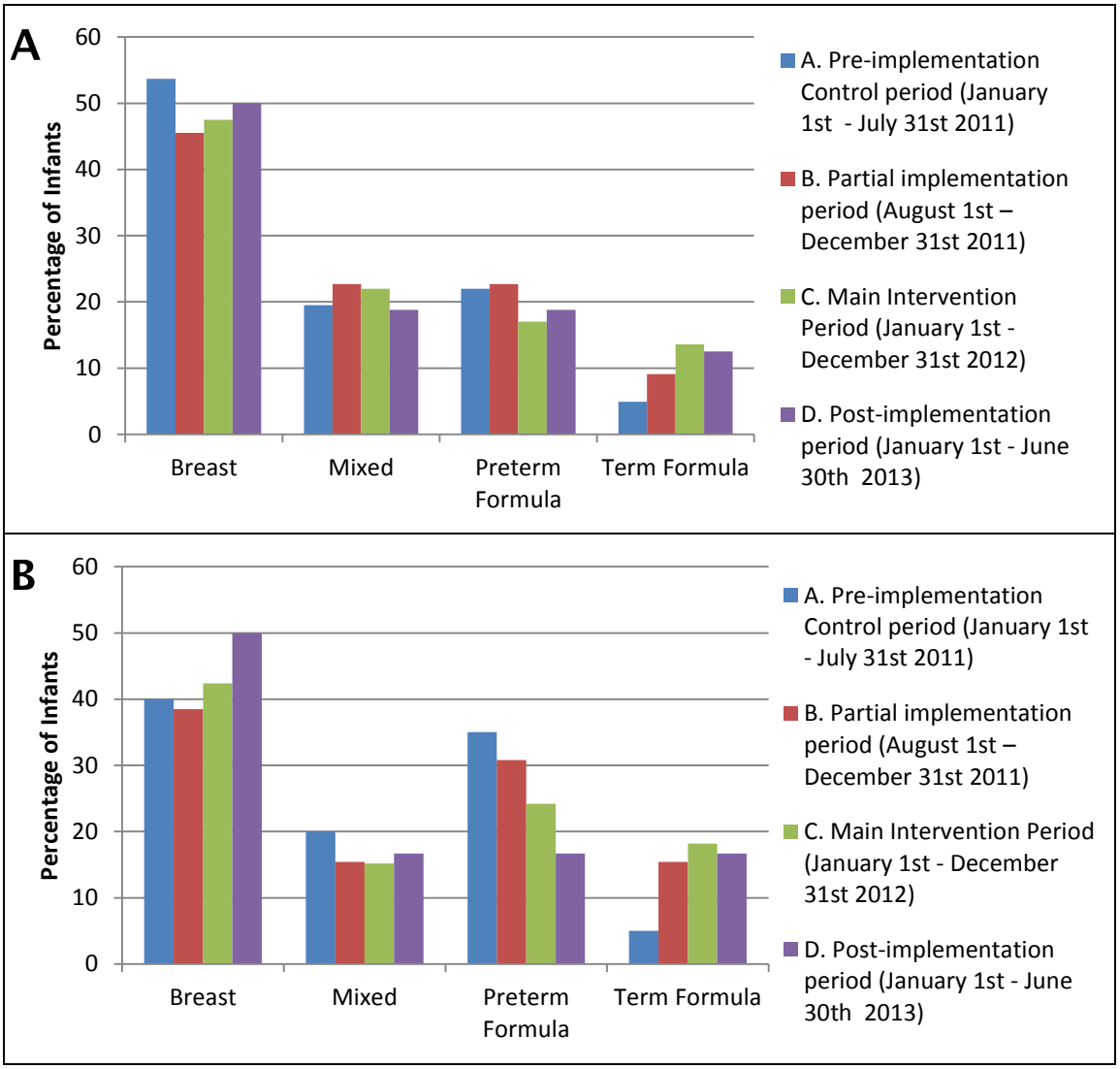


Figure 11.2: Type of milk feed at discharge to any destination (A) and home (B)

Period	Breast	Mixed	Preterm Formula	Term Formula
A. Pre-implementation period (January 1st – July 31st 2011)	22 (53.7)	8 (19.5)	9 (22)	2 (4.9)
B. Partial implementation period (August 1st – December 31st 2011)	10 (45.5)	5 (22.7)	5 (22.7)	2 (9.1)
C. Main Intervention Period (January 1st – December 31st 2012)	28 (47.5)	13 (22)	10 (17)	8 (13.6)
D. Post-implementation period (January 1st – June 30th 2013)	16 (50)	6 (18.8)	6 (18.8)	4 (12.5)

Table 11.2: Numbers (percentage) of infants on each type of milk feed at discharge (to any destination). Fisher's Exact for differences between periods, p=0.969

Period	Breast	Mixed	Preterm Formula	Term Formula
A. Pre-implementation period (January 1st – July 31st 2011)	8 (40)	4 (20)	7 (35)	1 (5)
B. Partial implementation period (August 1st – December 31st 2011)	5 (38.5)	2 (15.4)	4 (30.8)	2 (15.4)
C. Main Intervention Period (January 1st – December 31st 2012)	14 (42.4)	5 (15.2)	8 (24.2)	6 (18.2)
D. Post-implementation period (January 1st – June 30th 2013)	9 (50)	3 (16.7)	3 (16.7)	3 (16.7)

Table 11.3: Numbers (percentage) of infants on each type of milk feed at discharge home. Fisher's Exact for differences between periods, p=0.939

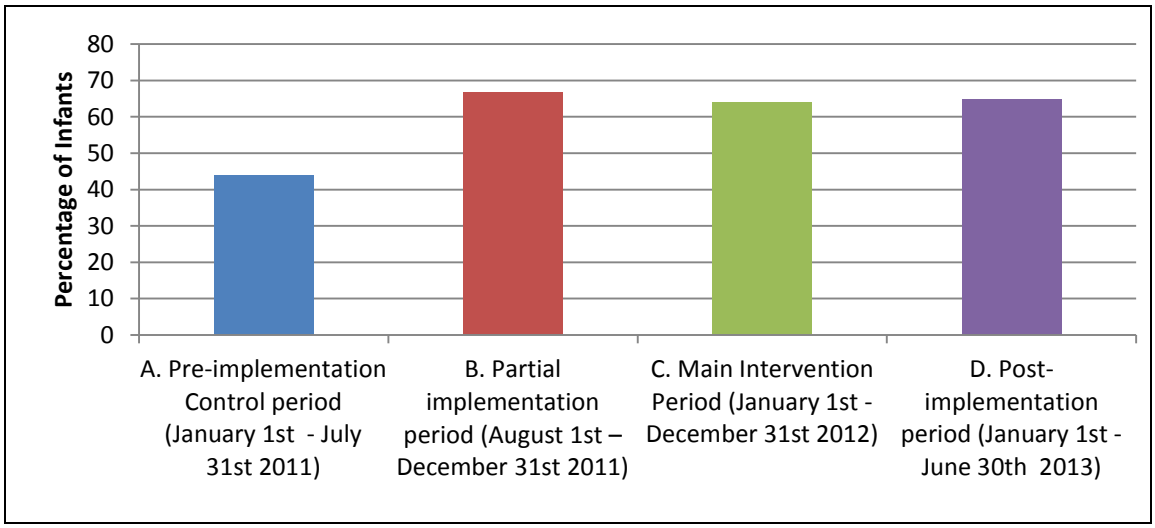


Figure 11.3 Percentage of infants who received fortifier if on maternal breast milk.

Period	Received Breast Milk Fortifier if on MBM
A. Pre-implementation period (January 1st – July 31st 2011)	18 (43.9)
B. Partial implementation period (August 1st – December 31st 2011)	14 (66.7)
C. Main Intervention period (January 1st – December 31st 2012)	39 (63.9)
D. Post-implementation period (January 1st – June 30th 2013)	22 (64.7)

Table 11.4: Number (percent) of who received fortifier if on maternal breast milk (MBM). Chi squared for difference between periods p=0.142

Period	Mean Length of stay (SD)
A. Pre-implementation period (January 1st – July 31st 2011)	65 (53.6)
B. Partial implementation period (August 1st – December 31st 2011)	41 (46.1)
C. Main Intervention period (January 1st – December 31st 2012)	25 (44.2)
D. Post-implementation period (January 1st – June 30th 2013)	64 (48.9)

Table 11.5: Mean length of stay in each study period. ANOVA for differences between periods=0.0564. (SD-standard deviation).

11.2 Adherence to Guideline

Guideline compliance audits using the method described in chapter 4 were carried out on a two monthly basis during the main intervention period in 2012 starting from the beginning of March, until the beginning of January 2013. A further audit was carried out following the end of the post-implementation period at the beginning of July 2013. Each audit was carried out on a single day, and data collected using the data collection tool in Appendix 4. Mean compliance across all seven audit periods is summarised in table 11.6. In addition, table 11.6 shows the mean compliance with just the measures of the audit that assessed the processes of nutritional care (this uses all the same audit points with the exception of those measuring the completion of the admission screening tool, which was felt not to be a marker of the processes of nutritional decision making and care). In general, compliance improved across all three periods although was variable in some areas, particularly the use of the screening tool, increasing feeds and switching to fortifier or formula milk appropriately. Average compliance with the guideline improved incrementally across the 12 month 2012 intervention period, with a slight decrease in compliance at the final audit in July 2013. Linear regression of mean audit compliance and mean nutritional process audit compliance against time showed that neither had a significant relationship with time. However, if only

the 12 months of the intervention period are used, mean overall audit compliance, and mean nutritional process audit compliance does increase over time, with coefficients of 0.86 and 1.1 respectively (r=0.86 and 0.92, p=0.028 and 0.009 respectively). Figure 10.8 below shows the mean audit compliance over time.

Audit Period		**Mar-12**	**May-12**	**Jul-12**	**Sep-12**	**Nov-12**	**Jan-13**	**Jul-13**
Number of infants audited		24	31	27	26	25	30	28
Screening Guideline element	1. Admission screening tool complete and in folder	33.3	22.6	51.9	38.5	20	23.3	14.3
	2. Correct risk category identified (where screened)	87.5	100	100	80	100	100	100
Parenteral Nutrition Guideline element	3. Parenteral Nutrition (PN) started in line with guideline	66.7	66.7	63.2	55.6	55.6	55.6	47.1
	4. Changed to bespoke PN or Preterm+sodium PN as per guideline	80	63.6	91.7	88.9	86.7	93.8	92.3
	5. On appropriate total fluid volume when PN flow rate decreased	88.2	85.7	85.7	100	85.7	92.9	92.3
	6. Lipid halved at correct total PN volume	60	66.7	80	75	88.9	90	100
Feed Guideline element	7. Feeds started in line with guideline	52	68	84.2	69.2	75	57.1	71.4
	8. Initial feed volume in line with guideline	100	89.3	100	90	84.2	81	95.5
	9. Feed volume increased in line with guideline	66.7	80	66.7	100	100	100	100
	10. Appropriate milk chosen	100	92.9	100	94.7	100	100	63.6
	11. Fortifier added/switched from DBM to LBW formula appropriately	63.2	100	66.7	100	100	100	100
Overall Average Guideline Compliance		**72.5**	**75.9**	**80.9**	**81.1**	**81.5**	**81.2**	**79.7**
Average Guideline Compliance Nutritional Care only (excludes items 1 and 2)		**75.2**	**79.2**	**82**	**85.9**	**86.2**	**85.6**	**84.7**

Table 11.6: Compliance with nutrition guideline audit points. Numbers represent percentage compliance

11.1 Normalisation Process Theory Scores

The modified NPT toolkit described in chapter 4 and shown in Appendix 3 was administered electronically to staff that had been recruited to the survey element of the study at two monthly intervals during the main intervention period in 2012 starting from the beginning of March, until the beginning of January 2013. A further questionnaire was carried out following the end of the post-implementation period at the beginning of July 2013 in the same way as the audits of guideline compliance. It is worth remembering at this point that the NPT toolkit was not originally designed to be used as a data collection tool and that it was used in this novel way in this study experimentally. Table 11.7 gives the numbers of respondents together with percentage response rate. Whilst 80 staff were recruited to the questionnaire element of the survey, several dropped out or had given incorrect email addresses, whilst others left the unit due to maternity leave or changes in employment. The percentage response rate takes this into account and is based on the number of remaining recruits at the point the questionnaire was administered. Table 11.7 shows that band 5 and 6 nurses, together with consultants seemed to be the most consistent responders. There were no junior medical/ANNP respondents for the latter half of the study period.

Time Period	Mar-12	May-12	Jul-12	Sep-12	Nov-12	Jan-13	Jul-13
Number of Respondents	44	52	39	26	24	18	16
Percentage Response Rate	57.9	74.3	58.2	41.3	40.7	31	27
Number (%) Consultants	4 (9.1)	4 (7.7)	4 (10.3)	4 (15.4)	4 (16.7)	3 (16.7)	4 (25)
Number (%) Junior Doctors/ANNPs	1 (2.3)	3 (5.8)	3 (7.7)	0 (0)	0 (0)	0 (0)	0 (0)
Number (%) Pharmacists	1 (2.3)	1 (1.9)	1 (2.6)	0 (0)	0 (0)	0 (0)	0 (0)
Number (%) Band 7 Nurses	4 (9.1)	4 (7.7)	2 (5.1)	3 (11.5)	5 (20.8)	2 (11.1)	2 (12.5)
Number (%) Band 6 Nurses	10 (22.7)	9 (17.3)	6 (15.4)	7 (26.9)	6 (25.0)	5 (27.8)	4 (25.0)
Number (%) Band 5 Nurses	19 (43.1)	23 (44.2)	18 (46.2)	10 (38.5)	6 (25.0)	5 (27.8)	4 (25)
Number (%) Band 4 Nurses	2 (4.6)	4 (7.7)	2 (5.1)	1 (3.9)	1 (4.2)	0 (0)	2 (12.5)
Number (%) Band 3 Nurses or lower	3 (6.8)	4 (7.7)	3 (7.7)	1 (3.85)	2 (8.3)	1 (5.6)	1 (6.3)

Table 11.7: Number of respondents and percentage response rate for each NPT questionnaire

Each of the 16 items in the toolkit were scored by respondents from 1 to 10, and the mean scores for each item at each survey time point are shown in figure 11.4, with the same data expressed as radar plots for each time period in figure 11.5..In general, the fuller the radar plot, the greater extent to which staff felt that the practices were part of 'normal practice' at that time.

It can be seen that over time the plots generally become fuller, with some key areas of the plots less full at different time points, indicating areas for improvement. The items relating to collective action and reflexive monitoring were scoring less highly early on in the intervention period, and improved over time, though did drop off again during the 2013 post-implementation period.

As discussed in chapter 9, results of the study to date were put up around the unit when initial NPT radar plots showed that staff did not feel able to see the benefit of the intervention in their work (indicated by the lower reflexive monitoring scores). Figure 10.6 highlights these areas more clearly by showing the combined mean score for each of the four areas of coherence, cognitive participation, collective action and reflexive monitoring, plus the overall mean score for each period,

In general, scores for each of the four domains increased sequentially across the study, and the overall mean increased sequentially across the study period, although, as for the audit data, there was some decrease in scores in the final post normalisation results. Figure 11.7 shows a small but statistically significant positive linear relationship between mean NPT scores and time.

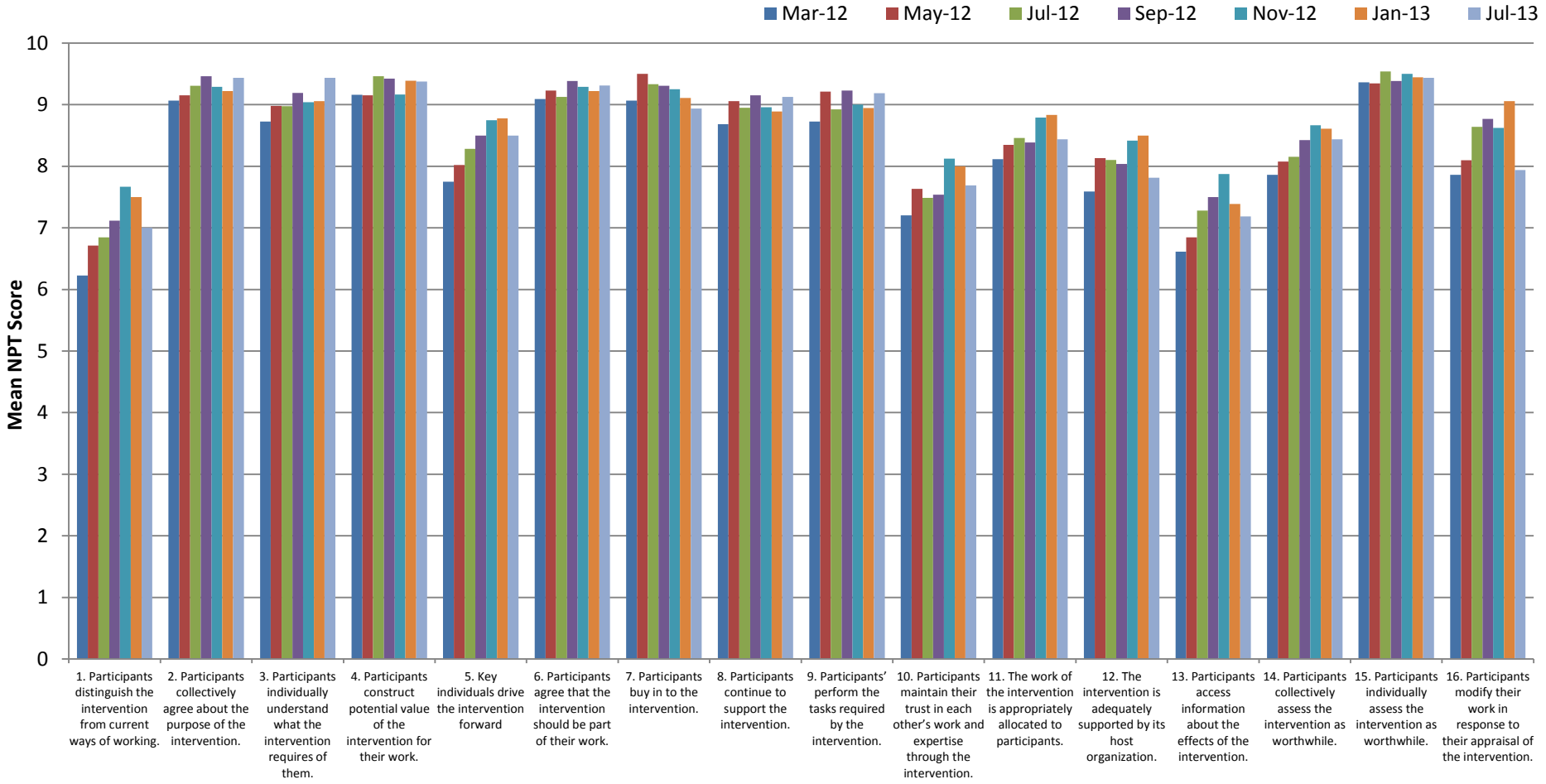


Figure 11.4: Mean scores for each item on the NPT questionnaire.

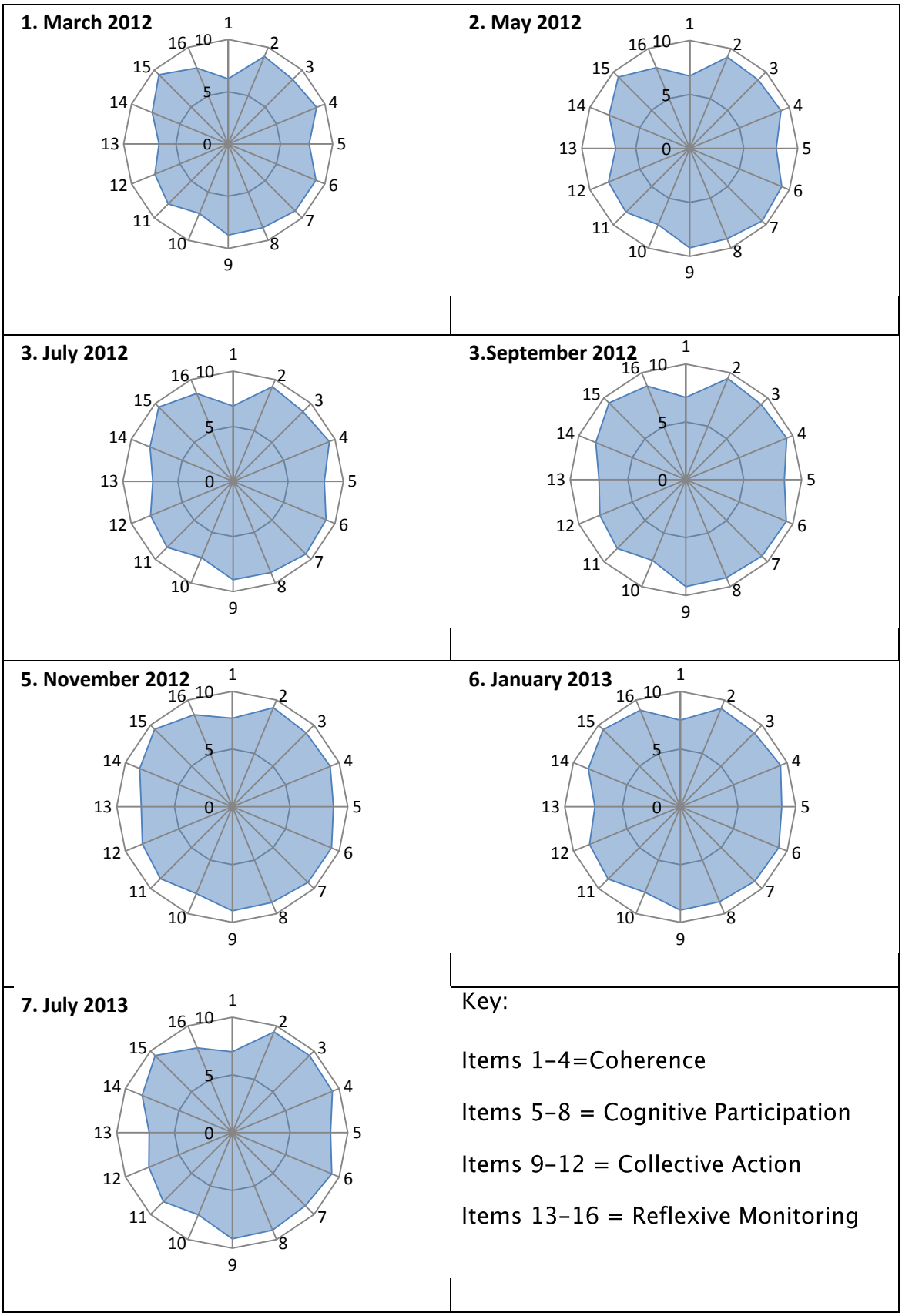


Figure 11.5: Radar plots showing the mean results of each NPT questionnaire during the study.

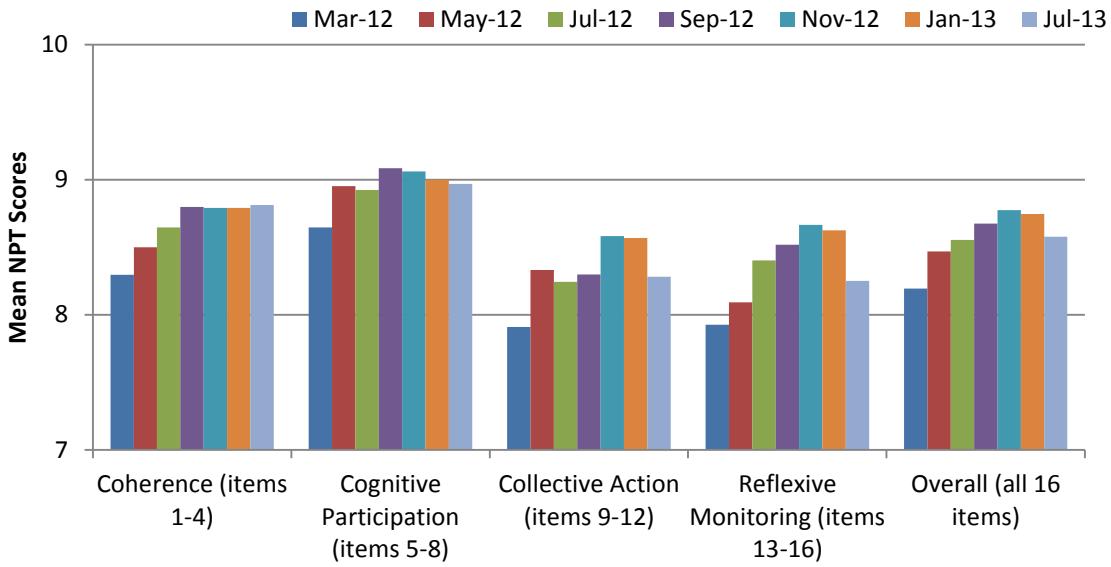


Figure 11.6: Mean scores across study periods for the fours domains of NPT, plus overall average score

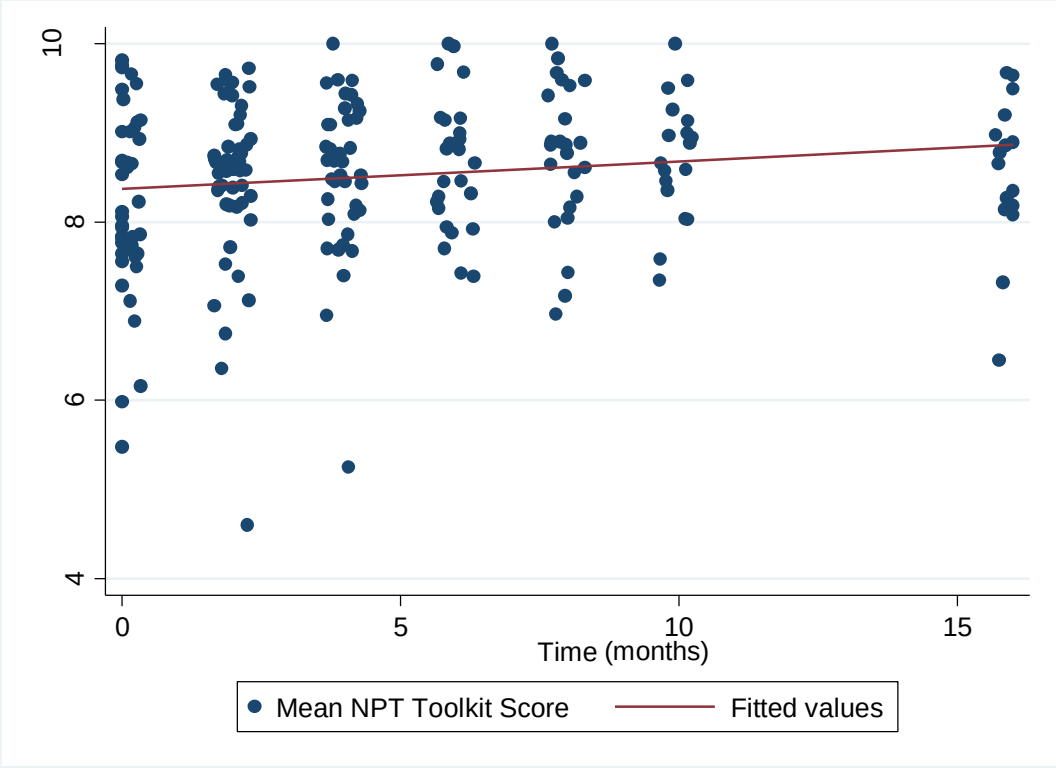


Figure 11.7: Scatter plot of mean NPT scores over time in months.
Equation of fitted line is: Mean NPT= 0.031*Time + 8.37. r=0.15, p=0.023

11.2 Relationship between Normalisation, Guideline compliance and Nutritional Care

11.2.1 Normalisation and Guideline Compliance

Figure 11.8 shows a plot of mean NPT scores and mean percentage guideline compliance over time, with both NPT scores and guideline compliance increasing together over time, then flattening out, suggesting that there is a relationship between the degree of normalisation and the extent to which staff comply with the guideline. Linear regression analysis showed that there is a significant association between the mean NPT scores across the entire study (including both the intervention and post-implementation periods) and both the mean overall audit compliance and mean nutritional process audit compliance, with coefficients of 0.80 and 0.95 respectively ($r=0.20$ and 0.21, $p=0.003$ and 0.002 respectively, see table 10.8). The addition of time as a variable into the linear regression models (to account for the repeated measures nature of the data – see chapter 4) is also shown in table 11.8. It can be seen that for prediction of both mean overall audit compliance and mean nutritional process audit compliance, the addition of time significantly contributed to the increases in compliance over the study and increased the predictive value of the model. However, despite this, the mean NPT scores remained a significant factor, showing that the measures of normalisation using NPT are associated with measures of clinical practice.

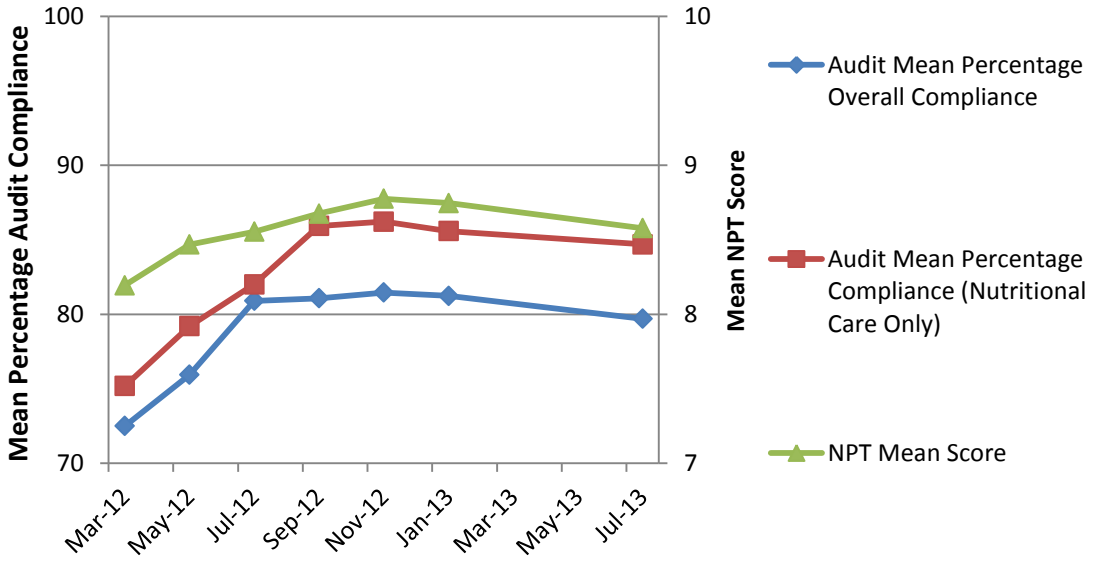


Figure 11.8: Relationship over time between mean NPT scores and percentage guideline compliance

Outcome	Mean overall audit compliance		Mean nutritional process audit compliance	
	Model with Time Excluded	Model with Time Included	Model with Time Excluded	Model with Time Included
Mean NPT Score Coefficient (p value)	0.80 (0.003)	0.38 (0.048)	0.95 (0.002)	0.40 (0.031)
Time coefficient (p value)	Omitted	0.54 (<0.0001)	Omitted	0.72 (<0.0001)
p value for model	0.0026	<0.0001	0.0018	<0.0001
r for model	0.2025	0.7063	0.2098	0.8076
r^2 for model	0.041	0.4988	0.044	0.6522

Table 11.8: Results of linear regression for mean audit compliance measures and mean NPT scores over time.

It is possible to look into the relationship of NPT to practice by breaking down NPT into its four component constructs of coherence, cognitive participation, collective action and reflexive monitoring. Table 11.9, in a similar way to table 11.8, gives the results of linear regression using the mean individual construct scores over time in relation to the mean overall and nutritional process audit compliance scores. It can be seen that when broken down in this way, the only construct which has a significant association with the mean audit scores, both before and after adjustment for the effect of time, is reflexive monitoring.

Outcome	Mean overall audit compliance		Mean nutritional process audit compliance	
	Model with Time Excluded	Model with Time Included	Model with Time Excluded	Model with Time Included
Mean Coherence Score Coefficient (p value)	0.34 (0.349)	-0.01 (0.962)	0.42 (0.320)	-0.05 (0.834)
Mean Cognitive Participation Score Coefficient (p value)	-0.31 (0.526)	-0.01 (0.984)	-0.35 (0.532)	0.05 (0.880)
Mean Collective Action Score Coefficient (p value)	-0.17 (0.697)	-0.20 (0.518)	-0.08 (0.879)	-0.12 (0.685)
Mean Reflexive Monitoring Score Coefficient (p value)	0.87 (0.017)	0.59 (0.027)	0.89 (0.034)	0.51 (0.044)
Time coefficient (p value)	Omitted	0.54 (<0.0001)	Omitted	0.72 (<0.0001)
p value for model	0.0085	<0.0001	0.0099	<0.0001
r for model	0.2482	0.7122	0.2059	0.8054
r2 for model	0.0616	0.5072	0.0424	0.6486

Table 11.9 Results of linear regression for mean audit compliance measures and mean individual NPT construct scores over time

11.2.2 Normalisation and Nutrient Intakes and Growth

Figure 11.9 shows a plot of mean daily energy and protein intakes based on birth month together with mean NPT scores over the intervention and post-implementation periods at each time point where the NPT questionnaire was used. Similar to the audit and NPT scores, protein intakes seem to trend towards an increase over 2012 (albeit with a degree of variability, including a dip around November), but fall away slightly during the post-implementation period. As with the mean audit scores, the change in protein intakes over the 18 month period of the intervention and post-implementation periods was not linear. Whilst mean protein intakes and mean NPT scores appear in general to mirror each other over time, there was no significant association between the two using linear regression, either with or without adjusting for the effect of time.

Energy intakes were reasonably constant over the intervention period, but again dropped off at the end of the post-implementation period. Linear regression showed no significant relationships between energy intake, time and mean NPT scores. Looking at growth in the same way using the mean change in standard deviation score between birth and discharge for weight and head circumference by birth months across the same intervention and post-implementation periods showed no significant associations with either time or mean NPT scores.

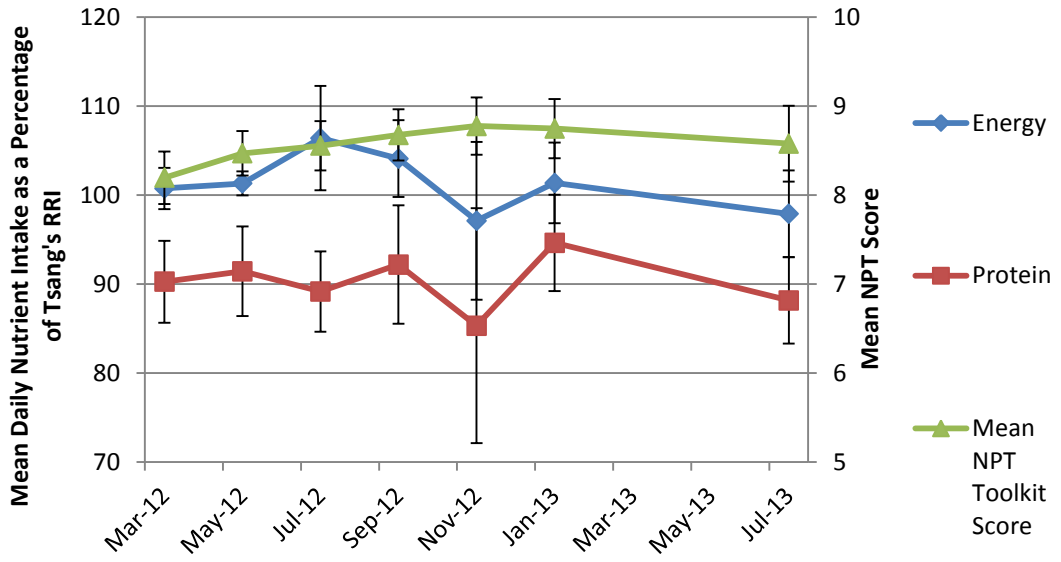


Figure 11.9: Mean Energy and Protein Intakes across the intervention and normalisation period, together with corresponding mean NPT scores. Error bars represent 95% confidence intervals

11.3 Summary

This chapter has presented the results of the study in terms of the effect of the intervention on changing the processes of care and practice, together with an assessment of the extent to which practices have become part of routine care using the NPT toolkit. These results are mixed regarding how successful the intervention appeared to be in changing practice. While there were improvements in audit compliance over time, together with some improvements in the process of care (shorter time to start PN and an increased number of infants who received breast milk fortifier), it is clear that some of the recommendations within the nutrition guideline were not being followed, with an increase in the time of starting milk feeds during the course of the study, and limited improvement in the use of breast milk. This is of interest given that the guideline audit compliance scores from the two monthly 'spot' audits generally increased during the intervention period. One explanation for this is that the more 'procedural' elements (i.e. screening, measuring, increasing/decreasing PN and milk feeds according to the flow charts in the guideline) are easier to implement, while more clinical elements which are more dependent on the infants themselves (i.e. decisions regarding commencement of feeds, adding fortifier and choice of formula) were less successfully implemented.

NPT scores generally increased over time, suggesting the intervention was becoming 'normalised' into practice. Audit compliance was associated with the mean NPT scores over time, showing the measures of normalisation using NPT can be related to real changes in practice. It is important to consider this in the context that the NPT toolkit was not originally designed to be used to measure 'normalisation' in this way, but was meant to help plan and develop an intervention. Whilst the r value for the association between NPT scores and audit compliance was small, it is still noteworthy that there was a significant relationship between this new theory, which was being used to measure practice change for the first time in this instance, and real measures of clinical practice.

Complex interventions require a means of monitoring and evaluating the extent to which the intervention is being used in order to ensure that any effects seen (or not) can be related to its use (or lack of use). The measures of

audit compliance and NPT scores both seem to provide a useful assessment of this. Whilst the previous chapter suggested that some improvements in growth and nutrient intakes were sustained beyond the intervention period into the post-implementation period, the results in this chapter show a small reduction in compliance and normalisation scores during the post-implementation period in 2013. Furthermore, it is of interest that initial NPT toolkit scores were high even at the start of the intervention, suggesting either that staff felt the intervention became part of routine care rapidly, or that the toolkit was perhaps measuring something slightly different than 'normalisation'. Another alternative is that staff were answering questions in the way they felt the study team would like them answered, and giving more positive responses; a common problem with questionnaires of this nature.

While this chapter and the previous one both provide some evidence regarding the impact of the intervention on practice and infant outcomes, they have not considered the factors that influenced the implementation of intervention and its attempt to become integrated into routine care, or how it affected staff practice at an individual level. The next chapter will look at these factors in more detail by presenting a qualitative analysis of the staff interviews looking at the factors influencing the implementation and normalisation of the intervention.

Chapter 12: Implementation Phase Results Part3 – Qualitative Assessment of Practice Change Process

The previous two chapters have both focussed on the results of the study in terms of the effect of the intervention on nutrient intakes, growth, nutritional processes and practice. However, one of the recurrent issues with complex interventions described in the literature is that whilst effects seen are associated with the intervention as a whole, it is difficult to know which elements of the intervention were most responsible for the effects seen or indeed if any individual aspects of the intervention had positive or negative effects on outcomes[34]. This chapter seeks to address this issue and understand the factors affecting implementation and the extent of integration of the intervention into routine care, and will present the results of the qualitative analysis of the staff interviews. The methods for the interviews and the qualitative analysis using the framework method are described in chapter 4, with the interview guide shown in Appendix 3. Copies of the completed analytical framework are provided in Appendix 16.

12.1 Interview sample

A purposive sampling strategy was used to recruit a selection of staff members of varying grades and experience, with an element of stratification to ensure the sample was representative of the whole staff group. Care was taken to recruit staff who were known to have negative attitudes towards the new practices in addition to those who had positive views. Similarly, staff members who had not agreed to be part of the questionnaire element of the study were also deliberately approached together with those who had taken part in the questionnaires.

Interviews' were carried out between the 20th March 2013 and 23rd May 2013. Altogether 22 members of staff were interviewed: two consultant neonatologists, three ANNPS, four senior sisters (band 7), eight sisters (band 6), three staff nurses (band 5) and two nursery nurses (band 4).

12.2 Results – Explaining Impact and the Factors Affecting Implementation

Whilst the majority of questions in the interview guide were based around the constructs of Extended NPT, some questions were about what factors they felt explained the impact of the intervention and its implementation on their practice and their patients. Once mapped to the analytical framework, a thematic analysis was carried out to draw out recurring themes within these two areas, and is described below.

12.2.1 Explaining Impact

Whilst it may be that it was a combination of approaches that caused any effects seen, I was interested to see what staff felt were the elements of the intervention that made the difference. This also led to an interesting insight into what the staff thought the actual intervention was. Several key themes emerged regarding what staff felt were the key factors explaining the effects of the intervention.

12.2.1.1 A Dedicated Nutrition Team

This was a recurring theme, with many interviewees citing the nutrition team as the key element explaining implementation. Generally this was felt to be due to two factors. Firstly, the nutrition team being identified as 'pushing' or 'driving' the intervention, with them reminding people about the guidelines, helping disseminate them , and playing an important role in communicating with the rest of the unit. One nurse explained her thoughts about the implementation process:

"I think it was the group of, people driving it, the group of nurses that – well not just the nurses and doctors that were part of the study, really drove it"

Secondly, the nutrition team and ward round were recognised as adding an important 'personalised' aspect to the standardised approach, with them reviewing individual infants and developing an individualised management plan for that infant. This was valued, as it meant that working to standards was negotiable, with staff able to follow the guideline and treat babies in a similar way, whilst feeling individual infants' needs were catered for.

12.2.1.2 The Guideline Itself

Staff generally felt that the guideline had been successful, with some citing specific practices in the guideline, such as the early use of more concentrated PN, as directly responsible for any improved outcomes seen. However, others were broader in their assessment, suggesting that it was the nature of the guideline itself, in terms of its ease of access and the fact it was easy to follow and use, that was the key factor in its perceived success. One staff member suggested that the guideline was important, but actually secondary to the nutrition team that had produced and disseminated it.

12.2.1.3 Seeing the effects for themselves

Many staff members remarked on how seeing the effects of the guideline in practice, with perceived better growth of the babies and more consistency in practice, was a factor that had encouraged people to follow it, for example:

"So I think it has been the engagement, and the, you know, the patting on the back, if you like, saying, actually, hey! What you're doing is, or what we are doing is working"

Generally this was mentioned as a secondary factor to the nutrition team or guidelines, but was a recurring theme in terms of continued guideline use.

12.2.1.4 Awareness of Nutrition

Another consistently recurring theme was that of the role of increased awareness on the unit. Staff recognised the importance of how well the guideline and practice changes had been publicised and advertised, with effective communication between the nutrition team and other staff regarding the changes but also the role of staff reminding each other to use the new guideline:

"I think that is probably why things have, have shown the improvement that they have, because people are much more aware of it, and tend to remind each other"

A culture of co-ordination and co-operation seemed to have emerged around the guideline, and staff recognised that there was an increased awareness of nutrition in general on the unit, with it being more of a priority.

12.2.1.5 Increased nursing involvement

Another factor that some staff felt had been important was increased involvement of nursing staff in nutrition, with better understanding of nutrition amongst nurses and a more pro-active role in nutritional decision making.

12.2.1.6 Consistency

One persistently recurring theme across all the interviews, was that of consistency. The role of the intervention in introducing consistency to nutritional care was recognised by the majority of staff and felt to be a good thing. Staff noted the benefit of people doing the same thing and being clearer about what to do. Some specifically mentioned how the new practices had meant that there was less opportunity for individuals' thoughts and beliefs (which may be incorrect) to drive nutritional decisions and more consistency, which was also seen as more predictable and beneficial. One nurse commented regarding the guideline:

"you've got something that's a rounded thing to refer to; you've got something that everyone can see, everyone can follow, and you're not having people kind of using their own ideas, initiatives, so you've kind of got something to see, something to look at and go, Oh yeah, that's fine, and follow it on"

12.2.2 Factors Affecting Implementation

Several common themes emerged when interviewees discussed the factors they felt had influenced the implementation process. Whilst some of these overlap with those described above, the specifics are different in the context of explaining implementation compared to when asked to explain effectiveness. These themes are described below.

12.2.2.1 Nutrition team

Again, having a dedicated nutrition team was highlighted as key factor in implementation. Several staff members commented that the continual reinforcement of the guidelines on the nutrition round was important, with the nutrition team having a role in raising awareness and driving the change process. The multidisciplinary nature of the team, with members from medical, nursing and allied health professional groups was valued, and the fact that the

staff implementing the change were familiar was felt to ease the process of change.

12.2.2.2 Guidelines

The nature of the guidelines themselves was identified as another key factor in implementation. Their ease of use, clarity and the easy to follow flow charts were repeatedly mentioned, but the most important factor as far as staff were concerned was the fact they were readily accessible at the cot side of every infant:

"They're quite user-friendly. Um, and the, the flow charts that are in all the baby's folders are an easy point of access so … And there's one in each room, so you can always find one, they're not … like I say, they're just user-friendly and easy to read, easy to use … and they make sense"

People also felt they offered a welcome degree of flexibility, and this was highlighted on several occasions, exemplified by one nurse:

"Yeah, there is flexibility, but not too much flexibility that doctors can interpret it and change it all according to their whims and wills".

12.2.2.3 Nurse Champions

Many people felt that the support and advice offered by the nurse champions aided implementation. One nurse typified the attitude of staff when she said:

"I do think the nursing input has been helpful..... they've come and given us teaching on how to do it; … they've given us, shown us more reason why it's important.... because I think, I think everyone gets a bit sceptical with these new things don't they… now it's just become sort of routine that that's what we do"

The fact they came from within existing clinical staff was viewed positively, as they were seen as one of the team and also had insight into the way people worked on the unit. One particular nurse badged them as advocates for change, whilst also noting that the new practices were becoming 'normalised' into practice:

"I mean because I guess we know the nurses …. that come and bring it in, you know, they're advocates for it, they tell us how important it is, so they've been

on that side that they can then bring it into practice and sort of lead by example I guess. And then because there's such a…. big team that come round, it's become part of the Unit; that's how we do it"

12.2.2.4 Screening Tool

Interestingly, whilst several staff members mentioned how the weekly use of the nutrition screening tool was seen as something of a chore, it was also highlighted by several people as a factor that aided implementation (even by those who had complained about it). It seems that the mandatory use of the screening tool made it difficult to resist the implementation process as a whole, with regular completion of the tool, together with consideration of nutritional risk, serving as an important reminder to both weigh and measure the infants and of the importance of nutrition. One nurse remarked:

"Doing the, the nutrition screening on a Sunday…. determining whether the baby's high risk, or moderate risk then you can refer to your chart, 'cos then, you know, it's set out then isn't it, who is more at risk …"

12.2.2.5 Nature of introduction

Several staff members identified that the guidelines seemed to have been introduced gradually, with one consultant noting it seemed to have 'crept in' whilst one nurse remarked on how it had been brought in gradually so that it 'did not feel like a big change':

"So I think it probably was brought in in the right way, in a good way anyway. It's not something that, felt like a big change, or something was imposed upon us. It just kind of came into Unit practice and seemed sensible, and we got on with it"

This suggests that a low speed and intensity of change reduces the work involved in changing and makes it minimally disruptive. Whilst generally people felt that the process had gone smoothly and had been done well, one nurse noted that she felt the changes were 'all hell to start off with', noting how some of the new practices described in the guideline seemed difficult initially (she did go on to say how she'd found things much easier over time).

12.2.2.6 Education and Awareness

The role of education and awareness was also highlighted by staff. Again the way in which the changes in practice had been publicised was mentioned, and how this had changed the outlook of staff regarding nutrition. Some staff felt this awareness was due to the education on nutrition at the start of the intervention, which had laid out the changes clearly. Another important factor suggested was that nutrition education had now become a part of induction for new staff, and with a relatively high staff turnover over the study period this had meant that many staff were taking the new practices as normal from the start of their employment.

12.2.2.7 Desire for consistency in practice

Many staff cited a strong desire for more consistency and uniformity in practice on the unit as a reason for the successful implementation. They felt people were keen to use and follow the guidelines as they wanted to be clearer about what they did and for similar infants to be treated the same. This gave the new practices legitimacy, and was described by one senior nurse:

"I think the publicity surrounding its implementation, and how it was different from what we did before; the fact that it was really needed, and that it was something that we had no proper guidance about, and we all felt that we were making things up quite a lot before that; and that's something that we weren't comfortable with, so we all felt it was necessary. It actually was necessary"

12.3 Themes within the Constructs of Extended NPT

The majority of the interview questions were aimed at exploring the 12 constructs of extended NPT. The answers to these questions were mapped to the constructs in the analytical framework (of note some content of the answers to a question exploring one construct were often mapped to another construct where relevant). Once this was done, thematic analysis was carried out within each construct and common themes drawn out, which are described below for each construct.

12.3.1 Potential

12.3.1.1 Individual Intentions

Generally staff felt motivated to follow the guidelines when they were first implemented, with a sense of growing commitment as the process continued due to perceived improvements in growth seen in the infants over time. One nurse described this:

"I just was a bit like, Oh OK, let's just see, and then I have become behind it because I've seen the difference it's made and realised how good it is for our babies, and that they actually are putting on weight, and it's just a set thing for, like, when we get new doctors you don't feel like you have to explain it all to them"

The perception that using the guidelines would improve practice and the growth of babies was consistently cited by staff as a motivating factor, with a sense that things could be done better and a need for babies to grow better. They appreciated by the effort invested by the nutrition team and sense that they were 'pushing' the guidelines, and were also motivated by the structure which the guideline offered to their work, removing uncertainties. This was coupled with a general desire and sense of need for the more consistent and structured approach that the guideline offered. Other motivating factors included the high awareness of nutrition that came in with the guidelines and an expectation that the guidelines had to be followed (from a clinical governance perspective). Several staff members also cited ease of use as a motivating factor. One nurse commented:

"I think with any kind of, like, change there's always a bit of resistance, but actually they, I don't know, it was perhaps the way they came in; it just seemed easy to use, so actually if they're easy to use it's easy to do it"

Of note, one member of staff said that they were initially 'couldn't be bothered to read' the guideline as it seemed too long, although they did feel that their motivation improved over time, particularly after it seemed to be making a difference. This was incongruous with the majority of staff though, so it may be that this particular nurse had difficulties due to her individual learning or working style.

12.3.1.2 Shared Commitments

Again there was a sense that the unit was generally committed to the guidelines and new practices, with one person suggesting there was 'near 100% commitment'. Similarly to individual intentions, there was a feeling that commitment increasing over time as people perceived benefits in the babies, with the unit 'slowly getting there'. Several people noted that the unit was positive towards the change, with the changes perceived as small and gradual. Again there was a strong perception of a need for a more standardised approach to nutrition. One person commented that the unit was accepting of the work required (e.g. measuring the babies more regularly) in exchange for the structure and guidance that came with it:

"I think it generally gets followed; I think they've been quite committed to the weighing and measuring and referring, you know, the, the Sunday night activities for the Monday morning, those things. I think that probably happened more smoothly than I thought it might do, because it's always tricky asking people to do extra things, but people are committed to it, and, you know, they pretty much ensure it gets done, and have got quite a nice attitude about it……possibly because they knew went hand-in-hand with the guideline, and because they needed the guideline and they felt the guideline had value, it was kind of, like, a payoff for having the guideline".

Another theme was that of the perceived effect of the guideline on different staff groups, with a general feeling that it was useful for junior staff to have guidance, while for new staff the guideline was part of their initial learning and so more easily accepted as 'standard':

"The new staff coming in actually because they were coming in whilst we were, introducing the Guidelines, they were quite good at following it through, whereas some of the staff that had perhaps been here for a little while, and you know, are stuck in their ways [chuckles] maybe, weren't quite so eager. But, you know, having new staff coming in and teaching that as the standard then I think that kind of helped to say that it was then important to try and make sure the other members of staff did the same"

At the same time it was felt that some senior staff (both medical and nursing) might find it harder to commit to the changes as they were used to more autonomy, meaning that these groups required more time to accept change.

The role of the nutrition team and key people helping keep the nutrition at the top of the agenda was also re-emphasized by several people in the context of the overall commitment by the unit.

12.3.2 Capacity

12.3.2.1 Social Norms

Generally staff interviewed felt that there were now increased expectations for nutrition across several areas including:

- An expectation for babies to grow better, with poor growth now unacceptable
- An expectation to start nutrition earlier and deliver more nutrition
- An expectation for appropriate nutritional decisions and plans to be made, with people prepared to challenge when this didn't happen
- An expectation for the babies to be measured and growth charts to plotted regularly

Staff also described a general focus on nutrition on the unit, noting how nutrition now had a raised profile with increased awareness on the unit, as illustrated by this senior nurse:

"You've raised awareness. Before babies always needed to be fed. And I think the old-fashioned way of looking at it was um, see what the baby tolerates and we always went very carefully, so when we used to put 10% dextrose up, and then we'd start introducing a bit of Vamin (PN) and stuff; and then their sugars would go sky high: Oh no, no, back off, back off. I don't think we actually considered the growth babies were missing out on in that time. Whereas now I think people are more tuned into the fact that you need to get food into these babies; you need to get calories and protein into them. So yeah, I think it's changed us… Raised awareness"

12.3.2.2 Social Roles

Whilst some interviewees mentioned that they felt the changes in awareness of nutrition and expectations may have been more prominent than a change in roles per se, staff generally recognised that roles regarding nutrition had changed, particularly for certain groups of staff, which fell into the three main themes described below. In addition, there was a feeling that nutrition was now a responsibility that was shared between all staff.

12.3.2.2.1 An Increased Role for Nurses

A recurring theme regardless of the background of the interviewees was that of an increased role for nurses in nutrition, with more responsibility for the measurement and plotting of growth, but more importantly an increased involvement in decision making. Nurses felt the guideline had allowed some restructuring of professional roles, empowering them to make more decisions and to question or challenge a lack of or incorrect decision making by medical staff. Nutritional decision making was now seen an activity that was shared by the team. Nurses also felt better placed to guide junior doctors in nutrition prescribing and decision making, as this nurse described:

"I think the nurses feel more able to make that decision with the Guideline. Obviously with the, sort of, say-so of the doctors as well, but I think, yeah, we could go to them and say: "This is what we think, this is what the Guideline says, are you happy to do that"? So I think we're probably doing it more but, obviously with the overseeing of the doctors, if you know what I mean"

In addition to having the guideline to inspire confidence, there was a feeling that nurses were driven by the desire for consistency:

"It's much more clear to follow now, rather than it, it used to seem. I guess like we would just do it quite individualised for that baby but now there's the flow chart to say what we do at certain days, weights, you know, preterm, things like that. So I think nurses can make the decision more based on the … we would know what to expect based on the flow chart, because obviously we get pressure from the milk kitchen that need to know how to make the feed up "

12.3.2.2.2 Junior Doctors Taking a Greater Role in Decisions

Similar to nurses, it was also felt by both medical and nursing staff that the guideline had caused a degree of restructuring which meant that junior doctors were now more likely or more able to make nutritional decisions, often without having to wait for a senior person to ask or defer to. Junior doctors were also more likely to ask nurses for advice. The guideline made it easier for medical staff to make decisions, though there was a concern from some senior nurses that some junior doctors followed the guidelines without thinking. One nurse noted how the guideline facilitated decisions:

"I think, like most things, especially for junior staff, medics and, and nurses and that, actually having something to follow is easier than, certain

consultants are doing certain things… if you've got one consultant on one week and then another one, they'll do different things – well they used to do different things with going up on, up on feeds: some will be more pro-active than others. Whereas this, now you've got a guideline everybody follows the same, same guideline. So I think, definitely, it's better"

12.3.2.2.3 Role of the Nutrition Team

Several members of staff (medical and nursing) identified that the nutrition team now fulfilled a specific role. The team was making more decisions and felt to be making a significant contribution to the 'work' of nutritional care. There was a concern that some nutritional decisions were being deferred to the Tuesday nutrition round, though generally staff felt that the guideline was enabling people to make decisions on a day to day basis with special individual cases deferred to the nutrition ward round (i.e. people making decisions despite the weekly nutrition ward round); one nurse talked about this:

"I think there is, the one fear that I had is that people would perhaps stop thinking for ourselves, and think: Ah! Nutrition day is Tuesday, and therefore everything can be all right so we can hold it on till Tuesday. But I think that's now because we are learning to work with a document; we can actually say, well actually if this baby needs something doing you don't wait for a Tuesday to come along, you use that document and you move the baby in the direction that you want them to go"

Some staff commented on how there was a perception that the nutrition team were checking what people were doing, with people considering what the nutrition team would make of their decisions each week:

"I think people know that the Nutrition Team is going to come round, so when they're making decision they're actually thinking about what you're going to make of what they've done as well"

Again demonstrating how the intervention had led to restructuring of professional roles, staff also noted that several nurses had become part of the nutrition team (as nurse champions) so their role had specifically changed. One interviewee (a nurse) also recognised that some of these nurses had returned to their normal roles but with increased knowledge and enthusiasm for the changes in practice:

"I think you've had a team of people and the team – several teams of people – and I think they will continue with their interest; the ones that are no longer on your research, the ones that are still interested, and you've got other people who haven't done your research that were also interested; so there's quite a collection of people, that want to make it work on the Unit"

12.3.2.3 Material Resources

Overall staff felt that they had adequate resources most of the time. Specific issues highlighted by some staff were insufficient supplies of some measuring equipment (incubator length measures, scales and tape measures) at times, particularly Sunday nights when all babies were measured, plotted and screened. Despite this most staff felt that they were able to manage on what was available. They did recognise that the incubator length measures had been supplied as part of the practice changes and felt the equipment was generally accessible. Several staff mentioned that time to carry out the work (specifically measuring and plotting) was not always available, and another commented that there were not always adequate numbers of staff to carry out the measuring and plotting, particularly at busy times. In terms of the physical copies of the guideline itself, several interviewees noted that there had not been enough flow charts in the babies' cot side folders initially although this had been resolved over time. Generally, people felt that there were enough copies of the guideline available and that they were readily accessible.

