THE NUTRIENT INTAKES AND FEEDING PRESCRIPTIONS OF LOW BIRTH WEIGHT INFANTS AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

by

Renette Andrea Reeding

Thesis presented in fulfilment of the requirements for the degree of Master of Nutrition in the Faculty of Medicine and Health Sciences at Stellenbosch University

Supervisor: Dr Evette van Niekerk
Co-supervisor: Mrs Hannelie Kemp
Statistician: Ms Tonya Esterhuizen

Faculty of Medicine and Health Sciences
Department of Interdisciplinary Health Sciences
Division of Human Nutrition

December 2017

DECLARATION

By submitting this dissertation electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously, in its entirety or in part, submitted it for obtaining any qualification.

Renette Andrea Reeding

December 2017

ABSTRACT

Objectives: To compare feeding prescriptions and actual nutrient intakes of premature, low birth weight (LBW) infants admitted to a tertiary hospital to international recommendations.

Methods: An observational, prospective study was undertaken. Patients consecutively admitted to the neonatal intensive care unit who met the inclusion criteria were enrolled. The infants' feeding prescriptions and intakes were obtained from hospital files and feeding charts on study days one, two, three, seven and 14 of life. Fluid, energy and macronutrient intake from intravenous (IV) fluids, parenteral and enteral feeds were calculated and compared with internationally recognised recommendations. Enteral feed advancements were assessed to determine whether full enteral feeds had been achieved on days seven and 14. Weight, length and head circumference (HC) were measured weekly.

Results: A total of 156 preterm infants (56% female; 44% male), with a mean gestational age of 30 weeks were included. The mean birth weight (BW), length and HC were 1 352g, 38.5cm and 28cm respectively. The majority of feeds prescribed (79.10 ml/kg/day) and intakes (34.93 ml/kg/day) on day one were in IV fluid form. Parenteral nutrition (PN) feed prescriptions only met a third of the recommended requirements of the infants (49.94 ml/kg/day, $n = 6$). Only minimal enteral feeds (24.13 ml/kg/day, $n = 48$) were prescribed, of which hardly any was administered. Thereafter, prescriptions and intakes for IV, PN and enteral nutrition (EN) were increased. By day seven, parenteral and enteral prescriptions and intakes were inadequate and not comparable to recommendations ($p < 0.05$). Enteral prescriptions and intakes had only met recommendations by day 14. Differences were seen between the enteral prescriptions and intakes on all study days for all BW categories, but were relatively comparable on day 14. Differences in fluid advancements were found between day one, two and three, and between day seven and 14 for prescriptions and intakes. By day seven and 14, decreased *z*-scores were observed for all anthropometry. Enteral intakes had a more positive impact ($p < 0.05$) on percentage weight loss on day seven than on day 14. Parenteral intakes in the VLBW group significantly influenced the regaining of BW on day 14 ($p < 0.05$).

Conclusion: This study showed that premature infants do not meet their nutritional requirements in the current clinical setting, with differences noted between prescriptions and intakes. Inadequate nutrition further exacerbates these infants poor growth seen during the

first two weeks of life as seen by either slow feed advancements or majority of infants not on full enteral feeds by day 14.

OPSOMMING

Doelwitte: *Om die voedings voorskrifte en werklike nutriënt innames van lae geboorte massa (LGM) babas wat in 'n tersiêre hospital opgeneem is, met aanbevole riglyne te vergelyk, en om vas te stel of nutriënt innames 'n impak op gewigsverlies na geboorte en die herwinning van geboorte massa gehad het.*

Metodologie: *'n Prospektiewe waarnemende studie is onderneem. Pasiënte wat opeenvolgend in die neonatale intensiewe sorg eenheid opgeneem is en aan insluitings kriteria voldoen het, is in die studie ingesluit. Voedings voorskrfte en nutrient innames is op dag een, twee, drie, sewe en 14 van lewe vanuit hospitaal rekords en voedingskaarte bekom. Vloeistof, energie en makronutriënt inname is vanaf intraveneuse vog, parenterale en enterale voedings bereken en met internasionaal erkende aanbevelings vergelyk. Die tempo waarteen enterale voedings verhoog is, is vasgestel om te bepaal of vol voedings op dag sewe en 14 bereik is. Massa, lengte en kopomtrek is weekliks gemeet om die impak van voeding op die persentasie massaverlies en herwinning van geboorte massa vas te stel.*