12.3.2.4 Informational Resources

Three key themes around informational resources arose:

12.3.2.4.1 Training on Measuring and Plotting

Several members of staff talked about training for measuring with most people feeling that they had received adequate training. Amongst those who had been trained there were some who would have liked more training, with recognition that others had not been trained at all. Several people identified that they had not received any or enough training, though recognised that others had been trained and that it was not always possible to get to teaching sessions. In most cases people did not feel that a lack of training had been an issue, and several highlighted that they had been supported by the nurse champions or colleagues in this area. The role of the nurse champions in delivering training, both in the clinical setting and on specific study days, was also mentioned.

12.3.2.4.2 Information and Education on Nutrition and the Guidelines

A need for education as part of the process was recognised by interviewees, together with acknowledgement that this was provided. Generally people felt they had received adequate teaching and education in nutrition. Again the nurse champions were highlighted as educators, but the role of specific lectures by me early on in the process and information within the guideline itself was also mentioned.

12.3.2.4.3 Support from Nurse Champions and the Nutrition team

As mentioned already, the role of the nurse champions in offering support and advice, with both them and the nutrition team available to answer questions, was a recurring theme.

12.3.3 Capability

12.3.3.1 Workability

There seemed to be consensus amongst staff that the guidelines were easy to follow and access. In particular, people found them clear, and the flow charts were especially useful, as described by this nurse:

"I think that the actual Guideline itself is quite long, which would probably have put people off it, but because the flow charts are very easy to follow you find the one right for your baby and you just follow it through. I think it's simple, it's standardised and everybody is following the same prescription, so everyone's doing the same thing. I think that's helped, just the fact that the flow charts are simple and they're by the baby's cot. Easily accessible"

Additional comments included the fact that the guidelines offered a degree of flexibility which made them more workable. One individual said that the nutrition ward rounds had been difficult for them as they found the number of people on the round and the assessment of babies disruptive to their work. She also disagreed with the concept of measuring babies 'all the time' and often didn't feel listened to when she raised issues.

12.3.3.2 Integration

The majority of staff felt that the new practices had indeed become part of routine care, with several interviewees stating 'it's just what we do now'. Other

comments include how things were becoming ‘automatic’ or ‘the norm’. One ANNP explained:

“I think it’s become part of the routine now; I think it’s become part of the norm, you know, this is part of the care, and this is how it should be”

Some staff felt that whilst the process of integration was happening, it had not yet got to the stage where they considered them fully part of routine care. Staff universally thought that t had been easy to integrate the new practices into care, which was put down largely to how well they fitted with existing practices, as one nurse responded:

“I think they fitted in quite reasonably. I mean it wasn’t excessively different; there was just, a slight little tweak here and there, and extra info, on this, or a slight change to what we’re going to do here. I don't think they were particularly tricky to implement”

A perceived need for the changes and a desire to make them work was also cited as a factor in integration. Regarding the weekly measuring of babies, staff felt that either this had fitted in well with the daily care of the infants so had been easy, or actually identified the routine measuring and plotting as an additional burden of work, though recognised it was happening regularly despite this.

12.3.4 Contribution

12.3.4.1 Coherence

It was clear to the majority of staff that the guidelines were necessary, with the key themes being a need for better growth (and better proportionality of growth), and a need for an actual guideline to aid clear decision making and provide structure and consistency to practice. There was also recognition that nutrition was important. A few people noted that while the reason for the guidelines wasn’t fully clear initially, it had become clearer as the study progressed; one nurse explained:

“It seems clearer now we can sort of see the results. I personally, always find it easier if you can see them … if you can see good results you can see why it was implemented in the first place. It does seem to be working”

Staff nearly all appreciated how the new practices were different from the old, with the introduction of clarity, structure and consistency in place of a previously ad hoc and variable practice cited most commonly. Example opinions included:

"We were a little bit ad hoc before in terms of, particular like going up on feeds and stuff. One person would say one thing, and then the next day somebody would say something different"

"Just complete lack of uniformity in practice two years ago, wasn't it?"

One member of staff noted how they felt that consistency was the major difference rather than any large changes in practice:

"I don't think it's overly different to what we did before. It just gives structure to what we do, did before"

Staff also noted a tendency to start nutrition earlier, more measuring of babies and clear improvements in the growth of the babies as other things that were different from before.

12.3.4.2 Cognitive Participation

All staff felt that their role in carrying out the work required by the guidelines was clear, though for some this was something that became clearer after implementation. One staff member commented:

"I think we all have our role in trying to, implement something that's new, and try to follow it, and help others I suppose to follow it"

There was a general willingness to carry out the work needed, with reasons for willingness including the rationale behind the guideline, clarity and the importance of nutrition. One member of staff was initially unhappy to follow the guideline though stated that this had got better with time. For one staff member, time pressures meant that it was sometimes difficult to do the work required.

12.3.4.3 Collective Action

All staff said that they still used the guidelines fairly consistently. Interestingly, one nurse stated that whilst she initially followed the guideline as she felt

pressure from the management to comply, over time she was doing it as she felt it was a good thing:

"I would say initially because we had to, and now because we like it because it's, it is easier because we're used to it. I think big groups of people can sometimes struggle with, Right, you're doing this, and you're a bit like, why should I? But now I think everyone's like, Mmmm, actually it's good, let's use it because it's good, rather than 'cos we have to"

Another nurse said she would regularly direct colleagues to the guideline:

"Yeah, I think people will refer to them, and because they're easily accessible, um, you know, I would always send them that way if I wasn't sure. So I think most people do use them fairly well now. They've become a part of the Unit, so they are just used now"

An ANNP also stated that whilst she followed the guideline most of the time, she did feel able deviate from it for clinical reasons occasionally.

Similarly, interviewees felt that other staff and colleagues on the unit were generally using them, with comments such as 'everyone is doing it'. New staff were perceived as a group more likely to use them, especially as they were entering a unit where it was already established practice. Nurses were also felt to be using it most, as more of the guideline was perceived to apply to them. Junior medical staff were another group felt to be using the guidelines more. Several staff members noted that whilst there were some people reluctant to follow them, they were increasingly persuadable. Senior staff and doctors were mentioned as groups who perhaps were sometimes not always following them although one respondent felt that no particular groups of staff were more or less likely to use them.

12.3.4.4 Reflexive Monitoring

A clear theme both in relation to questions specifically around being able to see the benefit of the guidelines and new practices but also across the interviews generally was that of the perception of clear benefits to both practice and the babies. Furthermore, a consistent theme across the interviews in general was how staff were driven on to use the new practices and guidelines by the obvious benefits they perceived in their work and the patients. Interviewees also noted the beneficial impact of feedback via the

nutrition team and AV system regarding the impact of changes, feeling spurred on to continue.

Every staff member interviewed perceived a benefit to their daily work in terms of practice and processes. These included:

- Easier to manage nutrition and make decisions, with clear guidance and less waiting for decisions to be made
- Improved consistency and uniformity of nutritional care with standardisation and better structure
- Increased awareness of nutrition and support by nutrition team and nurse champions

In relation to decision making, this nurse described the change in her view:

"And it's just easier to know actually, as a nurse, if the doctor hasn't done the ward round, … and we're waiting for them, and we want to increase feeds, and we're just following a guideline, we don't have to just necessarily wait for the junior doctor to ask the consultant what to do, because we've got the guideline in front of us".

Other nurses commented on the consistency:

"Well it's just consistent practice. And also, I mean you've showed us your outcomes which suggest the babies are growing better"

"care is standardised, everybody knows what they're doing; we're all singing from the same hymn sheet; babies seem to be growing better; um, nutrition just seems to be working better than it had previously"

Similarly most, but not all staff, perceived a benefit from the new practices in the babies they cared for in terms of improved growth of infants and better proportionality of growth. This was something they had appreciated over time rather than on a day to day basis. Several staff members commented that the babies 'looked better' especially when compared to babies transferred in from elsewhere:

"We can definitely see a difference between our babies that we've home grown, to ones that come in; they look different; … the others can just look kind of quite scrawny can't they?"

Staff also noted improved measuring and completion of growth charts. Some staff, particularly medical staff or ANNPs felt unable to comment on the benefit to the babies without more information or data/figures.

12.4 Constructing a Theoretical Framework for Practice Change

Mapping the qualitative interview data to the constructs of extended NPT provides valuable insight into the implementation process. Using these data, it is possible to develop a theoretically coherent explanation of *what the intervention was and how it worked*. This is important, as what was actually implemented as 'the intervention' in this study was interpreted and used by different groups in different ways in actual clinical practice. Figure 12.1 shows how the different elements of the intervention can be mapped to the major constructs of the extended NPT at a 'macro' (organisational) level, whilst figure 12.2 focuses specifically on the original NPT (the 'contribution' element of the extend NPT model) at the 'meso'(ward) level.

Going through Figure 12.1 in terms of the constructs of extended NPT, we first consider the construct of *capability*. The interview data demonstrated that the guideline itself had high workability, with staff feeling it was accessible and easy to use, with the flow charts cited as a key factor in its regular use. Having a clear practice guideline appears to have caused some restructuring of both social norms (with an increased role for nurses) and the relationships between staff and the intervention (with nurses feeling more involved in nutrition and also perceiving a benefit to their daily work and practice over time. This *normative restructuring*, with change in roles, interacts with the construct of *capacity*, with a clear perception of a change in *social roles*, particularly for nursing staff, who felt more involved with nutritional decision making and more empowered to question the nutritional management of the infants they were caring for. In addition, expectations for nutrition on the unit changed, with a shift in *social norms* so that nutrition had a higher profile and staff expected infants to be managed more consistently and effectively from a nutritional perspective. *Material and informational resources* did not seem particularly important to staff.

Looking at the construct of *potential*, the interview data illustrate a high level of intention amongst staff to make the changes work, driven by a desire for consistent and predictable nutritional care and a feeling that nutrition was something that could be done better. These qualitative data fit well with the high levels of intention measured using the TPB questionnaire at the start of the study. Furthermore, Figure 12.1 shows how this potential was increased by the *relational restructuring* that occurred, with staff seeing benefits to practice and feeling more involved increasing their intentions to use the new practices. Both the potential and capacity were able to act on *contribution* via the *mobilisation of resources*. The interviews demonstrated that the nutrition team was viewed as a major driver for change, and felt to be 'pushing' the changes on a regular basis, encouraging the normalisation of the practices, as illustrated by the diagram of *contribution* shown in figure 12.2, which contains all the theoretical constructs of the original NPT.

From figure 12.2 it can be seen that staff indicated that they found the intervention to be *coherent*, and were clear about the need for the change in practice, recognising the intervention as something new. Staff were clear regarding their role in the new practices and many were 'signed up' to the new practices, agreeing with the rationale behind them and keen for more standardised practice (indicating their *cognitive participation*). Indeed, this desire for more consistent practice was a major driver for change, and this belief that a change was needed allowed the staff to form a community of practice around the new guidelines and intervention. The interviews indicated that staff found the nurse champions helpful in understanding and carrying out the new responsibilities.

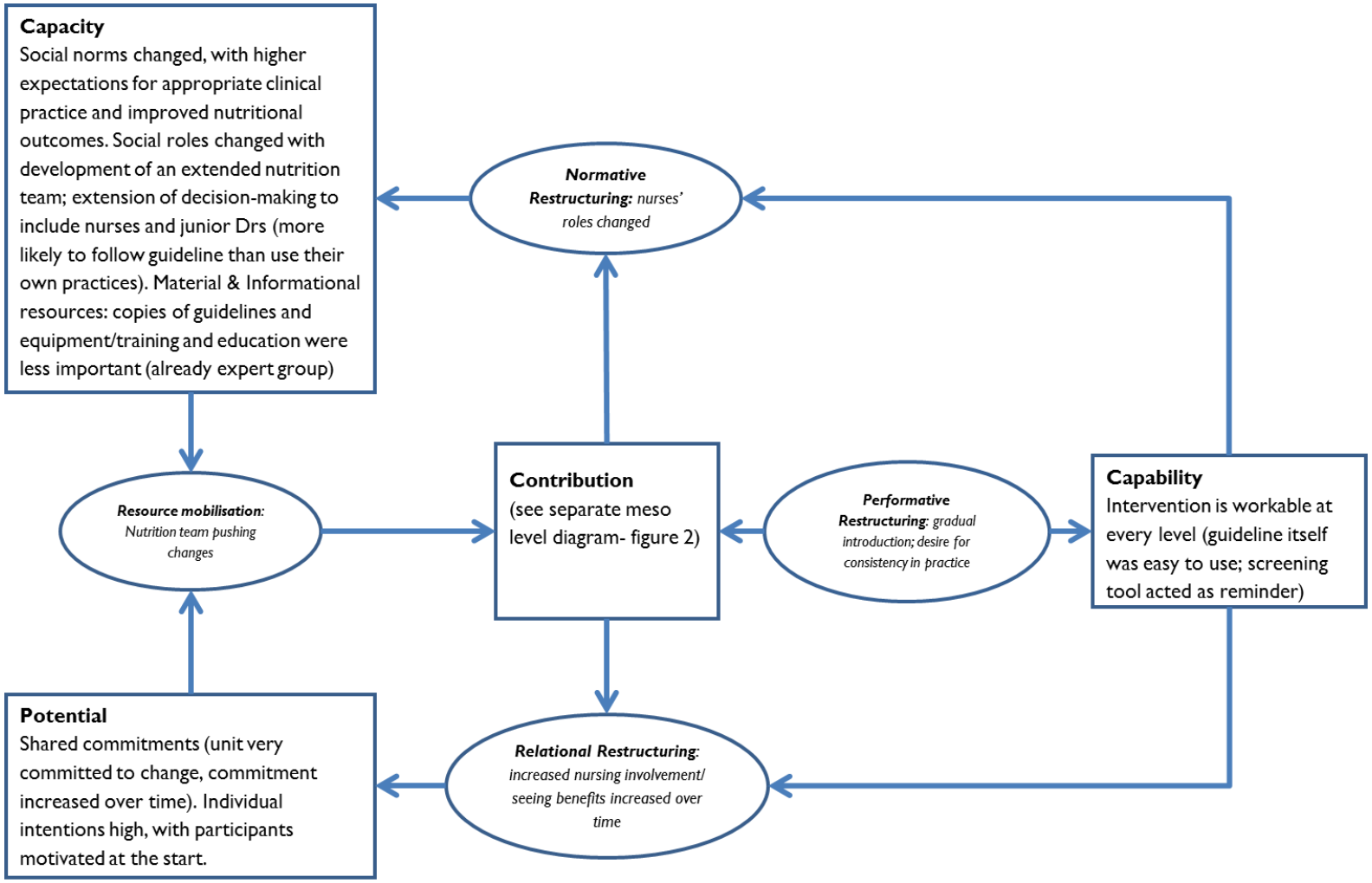


Figure 12.1: A theoretical framework for implementation at macro-level, based on extended NPT

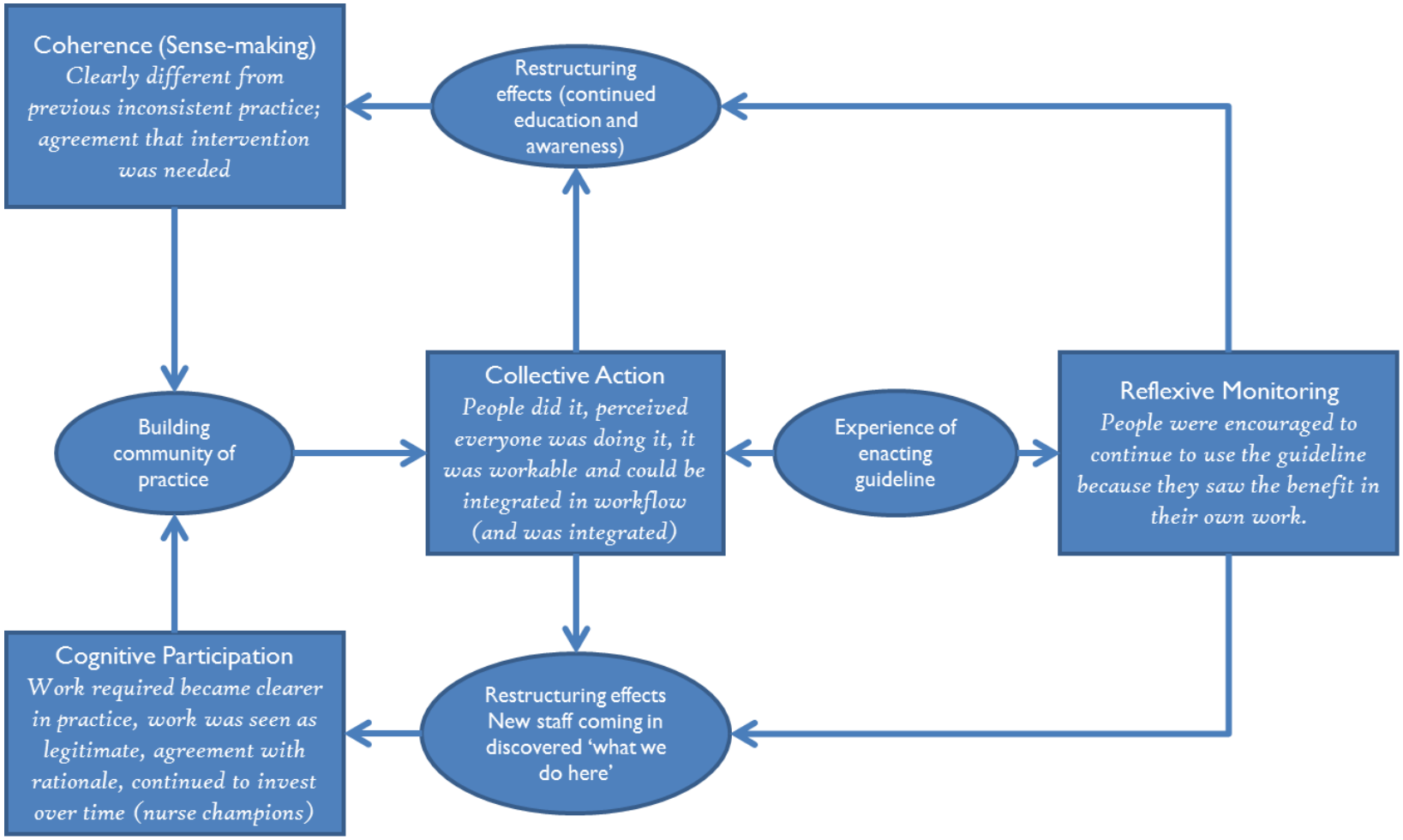


Figure 12.2: A theoretical framework for implementation at meso level, expanding the construct of *contribution* (based on NPT)

Staff thought that both they and their colleagues were using the guidelines in practice (*collective action*). In addition, the process and normalisation data show that they really *were* doing it in practice, linking together what staff *thought* they were doing and what they were *actually* doing. Staff also felt the new practices had integrated well into routine care, and these interview data suggest that they worked to accommodate them into practice. Once in use, the intervention led to restructuring effects. These included reinforcement and education by the nutrition team in response to staff demands, and a beneficial effect caused by the introduction of new staff, who entered an environment where the nutrition guidelines were 'just what we do here now', meaning that they used them immediately, with training on them as part of their induction.

The importance of *reflexive* monitoring came out strongly during interviews, which is consistent with the findings of the NPT questionnaires presented in the previous chapter. Perceiving a benefit of the new practices in their daily work, was consistently identified as a driver for staff in their continued use of the new practices. Figure 12.2 illustrates how, through the collective action of using the guideline, staff had a positive experience and saw the benefit in their work, which in turn reinforced their action. This also included some of the restructuring effects already discussed above.

12.5 Summary

Staff highlighted both the guidelines and the nutrition team as key elements of the intervention. They also valued the introduction of a consistent and predictable approach to care, which was something there seemed to be a desire for on the neonatal unit. The continued reinforcement of the practices and support in making them work by the nutrition team and nurse champions was repeatedly identified as a major factor in the success of the implementation process. Increased awareness, education and a gradual introduction with provision of feedback were also elements that were highlighted as important. A key element of the guidelines themselves was their ease of use and accessibility

Mapping the experiences of the staff regarding the implementation process to the constructs of extended NPT provides insight into the key drivers of the change process. Both individual and shared intentions were good, motivated by

a desire for consistency and to improve outcomes for the infants. The expectation for nutritional care on the unit changed to that of expecting infants to grow better and receive better nutrition. Most staff recognised a shift in roles regarding nutrition on the unit, with an increased role for nurses, who felt empowered to be more involved in nutritional decisions and prompt medical staff.

Some issues with the implementation process were highlighted, including a lack of measuring equipment and copies of the flow charts early on in the intervention. There were also issues identified around the nutrition ward rounds and the way they had worked initially, with a perception of large numbers of staff interrupting workflow on the unit, though this was felt to improve over time. In addition, there was acknowledgement that some staff may have had difficulty with the changes.

Overall, there was a sense from staff that the new practices had become reasonably well integrated into routine care. They were clear about the need for the change in practice and recognised the intervention as something new. They were clear about their role and generally felt that both they and the majority of their colleagues were following the new guidelines. What was very clear from the interviews was the large role that the NPT construct of reflexive monitoring played. Being able to see the benefit of the new practices in their daily work, both in terms of improved practice and benefits to the infants, was consistently identified as a driver for staff in their continued use of the new practices.

These interview data, taken in the context of the study as a whole, allowed theoretical frameworks based on extended and original NPT to be generated, which attempt to explain how the intervention acted to change practice. Key elements were changes in social norms and roles, with greater expectations for nutritional care and a shift towards greater nursing involvement in nutritional care and decision making. This was aided by a guideline which was felt to be useful and workable, with reinforcement of the new practices by the positive experience of using them and seeing benefit in both processes and patients.

These results, together with the findings of the other chapters and the implications and limitations of this study are discussed in the next chapter, which gives an overall discussion of the work in this thesis.

Chapter 13: Discussion

The study reported in this thesis has sought to deliver and evaluate a complex intervention intended to improve the nutritional care of preterm infants, and at the same time understand the process of practice change in a complex environment. The initial hypotheses of the study were:

1. *The introduction of a complex intervention for the nutritional care of preterm infants will improve their nutrient intakes and growth*

2. *The use of Normalization Process Theory to both guide and monitor the implementation of a complex intervention will result in improved integration into practice with subsequent improvement in clinical outcome measures*

This study also set out to study the factors that influence the implementation and adoption of a complex intervention into routine care

In this chapter I will discuss the findings of the study, and consider whether these hypotheses have been proven. The first hypothesis regarding the impact of the intervention to improve nutrient intake and growth will be looked at in terms of how effective the intervention was and how it relates to other work in this area. The second hypothesis focussing on NPT will be considered in three parts; the utility of NPT to guide and measure the implementation process, the impact this had on the integration of the intervention into routine care, and how this related to clinical outcomes. The potential issues and limitations of this study with regard to exploring each of these hypotheses will be discussed in each section. This will be followed by a discussion of the knowledge and experience gained in this work in relation to the process of practice change and the factors which affect it. Finally, the implications for practice and future work suggested by the findings of this thesis will be discussed.

13.1 The effect of the complex intervention for the nutritional care of preterm infants in improving their nutrient intakes and growth

13.1.1 The pattern of results seen in this study

Looking at the pattern of results described in chapter 10, the complex intervention was associated with the following changes in nutrient intakes and growth:

- Protein intake improved incrementally, with improvements seen after both partial and full implementation of the intervention compared to the pre-implementation period. These improvements appear to have been sustained into the post-implementation period.
- Weight gain also seemed to improve in an incremental fashion across all study periods, with a reduction in the fall of weight SDS experienced by preterm infants between birth and discharge. This also appeared to be sustained into 2013.
- Energy intakes were relatively stable across the pre-implementation and implementation periods, and appeared lower as a percentage of RRI after the implementation period.
- There was no statistically significant improvement in head growth, although there was a trend for a reduced fall in the difference in SDS for head circumference between birth and discharge across study periods, seen in the repeated measures analysis.

At first glance, this pattern of results suggest that the intervention had some success in improving protein intakes and weight gain, and this is important as the analysis of infant nutritional care during 2009 presented in chapter 6 highlighted protein intake and weight gain as areas in need of improvement. However, there are several issues to contemplate when considering the relative success of the intervention. Firstly, head growth was also identified as an issue from the 2009 analysis, and this has not been significantly enhanced by the intervention, although as mentioned above, there was a suggestion that head growth improved over the course of the study when looking at the pattern of results in the repeated measures analysis presented in chapter 10.

Secondly, in relation to this, there appears to have been little change in energy intake, as a result of the intervention, with, in fact, a fall in intake as a percentage of RRI toward the end of the study. This is not surprising, as energy intakes were already in excess of 100% during the pre-implementation period, so it makes sense that an intervention which aimed to deliver nutrients at

levels in keeping with Tsang et al's RRIs would maintain levels around 100%. This may explain why the energy intakes drifted down from in excess of 100% to around the 100% mark. However, it is perhaps a little surprising then that energy intakes appear to have fallen below RRI during the post implementation period. This may partly be explained by case-mix, with more unwell infants (as indicated by higher CRIB II scores) and a greater proportion of smaller or more premature infants. However, it may also suggest that certain elements of the intervention which were responsible for the maintenance of appropriate energy intakes were less consistently implemented during this time. In relation to this, as discussed in chapter 10 a new formulation of stock PN, 'Babiven', was introduced during the post implementation period, and the lower energy content of this product may explain the lower intake seen, especially given that the most significant fall in energy intake seemed to occur during the first two weeks of life, where PN would be the main source of nutrition. The fact that energy intakes fell but not protein most likely reflects the fact that the intervention was geared towards practices which improved protein intake to a greater extent than energy such as increased use of breast milk fortifier and early parenteral nutrition.

Thirdly, it seems that even partial implementation of the intervention (which focussed mainly on improved parenteral and enteral nutritional products) led to significant improvements in protein intake and growth. This could suggest that these elements alone may be responsible for the improvements associated with the intervention as a whole. However, looking at the repeated measures analysis results in chapter 10 it can be seen that there is an incremental 'dose response' pattern in protein intake and change in weight SDS at each sequential study period, suggesting that the full intervention was associated with a greater effect than those elements of the partial intervention in isolation. This sequential improvement in weight gain and protein intake appears to continue into the post implementation period, suggesting that improvements may have been sustained beyond the main intervention period.

It is useful at this point to consider the difference between statistical and clinical significance. Whilst some improvements seen may be statistically significant, what is perhaps more important is whether they are clinically significant. For instance, between the pre-implementation period (A) and the main intervention period (C), there was an increase in protein intakes of

0.33g/kg/day, or 6.3% of RRI, which seems relatively small. However, the observational study by Stephens et al described in chapter 2 did demonstrate a relationship between increased early protein intake and improved neurodevelopmental outcomes[43]. Therefore, an increase of 0.33g/kg/day across the entire stay may be important, especially as this difference was even greater in the post-implementation period (D) compared to the pre-implementation period at 0.47g/kg/day, although the findings of Stephens et al have yet to be proven in a randomised controlled trial (RCT). Similarly, the improvement in the difference in weight SDS between birth and discharge between the pre-implementation period (A) and the main intervention period (C) was 0.43 SD, which is the equivalent on a growth chart of about two thirds of the distance between marked centile lines. The observational study Ehrenkranz et al discussed in chapter 2 demonstrated an association between weight gain and rates of cerebral palsy, with infants with the greatest weight gain less likely to develop cerebral palsy, so this may be clinically relevant [42], though again these findings have not been proven in a RCT, so must be interpreted with caution. In addition, it is also important to consider whether weight gain in the absence of head growth or changes in length may represent excess adiposity, and this is considered in more detail later in this chapter.

Another important consideration here is the extent to which the improvements seen in this study are the result of the intervention itself. The comparison of infant outcomes in 2009 with the infants born during the 2011 pre-implementation period shows clearly that there were significant improvements in energy and protein intakes, but not growth, during the intervening years. This suggests that there was an underlying trend towards improved nutritional care prior to formal implementation of the intervention described in this study. This may have been due to changes in national policy or an increased awareness of nutrition amongst clinicians as a result of external influences, such as the publication of the ESPGHAN guidelines for the enteral nutrient intakes of preterm infants and the NCEPOD report highlighting failings in the delivery of parenteral nutrition to preterm infants, both published in 2010. Also during 2010, some of the work towards the nutritional aspects of this present project began, including recruitment of a Chief Investigator (Dr Alison Leaf, a supervisor of this project) and a research fellow (myself), which would have raised awareness of neonatal nutrition amongst clinical staff. It is of note

however that such influences were not identified by staff in the qualitative work presented in chapter 12.

More importantly, such underlying trends may have continued to influence practice and therefore outcomes, and so have been partly responsible for the changes observed during the intervention periods of this study. The effect of an underlying 'drift' toward improvements in practice cannot therefore be ignored, although the magnitude of the differences seen between pre-implementation and intervention periods during the study are relatively greater than those seen between 2009 and 2011 suggesting that there was an additional effect of the intervention over and above any underlying trend. The ITS analyses presented in chapter 10, whilst having important limitations, also support the possibility that there was an existing trend, as demonstrated by the fact that the slope for the majority of outcome measures seen during the 2011 pre-implementation period (A) is more positive than in any other period. However, without performing a RCT it is impossible to exclude confounders, so the emphasis in a study like the one presented here must be on plausible rather than definitive explanations.

13.1.2 This work in relation to other studies

During the time this study has been active, several other groups have used similar approaches in the preterm population in order to try and improve growth. Published in early 2012, Rochow et al described the introduction of a set of evidence based strategies aimed at improving the standard of nutritional care that preterm infants in their NICU received[221]. These included higher maximal intakes of parenteral amino acids and lipids, earlier enteral feeding with faster attainment of full feeds, daily adjustment of enteral feeds according to growth and the use of an electronic nutrition ordering system that tracked growth and energy intakes. Infants born during the intervention period (May 2005 to December 2007, n=123) were compared to those born in the preceding years (June 2001 to January 2005, n=115). The intervention led to significant improvements in energy and protein intake during early life and across stay compared to the pre-intervention period. There was also less pronounced weight loss immediately after birth, and infants in the intervention groups were heavier and had a larger head circumference at 36 weeks post-conceptional age, though there was no difference in average weight gain

across stay. These results are similar to those seen in the present study, though growth data are difficult to interpret as absolute weight and head circumference values were used rather than SDS or changes in SDS over stay, which account for normative data and size at birth. In addition, no statistical correction was made for baseline cohort characteristics such as weight and gestational age at birth.

In December 2012, Rogerro and colleagues published the results of their interventional study (intervention group January 2009 to December 2010, n=102) using a historical control group (January 2005 to December 2006, n=69), based around the introduction of nutritional practice changes [222]. These were focussed around improved PN, more controlled weaning of PN, early enteral feeding and tailored fortification of breast milk in response to weight gain. This study also demonstrated improved energy and protein intakes in the intervention group, together with a significant reduction in the fall in SDS score for both weight and head circumference between birth and discharge. Again, no statistical correction was made for baseline population characteristics. Unlike the present study, Rogerro et al were also able to show a significant improvement in head growth, although the magnitude of the change in head SDS is similar between the two studies. It may be that the present study lacked sufficient numbers and therefore statistical power to show a significant difference, as the intervention cohort in Rogerro et al' study was larger.

In 2013, Loys et al carried out another trial of improved nutritional policy, including earlier and higher parenteral and enteral nutrient intakes [223]. Like the other studies described above and the present study, this was a before and after study, comparing an intervention group (2009, n=37) to those born before the practices were introduced (2005-6, n=37). There was a significant reduction in the deficits in energy and protein accumulated over the first seven weeks of life (using Tsang's RRIs as the standard from which to calculate deficits). The intervention group showed significant reductions in the difference in SDS for length between birth and 36 weeks post-conceptional age, but not weight or head circumference. The present study was unable to look at length in detail due to a lack of comparative data in the pre-implementation group, despite regular measures of length in the intervention periods.

More recently, Moltu et al carried out a RCT of an enhanced feeding protocol compared to a standard one, enrolling fifty preterm infants [224]. Their enhanced feeding regimen included increased supply of energy, protein, essential fatty acids and vitamin A in parenteral and enteral feeds. They demonstrated significant improvements in energy and protein intakes in the first four weeks of life, with faster time to regain birth weight in the intervention group [224]. They also showed that infants in the intervention group maintained SDS for weight and head circumference between birth and 36 weeks post-conceptional age, a significant improvement compared to the control group [224]. However, they also noticed some detrimental effects of the enhanced nutrition in the intervention group, including a significantly higher septicaemia rate (which led to the trial being stopped early) and increased incidence of hypophosphatemia and hypokalaemia [225]. The authors attributed the metabolic disturbances to the increased protein intake leading to increased lean tissue accretion, which in turn increased the demand for phosphate and potassium. Infants with the most marked hypophosphataemia were more likely to develop septicaemia, so this was felt to be linked to the metabolic disturbances seen [225].

Whilst all four of the studies described above had results which are consistent with the present study, none of them included any kind of implementation study, nor did they include any process evaluation. This is important, as it means it is not possible to be sure to what extent the intervention was adhered to in practice, and could make implementing the intervention in other settings difficult. However, at the same time none of these studies used an intervention as multifaceted as the one used in the present study, relying on simple policy changes or reformulation of PN, which may make a process evaluation less important. These studies do support the idea, as suggested by the results of the present study, that improving the nutrient content of products alone does make a difference.

13.1.3 Implementing a standardised approach where robust evidence for practice may not be available.

While the intervention used in this study appears to have been associated with improvements in protein intake and weight gain, it is important to consider the implications of this for infants in the context of an intervention that was based on evidence that varied in quality; only a handful of the practice points

presented in chapter 2 were supported by evidence of a high level and grade. Given the complexity of the intervention in this study, combined with a large number of practice points covering all aspects of parenteral and enteral feeding, it may be that the present study was over-ambitious in trying to address the entirety of nutritional management, It may be that focussing on one or two practice points which are well supported by strong evidence (such as use of breastmilk for enteral feeding) would have been easier to implement, as it would have removed the *technical complications* due to the lack of a robust evidence base seen in this study. However, the decision to try and tackle all nutritional management was taken in order to try and maximise the impact on outcomes and also because there was a perceived need from staff for a comprehensive guideline. While this resulted in a guideline that was supported by staff, it meant that the implementation process was more complex and that the intervention as a whole was based on evidence, which whilst the best available, was variable in its quality and robustness. There is therefore a need to recognise this uncertainty when interpreting the results of the study, and the potential issues are discussed below.

13.1.3.1 Evidence for recommended nutrient intakes

Whilst Tsang et al's RRIs are well recognised and used in clinical practice, as discussed in chapter 2, their evidence base is variable, and it may be that the lack of improvements in head growth seen in this study is related to this. Nonetheless, there is evidence that achieving Tsang et al's RRIs can lead to improvements in growth[62], and the studies described above seem to corroborate this.

It is important to consider the possibility of adverse outcomes, and chapter 10 showed that rates of sepsis with coagulase negative staphylococcus appeared to increase during the main intervention period, though a similar increase was not seen in the partial or post implementation periods. While this study was not powered to detect differences in morbidity and mortality, these findings may still be a genuine effect of increased nutrient intake and warrants further investigation. Indeed, the possibility of a detrimental effect of enhanced nutrient provision, as highlighted by Moltu et al's study discussed above, should be considered. However, the mean intakes of potassium and phosphate in the first week of life in Moltu et al's intervention group were 1.33mmol/kg/day and 0.95mmol/kg/day respectively, which is a markedly

lower provision of phosphorous than the minimum recommended by Tsang et al of 1.5mmol/kg/day[225]. At the same time, protein intakes in Moltu's intervention group in the first week of life at 3.7g/kg/day were above Tsang et al's recommendations[14] of 3.5g/kg/day during the 'transition phase' and well above the 2g/kg/day recommended for the first day of life[225]. The picture in the study by Moltu et al is therefore one of excessive protein in the face of insufficient phosphorous, so whilst Tsang et al's RRIs may not necessarily be founded on a totally robust evidence base, it is perhaps understandable that some unexpected detrimental effects were observed.

13.1.3.2 Birth centiles as a target for growth

As discussed in chapter 2, the use of birth centiles as a starting point from which to measure postnatal growth is controversial. Since the study described in this thesis has been completed, Cole et al have published weight centiles for preterm infants born below 32 weeks gestation in UK neonatal units, based on longitudinal data provided by the Neonatal Data Analysis Unit from NHS electronic records [220]. Interestingly, these data demonstrated that while the UK-WHO NICM chart represented the birth weights of preterm infants reasonably well, the pattern of growth was different, with preterm infants dropping down across two marked centile lines for weight in the first two to three weeks of life and then tracking a lower centile thereafter. This led the authors to conclude that assigning an infant's target centile should be done once weight gain has stabilised rather than using the birth weight centile, as the latter could potentially encourage excessive and rapid weight gain. In the present study, the growth outcomes used were the change in SDS from birth based on the UK-WHO NICM reference data[69]. The pattern of growth in the 2011 pre-implementation period was similar to that described by Cole, with infants weight falling 0.68 standard deviations (approximately one marked centile lines on a NICM chart) by two weeks of age. However, in the 2012 intervention period, according to the non-repeated measures analysis presented in chapter 10, this fall at the end of week two was reduced to 0.57 standard deviations (just less than one marked centile line), and 0.44 SDs at discharge. These changes were further improved in the post-implementation period (0.34 SDs), a finding that was consistent in the repeated measures analysis also. This suggests that some of the fall in weight SDS seen by Cole is amenable to nutritional intervention, particularly early on.

Although the present study showed that weight gain could be increased, what is not clear is whether this is necessary or desirable. Whilst rapid postnatal growth has been associated with some improvements in neurodevelopmental outcomes, it is also associated with an increased risk of metabolic syndrome, obesity and heart disease in later life [226]. In fact even just two weeks of accelerated growth after birth has been associated with increased risk of insulin resistance in early adulthood and abnormal vascular tone [227]. It is not clear whether the increased growth seen in the present study is beneficial or detrimental with regard to these longer term outcomes, and infants will need to be followed up in order to ascertain this. It is likely that a balance needs to be found between any potential benefits of increased early growth from a cognitive perspective and the risks of increased metabolic and cardiovascular disturbance in later life. Avoiding an early deficit and hence the need for catch up growth may be the key issue here.

13.1.3.3 Weight as a measure of adequate growth

It is increasingly apparent that weight alone is inadequate to assess growth in the neonatal period. A systematic review carried out by myself and colleagues showed that preterm infants have significantly higher percentage body fat (due to a relative lack of lean tissue rather than an increase in fat mass) upon reaching term age, compared to infants born full term [46]. Of note the Rochow and Rogerro studies also looked at body composition as an outcome for their nutritional trials, both showing that their interventions had no impact on the body composition of the infants in the study compared to the historical controls [221 222]. This is interesting, as this may be a sign that, even with interventions to increase nutrient intake, whilst gaining more weight, the body composition of the infants remains abnormal compared to those born at term; Rogerro et al and Rochow et al found mean percentage body fats of around 16% and 17% respectively, which is consistent with other studies and higher than that seen in infants born at term (8.9–11.2%)[46 221 222 228]. This may indicate that despite increased nutrient intakes there is still a failure to promote lean tissue accretion in these infants. Given the higher delivery of both energy and protein seen, possible explanations for this pattern may be inadequate delivery of other essential nutrients not measured in these studies, or an effect of preterm birth independent of nutrition. Body composition is important, as alterations in the relative amounts of fat to lean tissue are likely to disrupt

normal patterns of growth and have been shown to affect metabolic function later in life [48 50]. There is therefore a need going forward to better measure and understand the impact of nutrition on body composition and associated longer term outcomes.

13.1.4 Limitations regarding the nutritional aspects of the study

Alternative explanations for the patterns of results seen have been discussed above, together with some of the limitations of the study. However there are some additional limitations regarding the nutritional outcomes which also warrant discussion. Firstly, as a controlled before and after study which uses a retrospective pre-implementation group, it is not possible to be sure that any of the changes seen during the study are a direct result of the intervention. As this was not a randomised controlled trial, it cannot control for causal mechanisms and confounders, and as such it is subject to limits on interpretation. Whilst the statistical analyses show associations between the progressive implementation of the intervention and changes in outcomes, it cannot prove causation. Multiple statistical methods have been used to try and ensure that the conclusions drawn are as robust as possible and a true reflection of the data, and some of the findings from the qualitative aspect of the study help to back up some of these findings as discussed below.

A further limitation is that of adequate patient numbers and statistical power to detect important differences. In the case of head circumference, the power calculation done at the start of the study based on the predicted number of infants to be born during the intervention period suggested that this study would only be able to detect an improvement of 1.2 SDs, so it is perhaps unsurprising that the smaller differences seen in the study are not statistically significant. In the case of mortality and morbidity data, as mentioned above, this study was not intended to look for differences in these outcomes.

Finally, another limitation is that whilst the intervention was planned to be delivered in a controlled and consistent way, there were some changes that occurred within the clinical environment. An example of this was the introduction of a new PN product (‘Babiven’) during the post-implementation period. This decision was made independently by the clinical staff and was out of the control of the study team but may have contributed to some of the patterns of results seen during the post-implementation phase.

13.2 The use of Normalization Process Theory to develop, guide and monitor the implementation of a complex intervention

13.2.1 Normalization Process Theory as a framework for implementing practice change

Looking back at the theory-led overview of systematic reviews of professional interventions using NPT presented in chapter 5, one of the hypotheses suggested by the findings was that "*Interventions that seek to restructure and reinforce practice norms and associate them with peer and reference group behaviours are more likely to lead to behaviour change*". In particular, interventions which facilitated either normative restructuring of practice, modifying peer group norms and expectations of practice (e.g. opinion leaders, educational outreach) or relational restructuring of practice, reinforcing modified peer group norms by emphasising the expectations of an external reference group (e.g. Reminders, Audit and Feedback), seemed more likely to successfully change practice. The intervention used in this study favoured these types of intervention components, with the nutrition team and nurse champions acting as opinion leaders and delivering education outreach, together with serial audits and a reminder in the form of the weekly screening tool. The fact that this study has demonstrated some improvements in practice and infant outcome provides some evidence that this hypothesis from the systematic review in chapter 5 may be true, and warrants further investigation in other studies of practice change.

The overview of systematic reviews presented in chapter 5 also demonstrates the utility of NPT to guide analysis of practice change interventions retrospectively. Whilst the theory-led analysis in chapter 5 helped inform the development of the intervention used in the present study, NPT was also used in a prospective manner in this study for the first time to actively develop and drive the intervention rather than perform a retrospective assessment of aspects of the implementation process. As such, and given some of the limitations of the study design described above, this should be considered an exploratory study of NPT in a clinical setting rather than a definitive one.

However, the theoretical frameworks discussed in chapter 12, together with the success of the study in changing practice and improving some of the infant outcomes suggest that NPT was useful for developing and implementing the complex intervention.

Prior to implementation, NPT was used to analyse the focus groups discussing the issues that might enhance or impede the uptake of the intervention, and again this highlighted important areas. In particular, they demonstrated that staff were clear about the reason and need for change in practice (*coherence*) and were willing to carry it out (*cognitive participation*) prior to the start of the study. This demonstrates that staff were in a good position to put the intervention into practice and perhaps explains the unexpectedly high NPT toolkit scores seen after the first questionnaire in March 2012, even though the intervention had not long been implemented. An alternative explanation for these high initial scores, as discussed in chapter 11, is that perhaps staff were answering more positively in order to please the study team, or it may be that the NPT toolkit captured something else other than 'normalisation' here; measuring staff *perception* of improvement and in turn, normalisation, rather than *actual* normalisation. It may be argued that if staff believe that the new practices are a success and have become part of routine care then this could be considered 'normalisation', even if the improvements in actual practice are less positive. Certainly in this study it seems that generally staff perceived improvements in care and increasing normalisation whilst the audit and infant outcome data suggest this process was not complete (although audit compliance of around 80% is high and would be considered to indicate successful implementation in most studies). Furthermore, the cause and effect relationship between NPT scores and normalisation is interesting; the act of measuring normalisation using NPT may itself have led to the positive scores and qualitative data seen in this study, or conversely, the NPT toolkit may have been detecting genuine increases in normalisation. Nonetheless, the fact that the NPT results are associated with parallel increases in audit measures (including high baseline measures) goes in favour of the NPT toolkit scores offering a reasonable measure of the uptake of the new practices, as discussed later in this chapter.

The focus groups highlighted the high value staff placed on *reflexive monitoring*, stressing the need to be able to see the benefit of the new

practices in their work. This proved to be important, as demonstrated by the improved audit compliance, and the peak in NPT *reflexive monitoring* and *collective action* scores seen in the second half of 2012 after publicity surrounding the interim infant outcome and audit results during August 2012.

Chapter 7 describes how NPT was used to guide the strategy for development of the intervention. In particular, the guidelines were aimed at encouraging *coherence* and *cognitive participation* by being clear about the reasoning behind the approaches used and how to use them. The interview findings show that they worked in this context, with staff repeatedly highlighting their ease of use and clarity. Similarly, the nutrition team, nurse champions and nutrition ward round aimed to provide feedback to aid *reflexive monitoring* and, based on the framework analysis of the staff interviews, seem to have achieved this.

It is perhaps important at this point to compare NPT to more 'traditional' ways of driving practice change. In particular, the 'Model for Improvement' (MFI) discussed in chapter 3 is commonly used in quality improvement projects to identify and address areas where practice is in need of improvement, and has been used extensively in the NICU setting. It could be argued that such a model may have had a similar effect in the present study, as by using the MFI 'Plan Do Study Act' (PDSA) approach, the shortcomings in current nutritional care could have been identified, a plan put together to address them using a guideline or similar, and then the effect measured using audits, with ongoing PDSA audit cycles identifying non-compliance and subsequent development of a strategy to address them. However, using the MFI to explore the processes used in this study would not have provided such rich information. For instance, whilst a lack of compliance would have been identified by the MFI approach, it may not have pointed out that the lack of compliance was due to a failure of staff to see the benefit of the new practice in their work (*reflexive monitoring*). The MFI tends to focus on one small specific step at a time, so whilst the MFI allows users to think about how they will change practice, again it does not provide a framework which allows them to think about how these changes will facilitate staff carrying out the work that needs to be done. It may also not have pointed to the need for a multifaceted, complex approach to practice change, with appropriate selection of interventions aimed at the most successful implementation.

PDSA cycles and the MFI focus on *improvement,* i.e. increased audit compliance or improved outcomes, identifying whether targets are being met. In contrast, NPT focuses on the work people do to enact a new practice, meaning that areas where work is not being done or encouraged in a certain way can be identified. At the same time, it can be seen how the PDSA approach can be used quickly and repeatedly to cause incremental change; repeated use over time may have led to changes in strategy that could have addressed shortfalls and perhaps delivered a similar result. The comprehensive implementation approach used in this study appears to have led to improved practice, outcomes and a degree of normalisation of the new practices, but it does not mean that other existing approaches would not have achieved the same result. However, it may be that the focus of NPT on normalisation is where its strength lies, as successful normalisation of a process may lead to it being sustained over a longer period after the end of a project, whilst models like the MFI require constant PDSA cycles to sustain them. While there is a suggestion that some improvements remained in place after the end of the study, the evidence for a sustained effect was only partial.

13.2.2 The utility of Normalization Process Theory to measure, guide and improve the integration of new practices into routine care

The audit compliance and NPT scores in Chapter 11 demonstrate that the guidelines were being used, and the interview data presented in chapter 12 suggest that staff were very positive and motivated about the new practices, were using the guidelines as part of routine care, and generally felt practice was changing and improving. At the same time however, outcome data in chapter 11 suggest that there was limited improvement in the majority of processes of care, with a greater time to start milk feeds and limited improvement in the use of breast milk. Chapter 10 suggests that there were some small improvements in infant outcomes. Overall therefore, while there are data to suggest that staff compliance and attitudes were affected in a positive way, objective measures of improvements in care and outcome demonstrated only a modest impact associated with the intervention.

The use of serial practice audits in conjunction with the NPT toolkit questionnaire provided a measure of the extent to which the new practices were adopted, and the fact that they both showed a similar pattern was

reassuring. Importantly, while the use of the NPT Toolkit to measure normalisation in the study was novel and experimental, it seems that the measure of 'normalisation' provided by the NPT toolkit does relate to practice changes in the 'real world'. The fact that the staff NPT toolkit scores, which are based on a subjective perception of how well the intervention has been integrated into normal practice, relate to objective measures of practice (the guideline compliance audit), suggests that the NPT toolkit has some utility for measuring the normalisation of new practices. Whilst there was a statistically significant relationship between the NPT scores and audit measures, the association was fairly weak, with an *r* value of just 0.2, meaning that NPT scores accounted for just 4% of the variability in audit scores. Similarly the effect size was small, with an increase in compliance of 0.8% for every extra point in mean NPT score. When time was included in the model, the *r* value for the model increased to 0.7, with the coefficient for the mean NPT score remaining a significant factor in the model, though its effect size reduced to 0.38% audit compliance for each additional mean NPT score point. Whether or not time should be included in the model is an interesting consideration. In an ideal implementation process, practice (and therefore guideline compliance) would improve over time, so it could be argued that this should not be adjusted for. However, including it allows the contribution of NPT measures in predicting normalisation to be seen without the effect of time. Including time also allowed some adjustment for the repeated measures nature of the data in the absence of identifiable longitudinal data, as discussed in chapter 4. The findings for the relationship between NPT scores and behaviour are not dissimilar to findings of other theories such as TPB, as discussed in chapter 3. TPB has been used extensively to predict both behaviour and intention, and has been shown in meta-analyses to have *r* values of 0.31 for objective measures of behaviour. In this context, the *r* value of 0.2 obtained in the present study suggests that the use of NPT to measure or predict normalisation of a new practice into routine care may have some validity and utility, and is worthy of further investigation.

Similar to the focus groups, the importance of *reflexive monitoring* came out strongly across both the interviews and the NPT questionnaire results. When the scores of the individual constructs of NPT were looked at in relation to the audit results, it was only *reflexive monitoring* that had a significant association with the audit compliance again with a *r* value of 0.25, similar to that seen for

overall NPT scores. *Reflexive motioning* accounted for 6% of the variability seen in the audit compliance and had an effect size of an improvement of 0.9% audit compliance for every point scored. Seeing the impact of actions is a feedback mechanism, and such 'feedback loops' are likely to be responsible for the efficacy of feedback based professional interventions, such as audit and educational outreach from other health professionals. In the context of this study, which took place in a complex environment; the feedback loop was clearly a potent mechanism for intervention. These findings are also consistent with those of the theory-led overview of systematic reviews of professional interventions using NPT described and discussed in chapter 5, which showed that those interventions which scored highly on *reflexive monitoring* were more likely to be successful.

The use of teaching and the AV system to help staff see the results of the study during the main implementation period in response to low *reflexive monitoring* scores demonstrates the utility of NPT to identify issues and make implementation a more dynamic process. It also illustrates how addressing such issues results in responsive changes that can be seen in subsequent NPT scores, suggesting that NPT offers a way to both *measure* and *guide* change.

In discussing the utility of NPT to guide practice change, it is again important to consider alternatives. In this case, it could be argued that as it was the *reflexive monitoring* construct of NPT that appeared to have the strongest effect, perhaps processes such as clinical audit or the PDSA cycles of the MFI described above could have been used in isolation to achieve a similar effect, without the need for the more extensive use of NPT described in this study. Both these processes, based on feedback to staff of data regarding performance, are strong in the domain of *reflexive monitoring*. However, to use these interventions *in place* of NPT would be to miss the other aspects of the theory, including the development of the intervention and the contribution of other constructs, and to miss the point of using a theory to guide implementation; in the present study, audit was used *alongside* NPT to measure and guide practice change. Whilst audit taps into one of the strongest constructs of NPT, there is evidence (some of which is discussed in chapter 5) that audit or similar measures alone are not enough to change practice significantly. Nevertheless, it must be recognised that perhaps the reason there is a significant relationship between NPT measures and audit measures is

through this shared construct of *reflexive monitoring*, rather than a property unique to NPT. Overall however, the use of a theory to guide implementation, together with a combination of interventions aimed at changing practice, is key to successful implementation and is something that comes out repeatedly in this thesis.

The MRC guidance on complex interventions emphasises the importance of having an understanding of how an intervention changes practice, and recommends the use of a process evaluation to enable an assessment of which elements of the planned complex intervention actually formed part of the intervention when used in practice, and to what extent those elements were adopted into practice. In this context, NPT has provided valuable additional information to that provided by the audit of guideline compliance. The audits measured how well the guideline was put into practice, but NPT, both as the toolkit questionnaire and through the analysis of the interview data, provided details of how the intervention was used by staff, which may prove useful should it be implemented elsewhere.

There is an important question to be asked about the extent to which the intervention in this study became 'normalised' (i.e. considered part of normal practice). Whilst chapter 10 provides some evidence that increased protein intake and weight gain were sustained into the post-implementation period, energy intakes continued to fall as discussed above, and audit measures of compliance and NPT scores also fell slightly at the end of the post-implementation period, although remained above baseline levels, suggesting that staff were continuing to work to deliver the intervention to a degree beyond that seen at the start of the study. However, six months may not be a long enough period to see any fall off in practice, so there is a case for repeating the 'post-implementation' audit of guideline compliance at a later stage to see if the new practices are being sustained well beyond the end of the study. In addition, whilst the study team 'withdrew' at the end of the intervention period to allow an assessment of how sustainable the changes were, many of the elements remained in place, including the guidelines, nutrition team, ward rounds and screening tool. While the nurse champions also remained in place, their role changed to a more research based role, with less emphasis on education and support (although they continued to work clinically for the majority of their time as they had done before). On the one

hand this means there was less of a 'withdrawal' of support, but more a reduction in education and deliberate reinforcement, and on the other hand it is also a testament to how the intervention was developed in order to be sustainable in clinical practice, utilising existing clinical staff and resources. This in part is due to the use of NPT during its development.

13.2.3 The relationship between Normalization Process Theory in practice and subsequent clinical outcome measures

Whilst there is some evidence above that the NPT scores can provide a potential measure of normalisation and practice change which is in turn associated with audit measures, there was no association between NPT toolkit scores and clinical outcomes. Chapter 11 shows that there was not a linear relationship between nutrient intakes and NPT scores over time. This is not unexpected, given that it is a common finding in studies of professional behaviour change, and one illustrated by many of the systematic reviews included in chapter 5; many professional interventions lead to improvements in practice and the processes of care, but not patient outcomes. As discussed above, this may be due to the fact that the intervention may not have been based on sufficiently robust evidence to produce the desired clinical outcomes. Another potential explanation is that greater compliance with the intervention was required, as chapter 11 demonstrated that that the maximum audit compliance was around 81%. Furthermore, looking in more detail at the audit results in Chapter 11, the points around the choice of feed at discharge and time to start milk feeds were not as well complied with, and these were outcomes where the intervention appeared to have no effect. Therefore, there may have been a failure to adequately share the findings of these audits contemporaneously with staff, and provide feedback that these needed to be improved on. Greater use of *reflexive* monitoring in this area might have led to further improvements in outcomes.