Resultate: *'n Totaal van 156 premature babas (46% vroulik; 44% manlik) met 'n gemiddelde gestasie ouderdom van 30 weke is ingesluit. Die gemiddelde geboorte massa, lengte en kopomtrek was respektiewelik 1352g, 38.5cm en 28cm. Die meerderheid voedings wat op dag een voorgeskryf (79.10 ml/kg/dag) en ingeneem (34.93 ml/kg/dag) is, was vanaf intraveneuse vog. Dertig persent van aanbevole totale parenterale voeding (49.94 ml/kg/dag, n = 6) en minimale enterale voeding (24.13 ml/kg/dag; n = 48) is voorgeskryf, maar bykans geen enterale voeding is ontvang nie. Daarna is voorskrifte en innames van intraveneuse, parenterale en enterale voeding verhoog. Teen dag sewe was parenterale en enterale voorskrifte en innames onvoldoende en nie vergelykbaar met aanbevelings nie ($p < 0.05$). Enterale voorskrifte en innames het eers teen dag 14 die aanbevelings bereik. Verskille is op alle studie dae tussen die enterale voorskrifte en innames vir alle geboorte massa groepe gesien. Verskille in die verhogings van vloeistof is tussen dag een, twee en drie en tussen dag sewe en 14 vir voorskrifte en innames waargeneem. Verlaagde Z-tellings is gedurende die twee weke vir massa, lengte en kopomtrek waargeneem. Enterale nutriënt innames het 'n groter impak ($p < 0.05$) op persentasie massaverlies op dag sewe as op dag 14 gehad. In die baie lae geboorte massa groep het parenterale nutriënt innames die herwinning van geboorte massa betekenisvol beïnvloed ($p < 0.05$).*

Gevolgtrekking: *Hierdie studie het getoon dat in die huidige kliniese opset daar nie aan die voedings voorskrifte en nutriënt innames van lae geboorte massa premature babas voldoen word nie. Stadige verhoging van voedings teikenend van ontoereikende voeding in die oorgrote meerderheid van hierdie babas, vererger die babas se swak groei gedurende die eerste twee weke van lewer verder*

ACKNOWLEDGEMENTS

I would like to extend my sincere gratitude to:

My supervisors, Dr. Evette van Niekerk and Mrs Hannelie Kemp for their invaluable time and input in assisting me with writing this dissertation, and for their expertise throughout the study.

The NICU nursing staff at CHBAH who helped me during the data collection period.

My family and friends, for their ongoing support and motivation, especially my colleague and dearest friend, Amina Dindar, for being a sympathetic ear and always being there for me.

My fellow students, Jessica Kotlowitz and Margot Bradfield, I cannot express enough appreciation for having such great friends and support on this journey.

Mitchell Taljaard, for your understanding and encouragement during this study. You are my rock.

Lord, God Almighty, for giving me strength and guidance to persevere despite the many trials and tribulations I've encountered on the road to reaching my goals.

CONTRIBUTIONS

The principal researcher, Renette Andrea Reeding, developed the idea and the protocol. The principal researcher planned the study, undertook data collection with the assistance of nursing staff in the unit, captured the data analyses, analysed the data with the assistance of a statistician (Tonya Esterhuizen), interpreted the data and drafted the dissertation. Dr Evette van Niekerk (supervisor) and Hannelie Kemp (co-supervisor) provided input at all stages and revised the protocol and dissertation.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF APPENDICES

LIST OF ABBREVIATIONS

AA	Amino acids
AGA	Appropriate for gestational age
ANOVA	Analysis of variance
APH	Antepartum haemorrhage
AAP	American Academy of Pediatrics
ASPEN	American Society of Parenteral and Enteral Nutrition
BPD	Bronchopulmonary dysplasia
BW	Birth weight
CHBAH	Chris Hani Baragwanath Academic Hospital
CHO	Carbohydrates
CM	Centimetre
CO_2	Carbon dioxide
CP	Cerebral palsy
CPAP	Continuous positive airway pressure
EFA	Essential fatty acids
ELBW	Extremely low birth weight
EN	Enteral nutrition
ESPEN	European Society for Clinical Nutrition and Metabolism
ESPGHAN	European Society for Paediatric Gastroenterology, Hepatology and Nutrition
EUGR	Extrauterine growth restriction
FP	Feeding prescriptions
GA	Gestational age
GI/T	Gastrointestinal/tract
GOR	Glucose oxidation rate
HC	Head circumference
HIV	Human immunodeficiency virus
HMD	Hyaline membrane disease
IUGR	Intrauterine growth restriction
IQR	Interquartile range
IV	Intravenous
KG	Kilogram
LBW	Low birth weight
LGA	Large for gestational age
LT	Length
MEF	Minimal enteral feeding
NEC	Necrotising enterocolitis

NI	Nutrient intakes
NICU	Neonatal intensive care unit
NNJ	Neonatal jaundice
NVD	Normal vaginal delivery
PIH	Pregnancy-induced hypertension
T/PN	Total/parenteral nutrition
SD/S	Standard deviation/score
SGA	Small for gestational age
VLBW	Very low birth weight
WAZ	Weight-for-age *z*-score
WHO	World Health Organisation
WT	Weight

DEFINITIONS OF TERMS

Appropriate for gestational age	Birth weight between the 10^{th} and 90^{th} percentile for gestational age.[1]
Actual intake	Refers to estimated nutrients (feed, IV fluid) received by the infant as recorded by the nursing staff.
Donor breast milk/ donor human milk	Breastmilk that has been donated voluntarily to a milk bank by women who are biologically unrelated to the recipient infant. This milk is pasteurised to eliminate any viral or bacterial contaminants.[2]
Extremely low birth weight	A birth weight below 1 000 g.[3]
Enteral nutrition	Providing nutrition directly into the stomach via a tube, catheter or stoma past the oral cavity.[4]
Extrauterine growth restriction	A weight, length and head circumference below the 10^{th} percentile of intrauterine growth expectation, based on postmenstrual age (PMA) at the time of hospital discharge.[5,6]
Feeding prescriptions	The type and volume of feeds (intravenous, enteral or parenteral nutrition) prescribed by the clinician.
Gestational age	Routinely based on the "gold standard" of early ultrasound assessments together with foetal assessments based on the clinical history of the last menstrual period (LMP).[7]
Glucose oxidation rate	The measure of the glucose infusion rate, how quickly glucose is oxidised in the body, and the rate of glucose the infant will receive.
Intrauterine growth restriction	"a foetus that fails to reach his potential growth", characterised by body weight below the 10^{th} percentile.[8]
Intravenous lipid emulsion	The emulsion of lipids for intravenous use when providing PN to infants. These lipid emulsions consist of triglycerides, phospholipids and glycerol which provide energy and essential fatty acids important for growth and development.[9]
Low birth weight	A birth weight below 2 500 g.[3]
Large for gestational age	A birth weight greater than the 90^{th} percentile for the gestational age.[10]

Minimal enteral feeding	Also known as "trophic feeds" , the provision of milk feeds in sub-nutritional quantities for a predetermined period.[11] Usually provided within the first 24–48 hours of life in stable infants to "prime" the gastrointestinal tract with very low volume feedings.[12–14]
Necrotising enterocolitis	A condition mainly affecting preterm infants, characterised by intestinal necrosis of the bowel, ranging from mucosal injury to full thickness necrosis and perforation.[15]
Nutrient intakes	The fluid and nutrients (energy and macronutrients) received by the infant.
Nil per os	Latin for nothing by mouth.
Pregnancy induced hypertension	Defined as a blood pressure ≥ 140/90 mmHG after two occasions of rest or ≥ 160/110 mmHG on one occasion in a previously normotensive woman.[16]
Postmenstrual age	The time elapsed between the first day of the last menstrual period and gestational age (at birth) plus the time elapsed after birth (chronological age) described in number of weeks.[17]
Total/parenteral nutrition	Feeding via bloodstream intravenously.[18]
Resting energy expenditure	Contributes 70% to total energy expenditure and is the total energy needed after accounting for physical activity energy expenditure and thermic effect of food.[19]
Small for gestational age	A birth weight below the 10th percentile of a certain reference for the gestation age.[20]
Very low birth weight	A birth weight below 1 500 g.[3]