Overall infant outcomes of the study discussed above and in chapter 10, did show that for the whole of the 2012 intervention period, there appeared to be a modest increase in weight gain and protein intakes associated with the intervention. It could therefore be argued that the increased NPT scores over time, combined with the increasing and reasonable audit compliance over the same period, suggest there was improving use and integration of the

intervention into routine practice during the intervention period, and this in turn was associated with the improved infant outcomes seen over the whole study period. Therefore, whilst there was no linear relationship over time between NPT scores and outcomes, this does not exclude a relationship between NPT and improved outcomes overall. Indeed, the qualitative data from the interviews support the conclusion that the use of NPT in this study to develop and guide the intervention led to improved implementation, and this is corroborated by the audit data. Using qualitative analysis of the interview data to produce the theoretical frameworks of how the intervention may have led to practice change, as illustrated in chapter 12, further demonstrates how the use of NPT as a framework for implementation helped enhance the integration and uptake of the intervention by staff on the neonatal unit. This is discussed in more detail below.

13.3 Understanding the Process of Practice Change

A major aim of this study was to understand the process of practice change in a complex environment such as NICU, and the way in which it sought to do this was by the use of a mixed methods approach. Whilst this is a strength of the study, integrating the quantitative clinical results of the intervention with the results of the mostly qualitative study of implementation represents a major challenge. As discussed briefly in chapter 4, these two different methodologies and approaches often seem at odds with one another and are the subject of ongoing epistemological debate regarding how and whether they should be integrated at all. However, using the qualitative methods to provide a *description* of the implementation process in the context of the measures of clinical practice and outcomes allows a comprehensive picture of the implementation process to be built up. Such an approach also allows more detailed evaluations of the intervention and insight into the complexities of changing practice in the clinical setting [229].

13.3.1 Implementation and integration of the intervention into practice

Taking the theoretical frameworks developed from the qualitative interview data described and discussed in chapter 12, together with the findings of the study overall, it can be seen how NPT can be used to explain how the

implementation process worked to change practice, although it is important to remember that the *success* of the intervention in changing practice was mixed, with only modest improvements in infant outcomes and audit compliance, and little improvement in some of the processes of care. Nonetheless, the cyclical nature of the frameworks show how these processes may go on to lead to sustained changes and 'normalisation' of the new practices, and there is some evidence of this from the audit and infant data, as discussed above. Figure 13.1 shows a simpler model of the key elements of the intervention and the mechanisms by which they drove the change process.

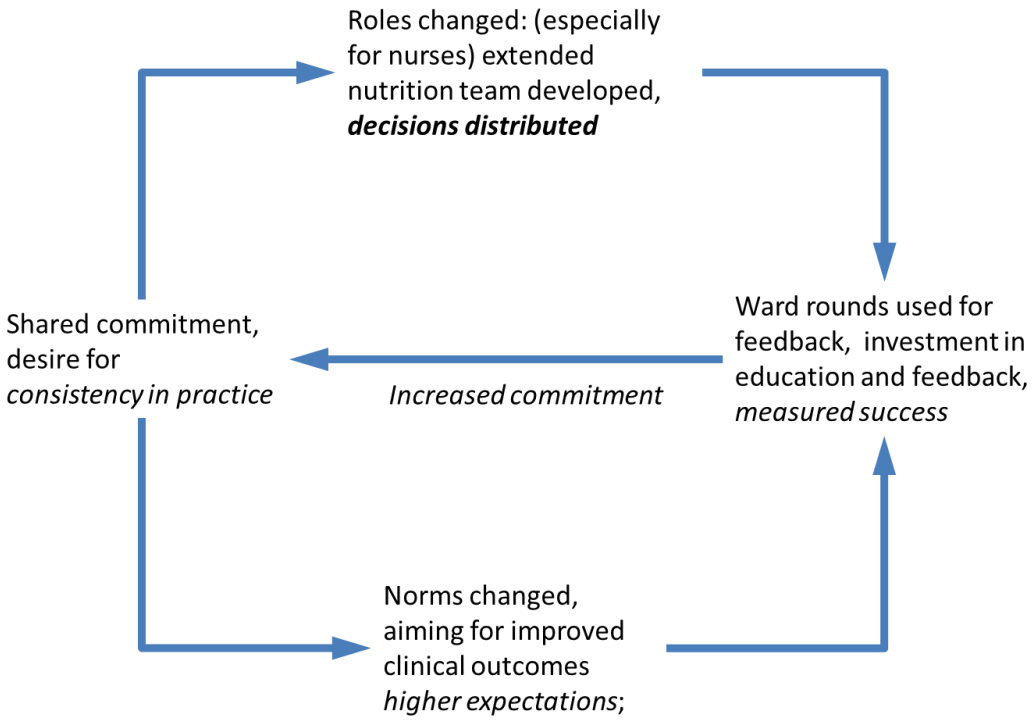


Figure 13.1: A simple model for the implementation of the complex intervention used in this study

Figure 13.1 illustrates how a shared commitment by staff to improve care, driven by a strong desire for consistency in practice was a foundation for the change process. This worked with the education and increased awareness surrounding the new practices, changing the accepted norms on the unit, with higher expectations for nutritional care and outcomes. The strong commitment to practice change allowed a change in roles and decision making to be facilitated by the introduction of the guideline. Indeed, looking at the interview data it is clear that the intervention harnessed the nursing staff as a driver for the change process. Given that the nurses spend the most time in the nursery

with the individual infants, it makes sense that putting them more in control of nutrition would result in things being more likely to be done, and done in accordance with the guideline (which was by the infant's cot at all times). There was a stronger desire for nutritional guidelines from the nursing team than for medical staff; Nurses spend a large amount of time with the infants and their families and they need to have a plan for the day to allow them to order feeds and plan their workload. They found the uncertainty surrounding feeding uncomfortable and acceptable, so wanted clearer and consistent guidance. Medical staff manage their workloads differently and are more mobile, moving about the unit, seeing and prioritising different patients. They are also trained to deal with uncertainty in a different way to nursing staff, so were more comfortable in deferring decisions till later or waiting for a senior opinion.

In this study there was a shift of decision making responsibility away from consultants (who previously had made the majority of feeding plans, with a feeling that different consultants made quite different plans) towards junior medical staff and nurses. The intervention therefore distributed decision making amongst these large groups of staff and away from specific individuals. These groups of people were able to use the guideline to make a plan and were more comfortable with decisions about feeding. Whilst the nutrition team were identified as a major driver for change, it seems that the guideline itself was the driver for this change in roles and responsibilities, because it facilitated decision making out of hours when the nutrition team or seniors were not available for advice. However, it can also be seen that the guideline alone would have been inadequate to cause change; the nutrition team facilitated the implementation process by attending to intervention design, workability and integration into workflow, reinforcing the changes and providing measures of success. Figure 13.1 also highlights their important role for *reflexive monitoring*, with the nutrition ward round used for feedback to staff and education. This further increased commitment to changes in practice, and it is likely that this mechanism led to some of the changes being sustained, as staff were continually encouraged to use the practices as they saw them working in daily practice. At the same time, a failure to properly exploit *reflexive monitoring* in terms of feeding back some of the areas of poor guideline compliance may be what led to the lack of improvements seen in the time to start milk feeds and choice of milk feeds at discharge described in chapter 11.

The distribution of decisions illustrated by figure 13.1 is one of the key factors that led to the modest improvements associated with the intervention and its perceived success by staff. This is of interest as it is not one of the 'professional interventions' listed by the Cochrane EPOC group; all of the other elements in figure 13.1 can be captured with the EPOC professional intervention taxonomy except for this one. This is important as the Cochrane EPOC professional interventions all rely on the individuals who were previously making decisions to continue making them but with a new agenda or focus. Their current practice will therefore need to be changed in line with the intervention. By shifting decision making to another group and providing them with the tools to take the responsibility it can be seen how this may be more likely to cause change, potentially circumventing existing and established practices. In this context, this study worked to change practice because it changed what people were able to do, rather than because it introduced a new behaviour.

One thing that comes across from the results of this study and its mixed effects on changing practice and infant outcomes, is that there are different levels of 'practice'. There are those that are relatively independent of the infants, such as completing screening tools, measuring, prescribing vitamins, changing feed and PN flow rates, there are those that are more dependent on the infants and their clinical condition, such as starting feeds, increasing feeds, choice of milk feed and adding fortifier, and finally there are those that are dependent on others, such as starting PN (this requires insertion of central line by medical staff) and breastfeeding (this requires motivated mothers and support from nursing staff). It seems that the more 'independent' levels of practice were more susceptible to the intervention used in this study, where there was some modest success, while those that are dependent on the infant's condition or on others were harder to influence.

There was a sense from the interviews that staff felt that the new practices had become, or at least were becoming, reasonably well integrated into routine care. Interestingly, this fits with the high scores seen on the NPT toolkit results, which suggest that the practices were becoming well normalised. Of note however, as discussed earlier in this chapter, there was a drop in NPT scores and audit compliance at the end of the six month normalisation period in 2013, suggesting that practice was beginning to slip. However, at the same

time the infant outcome data from the post-implementation period suggests that the improved protein intake and weight gain seen in the 2012 implementation period may have been maintained in 2013. One explanation for this is that staff had begun to 'drop' some elements of the intervention over time that they had not felt or found to be useful in practice. Whilst this had affected compliance scores, and their opinions reflected in the NPT scores, it had not altered the delivery of better nutrition to the infants. Figure 12.2 in chapter 12 illustrates how restructuring is part of the normalisation process, and indeed many practices are changed or adapted by users over time as they seek to fit them into existing practices and routine care. Another issue to consider is that NPT focusses on the introduction of a *new* practice; many elements of the intervention used in this study could be considered as standardisation of existing practices, rather than the introduction of new ones. In addition, it may be the case the staff were beginning to view the intervention differently and respond to questionnaires differently as they no longer considered the intervention to be new. This in turn raises the question of how long the NPT toolkit can be used usefully in the way it was in this study to measure normalisation.

13.3.2 The Role of the Clinical Environment

The findings of the focus groups and TPB questionnaire present a picture of a neonatal unit that was keen for nutritional practice to be standardised, giving the impression of an environment that was relatively 'ripe' for change. It is perhaps therefore unsurprising in this context that the intervention had some success in changing practice. Initial NPT toolkit scores were relatively high, suggesting that the practice was already relatively 'normalised' just two months into the intervention, and this may be a reflection of this positive setting. Similarly, given that the TPB survey demonstrated that attitude would be the most important factor in determining behaviour, and that the overall impression from the focus groups was that staff were positive towards the changes, it is perhaps not surprising that the intervention seems to have led to some improvements in practice and outcomes. However, there appears to be a disparity between both the positive attitudes and perceptions of success amongst of staff, and the limited effect of the intervention on some outcomes and measures of practice. This mismatch between what people think they are doing, and what they are actually doing in practice has previously been

highlighted in the context of neonatal nutrition by Kuzma-O' Reilly et al in their study of implementing 'potentially better practices' in nutrition (described in chapter 1), who identified a clear discrepancy between staff perceptions of practice and objective measures of practice [23].

The focus groups also identified several barriers to change, together with potential solutions as suggested by staff, and addressing these may also have facilitated the generation of an environment better able to implement the new practices. Data from the interviews in chapter 12 suggest that staff felt that many of these potential barriers had been addressed, and commented on the positive impact it had had on their ability to do the work being asked of them. Reflecting on the TPB findings in the context of the interviews, it seems that the education program, together with the support provided by nurse champions and nutrition team at ward level helped to promote a positive attitude towards the new practices amongst staff. The TPB survey also showed that intentions to follow the new guidelines were reasonably high at around 80% (depending on which measure of intention was used). This tallies well with the levels of guideline compliance seen in the serial audits, which were all around the 80% mark, suggesting that in this setting TPB was able to predict actual behaviour reasonably well.

Another environmental factor to consider here is that of staff turnover. During the study there was quite a high turnover of nursing staff (only 77% of the initial staff recruits to the NPT questionnaire were stil employed at the end of the study, with an equivalent intake of new staff to replace them), in addition to the regular turnover of junior doctors every six months. High staff turnover is often seen by those seeking to implement change as a barrier to implementation due to the loss of trained staff or the introduction of new individuals with their own practices. However, in the present study the introduction of new staff seemed to be beneficial, as new starters received training in the new practices and guidelines at their induction, and were being introduced to an environment where the new practise were being pushed by existing staff as the norm.

13.3.3 Limitations of the Implementation work in this study

Many of the alternative explanations for the findings of the NPT work in this study, together with some of the limitations of the work have already been

discussed in the previous sections of this chapter. However, there are some other important limitations that should also be considered. One limitation is that it is not possible to generalise the findings of the qualitative analysis of the interviews as they are specific to the setting. However, some concepts may be transferable and theoretical frameworks developed from the data, as has been done in this study, are more generalisable to other settings. Similarly, whilst purposive sampling was used to try and gain a diverse spread of responses, it is possible that more views could have been sought. Generally 20 to 30 participants are sufficient to ensure this, and certainly there were many responses that came up repeatedly.

Another limitation is the subjective nature of the analysis and interpretation of this work. One advantage of the framework method used to analyse the data is that it provides a clear and robust way of coding data and drawing together common themes, whilst ensuring all points are considered. The framework also provides an audit trail from the analysis back to the raw text of the interview. Therefore whilst the subjective nature should be remembered when interpreting findings, steps were taken to try and ensure the conclusions drawn were consistent with the data. In relation to the discussion on restructuring above, the interviews used in this study did not capture how the staff may have modified the intervention over time or why they might have modified it, nor does it address how 'modifiable' staff felt the intervention was (and whether this was a factor in their intention to use it). Another limitation of the interviews was that no senior managers were interviewed, which may have provided an opportunity to look at the factors influencing implementation at management level.

The majority of respondents to both the interviews and the questionnaires were nursing staff and not medical, meaning that the views of the medical team are less accounted for. However, the ratio of doctors to nurses in the responses was similar to that seen on the neonatal unit on a daily basis, so these differences are perhaps appropriate and likely to give a more realistic picture of the implementation process on the neonatal unit. Another limitation was the gradually declining response rate to the NPT questionnaires across the implementation period, and in relation to this, those who persistently responded may be more likely to be those with the most enthusiasm for the project. However, this in itself would not necessarily mean they would not have

given a reasonable account of normalisation, and the fact that the NPT results fit with audit measures corroborates this.

Regarding the statistical analysis of the NPT questionnaires, one issue and limitation that arose was that the anonymous nature of the respondents meant that responses from the same individual over time could not be linked together. This meant that it was not possible to perform more formal, longitudinal repeated measures regression modelling to analyse the data. However, this was compensated for by using a simpler general linear model with correction for time as discussed above, as this provides a more conservative estimate of significance. It is therefore likely that the significant associations seen between the NPT data and audit result over time are real, as a repeated measures longitudinal model would have been more likely to find significance.

It is also important to recognise that during the course of this study, NPT was extended to provide a more general theory of implementation at a higher level. Carl May, the author of both NPT and this 'Extended NPT' was involved in supervising this thesis, and so the work carried out during the study that is described here influenced the development of Extended NPT from the original NPT [153].More importantly, it must be acknowledged that whilst this thesis has tried to present a balanced view of the role of NPT in this study, together with a justification of its use in this study in chapter 3, its choice for use in this study was related to this relationship.

Finally, it is important to consider the dual role I had in the study as both the 'implementer' and 'researcher'. This was in addition to my existing role as a member of the clinical team, carrying out occasional clinical shifts as a neonatal registrar across the study period. I was also already known to the majority of staff as a result of previous rotation to Southampton neonatal unit earlier in my career. Staff responding to the questionnaires may therefore have been influenced in their choice of answers due to their working relationship with me, and those interviewed may have responded differently if they had been interviewed by someone who was unknown to them and unrelated to the study. Whilst my position at the centre of the study can be viewed as a limitation, it also had advantages. Several staff cited in interviews that they felt more able to carry out the work required of them by the intervention as the people promoting it were familiar to them and were trusted. Staff also

mentioned that they felt compelled to do it as they had seen the amount of work that had gone into putting the intervention together, and they trusted it was well researched. In some ways however, this too is an additional limitation in that it potentially limits the ability of the intervention in this study to be deployed elsewhere. However, it does demonstrate that the degree to which staff are familiar with, trusting of and favourable towards the implementers is a key factor in implementation, and highlights that the relationships between implementers and staff are important.

13.4 Implications for practice and future work

This study has essentially used nutrition in the NICU as a vehicle to understand implementation in a complex environment. Therefore, many of the lessons learned in this study regarding how to implement and drive practice change could be applied to other areas of practice in different clinical settings. In fact, the framework shown in figure 13.1 could easily be generalised to other implementation processes. Going forward, it is essential to try and establish what the 'bare bones' are of this intervention and the approach to practice change, such that those seeking to apply this work in other settings can use it most efficiently and require the least investment by their institutions. From the work in this thesis, key elements of interventions to change practice seem to include:

- Establishing an environment that is ready for change
    - This should involve an assessment of the baseline attitudes and intentions of staff, and the barriers and facilitators to change. The implementation strategy should then be tailored to any issues identified by the baseline assessment, and NPT offers a useful framework for thinking through this process guiding intervention development and implementation.
- Establishing a core group of people to help drive the change forward
    - This should ideally include a local multidisciplinary team who can be seen as experts, providing leadership for the change process and offering advice and support. Advocates of the change process at ward level, who can remind and support colleagues in the day to day use of new practices are also important
- Establishing systems to facilitate and maintain change
    - Guidelines are useful to provide structure to care and facilitate decision making by appropriate staff who may not have previously been involved in

such decisions. They should allow flexibility for experienced staff who wish to deviate from them in appropriate circumstances
    - Systems for reminding and/or reinforcing the change at ward level are vital and should ideally include a team of staff who can provide support and feedback in person, or regular visual reminders and feedback
- Establishing systems to measure the effectiveness of practice change and provide feedback to staff.
    - Audit and feedback are useful in assessing adherence to new practices, and demonstrating to staff how well they are doing. Using the NPT toolkit to measure normalisation and highlight areas for improvement is feasible, potentially useful and relatively easy to do if online questionnaires are used.
    - Ways of seeing the effect of the new practices in real time, such as the growth charts of infants and the perception of more efficient decision making regarding feeding in this study, help reinforce their use

An important issue to consider when translating these findings into other areas of practice or other clinical environments is that this study utilised considerable staff resources, of whom several were funded through research rather than clinical service budgets. In particular, staff time was required for developing, implementing and reinforcing the intervention, and for training staff. This this degree of support may not be available in some centres, so it is important to realise that implementing change and new practices does require some dedicated staff time.

Finally, as mentioned above, a major lesson learned from this project is the need for a clear evidence base for any intervention. This study used an intervention aimed at covering all nutritional practices, only a handful of which had a strong evidence base. A complex intervention aimed at implementing one or two practices with a good evidence base may have made implementation easier and perhaps had more impact on outcome.

13.4.1 Future work

The work carried out in this thesis has addressed several issues, but at the same time has also generated more questions and hypotheses regarding both nutritional care of preterm infants and approaches to the implementation of practice change. Firstly; this study, like others described above, has shown some benefit to infants from the introduction of practice changes to improve and standardise nutritional care. However, as discussed above, one limitation is the retrospective pre-implementation cohort. The findings from this and

similar studies suggest the need for a more conclusive trial of such a practice based intervention. The best format for this might be a cluster RCT, with neonatal units randomised to implement a similar complex intervention to the one used in this study, or continue with standard practice. Such a trial would need to include assessment of the longer term effects of improving early nutrition and rates of growth in relation to neurodevelopmental outcomes, metabolic consequences, body composition and cardiovascular risk. As discussed above, any cluster RCT would need the intervention be reduced to a more transferable and manageable format, so could use the framework developed in the present study (figure 13.1) to implement the complex intervention. This would allow an assessment of whether the framework is useful in other settings.

This study has also demonstrated the clinical utility of the NPT toolkit to guide the implementation of complex interventions. Blockages in the translation of clinical studies in to everyday clinical practice (a so-called 'T2 'block, as described in chapter 1[2]) are rife in medical practice[1], and NPT offers a novel and useful way to address this problem. Based on the present study, it can be hypothesized that scores of normalisation using NPT will relate to changes in clinical practice and outcome in other settings. This warrants formal testing, and such work is currently already underway as part of the 'Improving the normalization of complex interventions: measure development based on normalization process theory' (NoMAD) study[230], and could be included in any future cluster RCT like the one described above,

Looking in more detail at the findings of this study in relation to the constructs of NPT, other hypotheses can be developed. Firstly, coherence played a major role in this study, as there was a clear driver for consistency and recognition of a need to change, leading to high intentions to use the intervention. Therefore, it can be hypothesized that staff coherence is proportional to staff intention, and in turn will relate to measures of practice. Similarly, cognitive participation was also key, with staff indicating that their roles were clear. This cognitive participation went hand in hand with coherence, as staff 'bought in' to the intervention due to their desire for change. It could therefore also be hypothesized that high coherence of an intervention leads to increased cognitive participation. Following on from this, the present study demonstrated the importance of the *reflexive monitoring* aspect of NPT in driving practice

change. It can therefore be hypothesized that, in the implementation of complex interventions, the provision of 'real time' feedback on the success of the intervention will improve practice and outcomes. Finally, in this study, the intervention began to be integrated into practice, and a key factor in this was the distribution of decision making to nurses and junior doctors. Therefore it could be hypothesized that distribution of decisions to different, appropriately placed staff groups provided with the correct tools to make decisions results in more effective implementation. All these hypotheses could be formally tested in future studies using NPT, in particular the cluster RCT described above.

13.5 Conclusion

Referring back to Patton's framework for understanding complexity described in chapter 1, it is clear that standardising and optimising nutritional care of is a genuinely *complex* situation, with uncertainty and disagreement about how to address the problem most effectively. Whilst the lack of certainty regarding the best practice and evidence for nutritional care represents a *technical complication*, it is difficult to generate good quality evidence for practice in the absence of a robust system for the effective and consistent delivery of nutritional care. Similarly, without certainty about best practice, it is not possible to bring about effective change and address some of the *social complications* involved in nutritional decision making and the delivery of nutritional care. Therefore, this thesis attempted to address both of these complications together using a complex intervention, in order to try and move practice forward and deliver consistent care based on the best evidence currently available. In concluding this thesis, it is important to reflect back on the original hypothesis

1. *The introduction of a complex intervention for the nutritional care of preterm infants will improve their nutrient intakes and growth*

2. *The use of Normalization Process Theory to both guide and monitor the implementation of a complex intervention will result in improved integration into practice with subsequent improvement in clinical outcome measures*

The evidence presented in this thesis suggests that the implementation of the complex intervention was associated with modest improvements in infant

protein intakes and weight gain, although not in energy intakes or head growth. Whilst there is some evidence to support hypothesis 1, it is not possible to reject the null hypothesis, as the pattern of results suggests that some of the improvements seen may have been due to existing trends in practice or partial implementation of the intervention. In addition to the quantitative results, qualitative methods have suggested which elements of the intervention may have been more effective than others.

Similarly, there is also some evidence to support hypothesis 2, in that the use of NPT to guide and monitor the implementation of the complex intervention was demonstrated to result in improved integration of some components of the intervention into routine practice. However, it is again not possible to reject the null hypothesis here as it is clear that some aspects of practice, such as commencement of feeds and the use of breast milk, were not improved by the intervention, so its 'success' in changing practice was limited, and certainly not complete. It has been hard to demonstrate a direct association between the use of NPT and clinical outcomes but there is a suggestion of this in the pattern of quantitative and qualitative results seen. It is also an important finding that measures of normalisation using NPT appear to relate to objective measures of practice. Whilst results suggest that the intervention was being normalised into care towards the end of the study, it is likely that this is an ongoing and incomplete process, and it is not possible to tell at this stage how well the new practices will be sustained in the long term.

This thesis has also attempted to better understand the implementation of complex interventions, the process of practice change and the integration of new practices into routine care, and has been successful in this regard, producing some new insight into the way these occur, together with the generation of some theoretical frameworks which explain the processes which underpin them in the context of the complex intervention used in this study. Key elements included establishing an environment ready for change, the distribution of decisions and an emphasis on feedback and reflexive monitoring.

Overall, this thesis has allowed insight into the differences between *what people think* about a new practice, *what they say* (interviews), *what they actually do* (audit results and NPT questionnaires) and *whether it matters* (patient outcomes). This thesis began by highlighting the problems associated

with variable and inconsistent care, together with a discussion of the frequent 'T2' blockages that occur when translating evidence into practice. It can be seen how, using the right tools, more consistent practice can be introduced into routine care and perhaps begin to become normalised into practice. Complex interventions using multiple elements have the potential to change practice, and NPT may offer a way of enhancing the implementation and subsequent integration of new practices into routine care. Understanding and adjusting for the factors that influence this process should lead to improvements in clinical practice and patient outcomes.

Appendices

Appendix 1: Guidelines for the Nutritional Care of Infants in the Neonatal Unit

University Hospital Southampton NHS
NHS Foundation Trust

Guidelines for the Nutritional Care of Infants in the Neonatal Unit

Version: 1.0

Issued: December 2011

Review date: December 2014

Author: Dr Alison Leaf

The procedural aspects of this guideline can be found in the document entitled:-

Guideline Proforma – Guidelines for the Nutritional Care of Infants in the Neonatal Unit

Appendix 1

Contents

Executive Summary

Good nutrition is important at all stages of life. Babies are born at a time of rapid growth and formation of body tissues and organs, yet immature metabolism means they are unable to cope with either excess or lack of nutrients. Detail in both the quantity and quality of nutrients is critically important.

There is good evidence that mother's breast milk confers many advantages to baby, mother and to the formation of the parental bond. As well as containing just the right nutrients for human development, breast milk contains many factors which promote immune function and enable healthy intestinal development. Breast milk and breast-feeding should be encouraged in almost all situations.

Preterm infants and those with congenital abnormalities or metabolic disorders may require nutrient supplements or special feeds, and may require a period of intravenous nutrition until the gut is able to support their needs.

Measuring growth and monitoring biochemical well-being is crucial to optimising nutrition in high risk individuals.

These guidelines aim to provide both practical and theoretical guidance for the optimal nutrition of sick and preterm infants in the NNU at Southampton.

Appendix 1

1. Introduction

- Good early growth is essential for long term health and well-being of all babies.
- Achieving recommended nutrient intake in very low birth-weight and sick infants is difficult particularly in the first weeks of life and development of a significant nutrient deficit is common. It is then very difficult to 'catch up'.
- Protein intake is particularly difficult to achieve.
- These guidelines aim to support decision-making such that nutrient delivery can be optimised. Close monitoring of intakes, biochemical status and growth is essential to monitor how well this is achieved.
- ***Every feed and every day is important – being aware of daily intake of key nutrients is the first step to improving growth and development***
- SENNAT (Southampton Electronic Neonatal Nutrition Assessment Tool) has been developed to help us all measure and monitor nutrient intakes and growth

These guidelines are based on recommendations of:

- Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Journal of Pediatric Gastroenterology and Nutrition 2010[15]
- Nutrition of the Preterm Infant: Scientific basis and Practical Guidelines (second edition). Tsang RC, Uauy R, Koletzko B, Zlotkin S. Digital Educational Publishing 2005[14]
- Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR), Journal of Pediatric Gastroenterology and Nutrition 2005[75]
- Vermont Oxford Network 'Potentially Better Practices (PBPs) for Nutrition' as laid out in Pediatrics, 2003[23]
- Management and support of infant feeding in maternity facilities. Infant and young child feeding : model chapter for textbooks for medical students and allied health professionals., World Health Organisation 2009[77]
- Optimal feeding of low-birth-weight infants, World Health Organisation, 2006[78]

- UNICEF Baby Friendly Initiative, http://www.unicef.org.uk/babyfriendly

2. Definitions

AREDF	Absent or Reversed End Diastolic Flow (in umbilical artery, seen on antenatal scans)
AXR	Abdominal X-Ray
BMF	Breast Milk Fortifier
CPAP	Continuous Positive Airways Pressure
D/C	Discharge
DBM	Donor Breast Milk
DH	Department of Health
ELBW	Extremely Low Birth Weight (birth weight <1000g)
FBC	Full Blood Count
g	grams
IU	International Units
IUGR	Intrauterine Growth Restriction
IV	Intravenous
kcal	kilocalories
kg	kilogram
LBW	Low Birth Weight (birth weight <2500g)
LFT	Liver Function Tests
MBM	Maternal Breast Milk
mg	milligram
ml	millilitre
mmol	millimole
NBM	Nil By Mouth
NEC	Necrotising Enterocolitis
NICU	Neonatal Intensive Care Unit
NNU	Neonatal Unit
PBP	Potentially Better Practice
PDA	Patent Ductus Arteriosus
PDF	Post Discharge Formula
PN	Parenteral Nutrition
RCT	Randomised Controlled Trial
SD	Standard Deviation
TAT	Trans-anastamotic Tube
PN	Total Parenteral Nutrition
U&E	Urea and Electrolytes
VLBW	Very Low Birth Weight (birth weight <1500g)
VON	Vermont Oxford Network

Appendix 1

3. Roles and Responsibilities

BREAST-FEEDING AND LACTATION SUPPORT

- All staff: awareness of Trust Policy and NNU Guidelines
- 'Breast-feeding babes' – Lead Sandy Jackson: expert guidance for mothers breast-feeding on the post-natal wards
- NNU lactation support team – Lead Jess Macfarlane: expert guidance for mothers breast-feeding and/or expressing milk in NNU

PARENTERAL NUTRITION

- All staff: awareness of need for PN in high risk infants
- Nursing staff: awareness of location of 'stock' PN in NNU and knowledge and skills for PN administration appropriate to nursing skill level
- Medical staff: awareness of PN supplies available and how to prescribe; awareness of potential complications of PN and how to avoid
- Pharmacists: Amanda Bevan and Zoe Lansdowne: expertise in detailed composition of PN solutions and provision of PN in different situations on NNU

ENTERAL NUTRITION

- All staff: support for mothers in choice of feeding
- All staff: awareness of choices for enteral nutrition: maternal breast milk / breast-feeding; donor breast milk / milk bank; standard infant formula; formulas for preterm infants; special formulas for infants with specific gut or feeding problems
- Neonatal Dietitian (Anita Emm): expert knowledge of composition of breast milk and alternatives and guidance on making appropriate choices
- Surgical team: expert knowledge on potential feeding challenges in infants with congenital or acquired abnormalities of the gut, particularly following surgery.

FEEDING DIFFICULTIES

- All staff: awareness of common feeding difficulties of preterm infants and those with neurological complications
- Speech and language therapist: expert knowledge of structure and function of upper gastro- intestinal tract and how to optimise feeding potential of vulnerable babies

GROWTH MONITORING

- All staff: Awareness of importance of making accurate and regular measurements and plotting them on appropriate charts to monitor growth
- Nursing staff: Weigh babies at intervals as indicated by clinical condition (ideally three times per week)
- Medical and Nursing staff: Measure head circumference and length at intervals as indicated by clinical conditions (ideally head circumference at least weekly and length at least fortnightly)
- Medical and Nursing staff: Plot growth measurements on appropriate chart weekly (provided competent to do so)

SPECIAL CASES

- Neonatal Nutrition Team: Will review high risk or complex patients on weekly nutrition ward round

4. Related Trust Documents

- **Donor Breast Milk Guideline (to be found at: http://staffnet/TrustDocsMedia/DeptDivSpecific/DivC/WomenNewborn/NeonatalUnit/NeonatalGuidelines/DonerBreastMilkGuideline/DonorBreastMilkGuideline.doc)**
- Breastfeeding care pathway (on Neonatal Unit Guidelines on Unit Desktop PCs)
- Vitamins and supplements guideline (on Neonatal Unit Guidelines on Unit Desktop PCs)
- Parenteral Nutrition Guidebook, 4th edition (Hard copies in nurseries on Neonatal Unit)
- Princess Anne Breastfeeding Policy (to be found at http://staffnet/TrustDocsMedia/DeptDivSpecific/DivC/WomenNewborn/Obstetrics/ObstetricClinicalGuidelines/BreastfeedingTermInfantsGuideline/BreastfeedingTermInfantsGuideline.doc)
- Neonatal Unit Breastfeeding and Formula Feeding Guideline (currently being written)
- Neonatal Surgical Clinical Aids (to be found at: http://staffnet/Departments/DivisionC/Womenandnewborn/Neonatalservices/Neonatalsurgery/Neonatalsurgeryclinicalaids/Neonatalsurgeryclinicalaids.aspx)
- Central Venous Access Guideline (currently being written)
- Naso/Orogastric Tubes in Neonates - the safe placement of: Guidelines (to be found at:http://staffnet/TrustDocsMedia/DeptDivSpecific/DivC/WomenNewborn/NeonatalUnit/NeonatalGuidelines/NasoOrogastricTubesinNeonates-thesafeplace/NasoOrogastricTubesinNeonates-thesafeplacementofGuidelines.DOC)

Appendix 1

5. Guideline Information

1. AIMS AND OBJECTIVES

- To optimise use of breast milk and breast-feeding
- To achieve recommended nutrient intakes
- To achieve postnatal growth and body composition approximating fetal growth.
- To reduce the risk of nutritional deficiency states such as late anaemia of prematurity or metabolic bone disease.
- To reduce the risk of feeding related morbidities such as NEC or cholestasis
- To optimise long term neurodevelopmental outcome.

KEY PRINCIPLES

- All babies should be measured and have nutritional risk assessment on admission, and weekly during their stay
- Nutrition support should be started early: PN for high risk; enteral feeds for lower risk
- Mother's breast milk is the feed of first choice
- Feed tolerance should be assessed regularly and managed according to algorithms
- Protein intake should be documented and optimised in preterm infants
- High risk babies should be seen each week by the Nutrition Team
- Nutrition and feeding should be discussed in Discharge Planning and documented in the notes

AUDIT POINTS

- Use of Nutrition Screening Tool, on all NNU admissions (100%)
- Use of growth charts on all NNU admissions (100%)
    - Weight and Head Circumference plot weekly; length plot 2-weekly
- Lactation advice and support by 6 hours for all mothers of VLBW infants
    - 100% - unless mother too ill
- Breastfeeding rates at discharge
- Protein and energy intakes as recommended by Tsang 2005
- Use of nutritional supplements according to Guidelines
- Documentation of Nutrition Plan at discharge (100%)

2. ASSESSMENT AND MONITORING

(i) INITIAL ASSESSMENT

a. Growth Measurement

All infants should have weight, length and head circumference measured and plotted on the appropriate growth chart at admission. This information, together with other risk factors detailed below, will identify the degree of 'nutritional risk' – ie risk of becoming malnourished or developing nutrition and feeding related problems. Infants with multiple risk factors should be classified according to their highest individual risk factor. This will guide nutritional care and allow subsequent progress to be monitored.

b. Risk assessment – identify level of risk for nutrition and / or feeding-related problems

High risk

- Preterm <28 weeks
- ELBW < 1000g
- Severe IUGR (weight < 2nd centile with AREDF) <35 weeks
- Infant establishing feeds after episode of NEC or GI perforation
- Infants with severe congenital GI malformation: e.g. gastroschisis
- Severe Perinatal hypoxia / ischaemia

Moderate risk

- Preterm 28-31^{+6} weeks, otherwise well
- VLBW 1000 – 1500g
- Moderate IUGR (weight < 9th centile with AREDF) <35 weeks
- Baby on inotropes
- Baby on indomethacin/ibuprofen (NB avoid concomitant treatment with steroids)
- Baby >1500g with illness or congenital anomaly which may compromise feeding
- Symptomatic polycythaemia, with PCV $\geq$ 70%

Low risk

- Preterm 32-36^{+6} weeks, otherwise well
- AREDF / IUGR $\geq$35 weeks
- Term Infants >37 weeks

(ii) ON-GOING ASSESSMENT AND MONITORING

a. GROWTH

i. Weight should be measured at least twice a week, and plotted on CLOSE MONITORING WHO growth chart weekly. More frequent weights required for some babies should be plotted on a daily weight chart

ii. Head circumference should be measured and plotted weekly

iii. Length should be measured and plotted within the first week, and every 2 weeks thereafter.

iv. If a baby is too sick to be weighed and measured so cannot be plotted, mark the bottom of the growth chart at date with a triangle (△) at the day's date.

v. Targets for weight – changes in weight in the early days of life usually reflect fluid balance: aim for weight loss of no more than 10% from birth weight. Once baby is stable and growing, aim for gain of 15-20 grams/kg/day

vi. Head circumference and length: normally expect increase of 0.75 cm/week

b. BIOCHEMISTRY

i. **First week of PN**:
- Full PN Profile daily (FULL IP MG on eQuest, this includes U&E's, Calcium, magnesium phosphate and LFTs)
- FBC twice weekly

ii. **Second and subsequent week of PN**:
- Full PN Profile and FBC twice weekly if stable (daily if still unstable)

iii. **Triglycerides** should be measured weekly (ideally Mondays)when on IV lipid

iv. **If on PN for longer than 1 month, then Trace elements (Zn, Cu, Se, Mn – use special blood bottle in Dr's Office) and Vitamins (A, D and E) should be measured monthly. Consider measuring Iron status and clotting**

v. **When on enteral feeds:**
- Infants in the High and Medium risk categories need weekly FBC, U&Es, LFTs and Bone profiles once they are off PN and fully enterally fed. This can be extended to once fortnightly when babies are moved into Special Care.

c. SCREENING

i. A Neonatal Nutrition Screening form should be completed on admission and on Sunday/Monday when the baby has been weighed and measured each week on all babies to identify those requiring nutrition team review

d. NUTRITION TEAM REVIEW

i. Nutrition ward rounds take place on Tuesday mornings from 0900-1100. Nutrition team will see all 'high-risk' babies, and any others identified by nutritional screening on Sunday/Mondays.

3. NUTRIENT REQUIREMENTS

Nutrient requirement for Term and Preterm infants in the first weeks of life are summarised below. The figures shown below are based on the parenteral requirements for the first week, and the enteral requirements for the subsequent weeks (for a full list of parenteral and enteral requirements see Appendix 1).

Term infants – based on intake in 150 ml/kg breast milk; preterm infants based on recommendations in Tsang 2005 unless otherwise stated.

There are no specific guidelines for those babies born over 1.5kg and under term weight (2.5 kg) but it can be anticipated that their nutritional needs will be between those of preterm infants and term infants. Nutritional support should therefore aim to deliver nutrient intakes in this area.

It should be noted that these are just recommendations, and some infants may require more of certain nutrients such as Sodium and Potassium as dictated by the results of blood tests**.**

Nutrient Unit/kg/day	**Term infant**	**Preterm VLBW 1000-1500g 1st week (parenteral)**	**Preterm VLBW 1000-1500g After 1st week (enteral)**	**Preterm ELBW < 1000g 1st week (parenteral)**	**Preterm ELBW < 1000g After 1st week (enteral)**
Energy (kcal)	100	60-70	110-130	75-85	130-150
Protein (g)	1.5-2.1	3.5	3.4-4.2	3.5	3.8-4.4
Nitrogen (g)	0.24-0.34	0.56	0.54-0.61	0.56	0.61-0.70
Sodium (mmol)	1.4	2.0-5.0	3.0-7.0	2.0-5.0	3.0-7.0
Potassium (mmol)	2.0	0-2.0	2.0-3.0	0-2.0	2.0-3.0
Calcium (mmol)	1.25	1.5	2.5-5.5	1.5	2.5-5.5
Phosphate (mmol)	1.3	1.5-1.9	1.9-4.5	1.5-1.9	1.9-4.5
Vitamin D IU*	340	40-160	800-1000	40-160	800-1000
Vitamin A IU**	1150	700-1500	700-1500	700-1500	700-1500
Iron (umol)	17.9	0	35.8-71.6	0	35.8-71.6

*Vitamin D = dose quoted is total daily dose; ESPGHAN 2010 recommendation for enteral dose for preterm infants; term infants DH Dietary Reference Values 1991 (340 IU = 8.5 mcg Vit D)

**Vitamin A = dose quoted is total daily dose; term infants DH Dietary Reference Values 1991 (1150 IU = 350 mcg of Vitamin A retinol equivalent)

4. STANDARD NUTRITION SUPPORT –

(a) OVERVIEW - GETTING STARTED - EARLY PN AND TROPHIC MILK FEEDS

HIGH RISK / MEDIUM RISK (see flow charts for high [A] and medium risk preterm infants [B])

- Aim to introduce milk feeds gradually while maintaining calorie and nutrient intake with PN
- Before starting or increasing milk ensure baby is clinically stable and abdomen soft
- Ensure mother has lactation support to start expressing (see breastfeeding care pathway)

High risk preterm (<28 weeks; <1000g; severe IUGR/AREDFV <35 weeks)

Day 1 Start Stock Preterm PN at 60-90 ml/kg/day via UVC or long line, as soon as possible unless baby very unstable. Give fresh colostrum as mouth care or as trophic feeds

Day 2-3 Start trophic feeds: MBM 1 ml/kg 2-4 hourly (if no MBM can use DBM- see choice of milk chart);

Day 3-7 Change to Stock Preterm + Sodium PN when 6% weight loss from birthweight [231], additional sodium required, or by day 5, whichever soonest
Increase milk by 10-20 ml/kg/day as tolerated (see table); Aim to decrease PN flow rates with feeds only once baby on total fluids of 180ml/kg/day

Moderate risk preterm (28-31^{+6} weeks; 1000g <1500g; mod IUGR/AREDFV < 35 weeks)

Day 1 Start Stock preterm PN at 60-90 ml/kg/day via UVC or long line as soon as possible; if no central access consider peripheral PN

Day 1-2 Start colostrum/milk 1 ml/kg 2 hourly ('see choice of milk' chart)

Day 3-7 Change to Stock Preterm + Sodium PN when 6% weight loss, or by day 5, whichever is sooner. Aim to decrease PN flow rates with feeds only once baby on total fluids of 180ml/kg/day Increase milk by 20-30 ml/kg/day according to clinical condition and tolerance;

High / moderate risk term or near-term infants

All high/moderate risk babies should have a plan for nutrition support on admission and periods greater than 48 hours without protein and micronutrients should be unusual

Low risk

Day 1 Commence milk feeds 30-60 ml/kg/day, supplemented by IV fluids if necessary

Day 2-7 Increase milk feeds by 30 ml/kg/day as tolerated

NOTES

- If severely unwell or acidotic, PN may need to be delayed (though contains acetate)
- Babies with HIE undergoing therapeutic hypothermia, may tolerate trophic milk feeds
- For babies with surgical problems , see 'surgical guidelines' – section 6

4. (b) PARENTERAL NUTRITION

i) Indications for PN

- High or Moderate risk infants as described above
- Infants who are NBM and unlikely to achieve adequate milk intake in the next 5 days
- Infants who are not tolerating feeds such that they cannot take full feed volumes for 5 consecutive days

ii) Starting PN

- In high and moderate risk infants PN should be started as soon as possible as delay can result in significant and cumulative nutrient deficits.
- Birth weight ≤1500g – start as soon as possible after birth
    - Ideally within 6 hours
- Birth weight >1500g – if enteral feeding contra-indicated, start PN by
    - 48 hours in 1500-2500g
    - 72 hours in 2500-3500g if NBM
- Central line insertion (UVC or peripherally inserted central venous line) should be a priority for high and moderate risk infants
- If feeds are stopped on high or medium risk infant for any reason, re-stat PN

iii) Stock PN

- Infants should be started on Stock PN in the first instance as detailed below:
    - Preterm PN – For preterm infants (<37/40 gestation) where additional sodium is not indicated (ie until 6% weight loss, or day 5 of life)
    - Preterm + Sodium PN- For preterm infants (<37/40 gestation) requiring maintenance sodium. **This should be the PN of choice for the majority of preterm infants after the first few days following birth**, as it contains more protein.
    - Term PN – for Term infants (≥37 weeks gestation) at any point after birth.
- Stock PN comprises an aqueous solution (glucose, amino acids, electrolytes and trace elements) and a lipid solution (**which contains both fat- and water-soluble vitamins**). For adequate nutrition it is **important that the lipid is always given with the aqueous solution** at all times (except when well advanced on enteral feeds - see below).
-

iv) Pharmacy made ('bespoke') PN

- Neither PN alone nor unfortified full breast milk feeds fully meet the nutritional needs of preterm infants, so the period when a preterm infant transitions from PN to milk feeds is when they are at highest risk of poor nutrient intakes.
- Stock PN is designed to give the maximum possible nutrition at 130ml/kg/day. **Therefore, pharmacy can make bespoke PN, which provides more nutrition in a smaller volume, should be used whenever a preterm infant is receiving less than 130ml/kg/day of Stock PN**. This will occur whenever a preterm infant is increasing on enteral feeds, is fluid restricted, or receiving other infusions
- Bespoke PN may also be appropriate where infants have electrolyte requirements than cannot be met with Stock PN

v) Reducing PN as enteral feeds increase

- **Only once the infant is receiving 180ml/kg/day total fluids should the PN solution be decreased as enteral feeds increase** (unless there is a clinical decision to restrict fluids).
- Once the infant is on 90ml/kg/day enteral feeds, the rate of lipid infusion should be halved, and then stopped when the infant reaches 135ml/kg/day enteral feeds (beware with pharmacy made PN as this reduction in lipid may have already been done as part of the prescription). Any shortfall in total fluid volume due to the reduction in lipid should be made up by increasing the aqueous PN solution, to allow maximum protein to be delivered to the infant (though do not go above the maximum prescribed rate). This is important when infants are on Stock PN, but for those on bespoke PN, the reduction in lipid may have already been done/accounted for by the pharmacists when the PN was prescribed so may not be necessary (check with the pharmacists first). **Remember that once the lipid is stopped, vitamin intake will be inadequate until Abidec is started.**

vi) Peripheral PN

- PN should ideally be given via a central line. However, there are occasions in high nutritional risk infants with difficult access where the benefits of giving PN peripherally may outweigh the risks. Such decisions should be made by the Consultant responsible for the patient.

vii) Cautions on PN

SEPSIS - may affect lipid metabolism; measure triglycerides and if >2.8mmol/L consider reducing or stopping IV lipid for 12-24 hours in severely septicaemic baby (remember to restart/increase lipid when sepsis has resolved)

THROMBOCYTOPENIA – high concentration of polyunsaturated fats may impair platelet adhesion: reduce lipid to 1-2 g/kg/day if platelets <50.

CHOLESTATIC JAUNDICE – total and prolonged PN increases the risk, so try to give some enteral feed if at all possible; other risk factors include IUGR, sepsis and short bowel syndrome. Lipid solutions containing fish oil (eg SMOF) can reduce or reverse cholestasis, and should be considered in high risk babies if on PN for 4 weeks or more. Alternate day lipid may also be indicated in this situation, or if altered liver function - discuss with the pharmacists.

4. (c) ENTERAL NUTRITION

i. **Starting feeds** – see section 4(a) for guidance. Before starting feeds ensure baby is clinically stable and abdomen soft. In high-risk infants trophic feeding should be started within the first 72 hours if at all possible to minimise intestinal mucosal atrophy, and continued until ready to progress.

ii. **Choice of milk** – Mother's breast milk is almost always the feed of first choice, unless contraindicated by maternal illness or drugs. If no maternal milk available pasteurised donor breast may be used for high risk babies (parental consent required) in accordance with the DBM guideline. Preterm formula (LBW/Aptamil Preterm) is indicated for infants with gestation <34 weeks, or birth weight <1800 grams; Post discharge formula (Nutriprem 2) is indicated for preterm infants either as sole diet or in addition to breast-feeding from around 36 weeks (or at discharge) up to 6 months corrected. (see Flow Chart D)

iii. **Advancing feeds** – see section 4 (a) for guidance on volumes

- Before starting or increasing milk ensure baby is clinically stable and abdomen soft. Small gastric residuals can be tolerated if baby well. Passage of meconium and then changing stools is an important indication of gut motility. Glycerine suppositories may be useful if no stool passed for 48 hours.
- Feeds can be increased by 10-20ml/kg/day in high-risk, 20-30ml/kg/day in moderate risk and 30 ml/kg/day in low risk babies
- Test for residuals 4-6 hourly
- If baby vomits, or has residuals >25% of the previous 4 hours total feed volume and persisting or increasing examine and assess baby and refer to flow chart C

iv. Nutritional supplements

- BREAST MILK FORTIFIER (BMF, see high risk and moderate risk flow charts A and B) - 'multi-component' fortifier provides additional calories (carbohydrate), protein (cows' milk based), minerals and vitamins in a powder which is added to mother's breast milk. It should be more or less routine for babies with birth weight <1500g to receive fortifier once they have tolerated 150 mls/kg/day of MBM for 24 hours, unless significant gut or renal compromise. Blood Urea and albumin levels provide useful markers of protein status. In general, give ½ strength for 24-48 hours and then increase to full strength (2.2g sachet to 50 mls MBM), though it may be preferable to increase the fortifier by ¼s in high risk infants. For some extremely high risk infants it may be prudent to start fortifier when on 120-135 mls/kg/day of MBM and increase strength more gradually as PN is gradually reduced, in order to ensure the baby will be able to achieve enteral nutrient targets before stopping PN.

- Vitamins and Iron – breast milk provides insufficient vitamins (particularly vitamin A and D) for preterm infants, and virtually no iron. Abidec (multivitamins) and Sytron (iron) should be started according to NNU guideline

- Electrolytes and minerals
    - Small doses should be given as boluses, as scheduled on drug chart
    - Sodium : aim to maintain serum sodium 135-145 mmol/L
      If on > 4 mmol/kg/day, add to daily feeds in milk kitchen; if < 4 mmol/kg/day, give as divided bolus drugs (ideally as a four times daily regimen)
    - Phosphate: content of BM is low. Aim to maintain serum inorganic phosphate levels greater than 1.8mmo/L. Usually given as Potassium Acid Phosphate 0.5-2mmol/kg/day. If required as outpatient, may be preferable to use BMF

v. Nutrition at discharge

It is important to start discharge-planning well in advance. Breast-feeding at discharge is the preferred goal for all infants. However for preterm infants nutritional supplementation will be required. For those not being breast fed advice has to be given on choice of formula, so for all infants a pre-discharge nutrition assessment should be made and plan documented.

MUM PLANNING TO BREAST FEED

- Ensure lactation support is on-going re feeding technique
- Discuss with Out-reach sister re support at home
- **All preterm infants (<35 weeks) should have Abidec (1 ml) and Sytron (1 ml) daily**
- Assess growth
    - If growth has been good and weight, length and HC are no more than 0.67 SD (ie one centile line) below birth levels, then assess weight gain after 48 hours. If satisfactory can go home breast-feeding
    - If baby has had significant post-natal growth restriction and is >1.33 SD below birth (2 centile lines), discuss with Nutrition team / Dietician and consider discharge on BMF, with Outreach Support
    - For those with modest growth restriction, i.e. between one and two centile line drop, review overall pattern of growth and consider requesting nutrition review and Outreach support.

MUM PLANNING TO FORMULA FEED

- Babies <34 weeks gestation, with birthweight <2kg can be considered for discharge on Post-Discharge Formula (PDF) – 'Nutriprem 2'. This should be continued until 3 to 6 months corrected age.
- ELBW and VLBW babies who have been on LBW formula should be changed to PDF at approximately 36 weeks corrected age, or when beginning to take most feeds by bottle. For those who have had severe extra-uterine growth restriction, continuing with LBW formula to 40 weeks corrected age may be appropriate.
- Babies discharged on PDF should have Abidec 0.6 ml, but not Sytron.
- If changing to term formula, prescribe Abidec 1 ml (continue until at least one year post term) and Sytron1ml (continue until 6 month post term)

SOLIDS – can be introduced at 5-8 months REAL AGE (ie not corrected for prematurity)

5. MANAGEMENT OF COMMON GUT AND FEEDING PROBLEMS – see flow chart C

a. **Gastric aspirates / residuals** – preterm infants have immature gut motility, and aspirates/residuals and small vomits are not uncommon. Dark green bile stained aspirates, particularly in association with abdominal distension and / or tenderness are a cause for concern. However small milky / yellow aspirates up to 2-3 mls are frequently normal. They can be replaced, and feeds continued.

b. **Abdominal distension** – this is another common feature in preterm infants, due to poor gut motility. It tends to be more common in babies on nasal CPAP, with high volumes of air flowing into the upper airway and oesophagus. Tenderness, or systemic symptoms and signs such as apnoea, tachycardia or temperature instability should raise concern. If baby is otherwise well, a small glycerine suppository may help to stimulate peristalsis, and enable feeds to be continued.

c. **Suspected NEC** – classical features are blood and mucous in stools, bile stained aspirates and abdominal tenderness. Systemic signs such as tachycardia and hypotension occur in severe NEC. X-ray might show intramural gas ('pneumatosis coli'), dilated loops of bowel, free air, or a 'gas-less' bowel. In suspected NEC feeds should be stopped, and urgent attention paid to supporting ventilation, circulation and fluid balance.

d. **Suspected GOR** – mild milk reflux is common in newborn babies, including those born preterm and is usually self-limiting. It is rarely the cause of significant cardio-respiratory disturbance. However, apnoea and bradycardia are common in preterm babies and may occur in association with feeds. Try to avoid using gaviscon in babies who are having fortified MBM as the milk becomes excessively thick.

e. **Suspected Food Protein Intolerance** – food protein (e.g. cow's milk protein) intolerance can occur in young infants either breast fed or formula fed. Symptoms may include severe regurgitation, vomiting, constipation, peri-anal rash, blood in stools and iron deficiency anaemia. Non-intestinal features may include skin rash – atopic eczema, and colic. If this is thought to be the cause of symptoms, it is recommended that cow's milk protein be excluded from diet. If breast feeding, mother should exclude both cows' milk and egg products from her diet for two weeks, while continuing to breast feed. Formula fed infants should be tried on amino acid formula. If improvement is seen, a staged reintroduction should be carried out. If no improvement is seen on definite exclusion diet, food protein intolerance is unlikely. If exclusion diet is difficult to maintain, a trial of amino-acid formula may be breast fed infants. See review by Vandenplas et al.[232]

6. MANAGEMENT OF BABIES WITH SURGICAL BOWEL CONDITIONS WHICH MAY COMPROMISE NUTRITION

Information has been extracted from the NEONATAL SURGERY CLINICAL AIDS on SUHTranet:

(http://staffnet/Departments/DivisionC/Womenandnewborn/Neonatalservices/Neonatalsurgery/Neonatalsurgeryclinicalaids/Anorectalmalformations.aspx)

This website should be checked to ensure that the most up to date version of the guidance is used.

GASTROSCHISIS

All babies with gastroschisis will require PN.

For those treated with a Medicina Silo insertion at the cot-side a percutaneous long line should be sited on the Neonatal Unit but line insertion should ideally be delayed until after gut manipulation has ceased, i.e. once the silo has been removed and the defect closed, to reduce the chance of line colonisation. The median time to closure is 4 days. If it is felt that PN should be commenced before this time then this can be given via peripheral cannula. In babies in whom it is thought there may be a delay in defect closure it may be better to proceed with line insertion prior to closure. As some gastroschisis babies may go on to have intestinal failure and require long term central venous access, central lines should only be inserted by staff with considerable experience of line insertion so as to avoid loss of suitable veins.

If the baby is taken to theatre for primary closure or surgical silo creation a percutaneous long line can be inserted in theatre at the time if someone with the appropriate expertise is available.

Duration of PN may vary from 10 days to 6 weeks with a mean of 3 weeks. In rare cases gut function may be impaired for many months.

DUODENAL ATRESIA

A trans-anastamotic tube (TAT) can be placed during surgery, which allows feeding into the jejunum. A naso/orogastric tube will also be required for gastric decompression. Usually a 6Fr enteral feeding tube is placed nasojejunally and an 8Fr nasogastric tube placed down the other nostril. In preterm babies this may produce problems due to obstruction to both nostrils. In this situation it may be better to pass an orogastric 8Fr tube and leave one nostril patent.

Poor duodenal contractility may delay normal oral feeding for as long as 3 weeks. This may be overcome by transanastamotic feeding although there is evidence that this may delay eventual oral feeding. It is NOT usually necessary to place a long line or commence PN because of the use of TAT feeding. Duration of admission is about 7 - 10 days but may be longer if motility is very delayed.