CHAPTER 1

LITERATURE REVIEW

CHAPTER 1: LITERATURE REVIEW

1.1 EPIDEMIOLOGY OF PREMATURE BIRTHS

A premature infant is defined as an infant with a gestational age (GA) of less than 37 weeks. Premature infants are further sub-divided as moderate to late preterm (32 to < 37 weeks GA), very preterm (28 to < 32 weeks GA) and extremely preterm (< 28 weeks GA).[7,21]

Globally, premature births are a major cause of neonatal death and prematurity is the second most common cause of death in children under the age of five.[7,22] An estimated 15 million infants are born prematurely each year, equating to more than one in 10 births.[7] Survival rates around the world differ between high and low-middle income countries. Half of the preterm births (≤ 32 weeks GA) from low-income countries will die due to lack of cost-effective, feasible care such as breastfeeding support, warmth, and care for infections and breathing difficulties.[22] Data from Liu et al. showed that preterm birth is the direct cause of 35% of all neonatal deaths and that infections in moderate to late preterm infants is an indirect cause of neonatal death.[7] This data is taken from an estimated distribution of causes of 3.1 million neonatal deaths in 193 countries in 2010.[7]

In the South African context, the District Health Information System (DHIS) recorded 1 878 279 births during the period 1 January 2012 to 31 December 2013.[23] The National Perinatal Problem Identification Programme (PIPP) database represents 75.6% of all births in facilities using DHIS.[23] Data from PIPP reported 1 420 364 births during the same period as indicated by DHIS.[23]The highest rates of preterm births is reported in the Gauteng province.[23] South Africa is not listed in the top ten countries with the highest rates of preterm births per 100 live births according to WHO, but nine of the eleven countries with the highest rates are in Africa.[7] Data presented by Blencowe and Lui on preterm births and deaths worldwide reported 1 059 000 live births in South Africa in 2010 with a preterm birth rate of eight in every 100 births. South Africa is ranked 128 out of 184 countries with preterm birth rates, but 28th amongst countries with deaths due to complications related to preterm births, with 7 800 deaths reported in 2010.[7,24]

Despite high rates of preterm births, advances in the neonatal intensive care unit have increased the chances of survival for premature infants born at lower gestational ages and birth weights.[25]

1.2 NUTRITION AND THE PRETERM INFANT

Preterm infants have greater nutritional requirements than term infants due to rapid foetal growth and inadequate nutritional stores at birth.[26] Increased nutritional requirements are seen mainly in the most vulnerable preterm infants, especially those with morbidities.[26] It is well documented that early nutritional support is critical and often difficult to achieve for this vulnerable population, with ramifications for childhood development and health extending into adult life.[27] Accumulated nutritional deficits are observed in preterm infants within the first few weeks of life during their hospital stay due to insufficient intakes of energy and macronutrients.[3,28] Insufficient nutrition results in perinatal undernutrition and poor postnatal growth, which is associated with poor neurodevelopmental outcomes.[3,28] Being born prematurely places the infant at a high nutritional risk.[25]