EXOMPHALOS

Nutritional support: Most babies who have undergone primary closure will tolerate enteral feeding soon and not need PN. Most babies with a silo will require a long line and PN

MECONIUM ILEUS

Feeding may start when gut recovery from surgery allows. Usually start on MBM or standard formula feed grading up slowly. Feed may need to change to hydrolysed formula if weight gain inadequate on breast milk or standard formula. Occasionally PN is needed.
80-90% of babies with MI are deficient in pancreatic enzymes, and supplementation with 'Creon®' may be required. Further details are provided in Surgical Clinical Aids and treatment will usually be guided by advice from the CF team

OESOPHAGEAL ATRESIA and TRACHEO-OESOPHAGEAL FISTULA

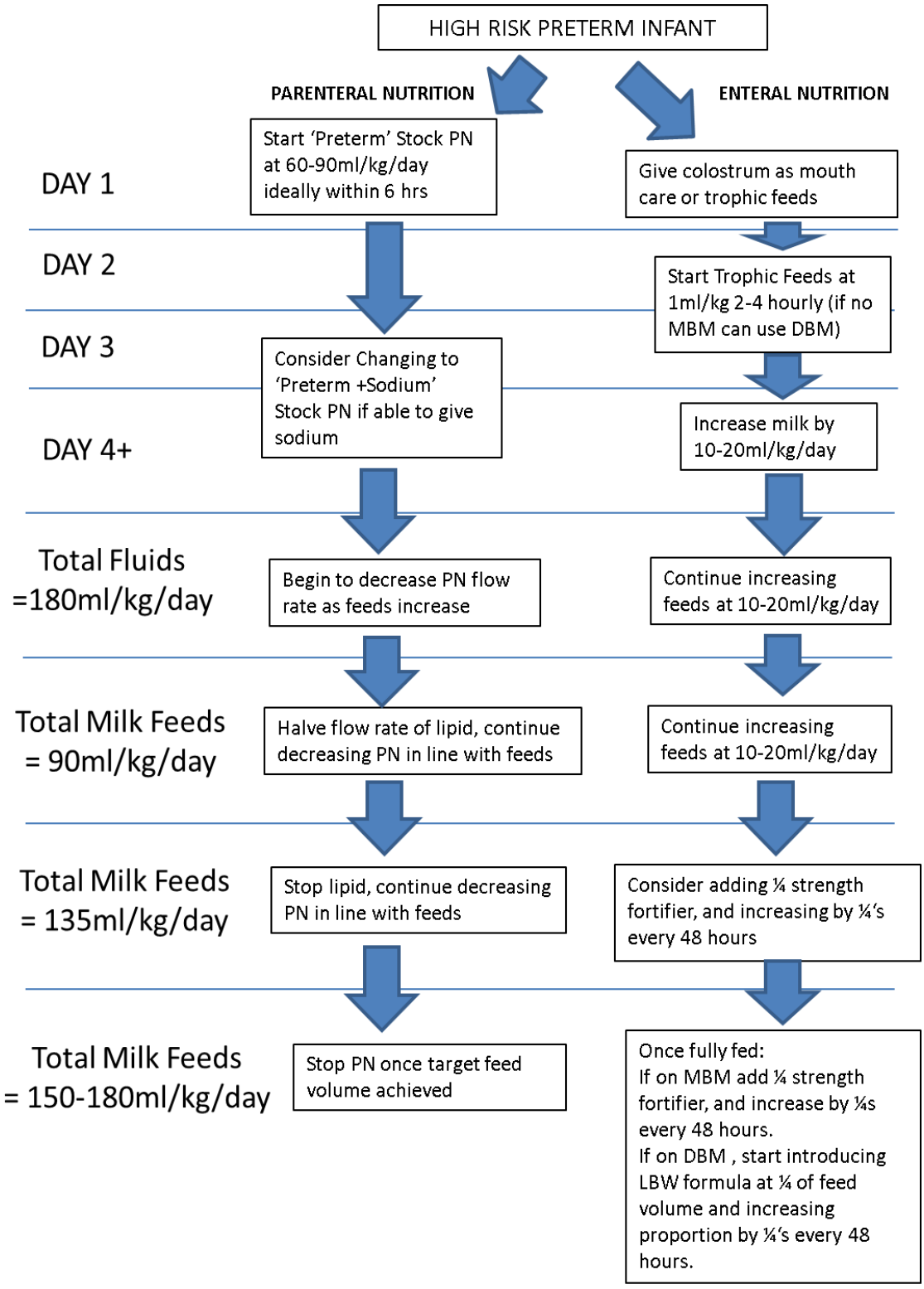
A trans-anastomotic tube (TAT) nasogastric tube will be placed at time of surgery and feeding usually commences via the TAT at 48hrs post-op. If the TAT falls out do not re-pass as this may perforate the anastomosis. Consult the surgical team immediately.

Oral feeding normally starts between 3 and 5 days post-op at the discretion of the surgical team.

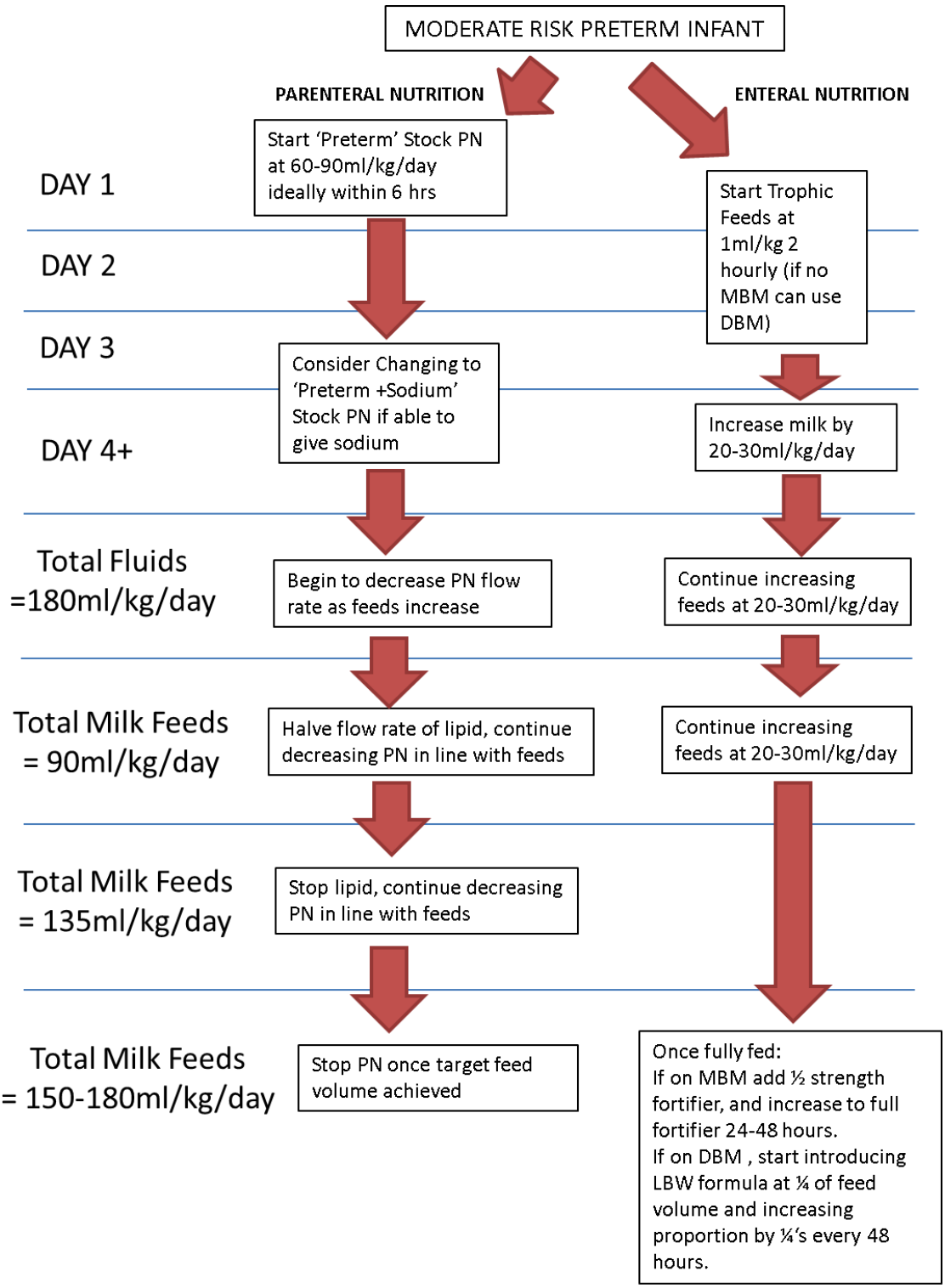
Gastro-oesophageal reflux prophylaxis: some surgeons use ranitidine post-op for 3 - 6 months. Others do not.

7. FLOW CHARTS

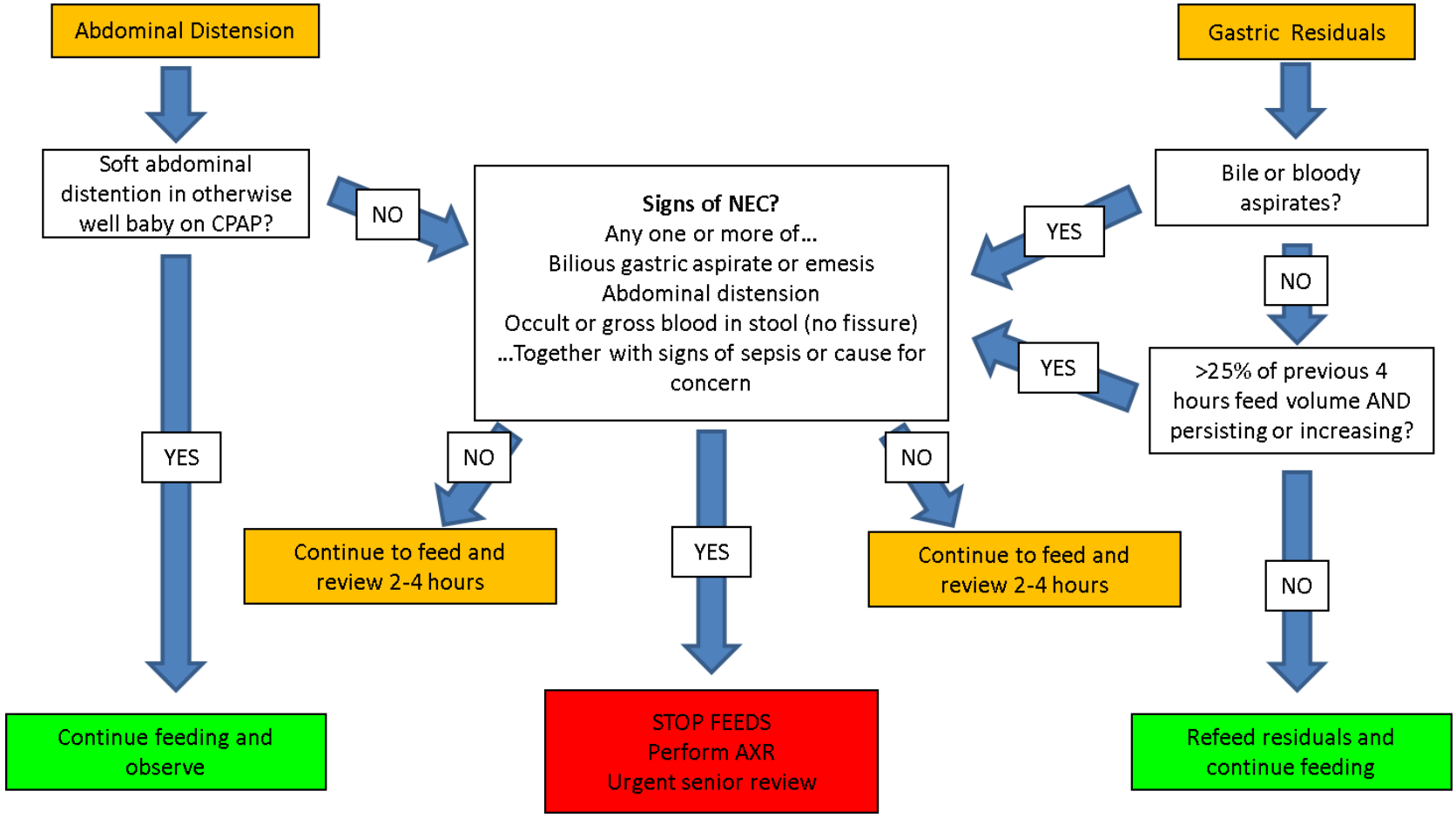
a. Starting and Increasing Feeds– HIGH RISK INFANTS



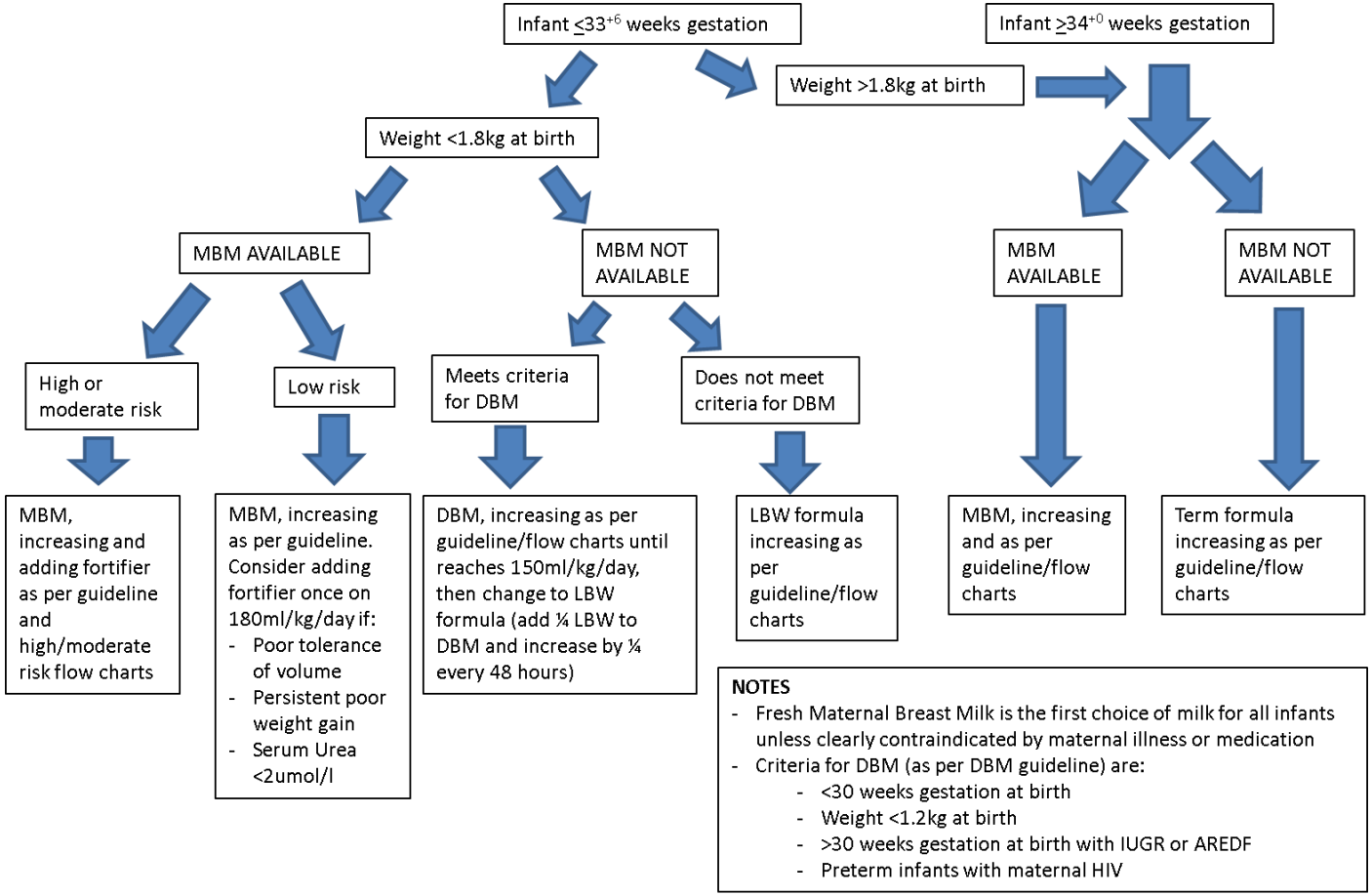
b. Starting and Increasing Feeds– MODERATE RISK INFANTS



b. Management of common feed related problems



d. Choice of Milk



Appendix 1

8. TABLES

a. Starting and Increasing Feeds

i. High Risk Infants (based on increases of 10-20ml/kg/day)

Weight (kg)	Start at (hourly)	Start at (2 hourly)	Increase hourly feed volume by*	Increase 2hourly feed volume by
less than 0.6	N/A	0.5	0.25ml every 24 hours	0.5ml every 24 hours
0.6-0.9	0.5	1	0.5ml every 24 hours	1ml every 24 hours
0.9-1.2	0.75	1.5	0.5ml every 12 hours	1ml every 12 hours
1.2-1.5	1	2	0.5ml every 8 hours	1ml every 8 hours
1.5-1.8	1.25	2.5	0.5ml every 6 hours	1ml every 6 hours
1.8-2	1.5	3	1ml every 12 hours	2ml every 12 hours

ii. Moderate Risk Infants (based on increases on 20-30ml/kg/day)

Weight (kg)	Start at (hourly)	Start at (2 hourly)	Increase hourly feed volume by:*	Increase 2hourl feed volume by:
1.0-1.2	1	2	0.5ml every 6 hours	1ml every 6 hours
1.2-1.6	1.5	3	1ml every 12 hours	2ml every 12 hours
1.6-2.0	2	4	1ml every 8 hours	2ml every 8 hours
2-2.4	2.5	5	1ml every 6 hours	2ml every 6 hours
2.4 and above	3	6	1.5ml every 8 hours	3ml every 8 hours

*Note that this refers to the actual feed **volume** based on 1 hourly feeds. Therefore if baby is 2 hourly fed then multiply the amount on this table by 2 to give the increase on the feed volume, if on 3 hourly feeds multiply by 3 and so on

b. Nutrient Content of Commonly Used Products per 100ml

Fluid Name / Nutrient	Preterm Stock PN	Preterm + Sodium Stock PN	Term Stock PN	Stock Lipid	Dextrose 10%	MBM/DBM	MBM with Full Fortifier*	Neocate LCP	Peptijunior	LBW Formula (Aptamil Preterm)	Post D/C Formula (Nutriprem 2)	Term formula	Infantrini
Energy (kcal)	63.0	59.8	70.2	166.7	40.0	69.0	85.0	71.0	66.0	80.0	75.0	66.0	100.0
Protein (g)	2.3	2.8	2.5	0	0.0	1.3	2.5	2.0	1.8	2.6	2.0	1.3	2.6
Carbohydrate (g)	12.1	11.0	13.5	0	0.0	7.2	10.0	8.1	6.8	8.4	7.4	7.3	10.3
Fat (g)	0	0	0	16.7	0.0	4.1	4.1	3.5	3.5	3.9	4.0	3.5	5.4
Sodium(mmol)	0.0	4.3	2.8	0.1	0.0	0.7	2.2	0.8	0.9	3.0	1.2	0.7	1.1
Potassium (mmol)	2.4	1.7	1.9	0	0.0	1.5	2.1	1.6	1.7	2.1	2.0	1.6	2.4
Calcium(mmol)	0.8	1.0	0.9	0	0.0	0.8	2.5	1.2	1.2	2.3	2.2	1.2	2.0
Phosphorous (mmol)	1.0	2.2	0.9	1.5	0.0	0.5	1.7	1.1	0.9	2.0	1.5	0.9	1.3
Iron (umol)	0.0	0.0	0.0	0.0	0.0	1.3	1.3	18.8	13.8	25.1	17.9	9.5	21.5
Vitamin A (IU)	0.0	0.0	0.0	3910.0	0.0	213.0	985.6	264.0	173.2	599.4	269.7	183.2	333.0
Vitamin D (IU)	0.0	0.0	0.0	680.0	0.0	0.0	200.0	51.0	52.0	120.0	68.0	48.0	68.0
Volume (ml/kg) required to reach recommended protein intake (ELBW infants)	152	125	140	Contains no protein	Contains no protein	292	152	195	211	146	190	292	146

Typical Values are used and are correct at 18/10/2011

*Based on Cow and Gate Nutriprem Breast Milk Fortifier

Appendix 1

9. SUPPORTING INFORMATION

GUIDELINES AND NUTRITIONAL CARE

There is good evidence from large epidemiological studies such as EPICure that preterm infants often fail to grow adequately, dropping to significantly lower centiles for weight and head circumference at discharge than those which they were born on[39 40]. There is also evidence that growth failure is also associated with poorer neurodevelopmental outcomes[42]. One significant causative factor for this failure of growth is that these infants receive inadequate nutrition, and there is evidence that they fail to achieve appropriate targets for nutrient intake[16 52]. Feeding practices across different neonatal units has been shown to be one of the factors responsible for the variability in lengths of stay and the level of postnatal growth restriction seen between different units offering the same level of care[17].

Although there is uncertainty around the definitive practice of nutritional support in preterm infants, there is evidence that standardisation of practice and the use of guidelines is beneficial. A systematic review and meta-analysis by Patole and De Clerk in 2005 showed that the use of standardised feeding regimens reduced rates of NEC, and in the context of the Vermont Oxford Network's 'Potentially Better Practices for Nutrition', the standardisation of practice was shown to reduce the time to start PN and enteral feeds, improve use of breast milk, reduce lengths of stay and a lower rate of infants being discharges with weights below the 10th centile [23 24]. Donovan et al studied aspects of nutrient intake and outcomes before and after the introduction of nutrition support guidelines in their NICU, showing significantly earlier initiation of both parenteral and enteral feeding, earlier achievement of full enteral feeding, and earlier regaining of birth-weight after introduction of guidelines[25].

ASSESSMENT AND MONITORING

Some babies are at higher risk than others of nutritional problems – under-nutrition, feed – related complications or both. Regular assessment of nutritional status and monitoring of growth will help identify infants with greater nutritional needs or a higher risk of poor growth or problems. Preterm infants in particular are at risk and should have their weight, head circumference and length measured at a minimum of once a week [23 78 233].

The following are things to consider when assessing nutritional risk

- Term babies with appropriate birth weight have good nutrient stores, designed to support them through the first few days when breast milk volumes are low. They are low risk.
- Preterm babies have low nutrient stores and are born at time of rapid growth – the earlier they are then the bigger the problem and the greater their nutritional risk. This is compounded by immature gut and metabolic function. They are moderate to high risk (depending on gestation) and need early nutrition support.

- Growth restricted babies have less nutritional reserve; they may also have reduced perfusion to the gut before birth and an increased risk of NEC. These babies will therefore be at greater risk compared to babies of a similar gestation.
- Congenital abnormalities such as gastrointestinal abnormalities, facial anomalies and cardiac problems (including PDA and associated treatment) will all affect nutritional status and increase nutritional risk.
- Acquired disorders such as hypoxic-ischaemic injury, sepsis and NEC will impact on the nutrition infants receive and in turn put them at higher risk of poor nutrition.
- Combinations of the any of the above factors will result in a greater overall risk.

NUTRITIONAL REQUIREMENTS

TERM INFANTS: breast milk provides appropriate nutrients for healthy term babies and breast-feeding should be supported and encouraged. Babies who are not being breast fed should be fed on a standard cows' milk based formula.
PRETERM INFANTS: evidence-based recommendations are available to guide nutrient intakes for preterm infants. The most comprehensive is Tsang 2005 [14], which gives guidelines for parenteral and enteral nutrition support, and specifies requirements for babies <1000g and 1000-1500g birth-weight, during both 'transition' phase (days 2-7 of life) and 'growth phase' (day 7 onwards). ESPHGAN 2010 [15] gives recommendations for enteral intake of fluid and nutrients, though is largely based on the Tsang recommendations. Growth is rapid in the third trimester of fetal life; infants born preterm thus have high requirements for nutrients, but immature physiological capacity to handle them. Breast milk is the optimal first choice for preterm infants' nutrition, however even at high volumes will not provide all adequate nutrients: supplementation with breast milk fortifier or preterm formula may be necessary. The tables in this guideline refer to the Tsang recommendations for energy and protein in VLBW infants and how they compare to typical feeds used in Southampton. Note that only LBW formula milk fed at 150ml/kg/day or fully fortified breast milk fed at 180ml/kg/day is able to achieve the recommended amounts). The full Tsang recommended nutrient intakes are given in Appendix 1. Essentially, the less mature, the lower the nutrient stores/reserves, the earlier nutrient provision is required

STANDARD NUTRITIONAL SUPPORT OF PRETERM AND SICK INFANTS

a. PARENTERAL NUTRITION

i. Early use of PN

The VON Potentially Better Practices for nutrition state that PN should be commenced as early as possible, ideally within the first 24 hours of life [23]. This helps prevent the net nutrient loss and catabolism that occurs when an infant is born prematurely. Significant nutritional deficits have been shown to occur in the first few days (up to 2 weeks) after birth, so introduction of PN early is a strategy

to help prevent this [16]. There is also good evidence that it promotes anabolism, prevents the loss of protein mass, improves calorie intakes, can improve growth and is safe [75 87-90].

ii. Protein intake

As described above, nutrient delivery in high risk groups is challenging, and the delivery of protein and energy early in life often fails to meet recommended targets. Whilst intravenous glucose given early on will meet energy needs in many cases, it contains no protein, which can only be administered using PN or milk feeds. Therefore, in high risk infants who cannot be fully fed quickly, it is vital to give the largest amount of protein possible as PN, as early as possible to try and prevent the accumulation of deficits. In view of this, Stock PN in Southampton has recently been reformulated to provide higher levels of protein in a smaller volume. Using high protein PN to deliver higher protein intakes in the first few days of life in preterm infants has recently been shown to have metabolic benefits in addition to the prevention of catabolism, including a reduction in hyperglycaemia and insulin use [234], and a significant reduction non-oliguric hyperkalaemia [235].

iii. Peripheral vs central PN

It is generally accepted that is preferable to given PN via a percutaneous central venous catheter ('long line') than via a peripheral cannula, in view of the decreased risk of extravasation, the difficulty associated in obtaining repeated peripheral access in preterm infants, and the ability to give higher concentrations of glucose and potassium. Central lines on the other hand have the disadvantage of the risk of catheter related infections. A Cochrane review in 2007 concluded that central PN was not associated with an increased risk of infection compared to peripheral PN, and there was some evidence that central PN resulted in a smaller number of catheters/cannulas per infant required to deliver the PN, together with improved nutrient delivery [236]. However, it also concluded that there was no significant difference in adverse events (including extravasation) when comparing central to peripheral PN. Therefore, whilst PN should be given centrally wherever possible, peripheral PN should be considered in some individual cases where there is significant nutritional risk and a delay or difficulty in obtaining central access [75].

iv. Monitoring and Complications

Careful monitoring of patients whilst on PN is important to ensure appropriate and adequate nutrition, and to identify potential complications, including liver disease, metabolic bone disease and catheter-related infection. Current recommendations regarding monitoring have been laid out by ESPGHANs guidelines on paediatric parenteral nutrition[75]., and can be found in the NNU Parenteral Nutrition Guidebook

b. ENTERAL FEEDING

i. Choice of milk

There is good evidence that maternal breast milk (and to some extent donor breast milk) is protective against NEC, so breast milk should be the food of first choice [20 106 109 237-239]. Ideally this should be the mother's own fresh colostrum. All mothers of preterm infants should have lactation support, and help with expressing within 6 hours of birth (ideally within half an hour according to current WHO recommendations)[77]. If no maternal milk available by 48 hours and the baby is ready for milk, consent should be sought to use DBM. However, as DBM is a limited resource and there is evidence it contains fewer nutrients than mother's own breast milk, DBM should be reserved only for the purposes of establishing feeds in high risk infants, as laid out in the DBM guideline).

Where breast milk cannot be used, preterm infants should receive a specialist high calorie and high protein formula ('LBW formula')[113 114 116].Preterm formulas are designed to meet the basic nutritional requirements of most preterm infants when fed between 150 and 180ml/kg. Preterm formulas can be used as soon as commencement of enteral feeding is recommended. Term formulas should not be used as they fail to meet the nutritional needs of premature infants. There is no evidence to support the use of term elemental/semi elemental formulas in the early stages of feeding unless there is a compelling clinical reason to do so.

ii. Starting Feeds

The objective of early feeding is to stimulate gut maturation, motility and hormone release. As starvation leads to atrophy of the gut, withholding feeds may render subsequent feeding less safe and protract the time to reach full enteral feeding [240]. No work has yet addressed whether initial feeds should be exclusively breast milk (mother's own or donor) or whether initial feeds should be delayed if only formula is available. However most evidence suggests that any enteral feed given early may be better than gut starvation [241].

Trophic feeding is defined as small volumes of enteral feeds up to 24 mls/kg/day given to promote gut function It has been shown to prevent changes of starvation in gut mucosa, but a systematic review of 9 trials of trophic feeds vs withholding feed, including 754 infants, did not find any difference in overall feed tolerance, weight gain or rates of NEC [97].

Due to concerns about NEC, commencement of enteral feeds is sometimes delayed in preterm infants. A Cochrane review of early vs delayed introduction of progressive enteral feeds did not show an increase in NEC with early feeds, but despite almost 1000 babies in 5 RCTs the conclusion was that data were insufficient [242]. The ADEPT trial randomised 404 preterm, growth-restricted

babies to early feeds (start day 2) or late feeds (start day 6): the early group achieved full feeding earlier, required less PN and had less cholestasis, and no difference was seen in incidence of NEC [243]. There is thus no evidence to support delaying feeds; there is a lack of good evidence to guide feeding policy in babies on inotropes and ibuprofen.

iii. Rate of advancing feeds

In standard risk infants a rate of increase of 30ml/kg/day is reported safe, whereas data are more limited in the high risk infant. Evidence points towards several days of trophic feeds followed by a rate of increase of 10-20ml/kg/day. There should be a low threshold for withholding stepped increases secondary to tolerance concerns in the high risk infants. There is limited data on this. A Cochrane review [244] including 4 RCTs and 496 babies, considered increase of up to 24 mls/kg/day as slow, and 25 or greater mls/kg/day as rapid. More rapid increase was associated with earlier tolerance of full feeds and faster weight gain, and no difference in NEC, but numbers were too small to make definite conclusions. This topic is being considered by NIHR for a multi-centre UK trial at present.

iv. Nutritional Supplements:

As mentioned above, the nutritional needs of preterm infants are greater than infants born at term, and as such breast milk is adequate to meet those needs [14]. In order to maintain the benefits of breast milk whilst optimising the nutritional status and growth of preterm infants' single multicomponent fortifiers (BMF) have been developed.

Concerns with the use of BMFs include tolerance and their effects to increasing osmolality and in turn the risk of NEC. Most studies have found no significant problems with the tolerance of fortified EBM [245], and a recent review of published evidence found no link between the relatively small increases in osmolality caused by the addition of fortifier to breast milk and NEC [246]. A Cochrane review concluded that the use of BMFs can lead to short term improvements in weight, length and head circumference and that while it is unlikely that further comparative studies with breast milk alone are to take place it recommends further research seeks to evaluate long term outcomes of BMF therapy and identify the optimum composition of BMF products [111].

Recommendations made in 2010 by ESPGHAN stated that the feed of choice for preterm infants (<1800g) was mother's own breast milk supplemented with BMF, or special preterm formula if breast milk not available [15].

v. Nutrition at Discharge:

Preterm infants are often discharged home with growth below that expected according to their birth centile. A review by ESPGHAN in 2006 looking at the evidence for feeding preterm infants after discharge recommended that infants discharged with an appropriate weight for their corrected gestational age should be discharged either breast feeding (where breast fed) or on regular formula (where formula fed). However, they also concluded that preterm infants discharged with a subnormal weight for their corrected gestation age should receive fortifier in addition to breast milk (where breast fed) or on special high energy/protein preterm infant formula (where formula fed) [76]. Recently, a Cochrane review looked at this in more detail, addressing the question of whether using fortifier in breast fed preterm infants after discharge improved growth. It concluded that using fortifier after discharge improved growth in infancy, though the evidence was limited [247].

Appendix 2: Statistical Analysis Plan

Understanding Change Management in Neonatal Intensive Care

An investigation into the factors affecting the successful integration into routine care of a complex intervention to improve the nutritional support of preterm infants

Appendix 2

1. Introduction

1.1 Preface

This study focusses on the implementation of a complex intervention aimed at translating current evidence in neonatal nutritional care into practice and improving the nutrient intakes and growth of preterm infants.

Importantly, this study also uses the sociological framework of Normalization Process theory (NPT[37 38]) to develop, assess and guide the intervention, its implementation, and subsequent integration into routine care. A specific tool was developed based on the NPT toolkit[35 36] to measure the process of normalization during the intervention period, highlighting areas needing more input from the study team and guiding the implementation process, enhancing the uptake of the new. By utilising this novel approach, this study measures and explores the process of a significant change in practice in a complex care environment, identifying the factors which promote and inhibit its integration into practice, and establishing how to embed new ways of working so that they become part of routine care. This is unique in offering the ability to integrate measures of implementation and normalization (provided by the modified NPT toolkit) with detailed clinical data on daily nutritional care, growth and outcomes.

The hypotheses that this study addresses are:

1. The introduction of a complex intervention for the nutritional care of preterm infants will improve their nutrient intakes and growth

2. The use of Normalization Process Theory to both monitor and guide the implementation of a complex intervention will result in improved integration into practice with subsequent improvement in clinical outcome measures

This research explores the dynamics of quality improvement in the context of neonatal nutritional care, studying the factors that influence the implementation and adoption of complex intervention.

1.2 Purpose of the analyses

These analyses will assess the efficacy of a complex intervention for the nutritional care of preterm infants in improving nutrient intakes and growth during its main one year intervention period, compared with period immediately before this where the intervention was partially introduced, and a pre-implementation group of infants cared for prior to any intervention. A further group cared for after the intervention period will also be compared to assess the degree to which the practices introduced as part of the intervention were sustained.

In addition these analyses will also assess the effect of the intervention on measures of practice and guideline compliance, together with the extent to which measures of infant outcomes and practice can be related to measures of normalisation using a novel NPT toolkit. As this was a dynamic implementation study with the intervention introduced in two stages, the step change in outcomes at each time point is of as much interest as the overall trend for change over the course of the entire study.

2. Study Objectives and Outcome Measures

2.1 Study Objectives

The primary objectives of this study are to:

1. Develop and implement a comprehensive package of care for the nutritional care of preterm infants (born at less than 30 weeks gestation or with a birth weight less than 1501g). Following implementation of the intervention (for 1 year), assess its' effect on improving:

    a. The delivery Energy (in kcal/kg/day) and Protein (in g/kg/day), compared with recommendations for this group of infants at 1 week of age, 2 weeks of age, 4 weeks of age, 6 weeks of age, 36 weeks post menstrual age and discharge.

    b. Growth (length, weight and head circumference) at 1 week of age, 2 weeks of age, 4 weeks of age, 6 weeks of age, 36 weeks post menstrual age and discharge.

2. Assess the factors which promote or inhibit the implementation, uptake and staff engagement of the complex package for the nutritional care of preterm infants. This includes:

    a. The effectiveness of the intervention in terms of changing practice and how successfully it is embedded and integrated 'normal' practice ('normalization')

    b. An assessment of the factors which impede or enhance the integration of the new practices into routine normal care ('normalization')

    c. The relationship between the effectiveness of the intervention at changing practice and the nutritional and growth outcomes described above.

    d. The effect of NPT to guide and assess the implementation process.

2.2 Outcome Measures

Infant outcomes

Primary outcome measures

1. Differences in mean daily energy and protein intakes during stay on NICU between pre-implementation and intervention periods
2. Differences in the change in weight and head circumference standard deviation scores between birth and discharge between pre-implementation and intervention periods

Secondary outcomes

1. Differences in mean daily energy and protein intakes during stay on NICU during the following time periods between pre-implementation and intervention periods
    a. First week of life
    b. Second week of life
    c. Fourth week of life
    d. Sixth week of life
    e. Week of 36 weeks corrected gestational age
2. Differences in the change in weight and head circumference standard deviation scores between birth and the following time points between pre-implementation and intervention periods:
    a. End of the first week of life
    b. End of the second week of life
    c. End of the fourth week of life
    d. End of the sixth week of life
    e. Week of 36 weeks corrected gestational age
3. Differences in mortality and morbidity between pre-implementation and intervention periods
    a. Mortality
    b. Numbers of infants with Necrotising Enterocolitis (NEC)
    c. Numbers of infants with Chronic Lung Disease (CLD)
    d. Numbers of infants with Retinopathy of Prematurity (ROP)

e. Numbers of infants with severe Intraventricular Haemorrhage (IVH)

f. Numbers of infants with Late Onset Sepsis (LOS)

g. Numbers of infants with Infection with Coagulase Negative Staphylococcus

h. Length of stay

Process and Practice Change Outcomes

Process Outcome Measures

The following measures of nutritional processes will be compared across study periods:

a. *Continuous outcome measures*

   i. Time of starting enteral feeds

   ii. Time of starting PN

   iii. Time of starting breast milk fortifier

b. *Dichotomous outcome measures*

   i. Numbers of breast fed infants that received breast milk fortifier

   ii. Numbers of infants discharged on breast milk, preterm formula and term formula

Practice Change Outcome Measures

The following measures will be used to assess and understand the changes in clinical practice over time

1. The change in percentage audit compliance over the intervention and normalisation periods
2. The change in the mean Normalisation Process Theory (NPT) toolkit questionnaires score over the intervention and normalisation periods
3. The relationship between percentage audit compliance and mean NPT toolkit scores over the intervention and normalisation periods
4. The relationship between percentage audit compliance and mean NPT toolkit scores over the intervention and normalisation periods and the primary infant outcome measures described above.

2.3 Derived variables

The main derived variables used will be those of Standard Deviation Scores (SDS) for infant weight, length and head circumference. These will be calculated from infant measurements using the LNS Growth add-in for Microsoft Excel, which calculates SDSs based on an infant's sex, gestational age at birth and current age. Further derived variables will be the difference in SDS (dSDS) between birth and a specific time point (see below for time points of analysis), to give a numerical and standardised indication of growth at different intervals during stay.

Whilst the primary nutrient intake outcomes will be energy and protein in SI units (kcal/kg/day and g/kg/day respectively), these values will also be converted into a percentage value of recommended amounts based on the 'Recommended Range of Intake' according to Tsang et al. Tsang's RRIs are given for three phases: Day zero, Transition and Growing. For the purposes of analysis, these phases are taken to be day zero, days one to six and day seven onwards respectively. Enteral RRIs are used once an infant is receiving 50% or greater of their total fluids enterally. Infants receiving intakes within the RRI are calculated as receiving 100% of recommendations, with amounts below or above these limits calculated as percentages using the lower and upper limits respectively

3. Study Methods

3.1 General Study Design and Plan

This study is essentially a before and after study, involving the development, introduction and assessment of a complex intervention to standardise the nutritional care of preterm infants. It consisted of a series of smaller phases as detailed in the subsequent sections. Figure 1 shows a detailed plan of the study, and a brief description of each phase is given below.

This study uses compares infant outcomes based on several different time periods to assess the effect of the intervention in improving nutritional care and outcomes:

A) Pre-implementation period (1st January 2011 and 31st July 2011). Data on infants born during this period was collected retrospectively after the study had finished in order to provide a more contemporaneous 'control' group. Initially period B below (the partial implementation period cohort) was planned to be used as this contemporaneous control. However, given that the intervention was being developed and partially introduced during this period, it was felt to be an inappropriate for comparison with the main 2012 intervention period.

B) Partial implementation period (August 1st – December 31st 2011). Data was collected prospectively during this period, during which some elements of the intervention (including improved nutritional solutions) were introduced, and staff were made aware of and consulted about the main intervention. In addition, the work with staff carried out during this period to develop the intervention would also be likely to begin to effect practice.

C) Main Intervention Period (January 1st– December 31st 2012) during which the full complex intervention was implemented

D) Post-implementation period (January 1st– June 30th 2013). This was used to assess the degree to which the new practices remained in place after the intervention period

In addition, data will be collected on a retrospective cohort of infants born during 2009, in order to inform the development of the intervention by assessing nutrient intakes and growth outcomes, and identifying areas where practice could be improved. These data from the 2009 infants will be summarised as described below, but will not be used as a comparator to assess the effectiveness of the intervention given the amount of time that has passed between 2009 and 2012.

3.2 Inclusion-Exclusion Criteria and General Study Population

To be included infants had to have been born at less than 30 weeks gestation or with a birth weight of less than 1501g. They also had to have been born in the study hospital and not transferred in from elsewhere after birth. Infants were automatically included from birth to receive the newly implemented service for the provision and monitoring of nutrition for preterm and VLBW infants (see below regarding the research approvals process).

All NICU staff were eligible for inclusion in the TPB questionnaire and the regular assessment of normalisation using the NPT Toolkit questionnaire and were recruited during November 2012. For interviews carried out after the intervention period, only staff who had been part of the NICU staff prior to the intervention were eligible to take part.

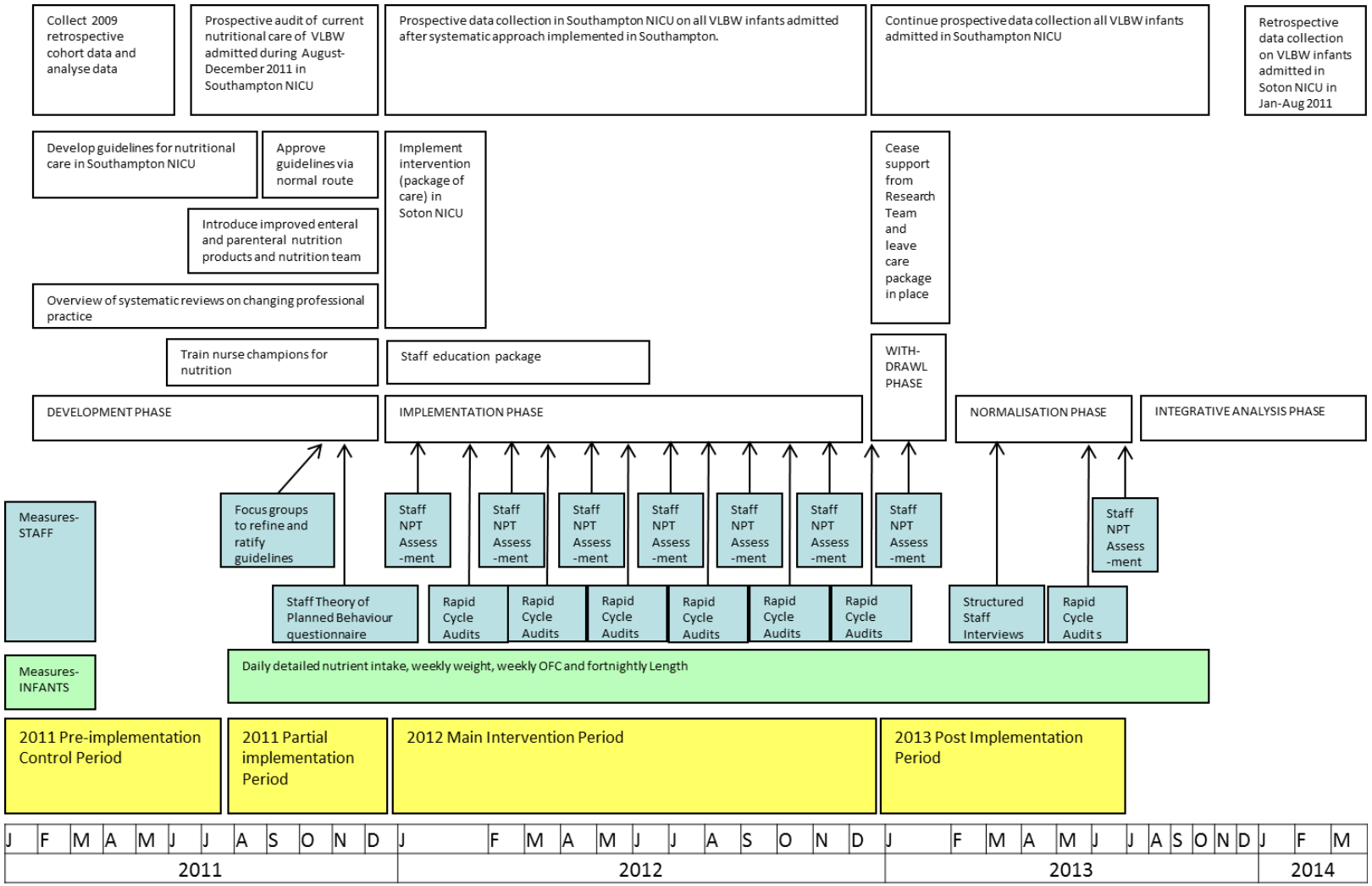


Figure 1: Plan of Investigation

3.3 Study Variables

Infant variables

A specially designed computer program (SENNAT) will be used to collect data on the type and amounts of fluid delivered to each infant on each day of their NICU stay. It will use this information to calculate the daily intake of various macro- and micronutrients

Nutrients that are of interest and will be used in the analysis of this study are:

- Energy (kcal/kg/day)
- Protein (g/kg/day)

Whilst the daily data will be used for an overall analysis, these nutrient intake data will also be summarised across various time points, and compared between study periods:

- First week of life
- Second week of life
- Fourth week of life
- Sixth week of life
- Week of 36 weeks corrected gestational age
- Entire NICU stay

For the purposes of interrupted time series analysis (ITS), nutrient intake data from all infants will be summarised across each calendar week for each study period

In addition, the same computer program was used to collected growth data, specifically:

- Weight
- Head circumference
- Length

These data will be collected each time they were measured during stay, and converted to SDS and dSDS as described above for the purposes of analysis. These derived variables will then be summarised and compared using the same time points above.

In addition, the following demographic variable will be collected for each infant

- Birth weight

- Gestational age at birth
- Sex
- Date of birth (and each subsequent day of stay)
- CRIB II score

The following binary variables will be collected for each infant

- Diagnosis with Necrotising Enterocolitis (NEC)
- Diagnosis with Chronic Lung Disease (CLD)
- Diagnosis with Late Onset Sepsis (LOS)
- Diagnosis with Infection with Coagulase Negative Staphylococcus (ICNS)

In addition, the continuous variable of number of days of stay (length of stay) will be collected.

Process variables

The following binary variables will be collected

- Whether infant received breast milk fortifier (breast fed infants only)

The following categorical variables will be collected

- Feed at discharge (breast milk, preterm formula, term formula and mixed feeding)

The following continuous variables will be collected

- Time of starting enteral feeds
- Time of starting PN
- Time of starting breast milk fortifier (breast fed infants only)

Practice Variables

The following practice based variables will be collected

- Percentage guideline compliance from each bimonthly audit
- Score (from 1-10) for each item on the 16 item NPT toolkit questionnaire completed by each staff member at each bimonthly NPT questionnaire point

Time variables

Each day of each infant's stay will be coded to a time period, with additional variable generated based on these time codes to as follows:

- 'Period' – this will assign each day of an infant's stay to a study period based on the infant's date of birth
- 'Study Period' – this will assign each day of an infant's stay to a study period based on the date of that day
- 'Exclude' – this will identify the days of infants stay which occur in a later study period to that in which they were born
- 'Crossover' – this will identify all the days of infants stay (regardless of when they occur) for all infants who crossover between study periods (ie those born in one period wo stay into the subsequent study period)

4. Sample Size

The sample sizes used for this study are pragmatic, based on the number of in-born infants during the defined periods. However, based on figures from 2009, it is estimated that 70 eligible infants will be born in Southampton in 2012 during the 1 year intervention period. These will be compared to infants born in the pre- and partial implementation groups born in 2011 (approximately 35 infants each). This will allow 80% power to detect a difference between groups in the mean daily provision of protein and energy over the course of the stay (from birth to discharge) of 0.39g/kg/day and 11.54kcal/kg/day respectively. For weight, length and head circumference the detectable differences of the change in SDS between birth and discharge for weight and head circumference will be 0.40 and 0.55 respectively (power for difference in SDS scores for length between birth and discharge could not be calculated due to a lack of data on length at birth).

5. General Considerations

5.1 Data Cleaning

The way that SENNAT collects data (based on a single day's total fluid intake up to midnight on that day) means that the first day of life and the last day of stay will not represent an entire day. These will therefore be dropped from the data set for each infant.

5.2 Analysis Populations

5.2.1 Study Period Populations

For nutritional data, the main analysis will be based on time periods, using study periods A-D described above, where the nutritional data collected between the dates of each period will be used to assess the effects at each period of the study. To recap, these periods are:

A. Pre-implementation period (1st January 2011 – 31st July 2011
B. Partial implementation period (August 1st – December 31st 2011)
C. Main Intervention Period (January 1st – December 31st 2012)
D. Post-implementation period (January 1st – June 30th 2013)

5.2.2 Infant Birth Period Populations

For growth and process outcomes, analysis will be based on individual infants born within each study period. This is slightly different to the time period approach above, as some infants born at the end of one period will have received care both in that period and the subsequent one. Including such infants in their period of birth will potentially skew results, as their outcomes will have been affected by the potentially great nutrition they received whilst cared for in the later period. Therefore, infants that fall into this category will have data from their overlapping period excluded, and for outcomes based on discharge (such as growth at discharge) will be excluded altogether from the analysis.

5.3 Covariates and Subgroups

Covariates

Analyses will be adjusted for the following covariates:

- Birth weight
- Gestational age at birth
- Sex

5.4 Multiple Testing

Where multiple comparisons occur (when comparing outcomes between all study periods), Tukey's method will be used to adjust the overall significance

of test results. Unadjusted significance will also be reported to allow the difference between two adjacent periods to be considered in addition to the overall comparison.

6. Summary of Study Data

Descriptive statistics will be used to summarise the demographic and outcome variables of the infants in all the study periods.

Variables of interest (listed as outcome measures above) will be tested for normality in order to help determine the nature of the analysis methods used. Normal plots and the Kolmogorov–Smirnov test will be used (the Shapiro–Wilk test will be used for outcomes where there are less than 200 cases), with a cut off value of $p<0.05$ accepted as evidence of a non-normal distribution. It is anticipated that nutrient intakes are likely to be negatively skewed with a non-normal distribution, whilst growth parameters are likely to take on a normal distribution.

For continuous variables, if the data are normally distributed, the mean and standard deviation will be calculated. If the data are not normally distributed, the median and interquartile range will be calculated.

For categorical or binary variables, these will be summarised as frequency and percentage of total.

For practice change measures using NPT survey results, scores will be summarised as mean and standard deviation for all staff at each time point (for both the total score and each of the four individual elements of NPT- coherence, cognitive participation, collective action and reflexive monitoring)

In general, all data will be listed and sorted by study period. All summary tables will be structured with a column for study period in the order of A-D given above, and will be annotated with the total population size relevant to that period.

7. Analyses

Analysis of TPB results

A questionnaire based on the Theory of Planned behaviour will be used early in the study to measure the attitudes and intentions of the staff prior to implementation[121]. This will be constructed and analysed in accordance with the method described by Francis et al[132]. Initially correlation analysis of measures of intention (both intention performance and generalised intention), direct attitude, subjective norms and perceived behavioural control and indirect attitude, subjective norms and perceived behavioural control will be

performed in order to establish which measure of intention worked best within the data. Direct measures of attitude, subjective norms and perceived behavioural control will then be entered into a multiple linear regression model as predictor variables with the preferred measure of intention as the dependent variable in order to establish which predictors were most important in the study population.

Indirect measures will then be calculated used the formulas in Francis et al's method (based on the Theory of Planned Behaviour[121]), with each belief statement weighted by the relevant outcome evaluation[132]. Weighted measures will then be regressed together with intention in the same way as the indirect measures, again to provide insight into the factors significantly affecting intention.

In order to determine the difference in beliefs between those with high and low intentions, respondents will be split into two groups (high and low intenders) using the median intention score. An independent samples t-test will then be used to identify the significant differences in beliefs between the two groups.

Comparison of Infant outcomes between study periods

Three methods will be used to compare the difference in the primary and secondary outcome measures between study periods. These multiple methods have been chosen to try and build up a comprehensive picture of the effects of the intervention over time and across study periods.

1. Comparison of non-repeated measures outcomes

   In the first instance, whilst nutrient intake and growth data will be available as repeated measures over time for each infant, a between study period comparison data will be made using single measures for each infant, with data reduced to a single outcome measure per infant in each group prior to analysis. For nutrient intakes, these will be summarised as the mean nutrient intake during the time period of interest (see outcome measures above), whilst growth measures will be summarised as the mean dSDS for each growth parameter. Depending on whether or not data are normally distributed, study groups will be compared using either a two way ANOVA (for normally distributed data) or the Kruskal-wallis test (for non-normally distributed data). If significant differences are found then comparisons between pairs of groups will be made using a post hoc analysis according to Tukey's method (normally distributed data) or multiple Mann-Whitney-U tests (non-normally distributed test). Infants will be assigned to a study period based on their year of birth. For infants who were born in one period, but were still in hospital during the time of the next study period, for nutrient intake data, data from the

overlapping period will be excluded from the analysis, whilst for measures of growth all data for overlapping infants will be excluded.

2. Interrupted time series analysis[164]

   As this technique uses linear regression with subsequent comparison of regression coefficients and constants between periods (segmented regression), strictly speaking this should be used with normally distributed data. However, as it provides a useful way of visualising and comparing the effects of the intervention over time and in each time period, it will be used but results interpreted in the context of the non-normal distribution of the data where present. In the first instance, data will be reduced to a single outcome measure per infant per time unit in each group prior to analysis. For nutrient intakes, these will be summarised as the mean nutrient intake **each week** across all study periods. The Prais-Winsten method will be used to correct for any auto-correlation in the data, which is likely given the repeated measures nature of the data[165]. If possible, multi-factor interrupted time series analysis will then be used to compare age and sex adjusted weight standard deviation scores and growth centiles in each study period, again taking into account the auto-correlated nature of the data due to repeated measures using the Prais-Winsten method. Segmented regression will be used for estimating intervention effects. For this analysis, as daily data will be used, study periods will be assigned based on the date of each measurement, rather than the birth date of the infant.

3. Modelling using mixed effects for repeated measures data

   This statistical technique is advantageous to the standard comparator tests above as it is able to account for repeated measures in the same infant (thus allowing all daily nutrient intake and growth data for each infant to be used). This technique also allows the addition of other potentially confounding variables and subsequent adjustment of the model. All study periods will be included in the analysis, with Tukey's method used to adjust significance values in view of multiple comparisons. Variables that will be added will be **sex, gestational age at birth** and **birth weight**.. For normally distributed data (growth data), a general linear model with mixed effects will be used. However, as this approach relies on data having a normal distribution, it cannot be used for non-normally distributed data. Therefore, for non-normally distributed data (likely to be the nutrient intake data), the generalized linear model will be used, as by introducing a random effect for the repeated element it is able to account for the non-

normal distribution of the data where present. For this analysis, as daily data will be used, study periods will be assigned based on the date of each measurement, rather than the birth date of the infant. It will not be necessary to remove overlapping days as the modelling approach using individual longitudinal data is able to account for this

Mortality and Morbidity

These are dichotomous outcome measures, so compared across study periods using Chi squared test (or Fishers Exact test where numbers are low).

Comparison of Process Outcome Measures between study periods

Continuous process outcome measures will be compared across study periods using either a two way ANOVA (for normally distributed data) or the Kruskal-wallis test (for non-normally distributed data). If significant differences are found then comparisons between pairs of groups will be made using a post hoc analysis according to Tukey's method (normally distributed data) or multiple Mann-Whitney-U tests (non-normally distributed test). Infants will be assigned to a study period based on their year of birth. For infants who were born in one period, but were still in hospital during the time of the next study period, data from the overlapping period will be excluded from the analysis.

Dichotomous outcome measures across study periods will be compared using Chi squared test (or Fishers Exact test where numbers are low).

Comparison of Practice Change Outcome Measures between study periods

Guideline compliance audit results will be summarised as mean percentage compliance across all audit points at each time period, and plotted over time. Linear regression will be used to assess the change over time.

Measures of the 'normalisation' of practice using scores form the Normalisation Process Theory (NPT) toolkit questionnaires answered by staff at two monthly intervals during the study period will be summarised as mean scores (both total score and scores for each of the four domains of coherence, cognitive participation, collective action and reflexive monitoring). These will be plotted over time, and linear regression used to establish the nature of the change over time.

In order to relate mean percentage audit compliance to NPT scores, the two plots will be overlaid, and multiple linear regression used to describe the nature of this relationship over time, with time included as variable to allow adjustment for the effect of time. Ideally, a repeated measures approach would

be used here given that the NPT results are the same group of staff answering the same questions repeatedly over time. However, the decision to use anonymous, untraceable questionnaires does not allow this. However, standard multiple linear regression with adjustment for time, is a more conservative approach than repeated measures, so would still give a reasonable measure of effects size with wider confidence intervals. Any statistical significance found using this method would therefore also be found by the less conservative repeated measures approach.