Nutritional goals for preterm infants are based on recommendations to provide a nutritional supply that will aid in achieving growth rates similar to intrauterine life, limits cumulative deficits and provides a positive nitrogen balance in the first few days of life.[6,14] There is no set standard for the precise nutritional needs of preterm infants despite consensus recommendations by nutrition experts on specific nutrient requirements.[3,29] The immature gastrointestinal (GI) tract of the preterm infant has anatomical and functional impairment to gut motility, digestion and absorption of nutrients that may limit tolerance to enteral feeds.[3,30] A nutritional regimen that provides both parenteral and enteral nutritional support is beneficial to the high-risk infant in that it improves growth without increasing the risk of adverse clinical outcomes.[27,28] Human milk is the optimal source of nutrition for premature infants as it's initially higher in protein, fat, amino acids and certain minerals such as copper and zinc.[31] Feeding preterm infants human or breast milk has beneficial effects, including decreased rates of NEC, sepsis, retinopathy of prematurity (ROP) and improved neurodevelopmental outcomes later in life.[31]Baby-Friendly Hospital Initiative (BFHI), also adapted to Mother-Baby Friendly Initiative is a global effort to promote, protect and support breastfeeding practises.[32] BFHI is an initiative that increases the likelihood of infants exclusively breastfeeding for the first six months of life.[32]

Ehrenkranz showed that adequate nutrition through early, aggressive enteral and parenteral nutrition support was associated with lower rates of death and short-term morbidities, and improved growth and neurodevelopmental outcomes without affecting the rate of NEC.[6,28] The American Academy of Pediatrics (AAP), the Canadian Pediatrics Society (CPS), the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the Scientific Basis and Practice Guidelines from Tsang provide the clinician with nutritional guidelines for parenteral and enteral nutrition for preterm infants (Table 1.1 and Table 1.2 respectively).[29,33–35]

1.2.1 Parenteral nutrition

Achieving adequate enteral intakes in preterm infants is challenging during the first few days to weeks of life.[36] Providing early parenteral nutrition (PN) is a potential strategy for minimizing this problem.[36] Evidence-based guidelines recommend initiation of PN immediately after birth in small preterm infants who are unable to tolerate oral or enteral feeding, as starvation for one day may be detrimental.[27,30,37]

PN may be provided as a sole-source or adjunct nutrition support with varying nutrient doses based on the infant's weight, age and condition.[37] However, PN practices are variable as indicated by a national observation study conducted in the United Kingdom, showing shortfalls in the nutritional adequacy of neonatal PN and delays in its initiation.[36,38] This study demonstrated the need for clearer guidelines on recommended nutrient intakes.[36,39] The German Society of Nutritional Medicine updated the European Society of Parenteral and Enteral Nutrition (ESPEN) PN guidelines for clinicians, which provides specific dosing ranges for energy, glucose, amino acids (AA), fat emulsions, minerals and vitamins for full or partial PN with gradual introduction and advancement of enteral nutrition.[37] Currently, there is only one manufacturer available in South Africa who produces paediatric, standard all-in-one PN bags. These PN formulations contains macro and micronutrients with some PN bags containing lower amounts of glucose substrates or others having no lipid substrates. Variations in PN formulations bears relevance when calculating energy and macronutrient prescriptions and should be taken into consideration when analysing infants' nutritional requirements.

Table 1.1: Recommended guidelines of parenteral nutrition in premature infants

PARENTERAL NUTRITION					
	AAP[29]	Koletzko[48]	Velaphi[40]	Tsang[34]	Elhassen & Kaiser[41]
Fluid ml/kg/day < 1 000g 1 000 – 1 500g	-	80–90 60–80	-	140–180 120–160	Day 1: 60–70 Advance by: 10–20 Goal: 130–180
Energy kcal/kg/day < 1 000g 1 000 – 1 500g	90–100	Day 1: 40–60 Goal: 95–125	110–120	105–115 90–100	120
Protein g/kg/day < 1 000g 1 000 – 1 500g	2.7–3.5	4.0	1.5–4.0	3.5–4.0 3.2–3.8	Initial rate: 2–3 Advance by: 0.5–1 Goal: 3.5–4
Lipids g/kg/day < 1 000g 1 000 – 1 500g	1–3	Minimum: 0.5 Goal: 3–4	2.5–3.5	3–4 3–4	Initial rate: 2–3 Advance by: 0.5–1 Goal: 3–3.5
Carbohydrates mg/kg/min < 1 000g 1 000 – 1 500g	6–12	Initial rate: 4.2–4.9 Goal: 8.5–11.8	6–8	13–17 9.7–15	Initial rate: 4–6 Advance by: 1–3 Goal: 12

1.2.2 Enteral nutrition

Enteral nutrition (EN) is the preferred route of nutritional support but is often delayed until four or seven days postnatally in preterm infants.[13,26,42] EN is challenging to achieve due to complications and perceived risks, such as feeding intolerances, infections, gastrointestinal (GI) anomalies or poor renal function.[13,26,42] Human milk is the preferred standard feed when initiating EN in preterm infants due to its trophic effect of stimulating maturation of the GI tract, and anti-infectious effects that reduce intestinal permeability and may protect against the incidence of NEC.[3,13,14,26,33] Mother's own preterm milk has a relatively high protein and fat content and anti-infective properties.[26] Donor human milk is the preferred alternative, but if not available, cow's milk-based artificial formula is an alternative option.[26]

Minimal enteral feeding (MEF), also known as trophic feeding, should be started within the first 24–48 hours of life in stable infants and is commonly used in combination with PN until full enteral feeds can be achieved.[13,14] MEF should not be considered part of total energy intakes while receiving total PN.[14] Priming the GI tract with MEF increases gut hormones such as gastrin and gastric inhibitory polypeptide and promotes intestinal maturation and motility.[12,14] Early trophic feeds support earlier achievement of enhanced enteral intakes that may also decrease feeding intolerance, resulting in a shorter period of PN, improved weight gains and bone mineralisation.[3,12,42,43]

1.3 NUTRITIONAL REQUIREMENTS OF THE PRETERM INFANT

The aim of this literature review and scope of the study is specific to the fluid, energy and macronutrient (protein, carbohydrate and fat) needs of the preterm infant. It does not include further analysis into the micronutrient requirements of preterm infants. The guidelines of enteral and parenteral nutrition for premature infants that are commonly recommended in practice are depicted in Table 1.1 and Table 1.2.

1.3.1 Fluid

Although water is not considered a nutrient, it is the most abundant component of the foetal and neonatal body, serving as a vehicle for parenteral and enteral administration of nutrients.[44] The purpose of fluid management of the preterm infant is to avoid dehydration or overhydration, to provide electrolytes and glucose concentrations, and to avoid abnormal acid-base balances.[29] Preterm infants are at risk of fluid mismanagement, leading to insensible losses through the skin which is porous with a thin keratin layer that varies according to gestational age and birth weight.[29,45] Transepidermal water loss signifies skin maturity and is exacerbated by a low weight to high surface area ratio, with the highest losses occurring during the first few days after birth.[45]

Non-aggressive fluid management is important in preventing morbidity and mortality, as aggressive fluid management has been associated with increased risk of patent ductus arteriosus and chronic lung disease.[46] Pulmonary fluid overload can lead to oedema and contribute to non-compliance from the organ and increased airway resistance.[44] A Cochrane review by Bell and Acarregui showed that restricting water intake in preterm infants had a significantly lower risk of PDA and NEC, and a non-significant decreased risk of BPD, intracranial haemorrhage and death.[47] However, this systematic review also showed that restricting fluids increased the risk of dehydration which may lead to hyperkalemia, cardiac arrhythmia, renal failure and death.[47]

Fluid requirements for preterm infants with birth weights ≥ 1 000 g are approximately 60–80 ml/kg/day on the first day and about 100 ml/kg/day for preterm infants < 1 000 g depending on insensible water losses and urine output.[29,45] Fluids are increased to a total of 120–140 ml/kg/day by day four of life, with daily increments of 20 ml/kg/day.[29]