A similar approach will then be used to relate mean percentage audit compliance and NPT scores to the primary infant outcome measures described above. Plots of mean percentage audit compliance and NPT scores will be overlaid with plots of energy intakes, protein intakes and the differences in weight and head circumference SDS between birth and discharge over time during the intervention period. Time series cross-correlation analysis will then be used to measure the relationship between the time series.

8. Reporting Conventions

P-values ≥0.001 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001". The mean, standard deviation, and any other statistics other than quantiles, will be reported to one decimal place greater than the original data. Quantiles, such as median, or minimum and maximum will use the same number of decimal places as the original data. Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

9. Technical Details

The majority of analyses will be carried out using Stata 12.1 Intercooled (Stata Corp.). However, the 'Generalised linear modelling using mixed effects for repeated measures data' will be carried out using the GLMMIX function in SAS 9.3 (SAS Institute Inc.), as this analysis method is not currently available in Stata.

Appendix 3: Questionnaires and Question Topic Guides Used in this Study

1. Question route used to guide focus groups

1. Please introduce yourself & say what you think your role is in the nutritional care of your patients.

2. What do you know about the new nutritional guidelines?

   Associated prompts:

   What is its purpose?

   What kind of impact do you think they might have on nutritional care of preterm babies?

   How important is it to have standardised nutritional guidelines for preterm babies?

3. How do you think you could support the implementation of these nutritional guidelines?

   Associated prompts:

   How will using them impact on your work?

   What will you need to do differently?

   What might need to change to ensure it gets fully completed?

   What would make following them easier?

   What other actions might therefore need to be taken & by whom?

4. What is your perception of the role of other professionals in relation to nutritional care of preterm babies?

   Associated prompts:

   How do you interact with other h/c professionals in relation to feeding?

Appendix 3

2. Elicitation Study for Theory of Planned Behaviour Questionnaire

Standardising Preterm Infant Nutrition – We Need Your Help

Please take a few minutes to answer the 9 questions below about how you feel about the introduction of a new package of care and guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants. Your answers will be helpful in planning how we implement the new package.

Firstly, please tick one of the boxes below which best describes your position.

○ Band 3 Nurse	○ Band 4 Nurse	○ Band 5 Nurse	○ Band 6 Nurse
○ Band 7 Nurse	○ Band 8 Nurse or higher	○ ANNP	○ Pharmacist
○ Dietician	○ SHO/ST1-3	○ SpR/ST4-8	○ Consultant

○ Other (Please Specify): _____

1. What do you believe are the **advantages** to using a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

2. What do you believe are the **disadvantages** to using a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

3. Is there anything else you associate with using a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

4. Are there any individuals or groups who would **approve** of using a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

5. Are there any individuals or groups who would **disapprove** of using a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

6. Is there anything else you associate with other people's views about using a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

7. What factors or circumstances would **enable** you to use a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

8. What factors or circumstances would make it **difficult or impossible** for you use a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

9. Are there any other issues that come to mind when you think about using a set of guidelines for the nutritional care, feeding, measuring and growth monitoring of preterm infants?

3. The Theory of Planned Behaviour Questionnaire

Development of Guidelines for Nutritional care in Southampton Neonatal Unit

Thank you for agreeing to fill out this questionnaire. Your answers will help inform our new set of guidelines for the nutritional care of preterm and term infants on Southampton Neonatal Unit. All the questions simply require you to tick a box to indicate your answer. It should take around 15 minutes to complete, and all questionnaires are anonymous and answers will be treated in strictest confidence.

1) Firstly, please select the option below that best describes your position	
Band 3 Nurse	
Band 4 Nurse	
Band 5 Nurse	
Band 6 Nurse	
Band 7 Nurse	
Band 8 Nurse or higher	
ANNP	
Pharmacist	
Dietician	
SHO/ST1-3	
SpR/ST4-8	
Consultant	
Other (Please Specify):	

Appendix 3

2) If a new set of guidelines for the nutritional care, feeding and measuring of preterm infants was introduced, how many of the next 10 infants you care for would you expect to use them on?	
0	
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	

3) I would regularly use and refer to a set of guidelines for the nutritional care, feeding and measuring of preterm infants if they were introduced							
	1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

4) Using a set of guidelines for the nutritional care, feeding and measuring of preterm infants is.....							
	1 Harmful	2	3	4	5	6	7 Beneficial

5) Using a set of guidelines for the nutritional care, feeding and measuring of preterm infants is.....							
	1 Bad	2	3	4	5	6	7 Good

6) Using a set of guidelines for the nutritional care, feeding and measuring of preterm infants is.....							
	1 Unpleasant (for me)	2	3	4	5	6	7 Pleasant (for me)

7) Using a set of guidelines for the nutritional care, feeding and measuring of preterm infants is.....							
	1 Worthless	2	3	4	5	6	7 Useful

8) Please look at the statements below and grade them from 1 to 7 depending on whether you strongly agree (7) or strongly disagree (1).

Using a set of guidelines for the nutritional care, feeding and measuring of preterm infants will.....

	1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree
....make my practice in this area more consistent and standardised							
....improve the nutrition of preterm infants							
....allow problems to be detected earlier							
....mean less flexibility in nutritional care and could cause problems for some infants							
....improve my knowledge of preterm infant nutrition							
....improve my confidence in the nutritional care for preterm infants							

9)

	1 Unimportant	2	3	4	5	6	7 Important
Improved consistency in nutritional care is:							
Improving the nutrition of preterm infants is:							
Spotting problems earlier is:							
Reduced flexibility in care is:							
Improved knowledge in preterm infant nutrition is:							
Improved confidence in preterm infant nutrition is:							

Appendix 3

10) Please look at each of the statements below and decide to what extent you agree with them, and rate them from 1(strongly disagree) to 7 (strongly agree)							
	1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree
My colleagues/team think that I should use a set of guidelines for the nutritional care of preterm infants							
I am expected to follow a set of guidelines for the nutritional care of preterm infants							
My managers think that I should use a set of guidelines for the nutritional care of preterm infants							

11) The next questions look at whether certain groups of professionals would approve or disapprove of you using a set of guidelines for nutritional care.							
	1 Disapprove	2	3	4	5	6	7 Approve
If I followed a set of guidelines for the nutritional care of preterm infants, Doctors would.....							
If I followed a set of guidelines for the nutritional care of preterm infants, Nursing staff would.....							
If I followed a set of guidelines for the nutritional care of preterm infants, the surgical team would.....							
If I followed a set of guidelines for the nutritional care of preterm infants, junior unit staff would.....							
If I followed a set of guidelines for the nutritional care of preterm infants, new unit staff would.....							

12)

	1 Not at all	2	3	4	5	6	7 Very much
Doctors' approval of my practice is important to me							
Nurses' approval of my practice is important to me							
The surgical team's approval of my practice is important to me							
Junior staff's approval of my practice is important to me							
New staff's approval of my practice is important to me							

13) I am confident that I could use a set of guidelines for the nutritional care, feeding and measuring of preterm infants if I wanted to

	1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

14) For me, using a set of guidelines for the nutritional care, feeding and measuring of preterm infants is....

	1 Easy	2	3	4	5	6	7 Difficult

15) The decision to use a set of guidelines for the nutritional care, feeding and measuring of preterm infants is beyond my control.

	1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

16) Whether I follow a set of guidelines for the nutritional care, feeding and measuring of preterm infants is not entirely up to me.

	1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Appendix 3

17)

	1 Unlikely	2	3	4	5	6	7 Likely
Guidelines will be difficult to find or access.							
Guidelines will be rigid and inflexible							
Guidelines will be clear, user friendly and easy to follow							
Guidelines will be supported by staff education and training to increase knowledge in that area							

18)

	1 Less likely to use them	2	3	4	5	6	7 More likely to use them
When guidelines are difficult to access I am....							
When guidelines are have no flexibility, I am....							
When guidelines are clear and easy to follow I am							
When guidelines are supported by staff education and training I am....							

4. The Normalization Process Theory Toolkit Questionnaire

Standardising Preterm Infant Nutrition (SPIN)- How are we doing?

The SPIN project at Southampton is looking at the impact of a new package of care in improving the growth of preterm infants; this includes use of a screening tool, nutrition guidelines and a nutrition support team. This questionnaire is designed to help us make the new package of care as effective as possible by identifying areas where more support or training is needed, or where changes need to be made. We would be grateful if you could take a few minutes to answer the short questions below

1) Firstly, please tick one of the boxes below which best describes your position.	
Band 3 Nurse	
Band 4 Nurse	
Band 5 Nurse	
Band 6 Nurse	
Band 7 Nurse	
Band 8 Nurse or higher	
ANNP	
Pharmacist	
Dietician	
SHO/ST1-3	
SpR/ST4-8	
Consultant	
Other (Please Specify):	

Appendix 3

2) Please look at each of the 16 short questions below and answer each one by giving it a score from 1 to 10, where 1 means 'Not at all' and 10 means 'Completely'.
Each question refers to the new nutritional guidelines and way of working that was introduced as part of the Standardising Preterm Infant Nutrition study.

	1	2	3	4	5	6	7	8	9	10
1. How different are the new nutrition guidelines and practices from your previous practice?										
2. Do you understand the purpose of them?										
3. Do you understand your role in delivering the new nutrition guidelines and practices?										
4. Can you see the benefits and value of them?										
5. Do you think the new guidelines and practices are being promoted by the people that matter?										
6. Do you agree that making the new guidelines and practices work well is part of your job?										
7. Are the new guidelines and practices something that you agree with?										
8. Are you able to support the new guidelines and practices and maintain them?										
9. Are you be able to use and follow the nutrition guidelines and practices?										
10. Can you rely on your colleagues and other professionals to follow the new guidelines and practices?										
11. Do you think that the work required by the new nutrition guidelines and practices has been allocated to the right staff members with the right skills?										
12. How much do you feel that the Trust supports the new nutrition guidelines and practices?										
13. Do you have sufficient information to judge whether the new nutrition guidelines and practices makes a difference to the preterm infants you care for?										
14. Do you feel staff on the unit as a group view the new nutrition guidelines and practices as worthwhile?										
15. Do you view the new nutrition guidelines and practices worthwhile?										
16. Have you changed the way you work as a result of the new nutrition guidelines and practices?										

5. Staff Interview Question Guide

1. The preliminary results of this study have shown that the introduction of the guidelines has had a significantly beneficial effect on the nutrient intakes and growth of preterm infants on the neonatal unit. How do you explain their success?
2. What factors about the way the guidelines were implemented and the content of the guidelines themselves do you think were responsible for them working (or not working) in practice?
3. How motivated were you to use the new nutrition guidelines and working practices? What were the factors that motivated you?
4. How committed do you feel the unit in general was to the new guidelines and working practices?
5. How do you think the guidelines changed people's roles and responsibilities regarding the nutritional care of babies on the unit?
6. Did the expectations of staff regarding nutritional care change following the introduction of the guidelines? How do you think they changed?
7. What resources (such as equipment or other material things) were needed to be able to carry out the new working practices and follow the guidelines? Were these available or were there any issues associated with them?
8. What knowledge and training did you need in order to carry out the new working practices and follow the guidelines? Was this made available and were there any issues associated with it?
9. How easy was it to follow the guidelines and carry out the work that they required?
10. How well did the new working practices and guidelines fit into the routine work on the neonatal unit? How easy was it to integrate them into other aspects of care?
11. Were you able to understand why the new guidelines and working practices were needed and see how they were different from previous practice?
12. Were you able to understand what the new guidelines and working practices required of you, and did you feel able and willing to carry it out?
13. Did you use and follow the guidelines? Do you feel your colleagues in general were also using and following them?
14. Could you see the benefit of carrying out the new working practices and following the guidelines whilst working? Were you able see the effects of them on practice and in the infants you cared for?

Appendix 4: Guideline Audit Proforma

Initials	Day	GA at birth	Birth-weight	Risk Cat	Risk cat in folder?	Correct risk cat?	Age PN started	Age PN switched to Bespoke/ +Sodium	Total fluids when PN decreased with feeds	Total milk feeds when lipid halved	Total milk feeds when FF added/ switched from DBM to LBW	Age Feeds started	Feeds started at	Feeds increased at	Milk chosen

Appendix 5: The AMSTAR Criteria

1. Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review.
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.
5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analysed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.
7. Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.
9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).
11. Was the conflict of interest stated? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

The AMSTAR criteria, adapted from [176]

Appendix 6: Characteristics of studies included in the overview of systematic reviews (chapter 5)

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Anderson 1996[248]	3	Review of techniques to improve prescribing behaviour	Primary Care	Primary care physicians	Techniques for promoting appropriate prescribing	Appropriate prescriptions and cost	1989-1996	Multiple	EM, DEM, REM, AF, EOV	9 RCTs included. Printed educational materials of little benefit, though combination of education and feedback more effective. Face to face educational interventions were successful. Specific strategies recommending changes in medication also successful	Specific strategies combining education and feedback can improve the quality of care. Little data on benefit to patient outcomes. More research is needed in this area.
Arditi 2012[249]	11	Effectiveness of computer generated reminders delivered in paper to healthcare professionals on the process and outcomes of care	Primary or secondary care	Any qualified health professional	Computer generated reminders delivered on paper	Objective measures of the process of care or patient outcomes	1946-2012	Single	REM, AF, EM, PMI	32 included studies. Moderate improvement in prof practice (median 7.0%, IQR 3.9-16.4). Improved care by median of 11.2% (IQR 6.5-19.6) compared to usual care, and by 4.0% (IQR 3.0-6.0) compared to other interventions. Providing a space on the reminder for a response from the clinician and providing an explanation of the reminders advice/content both significantly predicted improvement	There is moderate quality evidence that computer generated reminders delivered on paper achieves moderate improvements in the process of care. Reminders can improve care in a variety of settings and conditions.
Austin 1994[250]	3	Effectiveness of reminders on preventive care	Primary and Secondary Care	Family or internal medicine physicians	Reminders	Process and outcome of care	Not given	Single	REM	10 RCTs included but only 4 trials eligible for meta-analysis (narrative or qualitative synthesis of remaining 6 not done). Results showed significant improvements with reminders for cervical cancer screening (n=5345, OR 1.18, 95%CI 1.02-1.34) and tetanus immunisation (n= 4905, OR 2.82, 95% CI 2.66-2.98).	Reminders may increase provision of preventive care services

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Baker 2010[251]	11	Effectiveness of interventions tailored to address identified barriers to change on professional practice or patient outcomes	Primary and Secondary Care	Healthcare professionals responsible for patient care	Interventions tailored to address barriers vs no intervention or non-tailored intervention	Objective measures of professional practice or healthcare outcomes	1950-2007	Single	MAR	26 RCTs included in the review. 12 studies included in meta regression analysis, which gave a pooled OR of 1.54 (95% CI 1.16-2.01) with Bayesian analysis, and 1.52 (95% CI 1.27-1.82) in favour of tailored interventions. Of the remaining 14, 8 reported benefit for all outcomes, 2 reported benefit for some outcomes, and 4 showed no benefit or disadvantage.	Interventions tailored to prospectively identified barriers are more likely to improve practice than no intervention or dissemination of educational materials. It is unclear which elements of intervention explained effectiveness
Balas 1996[252]	6	Effectiveness of computerised information systems	Primary and Secondary Care	Providers and Patients	Computer-ised information interventions	Process or outcome of care	Not given	Single	REM	98 RCTs (97 comparisons) included in review. Computerised information interventions included reminders, feedback, medical records diagnosis assistance and patient education. 76 of 97 studies showed benefit for process of care, whilst 10 of 14 demonstrated improved patient outcomes. Vote counting method of analysis showed significant ($p<0.05$) benefits of provider and patient reminders in diagnostic tests and preventive medicine, computer assisted treatment planners for drug prescription, and computer assisted patient education.	Provider prompts, computer assisted treatment planners, interactive patient education and patient prompts can improve quality of care, and these modalities should be incorporated into information strategies

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Balas 2000[253]	8	Assess the impact of prompting physicians on health maintenance	Primary and Secondary Care	Providers	Physician prompts	Preventative care measures	1966-1996	Single	REM	The statistical analyses included 33 eligible studies, which involved 1547 clinicians and 54 693 patients. Overall, prompting can significantly increase preventive care performance by 13.1% (95% CI 10.5%-15.6%). Effect ranges from 5.8% (95% CI, 1.5%-10.1%) for Papanicolaou smear to 18.3% (95% CI, 11.6%-25.1%) for influenza vaccination. The effect is not cumulative, and the length of intervention period did not show correlation with effect size (R = −0.015, P = .47). Academic affiliation, ratio of residents, and technique of delivery did not have a significant impact on the clinical effect of prompting.	Improvement in preventive care can be accomplished through prompting physicians. Health care organizations could effectively use prompts, alerts, or reminders to provide information to clinicians when patient care decisions are made.
Bauer 2002[254]	3	Effectiveness of guidelines on improving practice or patient outcomes	Primary and Secondary Care	Providers and patients in mental health care	Introduction of guidelines together with any associated intervention	Guideline adherence (with patient outcomes where available)	1950-2000	Guideline	AF, EM, DEM, REM	41 studies identified (26 cross-sectional, 6 before and after studies and 9 controlled trials). Guideline adherence rates adequate in 27% of cross-sectional and before and after studies and 67% of controlled trials. 6 controlled trials and 7 cross-sectional/before and after trials included patient outcome data, with 4 (67%) and 3 (43%) showing improved outcomes in the intervention group respectively. Successful interventions tended to multifaceted and intensive, with the use of additional resources (note guideline studies where adherence not reported with patient outcomes excluded)	Certain interventions can improve guideline adherence, but usually require specific intervention. The impact on patient outcomes remains to be seen.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Beilby 1997[255]	5	Effectiveness of providing costing information to reduce costs by changing GP behaviour	Primary Care	GPs	Distribution of costing information to GPs	Objective Health provider performance	1980-1996	Single	EOV, REM, AF	6 included studies. 2 studies (n=467) showed significant benefit on drug prescribing, with one of these showing outreach more effective than printed materials. 3 studies (n=206) showed significant reductions in test ordering and associated costs (interventions were information provision, education and computerised feedback). 1 study (n=2827) showed non-significant reduction in specialist visits.	Provision of costing information can change GP behaviour, particularly for prescribing and test ordering. Interventions labour intensive, and costs of intervention and sustainability requires more study.
Blackwood 2014[193]	11	Effectiveness of protocolised ventilator weaning compared to standard care	Hospital adult ICU	Ventilated adult ICU patients	Protocolised ventilator weaning	Patient outcomes (Mortality, adverse events, QoL, weaning time, LOS)	1950-2014	Single	DEM	17 trials (2434 patients) included. Geometric mean duration of mechanical ventilation in the protocolized weaning group was on average reduced by 26% compared with the usual care group (N = 14 trials, 95% CI 13%to 37%, P = 0.0002). Reductions were most likely to occur in medical, surgical and mixed ICUs, but not in neurosurgical ICUs. Weaning duration was reduced by 70% (N = 8 trials, 95% CI 27% to 88%, P = 0.009); and ICU length of stay by 11 %(N = 9 trials, 95%CI 3%to 19%, P = 0.01). There was significant heterogeneity among studies for total duration of mechanical ventilation (I2 = 67%, P < 0.0001) and weaning duration (I2 = 97%, P < 0.00001).	Protocols appear to reduce duration of mechanical ventilation, weaning duration and ICU length of stay. Reductions are most likely to occur in medical, surgical and mixed ICUs, but not in neurosurgical ICUs. However, significant heterogeneity among studies indicates caution in generalizing results.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Boren 2009[256]	4	Effectiveness of computerized prompting and feedback on diabetes care	Primary Care	Providers and patients in primary or secondary care	Computerized prompting or feedback of diabetes care.	Processes and patient outcomes in diabetes	1970-2008	Single	REM	Fifteen trials were included in this review. 5 studies studied the effect of a general prompt for a particular patient to be seen for diabetes-related follow-up, 13 studies looked at specific prompts reminding clinicians of particular tests or procedures, 5 studies looked at feedback to clinicians in addition to prompting, with the remaining 5 studies looking at patient reminders in addition to clinician prompts. Twelve of the 15 studies (80%) measured a significant process or outcome from the intervention. Fifty processes and 57 outcomes were measured in the 15 studies (Table 2). Fourteen studies evaluated the effect the interventions had on the processes of care. Thirty-five of 50 process measures (70%) were significantly improved. Nine of the 57 outcome measures (16%) were significantly improved.	The majority of trials identified at least one process or outcome that was significantly better in the intervention group than in the control group; however, the success of the information interventions varied greatly. Providing and receiving appropriate care is the first step toward better outcomes in chronic disease management.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Brennan 2013[188]	7	Educational interventions to change the behaviour of new prescribers in hospital settings	Secondary care	New prescribers	Any educational strategy	Prescribing related outcome measures	1994-2010	Multiple	DEM, EM, EOV, REM, MAR, PMI, LOL	Sixty-four studies were included in the review. Only 13% of interventions specifically targeted new prescribers. Most interventions (72%) were deemed effective in changing behaviour. Of the 15 most successful strategies, four provided specific feedback to prescribers through audit and feedback and six required active engagement with the process through reminders. However, five and six of the 10 studies classified as ineffective also involved audit and feedback, and reminders, respectively. This means no firm conclusions can be drawn about the most effective types of educational intervention.	Very few studies have tailored educational interventions to meet needs of new prescribers, or distinguished between new and experienced prescribers. Educational development and research will be required to improve this important aspect of early clinical practice.
Bright 2012[257]	8	Effectiveness of clinical decision support systems (CDSS) to improve patient or health care process outcomes	Primary and Secondary Care	Any health care provider	Use of CDSS in clinical setting to aid decision making at the point of care	Objective measures of clinical, process, economic and implement-action outcomes	1976-2011	Single	REM	148 RCTs included, with 128 assessing process measures, 20 assessing clinical outcomes and 22 measuring cost. CDSSs improved process measures relating to preventative medicine (n=25, OR 1.42, 95%CI 1.27-1.58), ordering clinical studies (n=20, OR 1.72, 95%CI 1.47-2.00) and prescribing therapies (n=46, OR 1.57, 95%CI 1.35-1.82). CDSSs also improved morbidity (n=16, OR 0.88, 95%CI 0.80-0.96), though studies were heterogeneous. Other clinical outcomes showed no difference. Effects on the effects of CDSSs on implementation were variable and insufficient.	CDSS are effective in improving health care process measures but evidence for effects in clinical, economic, workload and efficiency outcomes remains sparse.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Brody 2013[198]	4	Effectiveness of inter-professional dissemination and education interventions for recognizing and managing dementia	Primary Care or secondary care	Providers and patients in primary or secondary care	Any interprofessional education intervention	Process or outcome of care	1990-2012	Single	EM	18 papers from 16 studies were included. Most studies found some improvement in clinician knowledge or confidence, or patient outcomes, though methods and patient and clinician populations were disparate.	While a significant evidence base for assessing and managing individuals with dementia has been developed, few studies have examined how to disseminate this research, and even fewer in an interprofessional manner
Bryan 2008[258]	8	Effectiveness of clinical decision support systems (CDSS) to improve outcomes in primary care	Primary Care	Providers and patients in primary or ambulatory care	Use of CDSS	Objective measures of process of care or health outcomes	200-2006	Single	REM	17 studies included (12 RCTs, 5 observational). Virtually all looked at process outcome measures, with 9 finding improvements from using CDSSs, 4 with variable results and 4 showing no effect from CDSS use.	CDSS have the potential to improve outcomes, but findings are variable, as are methods and types of implementation. More work needs to be done to determine effective implementation strategies for CDSSs.
Buntinx 1993[259]	3	Effectiveness of feedback and reminders on diagnostic and preventive care	Primary Care	Physicians in ambulatory care	Feedback and reminders	Number and costs of diagnostic tests ordered, guideline compliance	1983-1992	Multiple	AF, REM	26 trials included. 8 looked at impact on reducing costs (2 of 2 RCTs and 5 of 6 other trials showed significant reductions). 14 trials evaluated guideline adherence (4 of 4 RCTs and 1 of 3 other trials showed significant improvements.	Feedback and reminders may reduce costs of diagnostic tests and improve guideline adherence

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Chaillet 2006[182]	7	Effectiveness of strategies for implementing clinical practice guidelines in obstetric care	Secondary Care	Obstetric patients	Guideline implement-ation strategies	Objective measures of guideline compliance, process and patient outcomes	1990-2005	Guideline	DEM, AF, LOL, EOV, REM	33 included studies. Educational strategies (4 studies) were generally ineffective, whilst Audit and feedback (11 studies) showed significantly positive results in 9 studies. Quality improvement interventions (11 studies), Local opinion leaders (2 studies) and Academic detailing (1 study) had mixed effects. Reminders (2 studies) were generally effective and Multifaceted interventions (9 studies) demonstrated consistent benefit and high efficacy for changing behaviours. Studies where barriers to change were prospectively identified were more successful (93.8% vs 47.1%, p=0.04)	Prospective identification of efficient strategies and barriers to change is necessary for improved guideline implementation. Multifaceted strategies based on audit and feedback, perhaps facilitated by local opinion leaders seems most effective in the obstetric setting.
Chhina 2013[200]	7	Effectiveness of Academic Detailing (AD), as a stand-alone intervention, at modifying drug prescription behaviour of	Primary care	Family physicians	Academic detailing	Prescribing practice	1983-2010	Single	EOV	11 RCTs and 4 observational studies were included. Five RCTS described results showing effectiveness, while 2 RCTs reported a positive effect on some of the target drugs. Two observational studies found AD to be effective, while 2 did not. The median difference in relative change among the studies reviewed was 21% (interquartile range 43.75%) for RCTs, and 9% (interquartile range 8.5%) for observational studies. The median effect size among the studies reviewed was - 0.09 (interquartile range 2.73)	AD can be effective at optimizing prescription of medications by Family Physicians. Although variable, the magnitude of the effect is moderate in the majority of studies. AD may also be effective as a strategy to promote evidence based prescription of medications or incorporation of clinical guidelines into clinical practice.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Clarke 2010[194]	8	Effectiveness of guidelines for referral for elective surgical assessment	Primary care	GPs	Guideline	Appropriateness of referrals	1950-2008	Single	DEM	24 eligible studies (5 randomised control trials, 6 cohort, 13 case series) included. Interventions varied from complex ("one-stop shops") to simple guidelines. Four randomized control trials reported increases in appropriateness of pre-referral care (diagnostic investigations and treatment). No evidence was found for effects on practitioner knowledge. Mixed evidence was reported on rates of referral and costs (rates and costs increased, decreased or stayed the same). Two studies reported on health outcomes finding no change.	Guidelines for elective surgical referral can improve appropriateness of care by improving prereferral investigation and treatment, but there is no strong evidence in favour of other beneficial effects.
Damiani 2010[260]	9	Impact of computerised clinical guidelines (CCG) on the process of care	Primary and Secondary Care	All healthcare providers	CCG vs non-CCG	Objective measures of the process of care	1992-2006	Multiple	DEM, REM	45 studies included. 64% showed a positive effect of CCGs vs non-CCGs. Multivariate analysis showed the 'automatic provision of recommendation in electronic version as part of clinician workflow' was associated with increased chance of positive impact (OR 17.5, 95%CI 1.6-193.7).	Implementation of CCG significantly improves the process of care.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Davey 2013[261]	11	Effectiveness of professional interventions to improve antibiotic prescribing in hospitals	Secondary Care	Secondary care physicians and their patients	Any professional intervention	Objective measures of process and clinical outcomes	1980-2006	Multiple	DEM, REM, EOV, EM, AF	89 studies included. 76 had reliable outcome data (44 persuasive, 24 restrictive and 8 structural). For the persuasive interventions, the median change in antibiotic prescribing was 42.3% for the ITSs, 31.6% for the controlled ITSs, 17.7% for the CBAs, 3.5% for the cluster-RCTs and 24.7% for the RCTs. The restrictive interventions had a median effect size of 34.7% for the ITSs, 17.1% for the CBAs and 40.5% for the RCTs. The structural interventions had a median effect of 13.3% for the RCTs and 23.6% for the cluster-RCTs. When comparing restrictive vs persuasive, restrictive interventions had significantly greater impact at one and 6 months, but not longer term.	The results show that interventions to improve antibiotic prescribing to hospital inpatients are successful, and can reduce antimicrobial resistance or hospital acquired infections.
Davis 1995[187]	8	Effectiveness of CME	Primary and Secondary Care	Physicians (various grades)	Educational interventions aimed at modifying physicians practice	Objective measure of physician performance and healthcare outcomes	1975-1994	Multiple	DEM, AF, EM, EOV, LOL, PMI, REM	99 studies (160 intervention comparisons) met inclusion criteria. Overall 62% of interventions showed an improvement in either physician performance (70% of those studies which analysed it) or health care outcomes (48%). Effect sizes were small to moderate. For single interventions, 60% demonstrated a change in at least 1 major outcome measure with those likely to be effective including educational outreach, opinion leaders, patient education or reminders. For two-method interventions, 64% of studies were positive, and this increased to 79% for multifaceted interventions. Studies where a gap analysis had been done to inform the intervention were more likely to be positive.	Physician performance may be altered (albeit in a small manner) by certain CME interventions. Outreach or focussed CME better than traditional wider methods such as conferences, though it is these less effective methods that are most used.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Delpierre 2004[262]	4	Effectiveness of computer-based patient record systems (CBPRS) on medical practice, quality of care, and user and patient satisfaction.	Primary and secondary care	Providers and patients in primary or secondary care	Computer-based patient record systems (CBPRS)	Process or outcome of care, and patient/user satisfaction	2000-2003	Single	REM	26 articles selected. Use of a CBPRS was perceived favourably by physicians, with studies of satisfaction being mainly positive. A positive impact of CBPRS on preventive care was observed in all three studies where this criterion was examined. The 12 studies evaluating the impact on medical practice and guidelines compliance showed that positive experiences were as frequent as experiences showing no benefit. None of the six studies analysing the impact of CBPRS on patient outcomes reported any benefit.	CBPRS increased user and patient satisfaction, which might lead to significant improvements in medical care practices. The impact of CBPRS on patient outcomes and quality of care were inconclusive.
Dexheimer 2008[263]	8	Effectiveness of reminders on preventive care	Primary and Secondary Care	Physicians	Computer or paper based reminders	Use of preventive care interventions	1966-2004	Single	REM	61 studies included, with 264 preventative care interventions. Implementation strategies included paper based reminders (31%), computerised reminders (13% or a combination of both (56%). Average increase for all 3 strategies in delivering preventive care measures ranged between 12 and 14%. Computer generated prompts were the most commonly implemented reminders	Clinician reminders are a successful approach for increasing the rates of delivering preventive care, though their effectiveness remains modest.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Dexheimer 2014[264]	3	Effectiveness of implementation of asthma protocols to improve care	Primary and secondary care	Providers and patients in primary or secondary care	Implementation of asthma protocol using reminder-based strategies	Patient care and/or practitioner performance	1950-2010	Guideline	DEM, REM,	101 articles included in the analysis. Paper-based reminders were the most frequent with fully computerized, then computer generated, and other modalities. No study reported a decrease in health care practitioner performance or declining patient outcomes. The most common primary outcome measure was compliance with provided or prescribing guidelines, key clinical indicators such as patient outcomes or quality of life, and length of stay.	Paper-based reminders are the most popular approach to guideline implementation. Asthma guidelines generally improved patient care and practitioner performance regardless of the implementation method.
EHC 1994[185]	5	Effectiveness of strategies for implementing clinical practice guidelines	Primary and Secondary Care	Medical staff	Guideline implementation strategies	Objective measures of process or patient outcomes	1976-1994	Guideline	DEM, AF, REM, EM, EOV	91 studies included. 81 of 87 showed that guidelines significantly improved the process of care (adherence with recommendations in guidelines). Educational interventions (seminars, outreach and opinion leaders) are more likely to lead to a change in behaviour. Educational and implementation strategies closer to the end user and integrated into healthcare delivery are more likely to be effective. Attributes of guidelines play important role (see table in paper), with those that offer validity, flexibility, clarity and reliability are more likely to be effective. 12 of 17 showed significant improvements in patient outcomes.	Well-developed guidelines can change practice and improve patient outcomes. Guidelines accounting for local circumstances and disseminated with active education are more likely to be effective. Research is needed into potential barriers to guideline adoption and ways to overcome these.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Figueras 2001[265]	6	Effectiveness of educational programmes designed to improve prescription practices in ambulatory care	Primary care	Primary care practitioners	Educational programme	Prescribing practice	1988-1996	Single	EM	51 studies included, with 43 studying the efficacy/effectiveness of one or various interventions as compared to no intervention. Among seven studies evaluating active strategies, four reported positive results (57%), as opposed to three of the eight studies assessing passive strategies (38%). Among the 28 studies that tested reinforced active strategies, 16 reported positive results for all variables (57%). Eight studies were classified as a high degree of evidence (16%)	The more personalized, the more effective the strategies are. Combining active and passive strategies results in a decrease of the failure rate. Finally, better studies are still needed to enhance the efficacy and efficiency of prescribing practices.
Fleming 2013[203]	7	Interventions to reduce inappropriate antibiotic prescribing	Long term care facilities	Any qualified health professional	Interventions aimed at improving prescribing practice	Antibiotic use or adherence to guidelines	1946-2012	Multiple	LCP, DEM, EM, AF	4 studies included. 3 used educational materials for doctors and nurses (with 1 providing feedback to professional also) and 1 used educational material and feedback to doctors only. Multifaceted interventions involving small group education is most acceptable to nurses. The involvement of LCP was also beneficial.	LCP and education strategies and guideline may improve prescribing but quality of evidence is low

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Flodgren 2010[266]	10	Effectiveness of strategies to change the behaviour of professionals and organisation of care to promote weight loss in the obese	Primary Care	Healthcare professionals and obese or overweight adults	Interventions to implement an intervention to target weight reduction	Objective measures of professional practice or patient outcomes	1966-2009	Multiple	EM, EOV, AF, DEM, REM, MM	6 RCTs included with 4 targeting professionals and 2 targeting organisation of care. 3 trials evaluated educational interventions aimed at GPs, showing an improvement of 1.2 kg (95%CI -0.4-2.8) but results were heterogeneic. One trial found reminders could change practice in men (by 11.2kg, 95%CI 1.7-20.7) but not women (1.3kg, 95%CI -4.7-6.7). In another trial use of dieticians (5.6kg, 95%CI 4.8-6.4) or doctor-dietician team (6kg, 95%CI 5-7) improved weight loss.	Most included trials had weaknesses so difficult to draw firm conclusions about effectiveness.
Flodgren 2011[267]	10	Effectiveness of the use of local opinion leaders in improving professional practice and patient outcomes	Primary and Secondary Care	Healthcare professionals in charge of patient care	Local opinion leader to improve professional practice and patient outcomes	Objective measures of professional performance or patient outcomes	1966-2009	Single	LOL, EM, EOV, AF, REM, DEM, MM	18 studies included. Effect of interventions varied across the 63 different reported outcomes. However, for main comparisons, there was a 0.09 median improvement in compliance (risk difference) compared to no intervention, 0.14 compared to a single intervention, 0.1 compared to a single intervention and 0.1 when used as part of multiple interventions compared to no intervention. Overall across 15 studies, median adjusted risk difference was a 0.12 (=12%) absolute increase in compliance with the opinion leaders intervention group.	Opinion leaders alone or in combination with other interventions may successfully promote evidence based practice, though effectiveness is variable. The role of opinion leaders is not well defined in studies, so it is difficult to ascertain the optimal approach.

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Flodgren 2013[268]	11	Effectiveness of interventions to improve professional adherence to infection control guidelines on device-related infection rates and measures of adherence.	Secondary care	Secondary care providers and their patients	Guideline implementation strategies	Device related infection rates and measures of adherence	1950-2012	Guideline	DEM, AF, EM, REM, EOV, MAR	13 studies included (1 cluster RCT, 12 ITS studies). All included studies were at moderate or high risk of bias. The 6 interventions that did result in significantly decreased infection rates involved more than one active intervention, which in some cases, was repeatedly administered over time. The one intervention involving specialised personnel showed the largest step change (-22.9 cases/1000 ventilator days), and the largest slope change (-6.45 cases/1000 ventilator days). Six of the included studies reported post-intervention adherence scores ranging from 14% to 98%. The effect on rates of infection was mixed and the effect sizes were small, with changes was not sustained over longer follow-up times.	The low quality of the evidence provides insufficient evidence to determine which interventions are most effective. However, interventions that may be worth further study are educational interventions involving multiple active elements, repeatedly administered over time, and interventions employing specialised personnel.

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Forsetlund 2009 [269]	11	Effectiveness of continuing education meetings on professional practice and health care outcomes	Primary and Secondary Care	Qualified Health Professionals	Educational meetings (conferences, lectures, workshops, courses)	Objective measures of professional performance or patient outcomes	1966-2008	Single	EOV, EM, DEM, AF, REM	81 trials included in review. 30 trials (36 comparisons) included in meta-regression. Median adjusted risk difference (RD) showed 6% improvement in compliance (IQR 1.8-15.9) for educational meetings as part of larger intervention vs control. Used alone (21 comparisons, 19 trials) median RD 6% (IQR 2.9-15.3). For continuous outcomes median percentage change was 10% (IQR 8-32, 5 trials) vs control. For treatment goals median RD was 3% (IQR 0.1-4, 5 trials). Meta-regression showed higher meeting attendance associated with larger RD ($p<0.01$). Mixed interactive and didactic meetings were more effective than either used alone. Educational meetings less effective for complex behaviours.	Educational meetings alone or as part of larger interventions can improve professional practice and healthcare outcomes. The effect is likely to be small. Effectiveness may be improved by increasing attendance, mixing interactive and didactic formats and focusing on serious outcomes.

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Forsetlund 2011[270]	8	Effectiveness of interventions aimed at reducing potentially inappropriate use or prescribing of drugs in nursing homes.	Primary care	Primary care practitioners	Professional interventions to improve prescribing	Appropriateness of prescribing	1950-2010	Multiple	EOV, EM	Twenty randomised controlled trials were included from 1631 evaluated references. Ten studies tested different kinds of educational interventions while seven studies tested medication reviews by pharmacists. Only one study was found for each of the interventions geriatric care teams, early psychiatric intervening or activities for the residents combined with education of health care personnel.	Interventions using educational outreach, on-site education given alone or as part of an intervention package and pharmacist medication review may reduce inappropriate drug use, but the evidence is of low quality. Due to poor quality of the evidence, no conclusions may be drawn about the effect of the other three interventions.
Frampton 2014[271]	11	Effectiveness and cost-effectiveness of educational interventions for preventing catheter-BSI in critical care units in England	ICU	ICU staff and patents	Educational interventions	CLABSI rates, LOS, mortality, staff practice	1950-2011	Multiple	EM, EOV, AF, DEM	74 studies were included, of which 24 were prioritised for systematic review. Most studies were single-cohort before-and-after study designs. Diverse types of educational intervention appear effective at reducing the incidence density of catheter-BSI (risk ratios statistically significantly < 1.0), but single lectures were not effective. The economic model showed that implementing an educational intervention in critical care units in England would be cost-effective and potentially cost-saving, with incremental cost-effectiveness ratios under worst-case sensitivity analyses of < £5000/quality-adjusted life-year.	It would be cost-effective and may be cost-saving for the NHS to implement educational interventions in critical care units. However, more robust primary studies are needed to exclude the possible influence of secular trends on observed reductions in catheter-BSI.

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French 2010[272]	10	Effectiveness of interventions for improving appropriate use of imaging in musculo-skeletal conditions	Primary and Secondary Care	Health professionals, policy makes, patients and the public	Intervention to improve appropriate use of imaging for musculo-skeletal conditions	Objective measures of professional performance or patient health outcomes	1966-2007	Multiple	REM, DEM, AF, EOV, PMI, EM	28 studies included, with most aimed at health professionals and focussing on osteoporosis or low back pain. For any intervention in osteoporosis there was a modest improvement in practice (ordering of tests) with a 10% reduction (IQR 0-27.7), Patient mediated, reminders and organisational interventions appeared to have the most potential. Results for low back pain were variable.	Most interventions for osteoporosis demonstrated benefit, especially patient mediated, reminders and organisational interventions.
Garg 2005[273]	7	Effectiveness of Computerized Clinical Decision Support Systems on Practitioner Performance and Patient Outcomes	Primary and secondary care	Providers and patients in primary or secondary care	Computerized Clinical Decision Support Systems	Practitioner Performance and Patient Outcomes	1950-2004	Single	REM	100 studies were included. CDSS improved practitioner performance in 62 (64%) of the 97 studies assessing this outcome, including 4 (40%) of 10 diagnostic systems, 16 (76%) of 21 reminder systems, 23 (62%) of 37 disease management systems, and 19 (66%) of 29 drug-dosing or prescribing systems. Fifty-two trials assessed 1 or more patient outcomes, of which 7 trials (13%) reported improvements. Improved practitioner performance was associated with CDSSs that automatically prompted users compared with requiring users to activate the system (success in 73% of trials vs 47%; P=.02) and studies in which the authors also developed the CDSS software compared with studies in which the authors were not the developers (74% success vs 28%, P=.001).	Many CDSSs improve practitioner performance. To date, the effects on patient outcomes remain understudied and, when studied, inconsistent

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Giguere 2012[274]	10	Effectiveness of printed educational materials on professional practice and health care outcomes	Primary and Secondary Care	Any healthcare professionals provided with printed educational materials	Printed educational materials for clinical care, including guidelines	Objective measures of professional performance or patient health outcomes	1950-2007	Single	DEM	45 studies included (14 RCTs, 31 ITS). Based on 7 RCTs (54 outcomes), median risk difference in categorical practice outcomes was 0.02 (range 0-0.11) in favour of printed educational materials. Based on 3 RCTs (8 outcomes), the median improvement in mean difference for practice outcomes was 0.13 (range -0.16 to 0.36) in favour of printed educational materials. Only 2 RCTs and 2 ITS studies reported patient outcomes. Reanalysis of 54 outcomes from 25 ITS studies showed significant improvement in 27 patient outcome,	Compared to no intervention, printed educational materials may have a beneficial effect on professional practice outcomes. There is insufficient information on patient outcomes. The best approach for printed materials is unclear, as is their effectiveness compared to other interventions.
Gilbody 2003[202]	5	Effectiveness of organisational and educational interventions to improve the management of depression in primary care	Primary Care	Primary care physicians and their patients	Professional or organisational interventions to improve management of depression	Outcomes relating to the management of depression	1950-2003	Multiple	DEM, REM, LOL, EOV	36 included studies (29 RCT and non-RCTs, 5 CBA and 2 ITS). 21 studies had a positive outcome, with effective strategies including complex interventions incorporating clinician education, an enhanced nursing role and greater integration between primary and secondary care. Simple guideline implementation and educational strategies were generally ineffective.	There is potential to improve the management of depression in primary care. Commonly used guideline and educational strategies are generally ineffective.

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Goodwin 2011[196]	7	Implementation of falls prevention strategies	Primary Care	Community dwelling older people	Implementation strategy for fall prevention	Measures of successful implementation including behaviour change, attitudes, uptake	1980-2010	Single	EM	15 included studies (1 controlled trial, 3 cross-sectional, 4 cohort studies, 5 surveys, 1 process evaluation and 1 case series). Implementation methods included training (6 studies - generally positive results with improvements in outcomes), practice management changes (3 studies - mixed but generally positive results), peer/volunteer delivered programs (3 studies - positive results) and community awareness programs (3 studies - positive results).	There is evidence to support active training and support of healthcare professionals to implement falls prevention into clinical practice. Evidence is mixed, as is the use of community awareness programs and peer delivered prevention programs
Grimshaw 2004[275]	10	Effectiveness of guideline development, dissemination and implementation strategies to improve professional practice	Primary and Secondary Care	Medically qualified healthcare professionals	Guideline implementation strategies	Objective measures of provider behaviour and/or patient outcome	1966-1998	Guideline	DEM, EM, LCP, EOV, LOL, PMI, AF, REM, MAR, MM	235 studies (309 comparisons) included (110 cRCTs, 29 RCTs, 17 CCTs, 40 CBAs and 39 ITS). Majority of studies (86.6%) observed improvements in care, although this was variable both across and within studies. 73% evaluated multifaceted interventions (including 13 cRCTs, median improvement in performance 6%). Commonly evaluated single interventions were reminders (38 comparisons, median improvement 14.1% in 14 cRCTs), dissemination of educational materials (18 comparisons, median improvement 8.1% in 4 cRCTs), audit and feedback (12 comparisons, median improvement 7% in 5 cRCTs). No relationship between number of components and effects of multifaceted interventions.	Imperfect evidence base to support decision about which guideline dissemination and implementation strategies are likely to be effective under different circumstances.

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Gross 2001[276]	1	Effectiveness of implementation strategies for practice guidelines for appropriate use of antimicrobial agents	Primary and Secondary Care	Medical practitioners and their patients	Implementation of clinical guideline	Measures of appropriate use of antibiotics	1966-2000	Guideline	EM, EOV, AF, REM, DEM, LOL, MAR	40 included studies. Multifaceted implementation methods (23 studies) were most successful, though this made it difficult to determine the components critical to success. Individual methods more likely to be useful were academic detailing, feedback from other professionals (nurses, pharmacists, physicians), local adaptation of guidelines, small-group interactive sessions and computer assisted care.	Effective tools to implement change exist, and these should be used to improve practice in this area. Multifaceted strategies are most successful, but on an individual basis academic detailing, feedback and local adaptation are also useful.
Hakkennes 2008[180]	8	Effects of introduction of clinical guidelines and effectiveness of guideline dissemination and implementation strategies	Primary and Secondary Care	Allied health professionals	Guidelines and associated implementation and dissemination strategies	Objective measures of change in provider behaviour or patient outcomes	1966-2006	Guideline	DEM, EM, REM, EOV, LOL, AF	14 studies (27 papers) included, of variable methodological quality. 10 focussed on educational interventions. 6 studies used single interventions, 7 used multifaceted approaches and 1 used both. Most studies reported small effects in favour of the intervention group for process and patient outcomes. Multifaceted interventions were no more effective than single strategies.	No current evidence to support a set guideline implementation strategy for allied health professionals. Important to identify specific barriers to change using theoretical frameworks and then develop appropriate strategies.
Heselmans 2009[184]	8	Effectiveness of electronic guideline based implementation systems in ambulatory care	Primary Care	Physicians	Use of computer based guideline implementation systems	Objective measures of health professional practice or patient outcomes	1990-2008	Guideline	DEM, REM	27 studies included. None of the studies demonstrated improvements in 50% or more of their clinical outcome variables. Only 7 of the 17 studies reporting process outcomes showed improvements in the intervention group.	There is little evidence at the moment for the effectiveness of electronic multidimensional guidelines.

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Ivers 2012[205]	10	Effectiveness of audit and feedback on the practice of health professionals and patient outcomes	Primary and Secondary Care	Healthcare professionals responsible for patient care	Audit and provision of feedback to healthcare professionals compared to usual care	Objective measures of health professional practice or patient outcomes	1950-2011	Single	AF, EM, EOV, REM, DEM, LOL, LCP	140 studies included (108 comparisons, 70 studies). For professional practice outcomes (82 comparisons, 49 studies) weighted median adjusted RD was a 4.3% (IQR 0.5-16%) increase in compliance with desired practice. For continuous outcomes (26 comparisons, 21 studies), weighted median change was 1.3% (IQR 1.3-28.9%). For patient outcomes, weighted median RD was -0.4% (IQR -1.3-1.6, 12 comparisons, 6 studies) for dichotomous outcomes, with weighted median change of 17% (IQR 1.5-1.7) for continuous outcomes (8 comparisons, 5 studies). Meta-regression showed that feedback may be more effective where baseline performance is low.	Audit and feedback generally leads to small but potentially important improvements in professional practice. Effectiveness seems to depend on the baseline performance and how the feedback is provided.
Kahn 2013[277]	11	Interventions for implementation of thromboprophylaxis in hospitalized patients	Secondary care	Any qualified health professional	Interventions to increase implementation of VTE prophylaxis	Use of /adherence to prophylaxis	1946-2010	Multiple	REM, EM, AF, DEM, EOV	55 studies included with 54 included in analysis (8 RCT and 46 NRS). Alerts (reminders or stickers) were associated with a RD of 13% increase in prophylaxis (RCTs) and for NRS increases of 8-19% were seen, with education and alerts associated with significant improvements, and multifaceted interventions associated with significant benefits (multifaceted interventions had the largest pooled effect).	Significant benefits from alerts and multifaceted interventions. Multifaceted interventions with an alert component may be the most effective.

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Kastner 2008[278]	7	Effectiveness of tools that support clinical decision making in osteoporosis disease management	Primary and secondary care	Providers and patients in primary or secondary care	Computerized Clinical Decision Support Systems	Measures of patient outcomes and process of care	1966-2006	Single	REM, EM	13 RCTs met the inclusion criteria. Study quality was generally poor. Meta-analysis was not done because of methodological and clinical heterogeneity; 77% of studies included a reminder or education as a component of their intervention. Three studies of reminders plus education targeted to physicians and patients showed increased BMD testing (RR range 1.43 to 8.67) and osteoporosis medication use (RR range 1.60 to 8.67). A physician reminder plus a patient risk assessment strategy found reduced fractures [RR 0.58, 95% confidence interval (CI) 0.37 to 0.90] and increased osteoporosis therapy (RR 2.44, CI 1.43 to 4.17).	Multi-component tools that are targeted to physicians and patients may be effective for supporting clinical decision making in osteoporosis disease management.

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Loganathan 2011[279]	8	Effects of interventions to optimise prescribing in care homes	Primary care	Providers and patients in primary care	Interventions to optimise prescribing	Appropriate prescribing	1990-2010	Multiple	REM, EM, EOV	16 studies that met the inclusion criteria. Four intervention strategies were identified: staff education, multi-disciplinary team (MDT) meetings, pharmacist medication reviews and computerised clinical decision support systems (CDSSs). Six of the eight studies using complex educational programmes focussing on improving patients' behavioural management demonstrated an improvement in prescribing. Mixed results were found for pharmacist interventions. CDSSs were evaluated in two studies, with one showing a significant improvement in appropriate drug orders. Two of three studies examining MDT meetings found an overall improvement in appropriate prescribing. A meta-analysis could not be performed due to heterogeneity in the outcome measures.	Results are mixed and there is no one interventional strategy that has proved to be effective. Education including academic detailing seems to show most promise. A multi-faceted approach and clearer policy guidelines are likely to be required to improve prescribing for these vulnerable patients.
Mandelblatt 1995[280]	4	Effectiveness of interventions to improve physician screening for breast cancer	Primary and Secondary Care	Physicians	Interventions to improve physician behaviours regarding breast cancer screening	Measures of breast cancer screening	1980-1993	Multiple	EM, REM, AF	20 studies included. Interventions included physician reminders, audit and feedback, office systems and physician education. Most trials used 2 or more interventions, 65% used physician reminders. 11 of 16 trials using reminders showed significant benefits (effects size ranging in improvements of 6-28%). Audit and feedback was effective in all 4 studies using it (effect size ranging from 19-23% improvement). Physician education and office based systems had variable effects but were largely ineffective.	Physician-based interventions can be effective in increasing screening use. Interventions should emphasize community practices and practices for caring for underserved and older populations.

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McGowan 2009[281]	10	Effectiveness of interventions providing electronic health information to healthcare providers to improve practice and patient care	Primary and Secondary Care	Health professionals	Provision of electronically retrievable information	Objective measures of professional behaviour or patient outcome	1966-2008	Multiple	MAR, DEM	2 included studies, with neither finding any changes in professional behaviour following an intervention that facilitated electronic retrieval of health information. Neither assessed patient outcomes or costs	Overall there was insufficient evidence to support or refute the use of electronic retrieval of healthcare information by healthcare providers to improve practice and patient care.
Medves 2010[181]	5	Effectiveness of practice guideline dissemination and implementation strategies for healthcare teams	Primary and Secondary Care	Primary and secondary healthcare providers and their patients	Guideline implementation strategy	Objective measures of process, patient or economic outcomes	1994-2007	Guideline	DEM, EM, LCP, EOV, LOL, PMI, AF, REM, MAR, MM	88 included studies. 10 different dissemination and implementation strategies identified. Proportions of studies with significant positive findings were 72.3% for distribution of educational materials (59 studies), 74.2% for educational meetings (62 studies), 64.7% for local consensus processes (34 studies), 66.6% for educational outreach (12 studies), 81.3% for local opinion leaders (16 studies), 64.3% for patient mediated (14 studies), 82.2% for audit and feedback (45 studies), 85.2% for reminders (27 studies) and 77.7% for marketing (18 studies). Overall 72.7% of studies had significantly positive findings. More complex healthcare seemed to require more complex, multifaceted interventions	Team based care using practice guidelines locally adapted can positively affect patient and provider outcomes.

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O'Brien 2007[282]	10	Effectiveness of educational outreach visits (EOVs) on health professional practice or patient outcomes	Primary and Secondary Care	Health professionals	Educational outreach visits	Objective measures of professional performance	1950-2007	Multiple	REM, EOV, EM, AF, PMI, LCP, MAR	69 studies included. 28 studies (34 comparisons) combined, showing median adjusted RD in compliance with desired practice was 5.6% (IQR 3-9%). Adjusted RDs were consistent for prescribing (median RD 4.8%, IQR 3-6.5%, 17 comparisons), but varied for other professional performance (median RD 6%, IQR 3.6-16%, 17 comparisons). Meta-regression limited by the multiple potential explanatory factors (8) and showed no evidence for the observed variation in RDs (31 comparisons). 18 comparisons had a continuous outcome, with a median adjusted improvement of 21% (IQR 11-41%). Interventions including EOVs were slightly superior to audit and feedback (8 trials, 12 comparisons).	EOVs alone or when combined with other interventions have effects on prescribing that are relatively consistent and small, but potentially important. Their effects on other professional performance types are variable, though it is not possible from this review to explain that variation.
Oxman 1995[283]	8	Effectiveness of interventions to improve delivery of health professional performance and health outcomes	Primary and Secondary Care	Health professionals	Interventions to improve professional practice or health outcomes	Objective assessment of provider performance or health outcome	1970-1993	Multiple	DEM, EM, LCP, EOV, LOL, PMI, AF, REM, MAR, MM	102 included studies. Passive dissemination strategies resulted in no change in behaviour or outcome. Multifaceted, complex interventions had variable results ranging from ineffective to highly effective, and generally moderate overall	There are no "magic bullets" for improving the quality of health care, but there are a wide range of interventions available that, if used appropriately, could lead to important improvements in professional practice and patient outcomes.

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Perry 2011[284]	8	Effectiveness of educational interventions about dementia, directed at primary care providers (PCPs)	Primary care	Primary care providers	Educational interventions	Process of care and provider knowledge	1950-2009	Guideline	EM, REM	6 articles representing five studies (four cluster RCTs and one CBA) were included. Compliance to the interventions varied from 18 to 100%. Systematic review of the studies showed moderate positive results. Five articles reported at least some effects of the interventions. A small group workshop and a decision support system (DSS) increased dementia detection rates. An interactive 2-h seminar raised GPs' suspicion of dementia. Adherence to dementia guidelines only improved when an educational intervention was combined with the appointment of dementia care managers. This combined intervention also improved patients' and caregivers' quality of life. Effects on knowledge and attitudes were minor	Active educational interventions for PCPs improve detection of dementia. Educational interventions alone do not seem to increase guideline adherence. To effectively change professionals' performance, education probably needs to be combined with other organizational incentives.
Randell 2007[285]	8	Effectiveness of computerized decision support systems (CDSSs) on nursing performance and patient outcomes	Secondary care	Nurses and their patients in secondary care	Computerized decision support systems	Patient care and/or practitioner performance	1950-2006	Single	REM	Eight studies, three comparing nurses using CDSS with nurses not using CDSS and five comparing nurses using CDSS with other health professionals not using CDSS, were included. Risk of contamination was a concern in four studies. The effect of CDSS on nursing performance and patient outcomes was inconsistent.	CDSS may not necessarily lead to a positive outcome; further studies are needed. CDSS are complex interventions and should be evaluated as such. Contamination is a significant issue so it is important that randomization is at the practitioner or the unit level.