Table 1.2: Recommended guidelines for enteral nutrition in premature infants

ENTERAL NUTRITION				
	ESPGHAN[33]	AAP[29]	CPSNC[35]	Tsang[34]
Fluid ml/kg/day < 1 000g 1 000 – 1 500g	135–200	-	120–200	160–220 135–190
Energy kcal/kg/day < 1 000g 1 000 – 1 500g	110–135	105–130	105–135	130–150 110–130
Protein g/kg/day < 1 000 g 1 000 – 1 800 g	4.0–4.5 3.5–4.0	3.5–4.0	3.5–4.0 3.0–3.6	3.8–4.4 3.4–4.2
Lipids g/kg/day < 1 000g 1 000 – 1 500g	4.8–6.6	5–7	4.5–6.8	6.2–8.4 5.3–7.2
Carbohydrates g/kg/day < 1 000g 1 000 – 1 500g	11.6–13.3	10–14	7.5–15.5	9–20 7–17

The guideline for parenteral nutrition fluid on day one is to start at 60–80 ml/kg/day for preterm neonates > 1 500 g and 80–90 ml/kg/day for preterm neonates < 1 500 g.[48] The recommended parenteral fluid intakes for preterm infants weighing less than 1 500 g by day six of life, according to Koletzko et al., is 160–180 ml/kg/day and 140–160 ml/kg/day for preterm infants weighing ≥ 1 500 g.[48]

Data on enteral fluid intakes in preterm infants is lacking. Tolerated volumes of 96–200 ml/kg/day from combined parenteral and enteral studies serve as the lower and upper limits, with lower volumes more likely to reduce the risk of morbidities such as PDA or BPD.[33] While recommended fluid intakes range from a minimum of 135 to a maximum of 200 ml/kg/day, feeding rates of 150–180 ml/kg/day are likely to meet nutrient requirements.[33] When enteral feeds are at least 120 ml/kg/day, PN may be discontinued as basic fluid requirements will be met.[29] MEF of less than 25 ml/kg/day is not considered part of the total energy supply, but only when feeds increase above 40 ml/kg/day one can consider these feeds to be part of total energy intakes derived from PN and EN combined.[39] The Abnormal Doppler Enteral Prescription Trial (ADEPT) showed that the very premature infants (< 29 weeks GA) were only able to tolerate MEF for the first 10 days of life with median volume intakes of less than 20 ml/kg/day.[49] A randomized control trial (RCT) by Krishnamurthy et al. showed that preterm neonates weighing 1 000 – 1 499 g attained full enteral feeds of 180 ml/kg/day earlier when feed volumes of 30 ml/kg/day than those advanced by 20 ml/kg/day.[50] These infants reached full feeds by day seven in comparison to the nine days taken by the latter group.[50] Providing full enteral feeds has been shown to be more beneficial than PN in decreasing protein breakdown rates, but the volume of feed required to achieve this effect is unknown.[51]

1.3.2 Energy

Energy requirements are based on the preterm infant's basal metabolism, growth and compensation for any preceding accumulated nutrient deficits in utero or postnatally. Estimated requirements also need to take into consideration the infant's postnatal age, alteration in body composition and differences in resting energy expenditure.[3,33,52] Other factors determining energy requirements include the preterm infant's body size, postnatal age, physical activity, urine and stool losses, and clinical conditions and diseases.[52]

The current recommendation for energy supply from PN is 40–60 kcal/kg/day on the first day of life, with rapid increases to 95–125 kcal/kg/day within the first week of life.[48] The preterm infant's metabolism and growth, especially when ill, needs to be considered and adapted accordingly when recommending adequate energy intakes.[3,39,48]

Energy recommendations for EN for the first few days of life is not well-defined.[3] Energy intakes below 100 kcal/kg/day may not be adequate to meet the preterm infant's nutrient needs for achieving recommended growth rates.[14] ESPGHAN, AAP and the International Panel of Experts on Sustainable Food Systems recommend enteral energy intakes of 110–135 kcal/kg/day for stable growth in preterm infants.[33,52,53]

Parenteral and enteral nutrition recommendations differ; preterm infants are fed fewer calories with PN, compared with infants receiving more calories with EN, as there is no energy losses in their stools as they experience less thermogenesis.[48] Energy absorbed is stored in tissue, mainly as fat, but also in protein form.[14] Recommending increased energy intakes for preterm infants with poor growth may not be appropriate without evidence of fat malabsorption, since it is more likely that protein or other nutrients are limiting factors.[33] Therefore, recommendations should be based on adequate protein-energy ratios of 3.6–4.1 g/100 kcal in ELBW infants and 3.2–3.6 g/100 kcal for all other preterm infants with energy intakes > 100 kcal/kg/day. These protein-energy ratios may result in fat mass percentages closer to intrauterine references.[14,33,54] This recommendation is based on studies on preterm infants weighing more than 1 000 g.[54]