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Robertson 2010[286]	8	Effectiveness of CDSSs targeting pharmacists on physician prescribing, clinical and patient outcomes	Primary and secondary care	Providers and patients in primary or secondary care	Computerized Clinical Decision Support Systems	Practitioner Prescribing Performance and Patient Outcomes	1990-2009	Single	REM	21 studies were included (11 addressing safety and 10 addressing QUM issues). CDSSs addressing safety issues were more effective than CDSSs focusing on QUM (10/11 vs 4/10 studies reporting significant improvements in favour of CDSSs on ≥50% of all outcomes reported; P = 0.01). More studies demonstrated CDSS benefits on prescribing outcomes than clinical outcomes (10/10 vs 0/3 studies; P = 0.002). There were too few studies to assess the impact of system- versus user-initiated CDSS, the influence of setting or multi-faceted interventions on CDSS effectiveness.	Use of CDSSs to improve safety led to greater improvements than those for quality use of medicines (QUM). It was not possible to draw any other conclusions about their effectiveness.
Safdar 2008[287]	7	Effectiveness of educational strategies of healthcare providers for reducing health care associated infection (HCAI)	Secondary Care	Healthcare professionals	Educational interventions targeted at healthcare personnel	Incidence of HCAI	1966-2006	Multiple	DEM, EM, MAR, AF	26 studies included, using a number of different educational programmes, including feedback on audits or current practices, practical demonstrations, courses, self-study modules, posters, lectures and web based training. 21 of the studies showed significant reductions in HCAI rates after intervention (risk reduction ranging from 0-0.79).	The implementation of educational interventions may reduce HCAI considerably. Cluster RCTs are needed to determine the independent effect of education on reducing HCAI and associated costs.

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Schedlbauer 2009[288]	8	Effectiveness of CDSSs on prescribing behaviour	Primary and secondary care	Providers and patients in primary or secondary care	Computerized Clinical Decision Support Systems	Practitioner Prescribing Performance and Patient Outcomes	1950-2007	Single	REM	20 studies were included which used 27 types of alerts and prompts. Of these 27, 23 achieved improved prescribing behaviour and/or reduced medication errors. In many of the studies, the changes noted were clinically relevant. Positive effects were noted for a wide range of alerts and prompts. Three of the alert types with lacking benefit showed weaknesses in their methodology or design. The impact appeared to vary based on the type of decision support. Some of these alerts (n=5) reported a positive impact on clinical and health service management outcomes.	Most empiric studies evaluating the effects of CDSSs on prescribing behaviour show positive, and often substantial, effects. Additional studies should be done to determine the design features that are most strongly associated with improved outcomes
Shea 1996[289]	7	Effectiveness of computer based reminder systems on preventive care	Primary Care	Ambulatory care physicians and their patients	Computer based reminder systems	Objective measures of improvements in preventive practice	1966-1995	Single	REM	16 studies in included. 4 of 6 preventative practices assessed were improved by computer reminders, as were all practices combined (OR 1.77, 95%CI 1.38-2.27). Manual reminders also improved 4 of the practices and all practices combined (OR 1.57, 95% CI 1.20-2.06). A combination of computerised and manual reminders increased all 6 practices assessed (OR 2.23, 95%CI 1.67-2.98). No significant difference between computerised and manual reminders.	Manual and computer reminders can both separately increase the use of preventive practices, and in combination have a greater effect than either alone.

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Shiffman 1999[290]	7	Effectiveness of computer based guideline implementation	Primary and Secondary Care	Primary and secondary care physicians and their patients	Computer based guideline implementation	Objective measure of effectiveness in a practice setting	1992-1998	Guideline	DEM, REM	25 studies included. Guideline adherence improved in 14 of 18 studies where it was measured Documentation improved in 4 of 4 studies.	To evaluate the effect of information management on the effectiveness of computer-based guideline implementation, more of the confounding variables need to be controlled. In this review, different types of guidelines, settings, and systems make conclusions difficult.
Shojania 2009[291]	10	Effectiveness of point-of-care computer reminders on physician behaviour	Primary and Secondary Care	Physicians or physician trainees	Point of care computer reminders	Objective measures of the process of care and clinical outcomes	1950-2008	Single	REM	28 studies (32 comparisons) included. Computer reminders improved process adherence by a median of 4.2% (IQR 0.8-18.8%) across all reported process outcomes. In 8 comparisons reporting clinical outcomes there was a median improvement of 2.5% (IQR 1.3-4.2%), with blood pressure being the most commonly reported endpoint.	POC computer reminders generally achieve small to modest improvements in provider behaviour. No specific features of the interventions were associated with effect magnitude. Further work is needed to determine the factors associated with larger improvements

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Siddiqui 2011[292]	9	Effectiveness of physician reminders in faecal occult blood (FOB) testing for colorectal cancer screening	Primary care	Physicians in primary care	Reminders for FOB testing	FOB testing	1975-2010	Single	REM	Five studies (25287 patients) were included. There were 12641 patients in the Reminder and 12646 in the No-reminder group. All 5 studies obtained a higher percentage uptake when physician reminders were given, though this was only significantly higher in 2 of the studies. There was significant heterogeneity among trials (I2=95%). The combined increase in FOB test uptake was not statistically significant (random effects model: risk difference 6.6%, 95% CI: 2 – 14.7%; P=0.112)	Reminding physicians about those patients due for FOB testing may not improve the effectiveness of a colorectal cancer screening programme.
Steinman 2006[293]	7	Effectiveness of interventions to improve the prescribing of recommended antibiotics for acute outpatient infections	Outpatients	Outpatient prescribers	Interventions aimed at improving prescribing	Appropriate antibiotic prescribing	1950-2004	Multiple	EM, DEM, AF, EOV	26 studies reporting 33 trials were included. Most interventions used education alone or in combination with audit and feedback. Among the 22 comparisons amenable to quantitative analysis, recommended antibiotic prescribing improved by a median of 10.6% (interquartile range IQR 3.4–18.2%). Education alone reported larger effects than combinations of education with audit and feedback (median effect size 13.9% IQR 8.6–21.6% vs. 3.4% IQR 1.8–9.7% , P=0.03). This result was confounded by trial sample size, as trials having a smaller number of participating clinicians reported larger effects and were more likely to use clinician education alone. Active forms of education, sustained interventions, and other features traditionally associated with success were not associated with effect size.	Multifaceted interventions using audit and feedback were less effective than interventions using education alone. Although confounding may partially account for this finding, our results suggest that enhancing the intensity of a focused intervention may be preferable to a less intense, multidimensional approach.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Tan 2005[294]	11	Effectiveness of CDSSs on improving the mortality and morbidity of newborn infants and the performance of physicians treating them	Neonatal care	Physicians and infants in neonatal care	CDSS	Infant mortality and morbidity and physician performance	1966-2007	Single	REM	3 studies were included. Two looked at computer-aided prescribing. The first focussed on parenteral nutrition ordering. No significant effects on short-term outcomes were found and longer term outcomes were not studied. The second investigated the effects of a database program in aiding the calculation of neonatal drug dosages. Time taken for calculation was significantly reduced and there was a significant reduction in the number of calculation errors. The other study looked at the effects of computerised cot side physiological trend monitoring and display. There were no significant effects on mortality, volume of colloid infused, frequency of blood gases sampling or severe intraventricular haemorrhage.	There are very limited data from randomised trials on which to assess the effects of CDSSs in neonatal care. Further evaluation of CDSS using randomised controlled trials is warranted.
Thomas 1999[191]	10	Effectiveness of guidelines for professions allied to medicine	Primary and Secondary Care	Allied health professionals	Introduction of a clinical guideline to change AHP behaviour	Objective measures of the process or outcome of care provided by AHPs.	1975-1996	Guideline	DEM, EM, EOV, REM, LCP	18 included studies. 9 studies compared guidelines vs none, and of these 3 of 5 showed significant improvements in the process of care, 6 of 8 found improvements in outcomes of care. 3 studies compared 2 guideline implementation strategies with mixed results. 6 studies compared nurses operating in accordance with a guideline with standard (physician) care, with no difference between groups seen for process or patient outcomes.	There is some evidence that guideline-driven care is effective in changing the process and outcome of care provided by professions allied to medicine. However, caution is needed in generalising findings to other professions and settings

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Tinmouth 2005[295]	5	Effectiveness of behavioural interventions to reduce blood product utilisation.	Secondary Care	Hospital patients and clinicians	Intervention to change transfusion practice and the behaviour of clinicians	Number of units transfused or number of patients receiving transfusion	1966-2003	Multiple	REM, AF, EM	19 studies included, using both single (guidelines, audits, reminders) and multifaceted interventions. 18 studies demonstrated a relative reduction in the number of units given (9-77%) or proportion of patients receiving transfusion (17-79%). No particular intervention or combination of interventions seemed more effective than another.	Behavioural interventions, including simple interventions, appear to be effective in changing physician transfusion practices and reducing blood utilization. Clinical trials are still needed to determine the relative effectiveness of different interventions to change practices.
Wensing 1998[296]	7	Effectiveness of interventions to implement guidelines or innovations in general practice	Primary Care	Primary care physicians	Intervention to improve professional behaviour	Objective measures of provider behaviour	1980-1994	Guideline	DEM, AF, REM, EM, PMI	143 studies included, but only 61 'best evidence' (RCTs and CBAs) studies selected for analysis. For single interventions, 8 of 17 showed information transfer (IT) to be effective, 14 of 15 found in favour of information linked to performance (ILP), 3 of 5 showed learning through social influence (LTSI) to be effective and all 3 studies looking at management support MS showed significant improvements. For multifaceted interventions, 8 of 20 showed improvements for IT with ILP, 7 of 8 for IT with LTSI, 6 of 7 for IT with M, 3 of 3 for ILP with LTSI. 5 of 6 studies using 3 or more interventions showed significant improvements	Strategies using multifaceted interventions are more expensive but also more effective. All interventions had variable effectiveness. The combination of information transfer and LTSI or management support showed superior levels of improvement, as did reminders or feedback.

Study	Quality Score (0-11)	Focus	Inclusion Criteria					Single/ Multiple/ Guideline	EPOC Interv-entions	Main Results	Authors Main Conclusions
			Setting	Participants	Intervention	Outcomes	Period				
Worrall 1997[297]	6	Effectiveness of clinical practice guidelines on patient outcomes in primary care	Primary Care	Primary care physicians	Guideline dissemination and/or implementation strategies	Objective measures of patient outcomes	1980-1995	Multiple	DEM, EM, AF, REM	13 studies included (7 looked at hypertension, 2 at asthma, 6 at smoking). Only 5 of 13 (38%) showed statistically significant benefits. 6 studies used computer or automated reminders while the others used small workshops or education sessions.	There is little evidence that guidelines improve patient outcomes in primary medical care, but most studies published to date have used older guidelines and methods, which may have been insensitive to small changes in outcomes. Research is needed to determine if newer approaches are better
Wutoh 2004[195]	5	Effectiveness of internet-based continuing medical education (CME) interventions on physician performance and health care outcomes	Primary or secondary care	Practicing health care professionals or health professionals in training	Internet based education	Physician performance and health care outcomes	1966-2004	Single	DEM	16 studies were included. Six studies generated positive changes in participant knowledge over traditional formats; three studies showed a positive change in practices. The remainder of the studies showed no difference in knowledge levels between Internet-based interventions and traditional formats for CME.	Internet-based CME programs are as effective at improving knowledge as traditional formats of CME. It is unclear whether these positive changes in knowledge are translated into changes in practice Additional studies need to be performed to assess how long these new learned behaviours are be sustained.

Appendix 7: AMSTAR scoring of studies included in the overview of systematic reviews (chapter 5)

Study	1. Was an 'a priori' design provided?	2. Was there duplicate study selection and data extraction?	3. Was a comprehensive literature search performed?	4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	5. Was a list of studies (included and excluded) provided?	6. Were the characteristics of the included studies provided?	7. Was the scientific quality of the included studies assessed and documented?	8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	9. Were the methods used to combine the findings of studies appropriate?	10. Was the likelihood of publication bias assessed?	11. Was the conflict of interest stated?	Total
Anderson 1996[248]	Yes	Unclear	Unclear	Unclear	No	No	Unclear	Yes	Yes	No	No	3
Arditi 2012[249]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Austin 1994[250]	Yes	Unclear	No	No	No	Yes	No	No	Yes	No	No	3
Baker 2010[251]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Balas 1996[252]	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	No	No	6
Balas 2000[253]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8
Bauer 2002[254]	Yes	No	No	No	No	Yes	No	Not Applicable	Yes	No	No	3
Beilby 1997[255]	Yes	Unclear	Yes	Yes	No	Yes	No	No	Yes	No	No	5
Blackwood 2014[193]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Boren 2009[256]	Yes	Unclear	Yes	No	No	Yes	No	No	Yes	No	No	4
Brennan 2013[188]	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	No	Yes	7
Bright 2012[257]	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes	No	Yes	8
Brody 2013[198]	Yes	No	Yes	No	No	Yes	No	No	Yes	No	No	4
Bryan 2008[258]	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes	No	Yes	8
Buntinx 1993[259]	Yes	Unclear	Unclear	Unclear	No	Yes	No	Unclear	Yes	No	No	3
Chaillet 2006[182]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	7
Chhina 2013[200]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	7
Clarke 2010[194]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	8
Damiani 2010[260]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	9
Davey 2013[261]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Davis 1995[187]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	8

Study	1. Was an 'a priori' design provided?	2. Was there duplicate study selection and data extraction?	3. Was a comprehensive literature search performed?	4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	5. Was a list of studies (included and excluded) provided?	6. Were the characteristics of the included studies provided?	7. Was the scientific quality of the included studies assessed and documented?	8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	9. Were the methods used to combine the findings of studies appropriate?	10. Was the likelihood of publication bias assessed?	11. Was the conflict of interest stated?	Total
Delpierre 2004[262]	Yes	Unclear	Yes	No	No	Yes	No	No	Yes	No	No	4
Dexheimer 2008[263]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8
Dexheimer 2014[264]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	8
EHC 1994[185]	Yes	Unclear	Yes	No	No	Yes	No	Unclear	Yes	No	Yes	5
Figueras 2001[265]	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No	6
Fleming 2013[203]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	7
Flodgren 2010[266]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10
Flodgren 2011[267]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10
Flodgren 2013[268]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Forsetlund 2009 [269]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Forsetlund 2011[270]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	8
Frampton 2014[271]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
French 2010[272]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10
Garg 2005[273]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	No	7
Giguere 2012[274]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10
Gilbody 2003[202]	Yes	Yes	Yes	No	No	No	Yes	No	Yes	No	No	5
Goodwin 2011[196]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	7
Grimshaw 2004[275]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	10
Gross 2001[276]	Yes	Unclear	No	No	No	No	No	No	Unclear	No	No	1
Hakkennes 2008[180]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	8
Heselmans 2009[184]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	8

Study	1. Was an 'a priori' design provided?	2. Was there duplicate study selection and data extraction?	3. Was a comprehensive literature search performed?	4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	5. Was a list of studies (included and excluded) provided?	6. Were the characteristics of the included studies provided?	7. Was the scientific quality of the included studies assessed and documented?	8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	9. Were the methods used to combine the findings of studies appropriate?	10. Was the likelihood of publication bias assessed?	11. Was the conflict of interest stated?	Total
Ivers 2012[205]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Kahn 2013[277]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Kastner 2008[278]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	7
Loganathan 2011[279]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	8
Mandelblatt 1995[280]	Yes	Yes	No	No	No	Yes	No	No	Yes	No	No	4
McGowan 2009[281]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10
Medves 2010[181]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No	5
O'Brien 2007[282]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10
Oxman 1995[283]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	8
Perry 2011[284]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	8
Randell 2007[285]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8
Robertson 2010[286]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	8
Safdar 2008[287]	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	No	Yes	7
Schedlbauer 2009[288]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8
Shea 1996[289]	Yes	Unclear	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	7
Shiffman 1999[290]	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	No	Yes	7
Shojania 2009[291]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10
Siddiqui 2011[292]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	9
Steinman 2006[293]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	7
Tan 2005[294]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Thomas 1999[191]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10

Study	1. Was an 'a priori' design provided?	2. Was there duplicate study selection and data extraction?	3. Was a comprehensive literature search performed?	4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	5. Was a list of studies (included and excluded) provided?	6. Were the characteristics of the included studies provided?	7. Was the scientific quality of the included studies assessed and documented?	8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	9. Were the methods used to combine the findings of studies appropriate?	10. Was the likelihood of publication bias assessed?	11. Was the conflict of interest stated?	Total
Tinmouth 2005[295]	Yes	Yes	Yes	No	No	Yes	No	No	Yes	No	No	5
Wensing 1998[296]	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	No	No	7
Worrall 1997[297]	Yes	Unclear	Yes	No	No	Yes	Yes	Yes	Yes	No	No	6
Wutoh 2004[195]	Yes	No	Yes	No	No	Yes	Yes	No	Yes	No	No	5

Appendix 8: Published paper on the Neonatal Nutrition Screening Tool used in this study

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SHORT COMMUNICATION

Developing a new screening tool for nutritional risk in neonatal intensive care

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INTRODUCTION

Hospitalised children are at increased risk of malnutrition and preterm infants, in particular, often experience poor growth (1). This may be partly attributed to variability in nutritional care and a failure to meet nutritional targets, with the extent of nutritional deficits related to the degree of postnatal growth failure seen (2). One strategy to address this is the provision of specialist nutritional support while the infant is in the neonatal intensive care unit (NICU) (3) and, in relation to this, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommends the implementation of specialist paediatric nutrition support teams in hospital, with their role including nutritional screening (4). Nutritional screening enables nonspecialist staff to identify patients at nutritional risk and in need of further assessment and support by specialist staff. Where they exist, nutrition support teams are usually a limited resource, so using screening to identify patients in greatest need is important. When we established our neonatal nutrition team, we identified that no neonatal nutrition screening tool (NNST) currently existed. We therefore aimed to create a NNST that could be used on all infants in the NICU on a weekly basis by nursing staff to identify those at high risk of poor growth and in need of additional nutrition support during their stay.

A literature search was carried out to identify any paediatric screening tools already in existence that could be adapted for our purposes. Several tools were identified (5–11), with common features including assessment of nutritional intake, underlying disease processes and weight and, or, other anthropometry (Table 1). Few tools were relevant to the NICU population. For example, Mezoff et al.'s (9) tool was aimed at children admitted to intensive care with respiratory syncytial virus, a population that is perhaps reflective of NICU patients, although the youngest infants used in the validation of that tool were 28 days old and the specific nature of the disease was not ideal. Another tool, the Clinical Assessment of Nutrition score, is more neonatal, but aims to predict morbidity related to foetal malnutrition rather than direct nutritional support (10). The only NICU-specific tool is the Ohio Neonatal Nutritionists Screening Criteria for Identifying Hospitalised Infants at Highest Nutritional Risk (11). This complex tool for dietitians considers nutritional intake, growth, current diagnoses and postnatal age, although no published data are available regarding its validity, sensitivity or specificity.

Using the results of the literature search and consensus opinion, our multidisciplinary group, comprising two neonatologists with an interest in nutrition, a research fellow, a dietitian, a pharmacist and lead nutrition nurses, developed a NNST (Fig. 1), which considers underlying conditions associated with increased risk of poor growth. These include gestational age and weight at birth (1), diagnosis of absent or reversed end diastolic flow on umbilical artery Doppler, diagnosis of severe intrauterine growth restriction, defined as a birthweight below the second centile on the UK-WHO growth chart (12), need for gastrointestinal surgery or presence of severe gastrointestinal malformation

Appendix 8

Table 1 Summary of existing paediatric nutrition screening tools

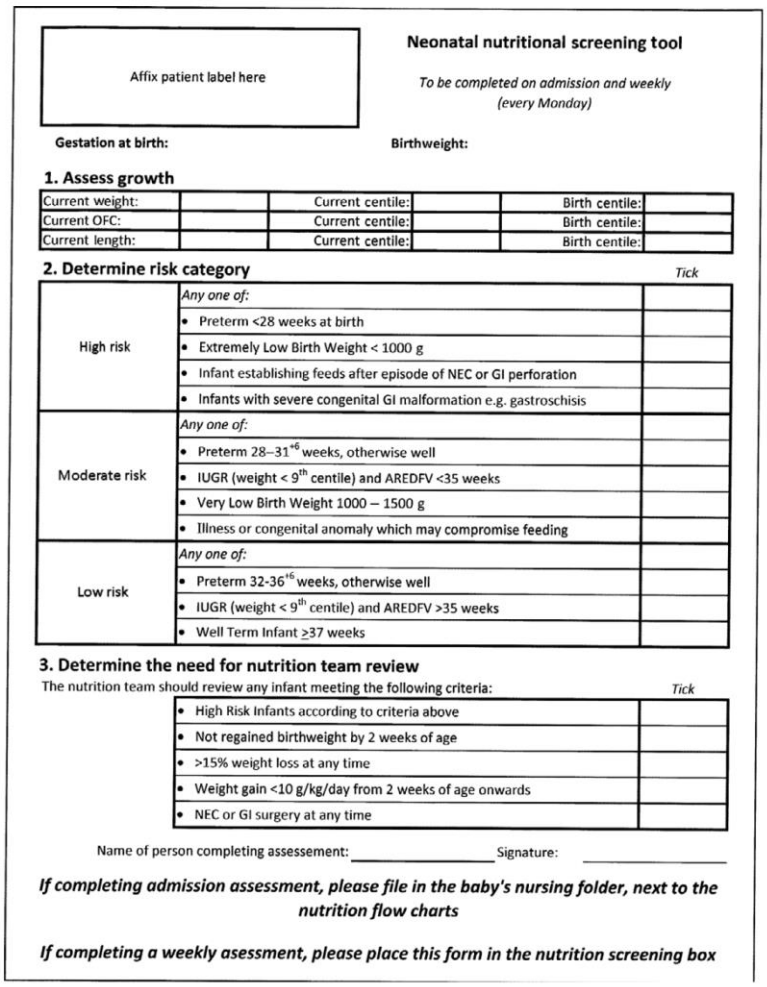
Tool	Target Population	Assessment criteria	Outcome
Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP) (5)	Children >2 years admitted to paediatric wards	Diagnosis with nutritional implications, nutritional intake, weight and height	High, medium or low risk
Screening Tool for Risk On Nutritional status and Growth (STRONGkids) (6)	Children >1 month admitted to paediatric wards (excluding PIC)	Subjective clinical assessment, disease with high nutritional risk, nutritional intake and losses, weight loss or poor weight gain	High, moderate or low risk
Paediatric Yorkhill Malnutrition Score (PYMS) (7)	Children >1 year admitted to paediatric wards	BMI, weight loss, nutritional intake, diagnosis with nutritional implications	High, medium or low risk
Paediatric Nutrition Risk Score (PNRS) (8)	Children >1 year admitted to paediatric wards	Pathology with nutritional implications, nutritional intake, pain	High, moderate or low risk
Nutritional Screen for Children's Medical Centre (Mezoff et al.) (9)	Children (>28 days) admitted to PIC)	Diagnosis with nutritional implications, nutritional intake, weight and height, weight loss, laboratory markers of poor nutrition (anaemia, low lymphocyte count, low serum albumin)	High or low risk
Clinical Assessment of Nutrition (CAN) Score (10)	Neonates soon after birth	Birthweight, length, head circumference, mid arm circumference and ponderal index	Well-nourished or malnourished
Ohio Neonatal Nutritionists Screening Criteria for Identifying Hospitalised Infants at Highest Nutritional Risk (11)	Hospitalised neonates	<1 week of age: >15% weight loss from birth or <1 kg at birth 1-2 weeks of age: <60 kcal/kg/day or continued weight loss >2 weeks of age: intake <66% energy requirement or <10 g/kg/day weight gain or low albumin/low phosphate/ high bilirubin/high ALP >2 months of age: any of above or no dietary iron or continued PN	High or low risk

BMI = Body mass index; PIC = paediatric intensive care, PN = parenteral nutrition.

(13), time to regain birthweight, maximum percentage weight loss from birthweight and minimum rate of weekly weight gain, from 2 weeks of age onwards. The cut-off for the latter was chosen as 10 g/kg/day, rather than 15 g/kg/day, as the latter is based on *in utero* growth and may not be applicable for full-term infants. This was important as the NNST tool is intended for all admissions. As with other tools, the NNST categorises infants as high, moderate or low risk. Only high-risk infants, plus those who meet any of the additional poor growth criteria at the bottom of the tool, constitute a positive screening result, requiring review by the specialist nutrition support team. However, the three risk categories allow the use of specific nutritional regimens for each group, meaning that appropriate nutritional care can be initiated prior to any formal nutrition review.

Once developed, the NNST was retrospectively applied on a weekly basis to all admissions to our NICU during 2010. The aim was to ascertain its sensitivity and specificity to detect infants on admission, or during their stay, who would go on to be discharged with faltering growth. Faltering growth was defined as a fall of 1.33 standard deviation scores (SDS) for weight between birth and discharge, corresponding to a fall across two marked centile lines on a UK-WHO growth chart. Infants who were <2 weeks old at discharge were excluded in view of the normal loss and regain of birthweight that occurs in the first 2 weeks after birth. Retrospective validation was necessary as prospective screening, and the associated nutritional intervention would have altered the outcome and made it impossible to assess the accuracy of the tool. Data were managed and analysed using Microsoft Excel 2010. There were 958 episodes of care, corresponding to 909 infants. Details of the population and screening results, together with details on specific groups of infants, are shown in Table 2. The NNST had a sensitivity of 89.6% and specificity of 75.1%.

We believe our NNST is the first tool of its kind that can be applied universally to the NICU population by nursing staff on a weekly basis and, in turn, direct the limited resource that is a nutrition support team. Weekly use of such a tool raises awareness of nutrition on the NICU and encourages regular monitoring and assessment of growth, as staff must measure and plot infants to complete the NNST. The NNST also allows the use of specific guidelines for the nutritional management of different risk groups, although it is important to remember that there is chance that some infants may have been wrongly classified by the tool and received inappropriate intervention. However, the incorporation of weekly growth measurements and plotting into the tool aimed to reduce the risk of such issues. In addition, sensitivity was high, making the tool suited for its purpose of identifying infants in greatest need of increased



Affix patient label here

Neonatal nutritional screening tool

To be completed on admission and weekly (every Monday)

Gestation at birth: **Birthweight:**

1. Assess growth

Current weight:		Current centile:		Birth centile:	
Current OFC:		Current centile:		Birth centile:	
Current length:		Current centile:		Birth centile:	

2. Determine risk category

		Tick
High risk	*Any one of:*	
	• Preterm <28 weeks at birth	
	• Extremely Low Birth Weight < 1000 g	
	• Infant establishing feeds after episode of NEC or GI perforation	
	• Infants with severe congenital GI malformation e.g. gastroschisis	
Moderate risk	*Any one of:*	
	• Preterm 28–31^{+6} weeks, otherwise well	
	• IUGR (weight < 9th centile) and AREDFV <35 weeks	
	• Very Low Birth Weight 1000 – 1500 g	
	• Illness or congenital anomaly which may compromise feeding	
Low risk	*Any one of:*	
	• Preterm 32-36^{+6} weeks, otherwise well	
	• IUGR (weight < 9th centile) and AREDFV >35 weeks	
	• Well Term Infant ≥37 weeks	

3. Determine the need for nutrition team review

The nutrition team should review any infant meeting the following criteria:

	Tick
• High Risk Infants according to criteria above	
• Not regained birthweight by 2 weeks of age	
• >15% weight loss at any time	
• Weight gain <10 g/kg/day from 2 weeks of age onwards	
• NEC or GI surgery at any time	

Name of person completing assessement: _____ Signature: _____

If completing admission assessment, please file in the baby's nursing folder, next to the nutrition flow charts

If completing a weekly asessment, please place this form in the nutrition screening box

Figure 1 Neonatal Nutrition Screening Tool.

Table 2 Characteristics of screening tool for all infants and specific population groups

	All Infants	Infants <28 weeks at birth	Infants <1000 g at birth	Infants with NEC or spontaneous perforation	Infants with other surgical conditions
Number of infants	909	78	88	27	80
Mean (SD) gestational age	36.3 (4.8)	25.6 (1.39)	26.2 (2.0)	27.5 (4.1)	36.5 (4.3)
Mean (SD) birthweight	2.66 (1.05)	0.78 (0.19)	0.75 (0.16)	1.06 (0.76)	2.54 (0.92)
Infants with faltering growth	115	29	27	18	13
True positives	103	29	27	18	13
False positives	210	49	61	9	67
True negatives	633	0	0	0	0
False negatives	12	0	0	0	0
Sensitivity (%)	89.6	100	100	100	100
Specificity (%)	75.1	0	0	0	0
Positive predictive value (%)	32.9	37.2	30.7	66.7	16.3
Negative predictive value (%)	98.1	–	–	–	–

NEC = Necrotising enterocolitis; SD = standard deviation.

nutritional support. Specificity was reasonable, although positive predictive value was low, meaning that two-thirds of infants might have been seen unnecessarily by the nutrition support team. However, overall the team saw only a third of all admissions, suggesting that it is a reasonable tool for targeting their expertise. While this was a retrospective validation, there would have been some nutritional intervention by the clinical team for infants they identified with poor growth, which could have altered the outcome and may explain the reduced specificity and positive predictive value.

Some existing paediatric nutrition risk screening tools have been subjected to similar evaluations. Compared to a full dietetic assessment, the Screening Tool for the Assessment of Malnutrition in Paediatrics and the Paediatric Yorkhill Malnutrition Score had sensitivities of 72% and 59%, respectively, with specificities of 90% and 92%, respectively (5,7). The higher specificity ensures fewer patients are seen unnecessarily, increasing efficiency. However, all tools must balance sensitivity and specificity, and we favoured sensitivity to prevent cases of poor growth being missed during this critical period. Our simplified approach to screening, which did not include an assessment of nutrient intake, may have also contributed to its lower specificity. This was a conscious decision to allow quick, easy and regular use by nursing staff caring for the infants. Elia and Stratton recently highlighted the importance of selecting a screening tool based on its purpose, setting, population, available evidence base, ease of use, acceptability and compliance (14). With this work, we were attempting to produce a tool that had reasonable sensitivity and specificity, but more importantly, could and would be used regularly by clinical staff.

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CONFLICT OF INTEREST AND FUNDING

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work. This work was supported by funding from the National Institute for Health Research Southampton Biomedical Research Centre. AAL and HEM's salary is supported by funding from the NIHR Southampton Biomedical Research Centre, and MJJ is a doctoral research fellow supported by the NIHR. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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Appendix 9: Published paper on the 'Nurse Champion' Role used in this study

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Developing the role of the nurse as a link advisor for research and a champion for nutrition in the neonatal intensive care unit

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Abstract A unique local practice initiative to develop a small group of nurses in the dual role of link advisors and champions for nutrition was part of a larger research project aimed at standardising nutritional care of preterm infants. Building upon the expertise of a small group of dedicated neonatal nurses, new clinical guidelines were successfully introduced and to date an incremental change in practice achieved. Furthermore, quality outcomes in terms of improving the research profile, bridging the research-practice gap, increased job satisfaction and personal practitioner recognition and achievement has contributed to the success of the project.

Background

There is good evidence that some preterm infants may fail to grow adequately, (Ehrenkranz et al., 1999; Wood et al., 2003). Poor growth can be associated with poor neurodevelopmental outcomes in extremely preterm infants, with a lower weight at discharge associated with an increased risk of neurodevelopmental impairment (Ehrenkranz et al.,

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2006). One reason for this poor growth may be that these infants receive inadequate nutrition in the first weeks of life. Recommendations for the optimal nutrient intake of preterm infants exist, (Agostoni et al., 2010; Tsang, 2005) however, there is evidence that these targets are not achieved (Embleton et al., 2001; Grover et al., 2008; Martin et al., 2009). Achieving recommended nutrient intakes in these infants is a major challenge, and feeding practices can be variable. This was demonstrated by Cooke et al. (2004) who showed that units offering the same level of care had significant variations in postnatal growth.

Variation in practice and outcome is increasingly being recognised as one of the major challenges in health care provision. Work by the Vermont Oxford Network (VON), consisting of over 800 neonatal units worldwide, has shown that variations in outcomes between essentially 'similar' neonatal populations and providers is often wide, demonstrating that these variations in clinical care are important. Members of the VON introduced eight 'potentially better practices' for nutritional care to try and make practice more consistent, and found reduced lengths of stay and improvements in growth following implementation (Kuzma-O'Reilly et al., 2003). Similarly, there is also evidence that the use of formal nutrition guidelines leads to significantly reduced rates of necrotising enterocolitis (Patole and de Klerk, 2005), earlier initiation of both parenteral and enteral feeding, earlier achievement of full enteral feeding, and earlier regaining of birthweight (Donovan et al., 2006).

Whilst it seems that a more standardised approach to the nutritional care of preterm infants is likely to result in improved nutrition outcomes, introducing new guidelines to standardise practice represent a major undertaking for any care group, particularly one as complex as a Neonatal Intensive Care Unit (NICU). Such an environment involves several processes for the delivery of nutritional care, with each process influenced by unit staff, together with their own practices and experience. Understanding the barriers to implementing a change in practice is key to the development of a successful intervention, (Grol, 1997; Grol and Grimshaw, 2003) and there is evidence that guidelines alone are often not enough to bring about or maintain a change in practice, and that more multifaceted implementation strategies are required (Grimshaw et al., 2004; Grol, 2001; Grol and Grimshaw, 2003; Mettes et al., 2010).

One potential strategy to aid guideline implementation is for dedicated members of staff to help champion the new ways of working. While many neonatal units might have a nurse or group of nurses who take the lead for nutrition within their unit, there is currently no specifically defined role for a 'Specialist Nurse in Neonatal Nutrition'. The role of Specialist Nurses has however, been developed in other areas of paediatrics to good effect, particularly in disease areas where good nutrition is crucial such as inflammatory bowel disease and diabetes (Heuschkel et al., 2008; Jefferson et al., 2003). Similarly, nurses have undertaken the role of 'link advisor' in a number of areas such as infection prevention and palliative care, and have been shown to positively impact on practice (Cotterell et al., 2007; Dawson, 2003). Such nurses act as a link between their own clinical area and their specialty, bridging the 'theory-practice' gap. This enables them to increase awareness of new ways of working and improve practice at clinical level, acting as clinical opinion leaders (Cooper, 2001). Nurses play a key role in research; however it can be difficult for clinical nurses to participate in research and at the same time difficult for research nurses to engage with local clinical practice. This is particularly important with the rapid growth of research associated with its' current promotion by the government as a core NHS role.

Taking the principles of both these models of 'specialist nurse' and 'link advisor', suggests that developing a unique and innovative nurse role which combines expertise in research and nutrition may offer a potential strategy to aid the improvement of the nutritional care of preterm infants. The work described in this paper regarding the development of the link advisor/champion for research and nutrition contributed to a larger research project to introduce a comprehensive package of care for the nutritional care of preterm infants (born at less than 30 weeks gestation or with a birth weight less than 1501 g) and assess its' effect on improving nutrient intakes and growth during NICU stay and neurodevelopmental outcomes at 2 years. This study was undertaken within the context of the National Institute for Health Research (NIHR) Nutrition, Diet and Lifestyle Biomedical Research Unit (later to become a Centre).

Aims

The aims of developing the dual role were to prepare experienced neonatal nurses to develop their research and nutritional knowledge and expertise. This was designed to bridge the research-practice gap through enhancing the implementation of the new nutrition guidelines and improving the uptake of new ways of working amongst staff as part of a research project aimed at improving nutritional care

though practice change. The nurses were considered to be 'Champions for Nutrition' on the unit.

Methods

Developing the link advisor/'champion for nutrition' role

Funding and recruitment

Funding was obtained from the Southampton NIHR Nutrition Biomedical Research Unit (later to become a Centre). Nurses were recruited from existing clinical staff with funding provided to the neonatal unit to backfill the vacancy. The matron, senior managers and multidisciplinary team were highly supportive of the initiative and encouraged staff to express an interest. Four nurses were available and in a position to be seconded.

Developmental activities

A role profile was developed to focus on the link advisor role for research (see Table 1). Nurses attended a local research induction, Good Clinical Practice (GCP) training and specific research study knowledge and skills training such as infant measurements. This level of training is usually provided to nurses in specific research roles. Dedicated training in nutrition was provided by local experts such as an academic consultant neonatologist with an interest in nutrition, a neonatal dietitian, a neonatal pharmacist, a speech and language therapist and a lactation specialist in small groups, initially as a formal study days, followed by informal support equating to approximately 2 h per week. Nurses also received education from clinical psychologists on the management of change and discussed techniques to deal with the associated challenges such as dealing with colleagues resistant to change. They also attended external courses relevant to neonatal nutrition. The link advisors had to demonstrate competence in growth measuring and plotting, calculating nutrient intakes, breastfeeding support and nutritional screening. They were prepared for individually leading a specified area of nutritional care together with associated audit activity to allow for an element of personal achievement and recognition within the overall project.

Role implementation

The 'nurse champions' helped shape the new nutritional guidelines, nutrition screening tool and were trained in use of a dedicated computer system for assessing nutrient intakes and growth (Johnson et al., 2012). They were released one day a week to work with the multidisciplinary nutrition research team and, continued to work clinical shifts for the remainder of their hours. Importantly, this meant that they were available as a resource to colleagues in working with the new practices introduced as part the new nutritional care package. Each week, on their research day, the nurses would wear a specific research uniform to emphasize that their time for the day was protected for research activity. Their role included data collection, growth measurements and staff training with a focus on supporting colleagues with new working practices, introduced as part of the research study. They became part of the multidisciplinary nutrition team, joining a consultant, a dietitian and a pharmacist on weekly ward rounds. As part of their development, each nurse took the lead for one specific area of practice development in relation to nutrition: measuring and plotting growth; breastfeeding; use of nutritional supplements and nutritional discharge planning. Their specific audit projects, to measure current practice in their area, were carried out on a three monthly rolling basis to measure compliance with the new guidelines as a measure of practice change in relation to their work.

Results

The development of this role has proved to be a resounding success in terms of raising the profile of both research and nutrition within the neonatal intensive care unit. As part of an ongoing process we have been evaluating the impact of the role using both quantitative (audit) and qualitative (staff feedback, appraisal and personal evaluation) methods, some of which are summarised below.

Audits of aspects of nutritional care

Serial audits have been carried out by the nurse champions looking at the changes in practice since they and the new guideline were introduced. The results clearly demonstrate improvements and are laid out below. See Table 2 for a list of audit standards.

Weighing, measuring and plotting

Following the introduction of the new practices on January 1st 2012, there was a considerable improvement in compliance with audit standards in terms of weighing; measuring and plotting on infants (see Fig. 1).

Use of nutritional supplements

There was again considerable improvement in the use of nutritional supplements (vitamins and Iron)

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Table 1 Role profile for research link advisors.

ROLE PROFILE
RESEARCH LINK ADVISORS

Requirements

- Be willing to act as the research link for your area
- Be enthusiastic, with good communication skills
- Be willing to learn, & undertake study to gain knowledge & remain updated
- Be willing to dedicate time to supporting clinical research studies in area of work
- Be willing & able to cascade information/updates related to clinical research to colleagues
- To have completed a research induction and Good Clinical Practice (GCP) training either through attendance or e learning on line
- Attend twice yearly meetings
- Have support and agreement from manager to undertake the role

Aims of the Role

1. Promote research within the clinical setting by gaining knowledge of the studies.
2. Promote research with users of the service.
3. Act as conduit between researchers and colleagues.
4. Facilitate clinical research activity by liaising with:
   - Lead research nurse/midwife/AHP
   - Principal Investigator (PI)
   - Other research staff
   - Colleagues in clinical area
5. To increase recruitment of children/adults into studies.
6. Where agreed, participate in clinical research under the supervision of the research nurse/midwife/AHP. (Outline of activities must be agreed using template overleaf).
7. Help to create a clinical research active environment.

Agreed Clinical Research Activities

Date of activity	Activity	Date &Notes of Review
	Research Practitioner induction	
	GCP Training (face to face or on-line)	
	List of additional training required i.e. study specific, body measurements	
	List of core activities	

Date agreed:

Research Practitioner:

Link Advisor:

in accordance with audit standards following the introduction of the nurse champions and the new guidelines (see Fig. 2).

Breastfeeding rates

In a baseline audit, breastfeeding rates were disappointing, with only 31% of infants going home breast fed, and 9% receiving mixed feeds. Of those discharged on formula milk, only 41% received the appropriate formula (preterm post-discharge formula). The reaudit of practice is ongoing, but several steps have been taken to address these shortcomings. These include the development of a breastfeeding guideline, which has had input from the nurse champions for nutrition, and ongoing staff training in breastfeeding support.

Table 2 Audit standards.

Audit	Criteria	Expected compliance
Growth chart audit	Appropriate Growth Chart available for each patient	100%
	Growth chart labelled	100%
	Weight plotted on Day 1	100%
	Head circumference plotted on Day 1	100%
	Length plotted on admission or by Day 7	100%
	One weight plotted per week	100%
	One head circumference plotted per week	100%
	One length plotted every 2 weeks	100%
Nutritional supplement audit	Preterm Infants should receive Iron and Vitamins in accordance with local guideline	100%
Feeding at discharge audit	Infants under 2 kg should be discharged either breastfeeding or on preterm formula if not breastfeeding.	100%

Appraisal of the link advisor/'champion for nutrition' role

Feedback from the nurse champions, multidisciplinary team, colleagues and managers has been generally positive. The nurses themselves have identified that having the opportunity to be part of a research project has offered a very different and exciting experience in their nursing career. They were positive about the training they received in both research and nutrition by experts in these fields, and considered that it had significantly helped develop their role, In particular, they felt that they are now seen by their colleagues as experts in the new nutritional practices, and a source of support and advice for colleagues to provide optimal nutrition to preterm infants. The nurses also valued their continued clinical work, and recognised that their new development role has been utilised while working clinically. They felt this to be incredibly motivating, particularly as they are able to see the success and impact of the project in their work. The nurses also felt that the working pattern meant that they did not lose their clinical skills, or forfeit their current relationship with NICU and the rest of their team, which tends

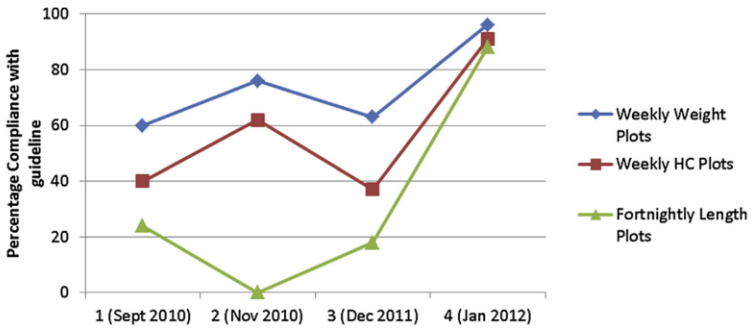

Fig. 1 Compliance with audit standards for measuring and plotting during the 4 audit periods.

Appendix 9

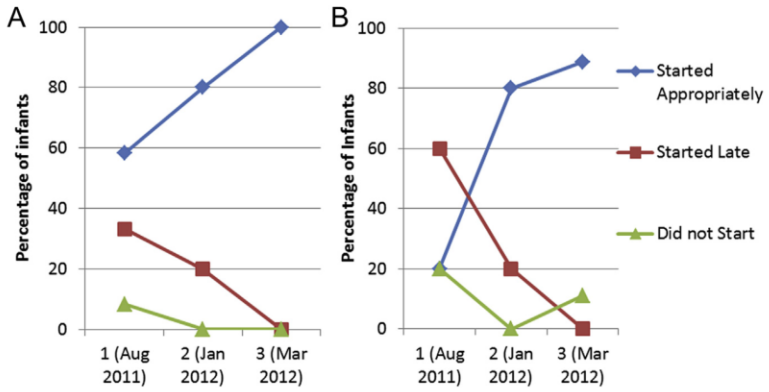

Fig. 2 Appropriate use of nutritional supplements across the 3 audit periods for vitamins (A) and Iron (B).

to happen when nurses change role completely from clinical to research.

One particular aspect of the new practices that represented a significant challenge was the introduction of weekly Nutrition Screening, that demanded regular measuring and plotting of infants' length and head circumferences in addition to routine weighing. The nurse champions instituted a rolling training programme in the measuring and plotting of infants, and also encourage use of the screening tool when on shift.

Another issue that the nurse champions cited as a difficult aspect of their role was the teaching and supporting of the more experienced ward staff in the new working practices, many of whom felt the new guidelines may limit their ability for autonomous decision making and practice. However, the nurses felt that generally people had accepted that they were there to help and that even the more resistant staff felt able to discuss things because they were seen as colleagues rather than outsiders.

Discussion

In this innovative approach to developing the research healthcare workforce, these research link advisors were also developed to act as 'Champions for Nutrition'. They are ideally placed to influence practice and specifically aid the implementation of new ways of working, acting as clinical opinion leaders in nutritional care. They work closely with nutrition team, which includes other relevant experts such as a neonatal dietitian, a lactation specialist and a speech and language therapist, and have also received support and specific teaching from all of these specialists. We believe this model has the potential to help bridge the research-practice gap in other areas of research. It is anticipated the use of nurses as link advisors for research and champions for the new nutrition guidelines and working practices in nutritional care will become embedded into 'normal' practice, and staff feedback and audit results so far have been encouraging. Further evaluation is planned to assess the success of the link advisors/champions in helping to implement and embed the new practices into routine care, including the use of staff questionnaires based on the sociological model of 'Normalization process theory' which considers the way in which new practices become embedded in normal practice (May and Finch, 2009; May et al., 2011; May et al., 2009). We also plan to continue serial audit measures, and are currently studying the impact of the new practices, together with the research link advisors, on nutrient intakes and growth in the preterm infants on the unit. The impact of the new role on other unit staff will also be assessed using an evaluative questionnaire. Should this prove successful we hope to share the project, together with the guidelines and a clinical 'tool-kit' of nutritional knowledge and skills with our collaborating tertiary neonatal unit. This in turn would ideally lead to expansion of this initiative at network level, and in addition the extension of this unique nursing role could link research and practice development in other areas of clinical practice. As the research team become less visible and active, it is envisaged that the link advisor/'Champion for Nutrition' role will continue to support the new practices as part of routine care. Ultimately, we hope that this novel role would become integrated into their clinical job description, and become a mandatory position within the core nursing team.

Disclaimer

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Appendix 10: Framework Analysis of Focus groups using EPOC Barriers to Change

Focus Group	A : Administrative Constraints	B : Clinical Uncertainty	C : Information Management	D : Patient Expectations	E : Perceptions of Liability	F : Sense of Competence	G : Standards of Practice
1	Everyone needs to be aware of changes Nutrition usually the first thing that slips Needs to be clear who is responsible for what. Midwives may need to some encouragement to engage with new practices Night staff often busy so can may not do work needed. however, should make time given length of shift, even after breaks Noted increased responsibilities of staff in room one, especially with transitional care. Not an onerous thing to be adding in to workload Could make Monday a busy day if Sunday night work not done	Whilst it is a guideline there is a need to treat babies as individuals Would not replace 'gut feeling'	Flowcharts should be easily available for people to look at in the nurseries Guidelines need to be constantly under review, so you now when things aren't working Important to have a sheet with key points on it and laminate it- make it easily accessible ?maybe nutrition folder in each room. Person in charge could be responsible for checking and that fluids prescribed appropriately Education and information important, as are copies of guideline to read and disseminate Education could be part of orientation programme but need to capture those on nights Nutrition should be discussed on ward round each day, with documented plan for next 24 hours. Nurse should be present needs to be a system in place for monitoring to ensure going up appropriately		Shouldn't always be down to those on nights, as long as it is done Feeding currently a joint decision, though can be the case that decisions aren't made until medics make them Nurse coordinators will need to make sure it is happening	Lots of junior staff with different skills and education. Not everyone will know how to measure or want to measure Guideline a lot to take in- will need to keep referring to it	Role in new guidelines is to use them a lead by example Need to take guideline as standard, with 'exceptions' only with good reason Not everyone is weighing and measuring regularly and this is a potentially huge change in practice. Need to make it routine to do this Feeding practices for small babies also a big change and difficult to implement

Focus Group	A : Administrative Constraints	B : Clinical Uncertainty	C : Information Management	D : Patient Expectations	E : Perceptions of Liability	F : Sense of Competence	G : Standards of Practice
2	Staff will need to read guideline and understand it, and seek advice if need clarification Study days good but a challenge to capture everyone- needs some sort of rolling/drop in session Doing head circumferences may be a challenge Could put screening tool in with new sets of notes to remind people to do it Putting copies of guideline round unit may not mean people read them	Sicker babies may be more of a challenge	Good to have structure to practice, especially if working by yourself. Also good to have something where everyone knows what happens and less ad hoc Will take a lot of inward digesting Nice summary at end Needs to be available in workplace with laminated copies Flowcharts important to pick out relevant bits, with details in back of guideline if people need more background	Guideline may reduce variability in advice given to parents, which can be variable and frustrating for parents Parents get focussed on weights, so measuring babies more often may alleviate this	People appreciate the a lot of work gone into guideline from 'our own team' Important for there to be consequences if not following guideline with reasons given when practices not done It has to be the norm to do measurements Need to get midwives to sign up to breastfeeding support within 6 hours Nurses are the one making decisions on feeding in the middle of the night. Some junior people may defer decisions to Tuesday for nutrition round, so nurses may need to take it upon themselves to make a decision and guidelines will facilitate this Unit previously introduced new practices in transfusion successfully- need to have someone leading the change and pushing it forward	Need for training in practical aspects, with assurance on the quality of measurements. Will need rolling education programme	More in guideline about nutrition at discharge and planning, which is new Need to make change the norm and routine, with certain things happening on certain days need to show people that the changes affect them, and they need to read/follow the guideline

Appendix 11: Framework Analysis of Focus groups using Normalisation Process Theory

Focus Group	A : Coherence	B : Cognitive Participation	C : Collective Action	D : Reflexive Monitoring
1	Recognition that similar to current practice but clear differences- formalising and providing structure Make nutrition more of a priority Less ad hoc-nice to have guidelines One person can't oversee everything anymore Something that could be improved on, with things being missed at times Important to have guidelines especially given expansion of unit ad increased staff Useful to have guideline for teaching purposes, especially as able to justify why we do what we do and all coming from same point Guideline provides basis to start and allows new knowledge in nutrition to be put into practice Will improve continuity of care and prevent unnecessary changes in care Is going to be a change in practice, especially for feeding of smallest babies More weighing and measuring 'Quite different to what we do at the moment' (in relation to weighing) Not a massive change from what we were doing before (overall guideline)	Important bits of guideline easily accessible and visual Flow charts should be easily accessible for everyone to look at Need to improve on feeding and nutrition, guidelines will help people focus Desire to have something for everyone to work from with continuity and a common document Belief that guideline will emphasise importance of nutrition and improve growth and development Good for junior people to have a guideline and useful for teaching Useful to have guidance in front of you. Should be with each baby in folder Will be some resistance but need to deal with it Recognition that not all babies will fit guideline Should be part of induction/orientation programmes Will give care more structure and less uncertainty Will allow nurses to have more awareness and prompt doctors Like the weaning for PN flow chart as this is currently ad hoc.	Need to ensure everyone is aware of guidelines and follows them Senior staff need to lead by example Flow charts with key points useful and need to be easy to access New staff need to be educated as part of induction Staff will need to be refreshed on measuring and learn to plot and document New work (measuring) needs to be as easy as possible- training and equipment, but not a challenge. Allocate measuring to same people/shift (nights on Sunday) will help it to be done, with clear responsibility of people (who are trained) Needs to be part of study days Medical team will need to refer to flow charts and guideline Everyone needs to be working together and discuss nutrition on ward round (by all teams). Joint decision making	Important to make nutrition higher up agenda again Perceived benefit to staff as will improve continuity and consistency of care Having a common, written structure for care would be good Will improve awareness of nurse in charge Guideline and flow charts will make it clear what should be happening and potentially raise issues when they occur Feeds will start earlier which is good System in place for monitoring feed increases helpful too. Monitoring weight and length beneficial too Staff keen to see a graph or similar to show visual impact of changes- pictorial illustration of benefits

Focus Group	A : Coherence	B : Cognitive Participation	C : Collective Action	D : Reflexive Monitoring
2	Good to have something structured, where everyone know what happens. Formalising it more and less ad hoc Guidelines have pulled together lots of things that were happening ad hoc, making it clear what the expectations are. Will help them make decisions. Now more about evidence than personal experience Standardised approach is new and important Profile of nutrition is now raised Not grossly different from previous practice but more formalised, less ad hoc. Won't come as a big surprise to unit More about nutrition at discharge, with formalised planning	Realisation that those who have had previously ad hoc behaviour will have to follow the guideline Appreciate having evidence base to back up practice Lots of work behind guidelines and has come from own team, which means people will take it seriously ('brownie points') People need to read it and ensure they understand it. Will mean more measuring, which was not being done before but should have been People need to remind each other to follow the guideline- feeling this should become indoctrined- should be the norm to measure the babies Need to make the guideline the norm and routine. Feeling that this is something people should know about and do. Need to know the content to be consistent. Other practice changes have occurred in the unit before and succeeded (eg blood transfusion policy) Need for this practice change to be lead by someone, 'pushing it forward'- nutrition team	Working together to follow standardised plan Hard copies of guideline need to be easily accessible, especially flow charts Should be part of study days Some practice is extension of that already done e.g. weighing and measuring Need to be a way of following up/ensuring things are done Quality of measurements should be ensuring- training Staff to remind each other at start of shift- nutrition nurses helpful Providing evidence in back of guideline reassures those who need it Nurses need to incorporate measuring in routine practice	Growth monitoring previously neglected, so will be good to improve on it Benefit of moving emphasis away from weight and calories to growth and protein May help resolution of lung disease (by growing) Audits have shown not doing head circumferences so need to improve. May benefit communication with parents as can show them a plan Might also improve early expressing of milk Highlight babies who are failing nutritionally and provide plan Might mean decisions deferred to nutrition ward round

Appendix 12: Teaching materials for staff training on preterm infant nutrition and growth

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Neonatal Nutrition

Dr Mark Johnson
Neonatal Clinical Research Fellow
NIHR Nutrition, Diet and Lifestyle Biomedical Research Unit
Southampton University Hospitals NHS Trust

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What we will cover

- Basic nutritional concepts
- Nutrient requirements
- Supplements to feeding and unusual milks
- Feeding methods
- Monitoring growth
- Anything else you like

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Why is nutrition important?

- A recognised goal in the nutritional care of preterm infants is to try and achieve rates and composition of growth similar to those seen in utero at the equivalent gestation
- Well established that infants born preterm tend to be shorter and lighter on reaching term equivalent age than those born at full-term (e.g. EPICure)
- Extrauterine growth restriction is well documented

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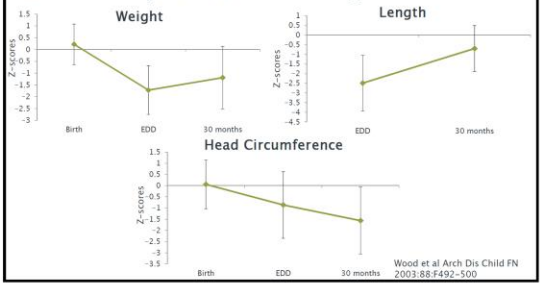
EPICURE

- Cohort study of infants <26 weeks gestation



Wood et al Arch Dis Child FN 2003;88:F492–500

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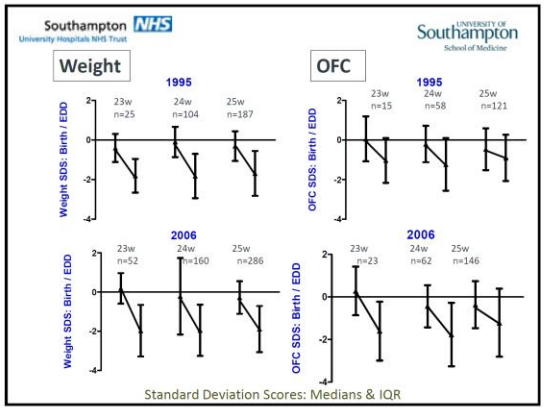

Standard Deviation Scores: Medians & IQR

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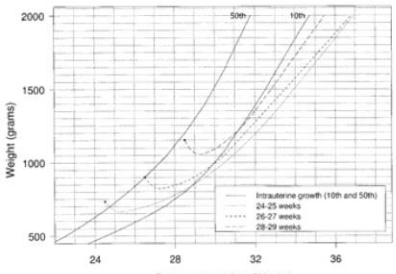
Extrauterine Growth Restriction



Ehrenkranz et al, Pediatrics 199:104:280–289

Appendix 12

Basic Principles of Nutrition

- Nutrients
- Balance
- Nutritional status

Nutrients

- Food contains nutrients
  - Macronutrients (Carbohydrate, Fat and Protein)
  - Micronutrients (Vitamins, minerals, trace elements)
- These nutrients
  - Provide energy
  - Provide specific nutrients which engage in chemical reactions

Balance

- There needs to be a balance between supply and demand
- Demands include
  - Fixed demands
    - Basal Metabolic Rate
      - Membrane function (NaK-ATPases etc)
      - Mechanical work (Cells and tissues)
      - Substrate Turnover (eg Protein)

Balance

- Variable Demands
  - Processing dietary intake
  - Physical Activity
  - Thermoregulation
  - Growth

Nutritional Status

- What you are
  - Body composition, reserves, genetics,
- What you eat
  - Supply of nutrients
- What you can do
  - Metabolic function
  - Physical activity

The Fetus

- What you are
  - Fat laid down from around 27 weeks
  - Iron, Calcium and Phosphorous stored from 28 wks
- What you eat
  - Intravenous nutrition supplied from placenta as glucose, amino acids, free fatty acids
- What you can do
  - Minimal physical activity
  - No need for thermoregulation, Lower BMR
  - Immature gut (though functional by 24 wks)

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The Term Infant

- What you are
  - Lots of fat stores (16–20% body fat)
  - Micronutrient reserves
- What you eat
  - Milk (lactose, protein, triglycerides)
- What you can do
  - Increased physical activity (inc feeding)
  - Thermoregulates (though well insulated!)

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Term infant requirements

- Average Term baby requires:
  - 100kCal/kg/day
  - 2.2g Protein
  - 2–3 mmol/kg Na
  - 2 mmol/kg K
  - 1 mmol/kg Ca

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Breast milk provides

- Average breast milk provides:
  - 0.7kCal/ml
  - 0.013g Protein/ml
  - 0.021 mmol Na/ml
  - 0.026 mmol K/ml
  - 0.0038 mmol Ca/ml
- Formula milk is similar
- So 150ml/kg/day provides:
  - 105 kcal/kg/day
  - 2g protein/kg/day
  - 3.1 mmol Na/kg/day
  - 4 mmol K/kg/day
  - 0.6 mmol Ca/kg/day

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The Preterm 24–26 week Infant

- What you are
  - No fat or micronutrient reserves
- What you eat
  - TPN (glucose, amino acids, free fatty acids)
  - Milk ((lactose, protein, triglycerides)
- What you can do
  - Increased physical activity
  - Need for thermoregulation and digestion
  - Higher BMR (breathing, no help from placenta)

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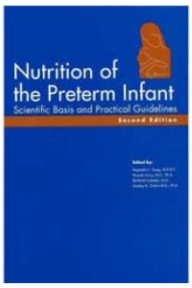
Preterm Infant Requirements



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Preterm Infant Requirements

- Day 0
  - 40–50 kcal/kg/day
  - 2g protein/kg/day
- Transition (day 1–7)
  - 75–90 kcal/kg/day
  - 3.5g protein/kg/day
- Growing (day 7+)
  - 110–120 kcal/kg/day
  - 3.5–4g protein/kg/day

Appendix 12

Energy and Protein for preterm infants

Fluid	10% Dextrose		
Rate	120	150	180
Energy	48	60	72
Protein	0	0	0

Fluid	Stock Preterm TPN	
Rate	120	130
Energy	89	96
Protein	2.5	2.7

Fluid	Stock Preterm TPN + Sodium	
Rate	120	130
Energy	88.9	96.3
Protein	3.0	3.2

Fluid	MBM		
Rate	120	150	180
Energy	84	105	126
Protein	1.6	2	2.3

Energy and Protein for preterm infants

Milk	MBM +Full Fortifier		
Rate	120	150	180
Energy	102	128	153
Protein	3	3.8	4.5

Milk	LBW		
Rate	120	150	180
Energy	96	120	144
Protein	3.1	3.9	4.7

Milk	Term formula		
Rate	120	150	180
Energy	79	100	118
Protein	1.6	2	2.3

Feeding premature infants

- Need top be started as soon as possible to prevent tissue loss
  - Urinary protein losses 1g/kg/day
  - Need 1.5g/kg to prevent catabolism
- Choice of feeding method
  - TPN
    - Aqueous bag ('Vamin')
    - Lipid
  - Milk Feeds

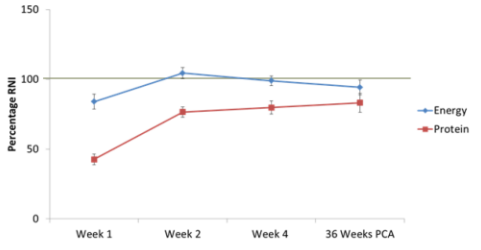
Sounds easy but....

- IV nutrition often sub-optimal
  - Fluid restriction (PDA etc)
  - Other infusions (UAC, PAL, Morphine)
- Enteral feeds can be complicated
  - Transition from in utero to ex utero means need to introduce feeds gradually
  - Concerns about metabolic and respiratory instability after birth
  - NECophobia!

500g baby

Fluids (ml/kg)	60	90	120	150
Infusions UAC/Morphine	33.6	33.6	33.6	33.6
Actual fluids for TPN(ml/kg)	26.4	56.4	86.4	116.4

Nutrition in 2009



p<0.001 for amount delivered for differences from recommendations (one sample t-test) for protein (all time points) and Energy at Week 1

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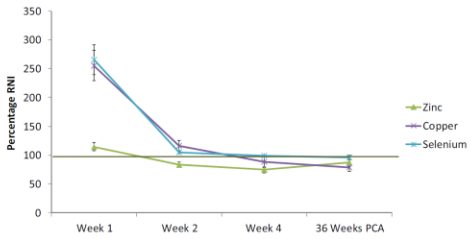
Trace Elements



p<0.001 for amount delivered for differences from recommendations (one sample t-test) for all except Copper at week 4 and Selenium at 36 weeks CGA.

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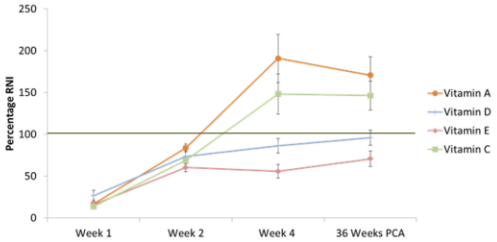
Vitamins



p<0.001 for amount delivered for differences from recommendations (one sample t-test) for all except Vitamin D at week 4 and 36 weeks CGA.

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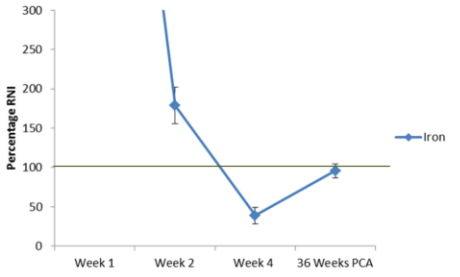
Iron



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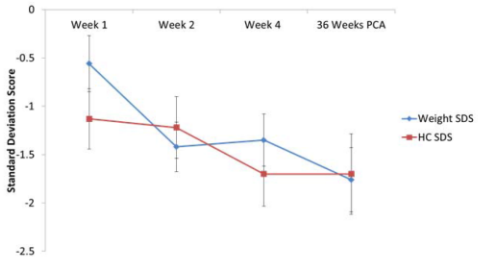
Growth



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Sounds easy but....

- IV nutrition often sub-optimal
  - Fluid restriction (PDA etc)
  - Other infusions (UAC, PAL, Morphine)
- Enteral feeds can be complicated
  - Transition from in utero to ex utero means need to introduce feeds gradually
  - Concerns about metabolic and respiratory instability after birth
  - NECophobia!

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NEC

- Ischaemic inflammatory condition of bowel
- Unknown cause but risk factors include
  - Feeding
    - BM vs Formula
    - Volume and Rate of feeding advancement
  - Prematurity
  - Ischaemia/asphyxia
  - Bacterial colonisation
  - IUGR and abnormal dopplers in utero

Appendix 12

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Signs of NEC

- Abdominal distension
- Increasing aspirates
- Bloody/mucousy stools
- Clinically unwell
- Tender abdomen

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Why feed?

- Prolonged TPN associated with
  - Infection risk
  - Jaundice and liver dysfunction
  - Poor growth
- Benefit of feeding on gut development
- Hunger!

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Starting Feeds

- Trophic feeding/MEN
  - Improves feeding tolerance and growth
  - Good for gut development
  - Does not increase risk of NEC
  - Up to 25ml/kg/day if no signs of NEC
- Delaying feeds
  - Currently no evidence that delaying feeds reduces the risk of NEC (ADEPT trial, 2 vs 6 days). Infants achieve full feeds more rapidly

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Increasing Feeds

- No clear guidance on this
  - Generally accepted to increase feeds by 10–20ml/kg/day if 'at risk' and by 20–30ml/kg/day if no risk factors
  - This is assuming infant tolerating feeds
- Aspirates can be a problem
  - Volume probably more important than colour

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Supplements

- Sodium (excess renal losses)
- Potassium
- Phosphate, calcium (poor stores, higher demand)
- Iron (demands vs stores vs availability)
- Vitamins (poor reserves)

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		Preterm Breastmilk* (/100ml)	Preterm Breastmilk + 2 sachets BMF (/100ml)
Vitamins			
Vitamin A	µgRE	ns	>130
Vitamin D	µg	ns	>5
Vitamin E	mg-α-TE	ns	>2.6
Vitamin C	mg	ns	>12
Thiamin (B_1)	µg	10	140
Riboflavin (B_2)	µg	30	200
Niacin (B_3)	µg	210	2610
Vitamin B_6	µg	10	120
Folic acid	µg	3.1	53.1
Vitamin B_{12}	µg	0.02	0.22
Biotin	µg	1	3.5
Pantothenic acid	µg	230	0.98
Vitamin K	µg	ns	>6.3
Minerals			
Potassium	mg	60	100
Chloride	mg	59	74
Calcium	mg	22	87
Phosphorus	mg	14	60
Magnesium	mg	2.5	8.5
Iron	mg	0.09	0.09
Zinc	mg	0.4	0.8
Iodine	µg	ns	>11
Copper	µg	63	94
Manganese	µg	ns	>8.1

Special Milks

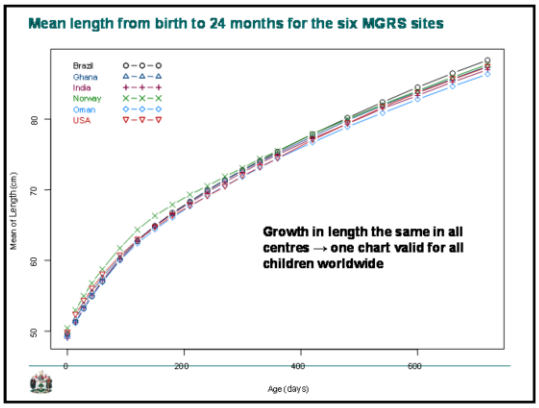
- Follow on Milks (extra Fe and vits)
- Thicker milks for colic/reflux
  - Omneo Comfort, SMA staydown, Enfamil AR
- Partially Hydrolysed (allergies)
  - Peptijunior (MCT rich)
- Hydrolysed (allergies, malabsorption)
  - Nutramigen 1+ 2, Pregestamil (has incr MCT)
- Amino acid based (allergies, malabsorption)
  - Neocate

More Special Milks

- High Energy Formulas
  - Infatrini, SMA HE
  - 100kcal per 100ml rather than 65-70
- Lactose Free Formulas (lactose intolerance)
  - SMA LF, Enfamil LF
- Soya Formulas (allergies, >6/12, CMP + lactose free)
  - Infasoy, Wysoy, Prosobee
- Low MCT feed
  - Monogen

Monitoring Growth

- How growth charts are generated
  - UK 1990 vs new WHO
- How are growth charts used
  - What are centiles
  - What are standard deviations
  - What is poor growth
  - How to plot growth



When to use the NICM chart

- Infants born before 32 weeks gestation
- Unwell infants born 32-36 weeks gestation
- Term unwell neonates needing close monitoring

  e.g. those with cardiac or renal disease
- Infants with significant growth or weight faltering

Data sources for the NICM Chart

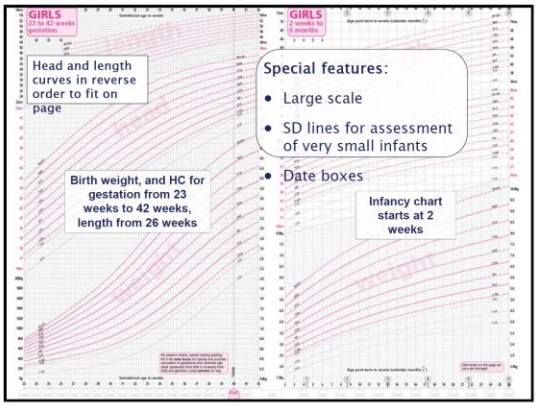
23 weeks gestation to 42 weeks:

- Reanalysed UK1990 data
- Describes size at birth only
- Does not describe how preterm infants should grow

2 weeks to 2 years corrected age charts:

- WHO growth standard

Appendix 12



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Preparing the chart using date boxes

- Start with *either*
  - a) estimated date of delivery (EDD)
  - *or* b) date of birth and known or estimated gestational age
- Use the calendar to fill in the date boxes
- Mark boxes up in pencil

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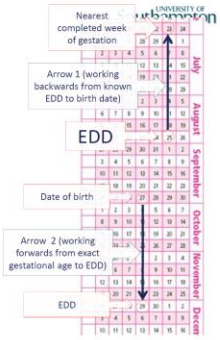
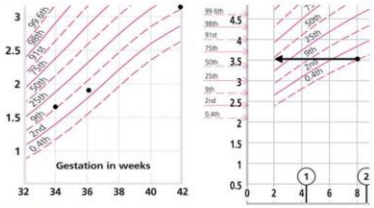
Use of the calendar to fill in the date boxes

- Move up or down column to find dates for each preceding (arrow 1) or succeeding (arrow 2) week on page 1 or fortnight on page 2
- At the end of year start again in same column at the top or bottom
- Ignore December 31st and leap years



Plotting pre-term infants

Transfer preterm to infancy section



Born 8 weeks preterm

Plot on preterm section of chart until 42 weeks (EDD+2)

Then plot on infancy section using gestational correction

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Making Measurements

- Weight
- Head circumference
  - Measure widest part of head above the ears, from prominent part of occiput to forehead. Take the average of 3 measurements.
- Length
  - Is a 2 person job
  - We now have neonatometers and incubator measures

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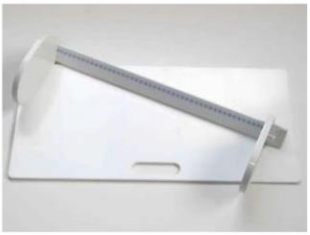
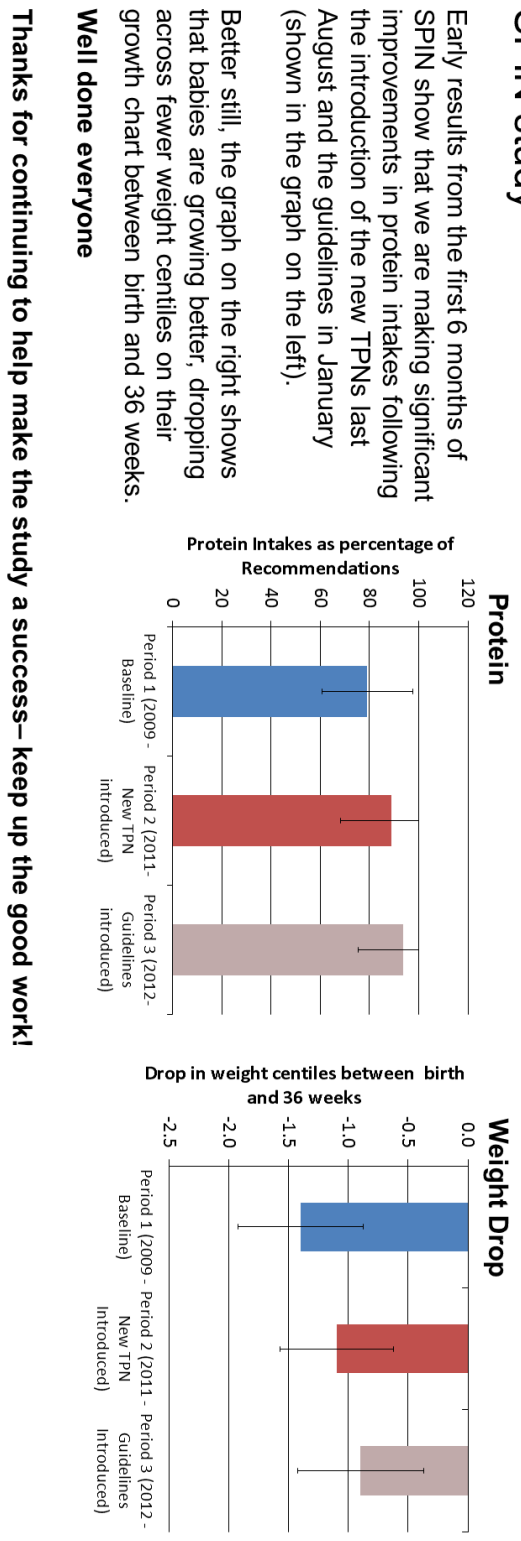
Incubator Measure



Appendix 13: Slide used on Neonatal Unit Audio Visual System to publicise results from the first six months of the study



Appendix 14: Statistical models from Interrupted Time Series Analysis

This analysis uses the raw nutrient intake and growth data, with excluded days included (assigned to appropriate study period), and collapsed by study week (using the means for nutrients). The outputs from stata are shown below.

In the sections below 'int' refers to the intercepts of the regression line of each interval being compared, whilst 'p' refers to the gradients of the regression lines of the two intervals being compared.

The following allowances have been made to try and give a more representative picture

- the first 2 months (8 weeks) have been removed to reduce effect of newly born infants with increasing intake without existing infants present.
- the data beyond 6 months post implementation will be also be removed, in order to reduce a similar effect of infants at the end of the study increasing intakes whilst others have been discharged (approximately 2 months data dropped)
- Period B (partial implementation will have a 1 month (4 week) run-in period to allow transition to new formulations etc
- Period C (full implementation) will have a 2 month (8 week run in period to allow new guidelines to become well used (a fits with audit data)

This means the periods will now look as follows:

- Period A = week 9 to 35 (6 months)
- Period B = week 36 to 60 (6 months)
- Period C = week 61 to 104 (10 months)
- Period D = week 105 to 131 (6 months)

Period A (pre-implementation 2011) vs B (partial implementation 2011)
Energy (kcal/kg/day)

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS	Number of obs =	52
Model	804.914338	3	268.304779	F(3, 48) =	7.05
Residual	1827.57932	48	38.0745692	Prob > F =	0.0005
				R-squared =	0.3058
Total	2632.49366	51	51.6175227	Adj R-squared =	0.2624
				Root MSE =	6.1705

Energy (kcal/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
intA	127.916	3.682996	34.73	0.000	120.5108	135.3212
intB	24.2982	3.596592	34.56	0.000	117.0668	131.5296
pA	.290493	.2284083	1.27	0.210	-.1687527	.7497386
pB	-.3548649	.2547847	-1.39	0.170	-.8671439	.1574141
rho	.3829656					

Durbin-Watson statistic (original) 1.207203
Durbin-Watson statistic (transformed) 1.856393

Comparison of intB-intA

(1) - intA + intB = 0

Energy (kcal/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-3.61779	4.817704	-0.75	0.456	-13.30443	6.068853

Appendix 14

Comparison of pB-pA

(1) - pA + pB = 0

Energy (kcal/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-.6453579	.3568642	-1.81	0.077	-1.362882	.0721658

Period A (pre-implementation 2011) vs B (partial implementation 2011)
Protein (g/kg/day)

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS		
Model	.533905461	3	.177968487	Number of obs =	52
Residual	1.92265252	48	.040055261	F(3, 48) =	4.44
Total	2.45655798	51	.048167804	Prob > F =	0.0078
				R-squared =	0.2173
				Adj R-squared =	0.1684
				Root MSE =	.20014

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
intA	3.423198	.1244884	27.50	0.000	3.172898	3.673499
intB	3.282241	.1214777	27.02	0.000	3.037994	3.526489
pA	.0184145	.0077168	2.39	0.021	.0028989	.0339301
pB	-.0057857	.0085999	-0.67	0.504	-.0230769	.0115055
rho	.4145211					

Durbin-Watson statistic (original) 1.197488
Durbin-Watson statistic (transformed) 1.862963

Comparison of intB-intA

(1) - intA + intB = 0

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-.1409572	.1608329	-0.88	0.385	-.4643335	.1824191

Comparison of pB-pA

(1) - pA + pB = 0

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-.0242002	.0121285	-2.00	0.052	-.0485862	.0001858

Period A (pre-implementation 2011) vs B (partial implementation 2011)
Energy (as a percentage of RRI per day)

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS	Number of obs = 52
Model	70.1009044	3	23.3669681	F(3, 48) = 1.16
Residual	970.964732	48	20.2284319	Prob > F = 0.3366
				R-squared = 0.0673
Total	1041.06564	51	20.4130517	Adj R-squared = 0.0090
				Root MSE = 4.4976

Energy (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
intA	103.7063	1.993956	52.01	0.000	99.69717	107.7154
intB	97.72459	1.954368	50.00	0.000	93.79507	101.6541
pA	.1738386	.1241989	1.40	0.168	-.0758801	.4235573
pB	.2489848	.1392382	1.79	0.080	-.0309724	.528942
Rho	.1191742					

Durbin-Watson statistic (original) 1.736553
Durbin-Watson statistic (transformed) 1.932159

Comparison of intB-intA

(1) - intA + intB = 0

Energy (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-5.981704	2.761571	-2.17	0.035	-11.53421	-.4291925

Comparison of pB-pA

(1) - pA + pB = 0

Energy (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	.0751462	.1880465	0.40	0.691	-.3029465	.4532389

Period A (pre-implementation 2011) vs B (partial implementation 2011)
Protein (as a percentage of RRI per day)

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS	Number of obs = 52
Model	201.066034	3	67.0220112	F(3, 48) = 3.35
Residual	960.502115	48	20.0104607	Prob > F = 0.0266
				R-squared = 0.1731
Total	1161.56815	51	22.775846	Adj R-squared = 0.1214
				Root MSE = 4.4733

```
------------------------------------------------------------------------------
Protein (as %RRI) | Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
------------------+-----------------------------------------------------------
       intA       | 90.47774   2.221692    40.72   0.000     86.01073    94.94475
       intB       | 84.59313   2.17521     38.89   0.000     80.21958    88.96668
         pA       | .3983261   .1381234     2.88   0.006     .1206104    .6760419
         pB       | .0167241   .1546033     0.11   0.914    -.2941267    .3275748
------------------+-----------------------------------------------------------
        rho       | .227765
------------------------------------------------------------------------------
Durbin-Watson statistic (original)    1.559962
Durbin-Watson statistic (transformed) 1.866869

Comparison of  intB-intA

 ( 1)  - intA + intB = 0

------------------------------------------------------------------------------
Protein (as %RRI) |  Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
------------------+-----------------------------------------------------------
       (1)        | -5.884609   3.027517    -1.94   0.058    -11.97184    .2026219
------------------------------------------------------------------------------

Comparison of  pB-pA

 ( 1)  - pA + pB = 0

------------------------------------------------------------------------------
Protein (as %RRI) |  Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
------------------+-----------------------------------------------------------
       (1)        | -.3816021   .2111567    -1.81   0.077    -.8061611    .042957
------------------------------------------------------------------------------
```

Period A (pre-implementation 2011) vs B (partial implementation 2011)
Change in Weight SDS from Birth

```
Prais-Winsten AR(1) regression -- iterated estimates

Source       | SS              df      MS                 Number of obs =      52
-------------+------------------------------              F(  3,    48) =   15.82
Model        | .543051058       3    .181017019           Prob > F      =  0.0000
Residual     | .549390446      48    .011445634           R-squared     =  0.4971
-------------+------------------------------              Adj R-squared =  0.4657
Total        | 1.0924415       51    .021420422           Root MSE      =  .10698

------------------------------------------------------------------------------
Weight SDS diff | Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
----------------+-------------------------------------------------------------
       intA     | -.48433    .0676338    -7.16   0.000    -.620317   -.3483431
       intB     | -.6600455  .0659779   -10.00   0.000    -.7927029   -.5273881
         pA     | .0184002   .0041917     4.39   0.000     .0099721    .0268282
         pB     | .0084342   .0046696     1.81   0.077    -.0009547    .0178232
----------------+-------------------------------------------------------------
        rho     | .4266093
------------------------------------------------------------------------------
Durbin-Watson statistic (original)    1.405723
Durbin-Watson statistic (transformed) 2.021892
```

Comparison of intB-intA

(1) - intA + intB = 0

Weight SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-.1757154	.0869208	-2.02	0.049	-.3504814	-.0009494

Comparison of pB-pA

(1) - pA + pB = 0

Weight SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-.0099659	.0066042	-1.51	0.138	-.0232446	.0033128

Period A (pre-implementation 2011) vs B (partial implementation 2011)
Change in Head Circumference SDS from Birth

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS		
Model	1.46521003	3	.488403344	Number of obs =	52
Residual	20.1623676	48	.420049325	F(3, 48) =	1.16
Total	21.6275776	51	.42407015	Prob > F =	0.3337
				R-squared =	0.0677
				Adj R-squared =	0.0095
				Root MSE =	.64811

Head Circ SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
intA	.0091448	.4180932	0.02	0.983	-.831488	.8497776
intB	-.2790717	.407695	-0.68	0.497	-1.098797	.5406541
pA	.0437406	.0259063	1.69	0.098	-.0083474	.0958286
pB	-.0173522	.0288457	-0.60	0.550	-.0753504	.040646
rho	.441419					

Durbin-Watson statistic (original) 1.157430
Durbin-Watson statistic (transformed) 1.834738

Comparison of intB-intA

(1) - intA + intB = 0

Head Circ SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-.2882165	.5336378	-0.54	0.592	-1.361167	.7847342

Comparison of pB-pA

(1) - pA + pB = 0

Head Circ SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-.0610928	.0409434	-1.49	0.142	-.143415	.0212295

Period B (partial implementation 2011) vs C (full implementation 2012)
Energy (kcal/kg/day)

Prais-Winsten AR(1) regression -- iterated estimates

```
Source       |  SS              df      MS              Number of obs =      69
-------------+------------------------------           F(  3,    65) =   10.68
Model        |  1681.77752      3      560.592507       Prob > F      =  0.0000
Residual     |  3411.92733      65     52.4911897       R-squared     =  0.3302
-------------+------------------------------           Adj R-squared =  0.2993
Total        |  5093.70485      68     74.9074242       Root MSE      =  7.2451
```

Energy (kcal/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
intB	115.3844	4.712617	24.48	0.000	105.9727	124.7962
intC	117.3717	3.54119	33.14	0.000	110.2995	124.444
pB	-.3227919	.3150267	-1.02	0.309	-.9519436	.3063599
pC	.1552522	.1411131	1.10	0.275	-.1265702	.4370745
rho	.4257895					

Durbin-Watson statistic (original) 1.151998
Durbin-Watson statistic (transformed) 1.998782

Comparison of intC-intB

(1) - intB + intC = 0

Energy (kcal/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	1.987292	5.527802	0.36	0.720	-9.052492	13.02708

Comparison of pC-pB

(1) - pB + pC = 0

Energy (kcal/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	.478044	.3565219	1.34	0.185	-.2339793	1.190067

Period B (partial implementation 2011) vs C (full implementation 2012)
Protein (g/kg/day)

Prais-Winsten AR(1) regression -- iterated estimates

```
Source       |  SS              df      MS              Number of obs =      69
-------------+------------------------------           F(  3,    65) =    7.26
Model        |  1.24755522      3      .415851739       Prob > F      =  0.0003
Residual     |  3.72220119      65     .057264634       R-squared     =  0.2510
-------------+------------------------------           Adj R-squared =  0.2165
Total        |  4.96975641      68     .073084653       Root MSE      =  .2393
```

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
intB	3.127774	.1535471	20.37	0.000	2.821119	3.434429
intC	3.210156	.1151283	27.88	0.000	2.980229	3.440083
pB	-.005125	.0102646	-0.50	0.619	-.0256249	.0153749
pC	.0045091	.0045883	0.98	0.329	-.0046544	.0136725
rho	.4151					

Durbin-Watson statistic (original) 1.189199
Durbin-Watson statistic (transformed) 1.938110

Comparison of intC-intB

(1) - intB + intC = 0

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	.0823821	.1806131	0.46	0.650	-.278327	.4430913

Comparison of pC-pB

(1) - pB + pC = 0

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	.009634	.0115939	0.83	0.409	-.0135206	.0327887

Period B (partial implementation 2011) vs C (full implementation 2012)
Energy (as a percentage of RRI per day)

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS		
Model	112.844325	3	37.6147751	Number of obs =	69
Residual	1732.87744	65	26.6596529	F(3, 65) =	1.41
Total	1845.72176	68	27.1429671	Prob > F =	0.2476
				R-squared =	0.0611
				Adj R-squared =	0.0178
				Root MSE =	5.1633

Energy (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
intB	104.009	2.200285	47.27	0.000	99.61477	108.4033
intC	102.6337	1.584686	64.77	0.000	99.4689	105.7986
pB	.2596875	.1479062	1.76	0.084	-.0357017	.5550766
pC	-.021765	.0634365	-0.34	0.733	-.1484565	.1049262
rho	.0362065					

Durbin-Watson statistic (original) 1.919720
Durbin-Watson statistic (transformed) 1.981169

Appendix 14

Comparison of intC-intB

(1) - intB + intC = 0

Energy (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-1.375309	2.705809	-0.51	0.613	-6.779183	4.028564

Comparison of pC-pB

(1) - pB + pC = 0

Energy (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	-.2814526	.1611277	-1.75	0.085	-.6032468	.0403416

Period B (partial implementation 2011) vs C (full implementation 2012)
Protein (as a percentage of RRI per day)

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS		
Model	513.892408	3	171.297469	Number of obs =	69
Residual	1847.44381	65	28.4222124	F(3, 65) =	6.03
Total	2361.33621	68	34.7255326	Prob > F =	0.0011
				R-squared =	0.2176
				Adj R-squared =	0.1815
				Root MSE =	5.3312

Protein (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
intB	85.00881	2.891349	29.40	0.000	79.23439	90.78324
intC	86.48625	2.121317	40.77	0.000	82.24969	90.72281
pB	.0282146	.1935565	0.15	0.885	-.3583444	.4147736
pC	.0532778	.0846771	0.63	0.531	-.1158341	.2223896
rho	.2736857					

Durbin-Watson statistic (original) 1.452871
Durbin-Watson statistic (transformed) 1.917906

Comparison of intC-intB

(1) - intB + intC = 0

Protein (as %RRI	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	1.477439	3.489917	0.42	0.673	-5.492407	8.447285

Comparison of pC-pB

(1) - pB + pC = 0

Protein (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	.0250631	.2143728	0.12	0.907	-.4030689	.4531952

Period B (partial implementation 2011) vs C (full implementation 2012)
Change in Weight SDS from Birth

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS	Number of obs = 69
Model	.022927974	3	.007642658	F(3, 65) = 0.57
Residual	.870593356	65	.013393744	Prob > F = 0.6364
Total	.89352133	68	.01314002	R-squared = 0.0257
				Adj R-squared = -0.0193
				Root MSE = .11573

Weight SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
intB	-.4366901	.0873502	-5.00	0.000	-.6111406	-.2622396
intC	-.5740514	.0675293	-8.50	0.000	-.7089167	-.4391862
pB	.009137	.005841	1.56	0.123	-.0025283	.0208022
pC	-.0034611	.0026873	-1.29	0.202	-.008828	.0019058
Rho	.534938					

Durbin-Watson statistic (original) 0.860734
Durbin-Watson statistic (transformed) 1.874817

Comparison of intC-intB

(1) - intB + intC = 0

Weight SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-.1373614	.0984179	-1.40	0.168	-.3339154	.0591927

Comparison of pC-pB

(1) - pB + pC = 0

Weight SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-.0125981	.0067798	-1.86	0.068	-.0261382	.0009421

Period B (partial implementation 2011) vs C (full implementation 2012)
Change in Head Circumference SDS from Birth

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS	Number of obs = 69
Model	.721680535	3	.240560178	F(3, 65) = 1.90
Residual	8.22238871	65	.126498288	Prob > F = 0.1380
Total	8.94406924	68	.13153043	R-squared = 0.0807
				Adj R-squared = 0.0383
				Root MSE = .35567

```
------------------------------------------------------------------------------
Head Circ SDS diff |   Coef.         Std. Err.      t       P>|t|      [95% Conf. Interval]
---------------+--------------------------------------------------------------
      intB         | -.5389364   .2334075   -2.31   0.024   -1.005083   -.0727895
      intC         | -.5150827   .1756443   -2.93   0.005   -.8658686   -.1642968
        pB         | -.0027119   .0156024   -0.17   0.863   -.0338721    .0284483
        pC         | -.0120037   .0069987   -1.72   0.091   -.0259811    .0019737
---------------+--------------------------------------------------------------
       rho         |  .4326858
------------------------------------------------------------------------------
Durbin-Watson statistic (original)    1.146426
Durbin-Watson statistic (transformed) 2.058333

Comparison of  intC-intB

 ( 1)  - intB + intC = 0

------------------------------------------------------------------------------
  Head Circ SDS diff      |   Coef.         Std. Err.      t       P>|t|      [95% Conf. Interval]
---------------+--------------------------------------------------------------
      (1)                 |  .0238537   .2732642    0.09   0.931   -.5218925    .5695999
------------------------------------------------------------------------------

Comparison of  pC-pB

 ( 1)  - pB + pC = 0

------------------------------------------------------------------------------
Head Circ SDS diff |  Coef.         Std. Err.      t       P>|t|      [95% Conf. Interval]
---------------+--------------------------------------------------------------
       (1)         | -.0092918   .0176807   -0.53   0.601   -.0446026    .026019
------------------------------------------------------------------------------
```

Period C (full implementation 2012) vs D (post implementation 2013)
Energy (kcal/kg/day)

```
Prais-Winsten AR(1) regression -- iterated estimates

Source       |  SS             df    MS                    Number of obs =      70
-------------+------------------------------                F(  3,    66) =    9.92
Model        |  1464.75192      3  488.25064                Prob > F      =  0.0000
Residual     |   3248.4294     66  49.2186272               R-squared     =  0.3108
-------------+------------------------------                Adj R-squared =  0.2794
Total        |  4713.18132     69  68.3069756               Root MSE      =  7.0156

------------------------------------------------------------------------------
Energy (kcal/kg/day)      | Coef.         Std. Err.      t       P>|t|      [95% Conf. Interval]
----------------+-------------------------------------------------------------
      intC                | 124.4064   3.308272   37.60   0.000    117.8012    131.0116
      intD                | 121.0212   3.988875   30.34   0.000    113.0571    128.9852
        pC                | .1715485   .1275446    1.35   0.183   -.0831025    .4261994
        pD                | -.3383739   .2716982   -1.25   0.217   -.8808368     .204089
----------------+-------------------------------------------------------------
       rho                | .3777179
------------------------------------------------------------------------------
Durbin-Watson statistic (original)    1.245008
Durbin-Watson statistic (transformed) 1.927175
```

Comparison of intD-intC

(1) - intC + intD = 0

Energy (kcal/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-3.385213	4.929116	-0.69	0.495	-13.22651	6.456085

Comparison of pD-pC

(1) - pC + pD = 0

Energy (kcal/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-.5099224	.3080836	-1.66	0.103	-1.125031	.1051863

Period C (full implementation 2012) vs D (post implementation 2013)
Protein (g/kg/day)

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS		
Model	1.28364993	3	.42788331	Number of obs	= 70
Residual	4.04096103	66	.061226682	F(3, 66)	= 6.99
Total	5.32461096	69	.077168275	Prob > F	= 0.0004
				R-squared	= 0.2411
				Adj R-squared	= 0.2066
				Root MSE	= .24744

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
intC	3.415881	.1224767	27.89	0.000	3.171348	3.660414
intD	3.31049	.1468653	22.54	0.000	3.017264	3.603716
pC	.0051947	.0047205	1.10	0.275	-.0042302	.0146195
pD	-.0078444	.0099996	-0.78	0.436	-.0278094	.0121205
rho	.4117355					

Durbin-Watson statistic (original) 1.174301
Durbin-Watson statistic (transformed) 1.803711

Comparison of intD-intC

(1) - intC + intD = 0

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-.1053913	.1800523	-0.59	0.560	-.4648774	.2540948

Comparison of pD-pC

(1) - pC + pD = 0

Protein (g/kg/day)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-.0130391	.0114044	-1.14	0.257	-.0358086	.0097305

Appendix 14

Period C (full implementation 2012) vs D (post implementation 2013)
Energy (as a percentage of RRI per day)

Prais-Winsten AR(1) regression -- iterated estimates

```
Source       | SS              df     MS                      Number of obs =      70
-------------+------------------------------                  F(  3,    66) =    8.03
Model        | 683.049196       3  227.683065                 Prob > F      =  0.0001
Residual     | 1870.31662      66  28.3381306                 R-squared     =  0.2675
-------------+------------------------------                  Adj R-squared =  0.2342
Total        | 2553.36581      69  37.0053017                 Root MSE      =  5.3234

------------------------------------------------------------------------------
Energy (as %RRI)    |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
--------------------+---------------------------------------------------------
      intC          |   101.5228   1.950853    52.04   0.000     97.62782    105.4178
      intD          |   100.2912   2.402623    41.74   0.000     95.49425    105.0882
        pC          |  -.0279124   .0753639    -0.37   0.712    -.1783813    .1225565
        pD          |  -.1998915   .1642308    -1.22   0.228    -.5277889    .1280058
--------------------+---------------------------------------------------------
       rho          |   .1742636
------------------------------------------------------------------------------
Durbin-Watson statistic (original)    1.646388
Durbin-Watson statistic (transformed) 1.939240
```

Comparison of intD-intC

```
 ( 1)  - intC + intD = 0

------------------------------------------------------------------------------
Energy (as %RRI)    | Coef.        Std. Err.      t    P>|t|     [95% Conf. Interval]
--------------------+---------------------------------------------------------
        (1)         | -1.231579    3.052456    -0.40   0.688    -7.326005    4.862847
------------------------------------------------------------------------------
```

Comparison of pD-pC

```
 ( 1)  - pC + pD = 0

------------------------------------------------------------------------------
Energy (as %RRI)    |   Coef.      Std. Err.      t    P>|t|     [95% Conf. Interval]
--------------------+---------------------------------------------------------
        (1)         |  -.1719791   .1820887    -0.94   0.348    -.5355308    .1915726
------------------------------------------------------------------------------
```

Period C (full implementation 2012) vs D (post implementation 2013)
Protein (as a percentage of RRI per day)

Prais-Winsten AR(1) regression -- iterated estimates

```
Source       |  SS             df      MS                     Number of obs =      70
-------------+------------------------------                  F(  3,    66) =    6.92
Model        | 655.286668       3   218.428889                Prob > F      =  0.0004
Residual     | 2084.13588      66  31.5778163                 R-squared     =  0.2392
-------------+------------------------------                  Adj R-squared =  0.2046
Total        | 2739.42255      69   39.701776                 Root MSE      =  5.6194

------------------------------------------------------------------------------
```

Protein (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
intC	88.83241	2.475293	35.89	0.000	83.89033	93.7745
intD	86.4824	3.005189	28.78	0.000	80.48235	92.48245
pC	.056226	.095474	0.59	0.558	-.134394	.2468461
pD	-.125244	.204843	-0.61	0.543	-.5342262	.2837382
rho	.3272249					

Durbin-Watson statistic (original) 1.344241
Durbin-Watson statistic (transformed) 1.852040

Comparison of intD-intC

(1) - intC + intD = 0

Protein (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-2.350016	3.749102	-0.63	0.533	-9.83534	5.135309

Comparison of pD-pC

(1) - pC + pD = 0

Protein (as %RRI)	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
(1)	-.1814701	.2305897	-0.79	0.434	-.6418572	.2789171

Period C (full implementation 2012) vs D (post implementation 2013)
Change in Weight SDS from Birth

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS		
Model	.187847456	3	.062615819	Number of obs =	70
Residual	1.37058641	66	.020766461	F(3, 66) =	3.02
Total	1.55843387	69	.022585998	Prob > F =	0.0361
				R-squared =	0.1205
				Adj R-squared =	0.0806
				Root MSE =	.14411

Weight SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
intC	-.7283148	.1134921	-6.42	0.000	-.954909	-.5017205
intD	-.6107918	.1262348	-4.84	0.000	-.8628276	-.3587559
pC	-.003398	.0043568	-0.78	0.438	-.0120967	.0053007
pD	.0105605	.0085823	1.23	0.223	-.0065746	.0276957
rho	.6660576					

Durbin-Watson statistic (original) 0.715365
Durbin-Watson statistic (transformed) 1.979178

Appendix 14

Comparison of intD-intC

(1) - intC + intD = 0

Weight SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	.117523	.1338585	0.88	0.383	-.1497342	.3847802

Comparison of pD-pC

(1) - pC + pD = 0

Weight SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	.0139585	.010556	1.32	0.191	-.0071171	.0350342

Period C (full implementation 2012) vs D (post implementation 2013)
Change in Head Circumference SDS from Birth

Prais-Winsten AR(1) regression -- iterated estimates

Source	SS	df	MS		
Model	.575619345	3	.191873115	Number of obs =	70
Residual	11.4008231	66	.172739745	F(3, 66) =	1.11
Total	11.9764425	69	.17357163	Prob > F =	0.3511
				R-squared =	0.0481
				Adj R-squared =	0.0048
				Root MSE =	.41562

Head Circ SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
intC	-1.068958	.3183215	-3.36	0.001	-1.704507	-.4334083
intD	-1.047317	.3559348	-2.94	0.004	-1.757964	-.3366704
pC	-.0113848	.012226	-0.93	0.355	-.0357948	.0130253
pD	.0228073	.0242054	0.94	0.350	-.0255204	.0711351
rho	.6541611					

Durbin-Watson statistic (original) 0.700575
Durbin-Watson statistic (transformed) 1.999096

Comparison of intD-intC

(1) - intC + intD = 0

Head Circ SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	.0216404	.382367	0.06	0.955	-.74178	.7850608

Comparison of pD-pC

(1) - pC + pD = 0

Head Circ SDS diff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]	
(1)	.0341921	.0296209	1.15	0.253	-.0249478	.0933321

Appendix 15: Statistical models from Repeated Measures Analysis using Generalised Linear Modelling

Generalised Linear Model with Mixed Effects for Energy delivered per kg per day (unadjusted)

Model Information

Response Variable	Energy Delivered Per Kg Per Day
Response Distribution	Gaussian
Link Function	Identity
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Restricted Maximum Likelihood
Degrees of Freedom Method	Containment

Number of Observations Read	10394
Number of Observations Used	10387

Dimensions

G-side Cov. Parameters	1
R-side Cov. Parameters	2
Columns in X	5
Columns in Z per Subject	1
Subjects (Blocks in V)	194
Max Obs per Subject	162

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	2
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Profiled
Residual Variance	Profiled
Starting From	Data

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	**0**	4	99394.475479	.	905.6749
1	**0**	5	99363.937155	30.53832448	95.90735
2	**0**	4	99361.13576	2.80139431	94.70402
3	**0**	2	99360.045511	1.09024907	36.60636
4	**0**	2	99359.679409	0.36610195	10.27021
5	**0**	2	99359.653399	0.02601068	1.729736
6	**0**	3	99359.652685	0.00071323	0.067122
7	**0**	3	99359.652684	0.00000108	0.000092

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics	
-2 Res Log Likelihood	99359.65
AIC (smaller is better)	99365.65
AICC (smaller is better)	99365.65
BIC (smaller is better)	99375.46
CAIC (smaller is better)	99378.46
HQIC (smaller is better)	99369.62
Generalized Chi-Square	8310442
Gener. Chi-Square / DF	800.39

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	ID	128.69	24.5616
CS	ID	48.5674	.
Residual		800.39	11.2540

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper	Mean	Standard Error Mean	Lower Mean	Upper Mean
1	115.17	1.7216	10190	66.90	<.0001	0.05	111.79	118.54	115.17	1.7216	111.79	118.54
2	115.77	1.6146	10190	71.70	<.0001	0.05	112.61	118.94	115.77	1.6146	112.61	118.94
3	117.87	1.3511	10190	87.24	<.0001	0.05	115.23	120.52	117.87	1.3511	115.23	120.52
4	120.45	1.8474	10190	65.20	<.0001	0.05	116.83	124.07	120.45	1.8474	116.83	124.07

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-0.6010	1.7566	10190	-0.34	0.7322	0.9862	0.05	-4.0442	2.8422	-5.1144	3.9124
1	3	-2.7039	2.0458	10190	-1.32	0.1863	0.5491	0.05	-6.7141	1.3064	-7.9605	2.5528
1	4	-5.2789	2.4757	10190	-2.13	0.0330	0.1429	0.05	-10.1316	-0.4261	-11.6399	1.0822
2	3	-2.1029	1.7791	10190	-1.18	0.2372	0.6383	0.05	-5.5902	1.3845	-6.6742	2.4684
2	4	-4.6779	2.3451	10190	-1.99	0.0461	0.1900	0.05	-9.2748	-0.08097	-10.7035	1.3478
3	4	-2.5750	1.9339	10190	-1.33	0.1830	0.5428	0.05	-6.3658	1.2157	-7.5440	2.3939

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|
1	115.17	1.7216	10190	66.90	<.0001
2	115.77	1.6146	10190	71.70	<.0001
3	117.87	1.3511	10190	87.24	<.0001
4	120.45	1.8474	10190	65.20	<.0001

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P
1	2	-0.6010	1.7566	10190	-0.34	0.7322	0.9862
1	3	-2.7039	2.0458	10190	-1.32	0.1863	0.5491
1	4	-5.2789	2.4757	10190	-2.13	0.0330	0.1429
2	3	-2.1029	1.7791	10190	-1.18	0.2372	0.6383
2	4	-4.6779	2.3451	10190	-1.99	0.0461	0.1900
3	4	-2.5750	1.9339	10190	-1.33	0.1830	0.5428

Generalised Linear Model with Mixed Effects for Protein delivered per kg per day (unadjusted)

Model Information

Response Variable	Protein Delivered Per Kg Per Day
Response Distribution	Gaussian
Link Function	Identity
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Restricted Maximum Likelihood
Degrees of Freedom Method	Containment

Number of Observations Read	10394
Number of Observations Used	10387

Dimensions

G-side Cov. Parameters	1
R-side Cov. Parameters	2
Columns in X	5
Columns in Z per Subject	1
Subjects (Blocks in V)	194
Max Obs per Subject	162

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	2
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Profiled
Residual Variance	Profiled
Starting From	Data

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	**0**	4	27459.48013	.	598.4016
1	**0**	5	27439.893771	19.58635840	53.14357
2	**0**	4	27439.141772	0.75199946	7.195221
3	**0**	2	27439.131893	0.00987896	1.545632
4	**0**	2	27439.131396	0.00049685	0.035475
5	**0**	2	27439.131396	0.00000026	0.00018

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics

-2 Res Log Likelihood	27439.13
AIC (smaller is better)	27445.13
AICC (smaller is better)	27445.13
BIC (smaller is better)	27454.93
CAIC (smaller is better)	27457.93
HQIC (smaller is better)	27449.10
Generalized Chi-Square	8155.36
Gener. Chi-Square / DF	0.79

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	**ID**	0.1349	0.02235
CS	**ID**	0.03731	.
Residual		0.7855	0.01103

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper	Mean	Standard Error Mean	Lower Mean	Upper Mean
1	2.8715	0.05375	10190	53.42	<.0001	0.05	2.7661	2.9768	2.8715	0.05375	2.7661	2.9768
2	3.0874	0.05044	10190	61.21	<.0001	0.05	2.9885	3.1863	3.0874	0.05044	2.9885	3.1863
3	3.2016	0.04218	10190	75.91	<.0001	0.05	3.1189	3.2843	3.2016	0.04218	3.1189	3.2843
4	3.3438	0.05769	10190	57.97	<.0001	0.05	3.2308	3.4569	3.3438	0.05769	3.2308	3.4569

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-0.2159	0.05496	10190	-3.93	<.0001	0.0005	0.05	-0.3236	-0.1082	-0.3571	-0.07472
1	3	-0.3301	0.06392	10190	-5.17	<.0001	<.0001	0.05	-0.4554	-0.2048	-0.4944	-0.1659
1	4	-0.4724	0.07733	10190	-6.11	<.0001	<.0001	0.05	-0.6239	-0.3208	-0.6711	-0.2737
2	3	-0.1142	0.05563	10190	-2.05	0.0401	0.1688	0.05	-0.2233	-0.00517	-0.2571	0.02872
2	4	-0.2564	0.07328	10190	-3.50	0.0005	0.0026	0.05	-0.4001	-0.1128	-0.4447	-0.06815
3	4	-0.1422	0.06045	10190	-2.35	0.0187	0.0865	0.05	-0.2607	-0.02373	-0.2976	0.01310

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|
1	2.8715	0.05375	10190	53.42	<.0001
2	3.0874	0.05044	10190	61.21	<.0001
3	3.2016	0.04218	10190	75.91	<.0001
4	3.3438	0.05769	10190	57.97	<.0001

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P
1	2	-0.2159	0.05496	10190	-3.93	<.0001	0.0005
1	3	-0.3301	0.06392	10190	-5.17	<.0001	<.0001
1	4	-0.4724	0.07733	10190	-6.11	<.0001	<.0001
2	3	-0.1142	0.05563	10190	-2.05	0.0401	0.1688
2	4	-0.2564	0.07328	10190	-3.50	0.0005	0.0026
3	4	-0.1422	0.06045	10190	-2.35	0.0187	0.0865

Generalised Linear Model with Mixed Effects for Energy delivered as a percentage of RRI per day (unadjusted)

Model Information	
Response Variable	Energy delivered as a percentage of RRI per day
Response Distribution	Gaussian
Link Function	Identity
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Restricted Maximum Likelihood
Degrees of Freedom Method	Containment

Number of Observations Read	10394
Number of Observations Used	10387

Dimensions	
G-side Cov. Parameters	1
R-side Cov. Parameters	2
Columns in X	5
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Subjects (Blocks in V)	194
Max Obs per Subject	162

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	2
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Profiled
Residual Variance	Profiled
Starting From	Data

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	**0**	4	93147.513061	.	840.0543
1	**0**	5	93130.201244	17.31181650	144.0159
2	**0**	4	93127.562436	2.63880830	225.5344
3	**0**	2	93123.883619	3.67881641	44.82335
4	**0**	2	93123.670484	0.21313506	14.65987
5	**0**	2	93123.642265	0.02821972	1.498265
6	**0**	3	93123.641952	0.00031207	0.032998

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics

-2 Res Log Likelihood	93123.64
AIC (smaller is better)	93129.64
AICC (smaller is better)	93129.64
BIC (smaller is better)	93139.45
CAIC (smaller is better)	93142.45
HQIC (smaller is better)	93133.61
Generalized Chi-Square	4576931
Gener. Chi-Square / DF	440.81

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	**ID**	57.1873	10.3171
CS	**ID**	18.1129	.
Residual		440.81	6.1915

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper	Mean	Standard Error Mean	Lower Mean	Upper Mean
1	105.31	1.1740	10190	89.70	<.0001	0.05	103.00	107.61	105.31	1.1740	103.00	107.61
2	102.69	1.1181	10190	91.84	<.0001	0.05	100.50	104.88	102.69	1.1181	100.50	104.88
3	100.75	0.9168	10190	109.89	<.0001	0.05	98.9493	102.54	100.75	0.9168	98.9493	102.54
4	96.5032	1.2621	10190	76.46	<.0001	0.05	94.0292	98.9773	96.5032	1.2621	94.0292	98.9773

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	2.6121	1.2594	10190	2.07	0.0381	0.1616	0.05	0.1435	5.0807	-0.6237	5.8479
1	3	4.5589	1.4163	10190	3.22	0.0013	0.0071	0.05	1.7826	7.3352	0.9197	8.1981
1	4	8.8020	1.7019	10190	5.17	<.0001	<.0001	0.05	5.4660	12.1381	4.4291	13.1750
2	3	1.9468	1.2573	10190	1.55	0.1215	0.4085	0.05	-0.5177	4.4113	-1.2836	5.1772
2	4	6.1899	1.6322	10190	3.79	0.0002	0.0009	0.05	2.9905	9.3893	1.9961	10.3837
3	4	4.2431	1.3575	10190	3.13	0.0018	0.0096	0.05	1.5822	6.9041	0.7551	7.7311

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|
1	105.31	1.1740	10190	89.70	<.0001
2	102.69	1.1181	10190	91.84	<.0001
3	100.75	0.9168	10190	109.89	<.0001
4	96.5032	1.2621	10190	76.46	<.0001

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P
1	**2**	2.6121	1.2594	10190	2.07	0.0381	0.1616
1	**3**	4.5589	1.4163	10190	3.22	0.0013	0.0071
1	**4**	8.8020	1.7019	10190	5.17	<.0001	<.0001
2	**3**	1.9468	1.2573	10190	1.55	0.1215	0.4085
2	**4**	6.1899	1.6322	10190	3.79	0.0002	0.0009
3	**4**	4.2431	1.3575	10190	3.13	0.0018	0.0096

Generalised Linear Model with Mixed Effects for Protein delivered as a percentage of RRI per day (unadjusted)

Model Information	
Response Variable	Protein delivered as a percentage of RRI per day
Response Distribution	Gaussian
Link Function	Identity
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Restricted Maximum Likelihood
Degrees of Freedom Method	Containment

Number of Observations Read	10394
Number of Observations Used	10387

Dimensions	
G-side Cov. Parameters	1
R-side Cov. Parameters	2
Columns in X	5
Columns in Z per Subject	1
Subjects (Blocks in V)	194
Max Obs per Subject	162

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	2
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Profiled
Residual Variance	Profiled
Starting From	Data

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	**0**	4	92662.385555	.	755.0893
1	**0**	5	92647.988486	14.39706933	142.9333
2	**0**	4	92644.220237	3.76824948	120.9658
3	**0**	2	92643.355833	0.86440353	52.3551
4	**0**	2	92642.972383	0.38344988	13.50835
5	**0**	2	92642.949679	0.02270405	2.254917
6	**0**	3	92642.949064	0.00061470	0.079812
7	**0**	3	92642.949064	0.00000078	0.000091

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics

-2 Res Log Likelihood	92642.95
AIC (smaller is better)	92648.95
AICC (smaller is better)	92648.95
BIC (smaller is better)	92658.75
CAIC (smaller is better)	92661.75
HQIC (smaller is better)	92652.92
Generalized Chi-Square	4373361
Gener. Chi-Square / DF	421.20

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	**ID**	53.2660	9.2083
CS	**ID**	15.0783	.
Residual		421.20	5.9129

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper	Mean	Standard Error Mean	Lower Mean	Upper Mean
1	79.5620	1.1285	10190	70.50	<.0001	0.05	77.3499	81.7741	79.5620	1.1285	77.3499	81.7741
2	83.5327	1.0783	10190	77.46	<.0001	0.05	81.4190	85.6465	83.5327	1.0783	81.4190	85.6465
3	85.6979	0.8805	10190	97.33	<.0001	0.05	83.9718	87.4239	85.6979	0.8805	83.9718	87.4239
4	86.7942	1.2135	10190	71.52	<.0001	0.05	84.4155	89.1729	86.7942	1.2135	84.4155	89.1729

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-3.9708	1.2222	10190	-3.25	0.0012	0.0064	0.05	-6.3664	-1.5751	-7.1110	-0.8305
1	3	-6.1359	1.3650	10190	-4.50	<.0001	<.0001	0.05	-8.8116	-3.4601	-9.6433	-2.6285
1	4	-7.2322	1.6380	10190	-4.42	<.0001	<.0001	0.05	-10.4430	-4.0214	-11.4410	-3.0235
2	3	-2.1651	1.2167	10190	-1.78	0.0752	0.2833	0.05	-4.5502	0.2199	-5.2915	0.9612
2	4	-3.2615	1.5747	10190	-2.07	0.0384	0.1627	0.05	-6.3482	-0.1747	-7.3076	0.7847
3	4	-1.0963	1.3117	10190	-0.84	0.4033	0.8374	0.05	-3.6674	1.4748	-4.4666	2.2739

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|
1	79.5620	1.1285	10190	70.50	<.0001
2	83.5327	1.0783	10190	77.46	<.0001
3	85.6979	0.8805	10190	97.33	<.0001
4	86.7942	1.2135	10190	71.52	<.0001

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P
1	2	-3.9708	1.2222	10190	-3.25	0.0012	0.0064
1	3	-6.1359	1.3650	10190	-4.50	<.0001	<.0001
1	4	-7.2322	1.6380	10190	-4.42	<.0001	<.0001
2	3	-2.1651	1.2167	10190	-1.78	0.0752	0.2833
2	4	-3.2615	1.5747	10190	-2.07	0.0384	0.1627
3	4	-1.0963	1.3117	10190	-0.84	0.4033	0.8374

Generalised Linear Model with Mixed Effects for Energy delivered per kg per day (adjusted for sex, gestational age and weight at birth)

Model Information

Response Variable	Energy Delivered Per Kg Per Day
Response Distribution	Gaussian
Link Function	Identity
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Restricted Maximum Likelihood
Degrees of Freedom Method	Containment

Number of Observations Read	10394
Number of Observations Used	10387

Dimensions

G-side Cov. Parameters	1
R-side Cov. Parameters	2
Columns in X	8
Columns in Z per Subject	1
Subjects (Blocks in V)	194
Max Obs per Subject	162

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	2
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Profiled
Residual Variance	Profiled
Starting From	Data

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	**0**	4	99384.332189	.	961.8778
1	**0**	5	99352.456422	31.87576758	101.5597
2	**0**	4	99350.359761	2.09666074	150.8515
3	**0**	2	99347.378655	2.98110602	32.11359
4	**0**	2	99347.183729	0.19492625	9.909188
5	**0**	2	99347.161075	0.02265393	0.988956
6	**0**	3	99347.160837	0.00023788	0.019506

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics

-2 Res Log Likelihood	99347.16
AIC (smaller is better)	99353.16
AICC (smaller is better)	99353.16
BIC (smaller is better)	99362.96
CAIC (smaller is better)	99365.96
HQIC (smaller is better)	99357.13
Generalized Chi-Square	8307391
Gener. Chi-Square / DF	800.33

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	**ID**	126.94	24.7560
CS	**ID**	49.7799	.
Residual		800.33	11.2532

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper	Mean	Standard Error Mean	Lower Mean	Upper Mean
1	114.51	1.7583	10189	65.13	<.0001	0.05	111.07	117.96	114.51	1.7583	111.07	117.96
2	115.21	1.6390	10189	70.30	<.0001	0.05	112.00	118.42	115.21	1.6390	112.00	118.42
3	117.49	1.3631	10189	86.19	<.0001	0.05	114.82	120.16	117.49	1.3631	114.82	120.16
4	120.25	1.8567	10189	64.76	<.0001	0.05	116.61	123.89	120.25	1.8567	116.61	123.89

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-0.6982	1.7585	10189	-0.40	0.6913	0.9788	0.05	-4.1453	2.7488	-5.2167	3.8202
1	3	-2.9740	2.0544	10189	-1.45	0.1478	0.4696	0.05	-7.0011	1.0532	-8.2527	2.3048
1	4	-5.7332	2.5047	10189	-2.29	0.0221	0.1006	0.05	-10.6429	-0.8234	-12.1689	0.7025
2	3	-2.2757	1.7816	10189	-1.28	0.2015	0.5774	0.05	-5.7680	1.2165	-6.8534	2.3019
2	4	-5.0349	2.3649	10189	-2.13	0.0333	0.1440	0.05	-9.6707	-0.3992	-11.1115	1.0417
3	4	-2.7592	1.9475	10189	-1.42	0.1566	0.4888	0.05	-6.5767	1.0582	-7.7632	2.2447

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|
1	114.51	1.7583	10189	65.13	<.0001
2	115.21	1.6390	10189	70.30	<.0001
3	117.49	1.3631	10189	86.19	<.0001
4	120.25	1.8567	10189	64.76	<.0001

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P
1	**2**	-0.6982	1.7585	10189	-0.40	0.6913	0.9788
1	**3**	-2.9740	2.0544	10189	-1.45	0.1478	0.4696
1	**4**	-5.7332	2.5047	10189	-2.29	0.0221	0.1006
2	**3**	-2.2757	1.7816	10189	-1.28	0.2015	0.5774
2	**4**	-5.0349	2.3649	10189	-2.13	0.0333	0.1440
3	**4**	-2.7592	1.9475	10189	-1.42	0.1566	0.4888

Generalised Linear Model with Mixed Effects for Protein delivered per kg per day (adjusted for sex, gestational age and weight at birth)

Model Information

Response Variable	Protein Delivered Per Kg Per Day
Response Distribution	Gaussian
Link Function	Identity
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Restricted Maximum Likelihood
Degrees of Freedom Method	Containment

Number of Observations Read	10394
Number of Observations Used	10387

Dimensions

G-side Cov. Parameters	1
R-side Cov. Parameters	2
Columns in X	8
Columns in Z per Subject	1
Subjects (Blocks in V)	194
Max Obs per Subject	162

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	2
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Profiled
Residual Variance	Profiled
Starting From	Data

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	**0**	4	27473.821715	.	639.5332
1	**0**	5	27452.174374	21.64734045	58.29848
2	**0**	4	27451.185209	0.98916519	10.43086
3	**0**	2	27451.164034	0.02117500	2.606152
4	**0**	2	27451.162536	0.00149780	0.089037
5	**0**	2	27451.162534	0.00000173	0.000793

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics

-2 Res Log Likelihood	27451.16
AIC (smaller is better)	27457.16
AICC (smaller is better)	27457.16
BIC (smaller is better)	27466.97
CAIC (smaller is better)	27469.97
HQIC (smaller is better)	27461.13
Generalized Chi-Square	8152.67
Gener. Chi-Square / DF	0.79

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	**ID**	0.1355	0.02296
CS	**ID**	0.03971	.
Residual		0.7854	0.01103

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper	Mean	Standard Error Mean	Lower Mean	Upper Mean
1	2.8698	0.05526	10189	51.93	<.0001	0.05	2.7615	2.9782	2.8698	0.05526	2.7615	2.9782
2	3.0852	0.05149	10189	59.92	<.0001	0.05	2.9842	3.1861	3.0852	0.05149	2.9842	3.1861
3	3.1999	0.04285	10189	74.67	<.0001	0.05	3.1159	3.2839	3.1999	0.04285	3.1159	3.2839
4	3.3425	0.05835	10189	57.28	<.0001	0.05	3.2281	3.4569	3.3425	0.05835	3.2281	3.4569

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-0.2153	0.05516	10189	-3.90	<.0001	0.0006	0.05	-0.3235	-0.1072	-0.3571	-0.07360
1	3	-0.3301	0.06453	10189	-5.12	<.0001	<.0001	0.05	-0.4566	-0.2036	-0.4959	-0.1643
1	4	-0.4726	0.07869	10189	-6.01	<.0001	<.0001	0.05	-0.6269	-0.3184	-0.6748	-0.2705
2	3	-0.1148	0.05591	10189	-2.05	0.0401	0.1689	0.05	-0.2244	-0.00518	-0.2584	0.02889
2	4	-0.2573	0.07426	10189	-3.46	0.0005	0.0030	0.05	-0.4029	-0.1117	-0.4481	-0.06650
3	4	-0.1425	0.06113	10189	-2.33	0.0197	0.0910	0.05	-0.2624	-0.02271	-0.2996	0.01454

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|
1	2.8698	0.05526	10189	51.93	<.0001
2	3.0852	0.05149	10189	59.92	<.0001
3	3.1999	0.04285	10189	74.67	<.0001
4	3.3425	0.05835	10189	57.28	<.0001

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P
1	2	-0.2153	0.05516	10189	-3.90	<.0001	0.0006
1	3	-0.3301	0.06453	10189	-5.12	<.0001	<.0001
1	4	-0.4726	0.07869	10189	-6.01	<.0001	<.0001
2	3	-0.1148	0.05591	10189	-2.05	0.0401	0.1689
2	4	-0.2573	0.07426	10189	-3.46	0.0005	0.0030
3	4	-0.1425	0.06113	10189	-2.33	0.0197	0.0910

Generalised Linear Model with Mixed Effects for Energy delivered as a percentage of RRI per day (adjusted for sex, gestational age and weight at birth)

The GLIMMIX Procedure

Model Information

Response Variable	Energy delivered as a percentage of RRI per day
Response Distribution	Gaussian
Link Function	Identity
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Restricted Maximum Likelihood
Degrees of Freedom Method	Containment

Number of Observations Read	10394
Number of Observations Used	10387

Dimensions

G-side Cov. Parameters	1
R-side Cov. Parameters	2
Columns in X	8
Columns in Z per Subject	1
Subjects (Blocks in V)	194
Max Obs per Subject	162

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	2
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Profiled
Residual Variance	Profiled
Starting From	Data

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	**0**	4	93068.657603	.	893.9164
1	**0**	6	93056.156278	12.50132466	142.005
2	**0**	4	93054.431545	1.72473291	39.00116
3	**0**	2	93054.363059	0.06848659	13.77971
4	**0**	2	93054.351818	0.01124117	0.937329
5	**0**	2	93054.351767	0.00005056	0.024609

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics

-2 Res Log Likelihood	93054.35
AIC (smaller is better)	93060.35
AICC (smaller is better)	93060.35
BIC (smaller is better)	93070.16
CAIC (smaller is better)	93073.16
HQIC (smaller is better)	93064.32
Generalized Chi-Square	4585831
Gener. Chi-Square / DF	441.79

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	**ID**	34.1212	6.6305
CS	**ID**	9.5515	.
Residual		441.79	6.2063

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper	Mean	Standard Error Mean	Lower Mean	Upper Mean
1	102.42	1.0031	10189	102.10	<.0001	0.05	100.45	104.39	102.42	1.0031	100.45	104.39
2	100.86	0.9835	10189	102.56	<.0001	0.05	98.9338	102.79	100.86	0.9835	98.9338	102.79
3	100.58	0.7695	10189	130.70	<.0001	0.05	99.0698	102.09	100.58	0.7695	99.0698	102.09
4	97.2719	1.0659	10189	91.26	<.0001	0.05	95.1826	99.3611	97.2719	1.0659	95.1826	99.3611

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	1.5594	1.1617	10189	1.34	0.1795	0.5359	0.05	-0.7178	3.8367	-1.4256	4.5444
1	3	1.8428	1.2198	10189	1.51	0.1309	0.4310	0.05	-0.5482	4.2339	-1.2914	4.9770
1	4	5.1492	1.4590	10189	3.53	0.0004	0.0024	0.05	2.2892	8.0092	1.4003	8.8981
2	3	0.2834	1.1281	10189	0.25	0.8017	0.9944	0.05	-1.9279	2.4947	-2.6152	3.1820
2	4	3.5898	1.4292	10189	2.51	0.0120	0.0582	0.05	0.7882	6.3913	-0.08259	7.2621
3	4	3.3064	1.2037	10189	2.75	0.0060	0.0307	0.05	0.9469	5.6659	0.2135	6.3992

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|
1	102.42	1.0031	10189	102.10	<.0001
2	100.86	0.9835	10189	102.56	<.0001
3	100.58	0.7695	10189	130.70	<.0001
4	97.2719	1.0659	10189	91.26	<.0001

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P
1	**2**	1.5594	1.1617	10189	1.34	0.1795	0.5359
1	**3**	1.8428	1.2198	10189	1.51	0.1309	0.4310
1	**4**	5.1492	1.4590	10189	3.53	0.0004	0.0024
2	**3**	0.2834	1.1281	10189	0.25	0.8017	0.9944
2	**4**	3.5898	1.4292	10189	2.51	0.0120	0.0582
3	**4**	3.3064	1.2037	10189	2.75	0.0060	0.0307

Generalised Linear Model with Mixed Effects for Protein delivered as a percentage of RRI per day (adjusted for sex, gestational age and weight at birth)

Model Information

Response Variable	Protein delivered as a percentage of RRI per day
Response Distribution	Gaussian
Link Function	Identity
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Restricted Maximum Likelihood
Degrees of Freedom Method	Containment

Number of Observations Read	10394
Number of Observations Used	10387

Dimensions

G-side Cov. Parameters	1
R-side Cov. Parameters	2
Columns in X	8
Columns in Z per Subject	1
Subjects (Blocks in V)	194
Max Obs per Subject	162

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	2
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Profiled
Residual Variance	Profiled
Starting From	Data

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	**0**	4	92655.690775	.	783.8821
1	**0**	5	92640.706152	14.98462395	145.2878
2	**0**	4	92637.09169	3.61446133	158.54
3	**0**	2	92635.730908	1.36078182	65.21602
4	**0**	2	92635.097453	0.63345497	21.46179
5	**0**	2	92635.037757	0.05969681	5.043639
6	**0**	3	92635.034618	0.00313826	0.391461
7	**0**	3	92635.034599	0.00001938	0.002223

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics

-2 Res Log Likelihood	92635.03
AIC (smaller is better)	92641.03
AICC (smaller is better)	92641.04
BIC (smaller is better)	92650.84
CAIC (smaller is better)	92653.84
HQIC (smaller is better)	92645.00
Generalized Chi-Square	4371798
Gener. Chi-Square / DF	421.18

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	**ID**	53.2417	9.3709
CS	**ID**	15.6388	.
Residual		421.18	5.9126

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper	Mean	Standard Error Mean	Lower Mean	Upper Mean
1	79.1850	1.1551	10189	68.55	<.0001	0.05	76.9208	81.4492	79.1850	1.1551	76.9208	81.4492
2	83.2507	1.0958	10189	75.97	<.0001	0.05	81.1028	85.3987	83.2507	1.0958	81.1028	85.3987
3	85.5303	0.8909	10189	96.01	<.0001	0.05	83.7840	87.2765	85.5303	0.8909	83.7840	87.2765
4	86.8184	1.2244	10189	70.91	<.0001	0.05	84.4183	89.2184	86.8184	1.2244	84.4183	89.2184

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-4.0657	1.2253	10189	-3.32	0.0009	0.0050	0.05	-6.4676	-1.6638	-7.2141	-0.9173
1	3	-6.3452	1.3746	10189	-4.62	<.0001	<.0001	0.05	-9.0397	-3.6508	-9.8771	-2.8133
1	4	-7.6333	1.6636	10189	-4.59	<.0001	<.0001	0.05	-10.8943	-4.3723	-11.9079	-3.3588
2	3	-2.2795	1.2206	10189	-1.87	0.0619	0.2422	0.05	-4.6722	0.1132	-5.4159	0.8568
2	4	-3.5676	1.5930	10189	-2.24	0.0251	0.1127	0.05	-6.6902	-0.4451	-7.6607	0.5254
3	4	-1.2881	1.3253	10189	-0.97	0.3311	0.7655	0.05	-3.8860	1.3098	-4.6934	2.1172

Study Period Least Squares Means

Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|
1	79.1850	1.1551	10189	68.55	<.0001
2	83.2507	1.0958	10189	75.97	<.0001
3	85.5303	0.8909	10189	96.01	<.0001
4	86.8184	1.2244	10189	70.91	<.0001

Differences of Study Period Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P
1	**2**	-4.0657	1.2253	10189	-3.32	0.0009	0.0050
1	**3**	-6.3452	1.3746	10189	-4.62	<.0001	<.0001
1	**4**	-7.6333	1.6636	10189	-4.59	<.0001	<.0001
2	**3**	-2.2795	1.2206	10189	-1.87	0.0619	0.2422
2	**4**	-3.5676	1.5930	10189	-2.24	0.0251	0.1127
3	**4**	-1.2881	1.3253	10189	-0.97	0.3311	0.7655

General Linear Model with Mixed Effects for Change in Weight SDS over stay (unadjusted)

Model Information

Dependent Variable	Change in Weight SDS over stay
Covariance Structures	Variance Components, Compound Symmetry
Subject Effects	ID, ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	5
Columns in Z Per Subject	1
Subjects	194
Max Obs Per Subject	162

Number of Observations

Number of Observations Read	10394
Number of Observations Used	3820
Number of Observations Not Used	6574

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	6933.03471419	
1	3	3957.92395369	0.28223230
2	1	3956.09798775	0.01714840
3	1	3955.93932476	0.00011392
4	1	3955.93814710	0.00000001

Convergence criteria met but final hessian is not positive definite.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
Intercept	**ID**	0.1862
CS	**ID**	0.01477
Residual		0.1403

Fit Statistics

-2 Res Log Likelihood	3955.9
AIC (smaller is better)	3961.9
AICC (smaller is better)	3961.9
BIC (smaller is better)	3971.7

Least Squares Means

Effect	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Study Period	1	-0.9409	0.05031	3628	-18.70	<.0001	0.05	-1.0395	-0.8422
Study Period	2	-0.6773	0.04596	3628	-14.74	<.0001	0.05	-0.7674	-0.5872
Study Period	3	-0.4761	0.04051	3628	-11.75	<.0001	0.05	-0.5555	-0.3966
Study Period	4	-0.3419	0.05240	3628	-6.53	<.0001	0.05	-0.4447	-0.2392

Differences of Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-0.2636	0.04177	3628	-6.31	<.0001	<.0001	0.05	-0.3455	-0.1817	-0.3709	-0.1562
1	3	-0.4648	0.05502	3628	-8.45	<.0001	<.0001	0.05	-0.5727	-0.3569	-0.6062	-0.3234
1	4	-0.5989	0.06753	3628	-8.87	<.0001	<.0001	0.05	-0.7313	-0.4665	-0.7725	-0.4254
2	3	-0.2012	0.04567	3628	-4.41	<.0001	<.0001	0.05	-0.2908	-0.1117	-0.3186	-0.08387
2	4	-0.3354	0.06175	3628	-5.43	<.0001	<.0001	0.05	-0.4564	-0.2143	-0.4941	-0.1766
3	4	-0.1341	0.04829	3628	-2.78	0.0055	0.0282	0.05	-0.2288	-0.03945	-0.2583	-0.01002

General Linear Model with Mixed Effects for Change in Weight SDS over stay (adjusted for sex, gestational age and weight at birth)

Model Information

Dependent Variable	Change in Weight SDS over stay
Covariance Structures	Variance Components, Compound Symmetry
Subject Effects	ID, ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	8
Columns in Z Per Subject	1
Subjects	194
Max Obs Per Subject	162

Number of Observations

Number of Observations Read	10394
Number of Observations Used	3820
Number of Observations Not Used	6574

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	6465.63045887	
1	2	3947.30309567	0.80360565
2	1	3947.16167773	0.80268626
3	1	3947.15283173	0.80262817
4	1	3947.14884045	0.80260194
5	1	3947.14835214	0.80259884
6	1	3947.14798470	0.08308832
7	2	3923.89224704	0.00030622
8	1	3923.38073872	0.00145830
9	1	3923.37148052	0.00000065
10	1	3923.37147627	0.00000000

Convergence criteria met but final hessian is not positive definite.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
Intercept	**ID**	0.1560
CS	**ID**	-0.00121
Residual		0.1405

Fit Statistics

-2 Res Log Likelihood	3923.4
AIC (smaller is better)	3929.4
AICC (smaller is better)	3929.4
BIC (smaller is better)	3939.2

Least Squares Means

Effect	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Study Period	**1**	-0.9392	0.04721	3627	-19.89	<.0001	0.05	-1.0317	-0.8466
Study Period	**2**	-0.6933	0.04327	3627	-16.02	<.0001	0.05	-0.7782	-0.6085
Study Period	**3**	-0.5098	0.03716	3627	-13.72	<.0001	0.05	-0.5827	-0.4370
Study Period	**4**	-0.3911	0.04866	3627	-8.04	<.0001	0.05	-0.4865	-0.2957

Differences of Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-0.2458	0.04090	3627	-6.01	<.0001	<.0001	0.05	-0.3260	-0.1657	-0.3510	-0.1407
1	3	-0.4294	0.05238	3627	-8.20	<.0001	<.0001	0.05	-0.5321	-0.3267	-0.5640	-0.2947
1	4	-0.5481	0.06425	3627	-8.53	<.0001	<.0001	0.05	-0.6741	-0.4221	-0.7132	-0.3830
2	3	-0.1835	0.04404	3627	-4.17	<.0001	0.0002	0.05	-0.2699	-0.09718	-0.2967	-0.07033
2	4	-0.3022	0.05925	3627	-5.10	<.0001	<.0001	0.05	-0.4184	-0.1861	-0.4545	-0.1500
3	4	-0.1187	0.04683	3627	-2.53	0.0113	0.0549	0.05	-0.2105	-0.02690	-0.2391	0.001649

General Linear Model with Mixed Effects for Change in Head Circumference SDS over stay (unadjusted)

Model Information

Dependent Variable	Change in Head Circumference SDS over stay
Covariance Structures	Variance Components, Compound Symmetry
Subject Effects	ID, ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	5
Columns in Z Per Subject	1
Subjects	194
Max Obs Per Subject	162

Number of Observations

Number of Observations Read	10394
Number of Observations Used	895
Number of Observations Not Used	9499

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	2543.19451212	
1	2	2200.72356697	0.00211767
2	1	2200.71945577	0.00000126
3	1	2200.71945327	0.00000000

Convergence criteria met but final hessian is not positive definite.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
Intercept	**ID**	0.5084
CS	**ID**	0.01607
Residual		0.5016

Fit Statistics

-2 Res Log Likelihood	2200.7
AIC (smaller is better)	2206.7
AICC (smaller is better)	2206.7
BIC (smaller is better)	2216.5

Least Squares Means

Effect	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Study Period	1	-0.9886	0.1537	745	-6.43	<.0001	0.05	-1.2904	-0.6869
Study Period	2	-0.8186	0.1377	745	-5.94	<.0001	0.05	-1.0890	-0.5482
Study Period	3	-0.6850	0.08650	745	-7.92	<.0001	0.05	-0.8548	-0.5152
Study Period	4	-0.5708	0.1201	745	-4.75	<.0001	0.05	-0.8066	-0.3351

Differences of Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-0.1700	0.1968	745	-0.86	0.3878	0.8233	0.05	-0.5563	0.2162	-0.6767	0.3366
1	3	-0.3036	0.1748	745	-1.74	0.0829	0.3054	0.05	-0.6469	0.03962	-0.7538	0.1466
1	4	-0.4178	0.1947	745	-2.15	0.0322	0.1396	0.05	-0.8000	-0.03567	-0.9190	0.08339
2	3	-0.1336	0.1457	745	-0.92	0.3595	0.7958	0.05	-0.4196	0.1524	-0.5087	0.2415
2	4	-0.2478	0.1787	745	-1.39	0.1660	0.5082	0.05	-0.5986	0.1031	-0.7079	0.2124
3	4	-0.1142	0.1332	745	-0.86	0.3916	0.8269	0.05	-0.3758	0.1474	-0.4572	0.2288

General Linear Model with Mixed Effects for Change in Head Circumference SDS over stay (adjusted for sex, gestational age and weight at birth)

Model Information

Dependent Variable	Change in Head Circumference SDS over stay
Covariance Structures	Variance Components, Compound Symmetry
Subject Effects	ID, ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	8
Columns in Z Per Subject	1
Subjects	194
Max Obs Per Subject	162

Number of Observations

Number of Observations Read	10394
Number of Observations Used	895
Number of Observations Not Used	9499

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	2391.18398666	
1	2	2154.79715874	0.00000007
2	1	2154.79715868	0.00000000

Convergence criteria met but final hessian is not positive definite.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
Intercept	**ID**	0.3400
CS	**ID**	-0.00008
Residual		0.4995

Fit Statistics

-2 Res Log Likelihood	2154.8
AIC (smaller is better)	2160.8
AICC (smaller is better)	2160.8
BIC (smaller is better)	2170.6

Least Squares Means

Effect	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Study Period	1	-1.0574	0.1349	744	-7.84	<.0001	0.05	-1.3222	-0.7926
Study Period	2	-0.9077	0.1251	744	-7.26	<.0001	0.05	-1.1533	-0.6621
Study Period	3	-0.7377	0.07475	744	-9.87	<.0001	0.05	-0.8844	-0.5909
Study Period	4	-0.6449	0.1050	744	-6.14	<.0001	0.05	-0.8510	-0.4388

Differences of Least Squares Means
Adjustment for Multiple Comparisons: Tukey-Kramer

Period based on date in study	Period based on date in study	Estimate	Standard Error	DF	t Value	Pr > |t|	Adj P	Alpha	Lower	Upper	Adj Lower	Adj Upper
1	2	-0.1496	0.1760	744	-0.85	0.3956	0.8304	0.05	-0.4952	0.1959	-0.6029	0.3036
1	3	-0.3197	0.1524	744	-2.10	0.0363	0.1548	0.05	-0.6189	-0.02050	-0.7121	0.07272
1	4	-0.4125	0.1713	744	-2.41	0.0163	0.0765	0.05	-0.7488	-0.07613	-0.8536	0.02867
2	3	-0.1701	0.1339	744	-1.27	0.2045	0.5823	0.05	-0.4329	0.09281	-0.5149	0.1747
2	4	-0.2628	0.1614	744	-1.63	0.1039	0.3632	0.05	-0.5797	0.05403	-0.6784	0.1527
3	4	-0.09277	0.1200	744	-0.77	0.4397	0.8666	0.05	-0.3284	0.1428	-0.4018	0.2162

Appendix 16: Framework Analysis of Interviews

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
1	Band 6	Puts success down to having a dedicated team encouraging everyone to do things- this was the main factor; people "really pushing it...emphasizing the importance of it" Felt guidelines were a secondary factor (and came from the team) Normally guidelines not disseminated well but having people was a big help.	Having a dedicated team was a major help in dissemination- people encouraging it and making it work. Feels practice would slip without continuous reinforcement. Guidelines quite user friendly, especially flow charts which are all easy to access at cotside. "They're quite easy to use, and nice to use"	Felt motivated to use guidelines, especially as they seemed so easy to use and seemed to make a difference.	Generally felt unit committed to new practices. This in part due to a feeling it is making a difference to the babies. Standardised approach and ease of use also helped commitment.	Feels people have more expectations about nutrition and that Southampton now has a reputation for good nutrition and outcomes.
2	Band 6	Felt success down to specific clinical practice changes brought in by the guideline. Also felt increased growth monitoring has meant that the benefits are more obvious and encouraged use of guideline	Teaching and support from nurse champions been helpful, advocates for changes. Nutrition team involvement key	Motivated to follow guidelines by the nutrition team and ward round	Felt unit committed to guidelines, though this has increased over time	Can now see the importance of nutrition more than previously, with more expectations for nutrition. Expect nutrition to be started earlier.
3	Band 4	Puts success down to fact there is a guideline so people know what they are doing. Having the actual guideline itself, readily available was key. Nutrition team also played a part, particularly in relation to improving consistency. Having the same people on the team also helped.	Having a dedicated team made a big difference to practice and helped people be more consistent.	Motivated to following guidelines, mostly due to the benefits for the babies.	Rest of unit seem committed to guideline- can't think of any negative comments. People positive about the changes.	Didn't feel expectations of people changed by guideline.

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
4	Band 5	Word of mouth a major factor, with people reminding each other to use guideline. Increased awareness.	Having actual guidelines in a folder that was easily accessible was key, especially for those working shifts who did not interact with nutrition team. Flow charts important as made it easy to use.Nutrition team also a major factor, and helped reinforce guideline.	Felt motivated to use guideline as was going to help the babies, particularly in relation to monitoring growth more closely.	Felt mostly there was commitment from the unit. Also noted that influx of new staff who had been told that the guideline was the standard helped the established members of nursing staff to use it.	Felt expectations of staff around nutrition changed, particularly around measuring and screening
5	Band 6	Having nutrition team to remind people to measure and follow guideline. Seeing the positive results have also made people more likely to follow it.	Fact guideline is very clear made it easy to follow. The weighing and measuring of babies on a Sunday and screening on a regular basis helped reinforce the practices. Nutrition team reminding people a key factor too.	Initially reasonably motivated to follow guidelines, but became more committed when saw improvements in the babies growth.	Unit generally committed and open to change. Didn't feel massive changes introduce but rather more support.	Nutrition research raised expectations. Increased focus on nutrition has also changed expectations of measuring and growth charts

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
6	ANNP	Attributes success to how well advertised the changes have been. Good awareness of nutrition team activities and seeing end point has provided proof it is important. Nurses understanding has got better which has helped. Different modes used to get team on board a factor Ease of access to guidelines key also Clear end point and benefit to babies helped push the change	Attributes success to how well advertised the changes have been. Good awareness of nutrition team activities and seeing end point has provided proof it is important. Nurses understanding has got better which has helped. Different modes used to get team on board a factor Ease of access to guidelines key also Clarity and accessibility key feature of guideline The fact staff knew implementer was important, as they were familiar and approachable, and delivered clear information on the project.	Motivated to comply as completely agreed with need for better growth in babies. Seeing that the guideline was being pushed by key people (nutrition team) in a structured way increased motivation and made it be taken seriously	Feels that nutrition still a top-down approach with nutrition team and senior doctors at the top, diluted out towards nurses and junior staff Does feel key people (medical staff, ANNPS and senior nursing staff) have been 'hit' and help keep it on the top of the agenda	Nutrition becoming more of a thought and featuring on most ward rounds, which it wasn't before. Staff now expecting nutritional decisions to be made. Expectations gradually changing
7	Band 6	Adherence to guideline main factor in successPuts this down to the core group of people driving it (Nutrition team nurses and doctors) and publicity at the start.Availability and accessibility of guidelines in the folders in the rooms helped too (especially flow charts).Weekly nutrition ward round also a factor in reinforcing	Level of publicity, including AV system important.Various staff involved	Motivated to comply, partly as involved in start with focus groups.Aware of a 'push' at the start following on from this which helped motivation	Feels unit very committed to using the guidelinesPeople appreciate the clear guidance on feeding and aspiratesLike having clear rules to follow	Nutrition now more in the forefront of people's mindsExpectation now to get nutrition started earlier.

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
8	Band 5	Attributes success to logical order of guideline and that it's easy to follow and easy to find in baby's folder.	Helped that nurses from unit became part of team, and that they knew how 'everybody's mind worked' Fact that people knew the need for the guideline was helpful New staff starting being shown it 'from the off' has helped, especially given lots of new nurses over past 18 months. Guideline easy to get hold of and follow	'Always' follows the guideline, motivated to do so as felt nutrition was done poorly, with poor growth and breastfeeding, so felt it was needed	Unit really committed to new practices. Everybody know why they're doing it and it's clear there is now something where there was nothing before	Expectations have changed and are more positive as can see the results.
9	Band 4	Guideline was the key thingSuccess due to guideline being a rounded thing people can refer to and not having peoples using their own ideas and initiativeHaving guideline to follow is important, as remove people's opinions that may not be right	Key to getting people to follow guideline was that it had lots of people's inputsAlso that guideline clear, concise and easy to understand made more likely to follow itIn depth guideline with lots of steps helpedHandy having people (nurse champions) around to go to for advice and also felt supported by nutrition team who had research to back up theory Gradual introduction and support made a big difference	Very motivated to use the guideline as it gave reassurance and meant didn't have to constantly ask questions. Having guidance was motivating	Took a lot for some people who have been on unit for a long time to be won over, but generally has happenedGenerally a commitment across the unit.	Thinks expectations have changed, with people definitely more confident with nutrition with a greater emphasis on nutrition.People able to say if they think something's not right with nutritional management.

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
10	Consultant	Guideline well publicised and implemented, easy to get hold of and fact is in every baby's folder means it's available on ward round. This means it becomes part of what you do on the ward round. Made decisions easier- 'switch off your brain and go with the guideline', which is definitely a good thing.	Guideline sort of crept in from their perspective, so it was the nutrition round that has highlighted everything to medics. Way it was brought in more relevant to nurses who had to do more measuring etc. Seems to been brought in in the right way, as it's not felt like a big change or something that was imposed upon us- came into unit practice and seemed sensible so we got on with it. Nurse champions good for spreading the word around Guideline itself was key, as was the fact it was user friendly and could be used on the ward round.	Motivated to follow guideline to get better outcomes. Helped by presentation of nutritional outcomes by implementers, knowing it could make a difference. Also found guideline helpful, particularly as standardised care and made things consistent from week to week	Feels nursing team quite committed to guideline- have just taken it on and are doing what they are meant to be doing.	Expectations have changed- we don't accept faltering growth anymore and try and do something about it rather than let it go/make excuses. Definitely now more aggressive in managing nutrition.
11	Band 6	Success due to more standard way of approaching nutrition, with more consistency. Better PN also helped	Whilst guideline quite long, the flow charts are very easy to follow. Simple and standardised so everybody is doing the same thing. Also helps that flow charts by every baby's cot.Nutrition team pushing the guideline all the time also a factor, with them enforcing it, together with the advertising and awareness probably the key factor in success.	Nice to have a guideline as a standard. Motivated to follow them as they were easy to follow and to help colleagues, especially junior ones.Guidelines provide something to support decisions.	Thinks majority of people are committed to the guideline. Few who are reluctant but this will always happen.	People like the support and the overall approach to change, which maybe has affected their expectations.Expectation for babies to get better nutrition now.

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
12	Consultant	Explains success by the effective communication between the nutrition team and the rest of the unit. Big decisions now centralised to nutrition round which means there is uniformity of practice. Increased nursing involvement also a factor, as has awareness of research.	Clarity of guidance a major factor in people following guideline People keen for more uniformity which meant they followed the guideline Increased awareness of nutrition due to nutrition team being around	Motivated to follow guideline as had worked with lead nutrition team member before so felt there was good leadership from the top. Expectation to follow guideline from a governance point of view.	Unit undoubtedly behind new practices	Expectations have changed- profile of nutrition now high up on unit agenda
13	Band 6	Success down to having a protocol to follow and everyone is doing the same thing.	People following guideline as everyone is talking about it, measuring babies and seeing Tuesday morning nutrition roundKey factor was changing people's outlook on nutrition, and guideline helped this.Guideline followed as very clear and in every nursery and baby's foldersHaving nurse champions on the unit, teaching staff also helpful	Motivated to follow guideline as had learnt about nutrition from teaching and knew babies weren't growing very well	Near 100% commitment from unitHas been frustrating at times but slowly getting there.Everyone seems to be following the guideline	Expectations have changed, as we are all wanting more from nutrition and expecting to make it work and make improvements

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
14	Band 7	Reason for success is that beforehand we had nothing to go on except everyone's individual thoughts, never knowing what the next person would want. Consistency was key	Lots of education about what guidelines were about People (nutrition team) available to discuss and ask for clarification during initial use. Good that nutrition team a mixture of nurses and doctors that were your colleagues, so you were familiar with them. Similarly nurse champions also helpful as they were colleagues Reason guideline successful was engagement by the people who have written it- this meant people thought it was going to work Amount of group participation felt like a 'group hug', with a 'patting on the back' when saw that it was working. feedback was beneficial	Felt motivated to follow guideline as knew things could be done better. Also motivated as the document itself was workable and encouraged you to use it. Felt nutrition team approachable and could be engaged with	In general the unit has embraced the changes Education needs to be a continuous and evolving process as staff change. Needs to be a living breathing moving thing that moves forward with us	Have learned that we can do better by our babies and expectations should be higher

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
15	Band 6	Success due to more concentrated feeds started earlier, with a more structured way of feeding	Lots of publicity and nurses taught, cascading the information on.Something we have to do -a proper nutritional study and is benefitting the babiesGuideline works as clear what to do and much easier than beforeGuideline is central to the processNutrition folder good as can see what baby should be gettingRemoves individual doctors assumptionsGood flexibility in guideline but not so much that allows doctors to change according to the whimsHaving own nurses in research team responsible for it working- felt good about itMore structured feeding was wanted as previously hit-and-miss	Happy to follow guidelines as were simple and well set out, structured and individualised to the baby. Motivated by consistency	Nursing staff committed to it- 'something we have to do'Guideline good to direct new doctorsPerhaps doctors/surgeons would like more control	People more tuned in to what is happening and know it's not right when babies don't get appropriate nutritionRaised awareness of nutrition

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
16	ANNP	Success due to re-emphasizing importance of looking at individual babies and work out what they are receiving nutritionally People more aware of nutrition and tend to remind each other about process of increasing feeds Highlighted that nutrition has been a problem in the past has helped too Increased awareness a big part of success.	Having formalised nutrition round each week a selecting high risk babies important Huge change in way people looking at things and encouraged people to have a discussion about the baby Guideline has been important, but having formal nutrition round where you can get advice probably key. However, guideline means can get guidance on days between nutrition rounds. Having info in red folders at cotside has made a difference in getting people to follow the guideline	Seeing the amount of effort put into getting everything together for the guideline was motivating. Made more aware that things were changing too Guideline extremely useful, especially out of hours.	Thinks unit fairly committed to new practices Lots of new nursing staff who receive lots of information in their learning package including nutrition Junior staff may not pick up on things unless senior person directs them May be assumption that process is happening but if you look closely its being overlooked, perhaps due to new staff or skill mix Generally people more aware of it, even new staff get used to nutrition round which emphasizes importance.	Expectations of staff for babies to get nutrition and grow well have changed. more aware of it and considering growth, supplements, correctness of feeds Looking at things in more detail and thinking about compliance with guideline-feel responsibility to meet it
17	Band 7	Having a guideline for all different babies explains success, as before it was all a bit ad hoc. Consistency importantPeople following guideline because it is in each file and really easy to follow.Guidelines 'really good; so that's why they're followed'	Guidelines useful and good so followedEasy to follow guidelines and classify babiesCombination of guideline and nutrition ward round important, plus having people around to askWard round on Tuesday may be more important than guideline, as it is a catalyst	Motivated as important to get nutrition correct, and unit prides itself on this (notes seeing babies from elsewhere who haven't had proper nutrition)Driven by people that were around	Unit committed as the team around got everybody motivated 'whether they wanted it or not'People don't talk positively about working Sunday nights but are doing the nutrition forms	Now have a high standard of expectations around nutrition. Always been good at nutrition but now better

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
18	Band 5	Nutrition round seems to have helped- assessing each baby individually looking at growth and nutrition. Team made up of nutritionist, doctors and consultants Working from guideline means every baby treated the same, but then individual needs worked out by team important (personal element)	Having guideline there next to every baby's cot side has helped- saved time as not had to look for them. Having teaching on guideline and nutrition round on Tuesday to discuss it and ask questions of helped Having it a cotside and being easy to follow main things Screening on Sunday to determine risk and then follow guidelines important. Screening difficult and lengthy but gets done and good to do it.	Took a while to get used to but easy to follow Happy to follow guideline as better for babies and all doing the same thing	Thinks everyone has been quite into doing it We've all worked as a team to get and do it. Didn't feel that anyone was 'really anti'	Guideline has highlighted areas we were weak in and can now see where were going wrong Now more of a focus on nutrition

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
19	Band 7	Success explained by more consistency in what we're doing and helping nurses to be pro-active in the decision making.Nursing staff generally more aware of the next stage or actions to be taken, more likely to guide doctors about prescribing or ask regular questions	Teaching session at the beginning was most responsible for making it work- presented what was going to do before implementing it made people aware of what was going to happen. Put into front of mind and made everything else fit into placeFor junior staff the presence of the nurse champions that keep reiterating pints and driving things forward also importantPublicity surrounding implementation key, as was how it was different from what was done before and really needed as had no proper guidance. All felt it was necessary	Very motivated to use guidelines due to fact they were necessary as previously felt 'was making it up'. Previously felt feeding was a 'little bit made-up'- more art than science	Generally gets followed and feels people quite committed to it. This may be due to desire to have a guidelines (measuring babies more was the 'pay off' to have a guideline)	Now more pro-active about nutrition, with a push towards early PN

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
20	Band 7	Success due to guidelines - have altered culture with girls doing the research and research team, made everybody think more about what we're doing and when we should change People were interested in nutrition before but now more regimented Now more consistency in guidelines and less of people's individual thoughts, which is a good thing	'All a bit of everything' helped success Guidelines were referred to as people didn't know it before Having the nurses and people around to help with the initial putting in has helped as well Visual flow charts and physical guideline important Nutrition rounds where questions asked about whether guideline being followed and why not has been important too.	Nutrition now come to the forefront and is an important part of what we do so that did motivate. Letting babies down now also lets them down in later life	Thinks unit is committed- enough people interested and committed when new documents come in and also getting trained and guidelines pointed out.	More expectation that babies will get measured (more the norm that they will be measured). Better planning Expectation for babies to grow better (bigger and not fatter)
21	ANNP	Having guidelines was factor in success but also now thinking about nutrition more. Physical guideline definitely important, especially for junior medics and nurses. Everyone doing the same and not consultants doing different things each week	Have a team of people to remind people was good, especially nurses that helped implement it. Having guideline in every babies notes so easily available also goodBabies being seen every week by the nutrition team is good. Having forms to fill in each week is a good reminder to do measuring. Nurses from nutrition team make sure it is done too. Easy to follow and accessible guideline important, and having nutrition round each week keeps it at the forefront	Going to focus groups and hearing about plans, plus knowing that babies don't grow very well on the neonatal unit was motivatingFelt it was a good project and something simple to implement and follow	Most permanent staff are relatively committed to guidelines and new practices. No one is asking about what to do so it must be clear from the guideline, so people must be following it.	Expectations have changed- taking nutrition more seriously and nutrition more in the forefront

Subject	A : Role	B : Explaining Success	C : Factors affecting implementation	D : Individual Intentions	E : Shared Commitments	F : Social Norms
22	Band 6	Feels success explained by focus on PN - giving earlier and for longer, and more concentrated	'All hell' to start off with Measuring seemed unnecessary but has got better over time Guidelines being followed - getting easier to understand Flow chart quite handy Not a clear path for all babies Nutrition nurses and their uniforms helping- will do it with you People following the guideline so they don't get into trouble Guideline is flexible though this depends on how senior/junior you are	Initially not motivated at first. Felt like lots of stuff to read- can't be bothered to read it. However, did feel it was right to get the nutrition right and that everyone had to work together to get it right and unless actually do it will never get better. Therefore happy to try it and see if it proved better. Got used to it.	Felt for the unit in general it was confusing for everybody - 'lots of moans and groans' At the start though people felt they had to do it, but are committed to it because they want the best for the babies	Doesn't know if expectations around nutrition on the unit have changed

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
1	Feels roles have changed. Nurses taking more responsibility for measuring Nurses feel more able to make decisions or prompt/challenge doctors regarding nutritional decisions. This is driven by a desire for consistency from nurses. Junior doctors more comfortable/confident in making decisions than before.	Some issues regarding availability of weighing and measuring equipment (especially length measurer), though these were accessible. Time to carry out measures, plus an additional staff member to help with measuring and documenting was also an issue.	Felt never received any training, particularly in relation to plotting, though recognises that many people did get some training. Did get adequate teaching on nutrition.	Guideline easy to read, access and follow. Makes sense "one of the best guidelines we've got"	Feels guidelines integrated well into routine care and did not require any changes to be made to practice in order to put them in place. Puts ease of integration down to persistence of team and ease of use. "part of routine now"
2	Lots of nutritional decision making now made by nutrition team Junior doctors taking on more decisions for nutrition. Greater role for nurses in measuring, with this meaning its more likely to get done. Perhaps expectations changed more than roles	Felt had adequate resources, particularly regarding breast pumps, weighing and measuring equipment and growth charts. Having all equipment needed made guidelines easier to follow.	Felt there has been adequate training and information, particularly via nurse champions, guidelines themselves and AV system.	Easy to follow the guideline in practice. Made easy by availability of equipment	New practices have become part of routine care, particularly due to fact they can see it's working/making a difference Integrated into practice
3	Noted specific changes in roles as people became part of nutrition team. Shift in measurement of head circumference from doctors to nurses. Increased confidence of staff to take part in nutritional decisions or ask questions.	Felt provided with everything needed to follow guideline, particularly measuring equipment. Remembers new length measurers and scales.	Felt adequately trained for new practices. Found training days on measuring and plotting useful.	Guidelines straight forward.	Feels guideline now part of routine care- just what everyone is doing.

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
4	Noted that some nurses had become part of nutrition team.Increased role of nurses in measuring and plotting. Some more nutritional decision making by junior medical staff over time.	Felt provided with the right equipment but perhaps could have done with more scales and measurers due to increased demand. Initially not enough copies of flow charts in baby folders but this improved.	Training in measuring and plotting was useful and needed.	Flow charts made guidelines easy to use. Easier to follow guidelines for medical babies, surgical babies more difficult with some disagreement between guidelines and preferred surgical management	Was easy to integrate guideline into practice and seems to have become part of routine care.
5	Feels more awareness of nutrition rather than necessarily changed roles. Nurses now working with doctors rather than doctors making decisions in isolation- more of a team decision. Guideline has facilitated junior doctors making decisions. Nutrition team doing bulk of work, though everyone contributing	Felt had appropriate and adequate amounts of equipment and copies of guideline.	Felt had enough training	Guideline clear and easy to follow	Easy to integrate into routine care "It's just that is what you do now"

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
6	Notes some staff have become part of nutrition team. Now a feeling that people are responsible for how a baby grows. Nurses now increasingly questioning why nutrition not being delivered as per guideline or decisions not made by medical staff	Needed accessibility of guidelines and this was available	Felt needed and was given clear information regarding guideline. Would have liked perhaps more teaching, but felt what was given was enough to implement it.	Guidelines accessible and clear Easy to follow given complex topic Nutrition screening/review sheets help drive nutritional awareness and management for medical staff, supporting decision making. Also aids flexibility which is often needed. Review sheets also aid transparency of rationales for deviations from guideline.	Feels guideline is becoming, but has not yet fully become part of routine practice. Guidelines and practice seemed to integrate well into routine care, and now there is generally always consideration of nutrition on daily ward rounds (though this may be a general trend in neonatology rather than specific to Southampton). Has noticed nurses asking more questions about nutritional management.
7	Clear culture change to measure babies (nursing staff)Feeling that nutrition decisions may be being deferred to nutrition round on TuesdaysOn other hand people are using the guidelines to guide nutrition decision making.More junior nurses feel empowered to make feeding decisions, especially with new doctors- more likely to guide them into making a decision that fits with the guideline.	Felt had access to necessary equipment but sometimes not always enough at key times (e.g. Sunday nights)Copies of guideline very accessibleTime can be an issue	Felt adequate teaching and training in measuring for themselves, though aware not everyone got it	Guidelines accessible and flow charts make it easy to follow them.	Thinks new practices integrated into routine care. Felt not much deviation from was already happening but provided a framework.Easy to integrate into practice

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
8	People now have a role to follow guideline Measuring being done by nurses more than before (though unclear whose job it was before) Decision making more joint now between doctors and nurses rather than just doctors before Junior doctors more comfortable making a nutritional plan even if not with a more senior doctor due to guideline.	Feels there was enough equipment, though sometime a shortage of tape measures. Copies of guideline not an issue	Did get training in measuring Felt had all training that was needed	Very easy to follow guideline	New practices mostly integrated into unit, and were easy to integrate. Has mostly become part of routine care, particularly for measuring though plotting not always consistent
9	Has noticed a change in decision making around nutrition- feels more confident to make nutritional decision themselves, More involvement of nurses in nutritional issues.Junior doctors now don't always need to check with the big boss	Not excessively problematic but more measuring equipment would have made things easier, especially on a Sunday night.Enough copies of guideline which were easy to access.	Did not attend training sessions so would have liked more training as would have improved confidence. However did not feel anything was particularly lacking and felt able to ask. Could easily access nurse champions for help.	Guideline easy to use- pretty simple and self-explanatoryClearness and easiness of it all good	New practices fitted well with routine care- not excessively different or tricky to implementNow part of routine care for most part, people regularly using guideline

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
10	Nurses have assumed more responsibility for making decision about feeds, meaning they get implemented earlier in the day with less waiting or stopping of feeds. Seems to be easier for junior doctors to follow the guideline and make decisions about feeds. Making more decisions than previously perhaps.	Felt had adequate material resources.	Felt had adequate training	Easy to follow guideline - not complex at all really	New practices seems to be fitting into routine care quite nicely Measuring etc. seems to fit with nurses work, and is being done. Measuring element seems to have become part of routine care though nutritional management perhaps still needs highlighting occasionally, but overall seems to have integrated relatively easily
11	Junior staff now realised their input can help and people generally realise how important nutrition is.Nurses role has taken on length measuringMore involvement from nursing staff in nutritional management, flagging up flow chartsJunior doctors now don't always need to go and check their feed plan with seniors like before	Generally enough equipment though sometimes difficult to length sick term babies.	Lots of education about the equipment has been good and enough to follow guidelinesNutrition nurses and team available for questions.Lots of info provided in guideline and lectures	Flow charts make guideline easy to follow. straight forward and basic 'it's not rocket science'	New practices easily integrated into routine care. Actually easier than it was before due to structure and guidance.Definitely part of routine care

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
12	Role changed for good and bad. More empowerment of nutrition team to take decisions but these decision now more focussed on nutrition rounds Disadvantage is that you can get put-off a bit and leave decision making to someone else. Now natural defence mechanism is to refer to nutrition team but this stops you thinking. More junior people now able to make nutrition decisions as shielded by a governance tool (guideline)	Had enough material resources, especially paper copies of the guideline and flow charts	Had adequate training	Pretty easy to follow guideline	New practices fitted in easily because there was a need for it. Complexities of care/debate affected integration but felt this is normal part of medicine Seems part of established practice but will take more time for it to be routine
13	Nurses feel more responsible for nutrition and are more involved in nutrition planMore collective decision making now- nutrition team getting more influence on feeds, but nurses have more involvement and are asked for advice by the junior doctorsGuideline means that junior doctors more able to make decisions that they would have previously referred to consultantsJunior nurses also more involved	Had the right equipment and found the incubator measures very useful. Could have done with some more scales on busy nights	Taught to measure by nurse championsFelt had enough training	Very easy to use guideline and put it into practiceHaving flow charts in red folders helped as they are by bed when discussing baby	New practices integrated 'perfectly' in unit- it 'just happened'Now normal practice to follow guideline 'it's what we do'

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
14	Concerned that people might stop thinking for themselves and defer decision to the nutrition round. However, guideline has allowed people to move babies on and not wait till Tuesday, with nutrition round focussing on more challenging babies Easier for junior members of staff to be enabled to make decisions- has empowered more people to get involved and think about nutrition	Had enough measuring equipment but concerned not always used properly.	Found guideline easy to follow and felt very well educated in it Some staff need more training in measuring and plotting	Guideline is a workable document, using it all the time and easy to follow. Initially needed to refer to it for each baby but are now learning it.	Felt easy to integrate new practices into routine care as feeding part of daily care. Measuring potentially extra but feels this should have been being done for years Nutrition now part of routine care and something you automatically think of and is not unusual to do.
15	Real shift in roles. Nutrition team making decisionsPeople consider what nutrition team will make of their decisions, which is making them thinkAwareness of nutrition team checking what people doGuideline gives more scope to junior doctors to make decisions	Actual guideline most important material resource, which was availableOnly thing would have been more scales	Had enough training- there to learn and cascade to othersNo reason why a single nurse on the unit should not be following the guideline	Relatively easy to follow guidelineSome flexibility which is good, but not too much as to allow people to change according to their whimsNutrition folder good as can see exactly what baby should be getting	No problem to integrate guidelines into routine care, made things clearerMeasuring on Sunday can be hectic but people have been doing it. Teaching from nurses has helpedNow part of routine care- 'what we do here' 'everybody's accepted it'

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
16	Despite nutrition round, people still make decisions and also use nutrition round plan for the week. Roles changed in that have dedicated people coming round regularly and a team of nurses Nutrition discussed more at handover Junior doctors perhaps making more decisions or at least make a plan to discuss with the consultant	Needed flow charts to be in folders and they weren't always there initially but got better	Happy with what training had been provided Aware that other training going on but not always able to get to it but considers this part of way system works Able to catch up when come back and read about what has changed	Very specific guideline which is good. Know what is happening Real change to how we look at things No more delays like there used to be	Thinks new practices did fit in with everything else on unit. Often not always at top of the list though as other things intervene Has become part of routine now- part of the norm and how it should be
17	Nutrition now everybody's responsibility, which it wasn't beforeNurses now have a part in everything rather than decisions just made by the daily ward roundBefore most senior people were making nutrition decisions, now everyone can go to the guideline and a say 'shouldn't we be doing this today'. Guideline gives junior staff more involvement as now have something to look at.All babies get the same treatment, but still flexibility	Thinks there was enough support and equipment	Thinks had enough training on measuring and nutrition. Unsure if more junior people did	Guidelines in each file and easy to follow and usefulFlow charts the best thing	Thinks new practices now normal practice

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
18	As a nurse guideline makes it easier to think rather what they should be doing than relying on doctors to make decisions- given more involvement in decisions as feel makes sense and not making it up. Perhaps less the case for the aspirate part of guideline than feeding. Noticed now nutrition not had be a consultant decision, though unsure if it was before	Always fighting over the scales so sometimes can be a problem. Would like more scales with measurer on Incubator measures good - don't always seem to be fighting over that Sometimes laminated flow charts on folders missing	Had some trained as part of modules from implementer which was enough Teaching on measuring by nurse champions, also happy with measuring as worked in outpatients, though maybe would have liked more	Once get into guidelines they're very easy to follow	Has now become part of routine check to check what feeds baby is on- has become part of routine practice Not that difficult to fit it with checks and cares
19	Nursing staff more aware of next stages or actions and more likely to guide doctors as to what they want prescribingFeels nutrition decisions have always been done as a team.Perhaps decision now taken away from team and put onto the nutrition team/deferred for special cases though not for all babies on a daily basisGuideline has guided junior doctors to enable them to make decisions	Paper copies of the guideline were needed and there were enough of these.Equipment not an issue	Guideline really clear wasn't ambiguous and designed to take away ambiguity of decision making. Didn't feel needed any other training.Didn't have formal measuring training but felt supported by nurse champions	Very easy to follow guideline and do the work required	Feels now what we normally doEasy to fit into routine carePart of what we do- new staff juts take it as read that that's what happens. New staff may be more au fait with it than staff who've been in unit longer - has been really nice for them to have structure

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
20	Team of people on unit with interest Noted those who have joined team and now left but continued interest Guidelines have allowed junior nurses to say when things aren't being done Nutrition team has people from different areas which is a change	Probably wasn't enough copies of guideline to start with- not in every folder- now better Work has been done in teaching people to measure and plot Still not enough lengthers and scales	Thinks probably did have enough teaching	Flow charts visual and helpful Wasn't relatively easy to follow but got better as got used to it	Thinks new practices have integrated relatively easily Notes weighing and measuring overnight not always possible and not always handed over- doesn't roll on a 24 hours basis Most people wanted it to work and go forward Now more or less what we do routine, though still not good at written communication and talking to mothers
21	Nurses now doing all the measuring and getting more involved.More shared responsibilityLack of decision on feeds now happening lessUnsure if less emphasis on doctors making decisions, though feels should and may be less with guidelineNow less necessary to ask a senior person about feedsNow doing less as nurses doing more and easier to make decisions as things better documented	Can't remember any problems - not difficult to come across copies of the guideline	Maybe would have liked more teaching but haven't had trouble following guideline, so not an issue	Guideline easily accessible and easy to followNot had any particular problems with guideline. Structured and nice to useFeels able to deviate from guideline when necessary as long as able to rationalise and give a reason - so this has not been a problem	Fluids thought about on a daily basis so it fits nicely with routine care.Easy to integrate into care as available by cot, with nice flow chart that can be followed easilyPretty much part of routine careBeen taken up quite well and people happy to follow it.

Subject	G : Social Roles	H : Material Resources	I : Informational Resources	J : Workability	K : Integration
22	Doesn't think roles have changed particularly Now feels less able to make decisions around feeding than before, though this is not just due to nutrition guideline and more for surgical babies. As a senior person guidelines may have taken away some autonomy Junior staff can sometimes be a bit like sheep- do make decisions but need more experience to be more flexible Guidelines have been a good thing for junior staff Junior doctors often don't have a clue and rely on nurses, but guideline helps them understand what we're doing Consultants will always do what they want (for all things not just nutrition guidelines)	Unsure if incubator measurers are the most suitable (?could be disposable or similar) Equipment for measuring difficult to use, so may also not be the best Seemed to have enough scales	Able to ask if unsure Supported by nutrition nurses	Felt nutrition rounds 'tricky'. Too many people at a busy time when other stuff going on. Disturbing babies too much sometimes Sometimes didn't feel listened too, especially given experience. Also questioned the expertise of others on team 'All hell' to start off with Disagreed with idea that babies had to be measured no matter what- not a priority for them Easy to follow guideline with some flexibility if senior. Flow chart handy. 'Not that difficult really'	Guidelines and practices did fit in with existing work. Easy enough to do Practice still seems separate rather than normal practice by is getting better, becoming part of what we do Perhaps new people more likely to accept as normal practice

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