1.3.3 Protein

Protein and amino acids (AA) are key factors for adequate growth and should be given as part of an early nutritional intervention.[52,55] Early administration of AA is beneficial in reducing the number of preterm infants with anthropometrical measurements below the 10th percentile.[52] Proteins form a major part of functional and structural components of all the cells in the body.[55] A positive nitrogen balance can be achieved with low energy intakes when adequate AA and proteins are provided.[55] Protein turnover is three times higher in preterm infants than in adults due to their metabolically active intestines and, therefore, higher protein and energy demands per kilogram body weight.[55]

Protein needs are the highest at the beginning of the last trimester and decline slightly towards the end of the gestation period.[3] Foetal protein accretions are about 2–2.5 g/kg/day with foetal AA uptakes of 3.5–4.5 g/kg/day during the last trimester up to term.[39]

Experts recommend initiating parenteral AA within hours after birth, and minimum intakes of 1.5–3 g/kg/day, advancing rapidly to 4 g/kg/day within 2–3 days, have been shown to reduce a negative nitrogen balance.[3,28,37,39,48] ASPEN recommendations are similar, with slightly lower protein dosages for septic infants.[37] It has been observed that high AA uptake reduces the occurrence and severity of neonatal hyperglycaemia, stimulates growth and is not associated with AA overload as seen with increased biomarkers of acidosis, hyperammonaemia, raised blood urea nitrogen or hyperaminoacidaemia.[29,48,54] Positive nitrogen balance and anabolic states can be achieved with AA intakes of 2.5–3 g/kg/day and parenteral lipids and glucose energy intakes of 60 kcal/kg/day.[29] Early administration of high doses of parenteral AA is no longer considered a risk, but has been found to be both effective and safe.[56]

There is limited data defining optimal protein, especially AA intakes, despite good evidence that inadequate intake results in poor growth and lower cognition.[57] Consideration should also be given to the quality of protein, specifically amino acids and not only protein quantities.[33] Receiving protein via the enteral route is difficult to quantify as proteins in the gut need to be digested, absorbed and pass the gut and liver before reaching the systemic circulation.[55] A considerable portion of enteral protein intakes does not reach the systemic circulation and is not available for growth of other tissues.[55] Therefore, a practical approach is to provide relatively high doses of AA from PN, while increasing enteral nutrition for preterm infants at risk of protein deficits due to poor tolerance of enteral feeds.[55]

Current recommendations for enteral protein intakes suggest an initial safe intake of at least 2–2.5 g/kg/day, with gradual increases to 3.5–4.0 g/kg/day (12–14.5% of total energy) for stable preterm infants weighing 1–1.8kg. Higher protein intakes of 4–4.5 g/kg/day are most likely safe for the smallest preterm infants (up to 1 kg) or for those where catch-up growth is needed when on full enteral feeds, gradually declining to 2–2.5 g/kg/day close to term age.[33,55,58]

1.3.4 Fats

Preterm infants receive most of their energy from their fat stores at birth.[59] Preterm infants however, rely on parenteral and enteral intakes of fat due to their limited fat stores.[29,59] Fat provides 40–50% of the preterm infant's total energy needs.[29]

Intravenous lipid emulsions (IVLE) from PN are used as a high-density non-carbohydrate energy substrate with a low volume and osmolarity for easy infusion into the peripheral veins.[29,39,48,59] IVLE is a source of essential fatty acids (EFA), which are crucial for the structural composition and myelination of the brain.[3] EFA deficiency can occur within 2–3 days if preterm infants are fed PN without lipids.[48] A minimum fat intake of 0.5 g/kg/day protects against EFA deficiency.[29] Initiating lipids within the first two days of life in very preterm infants appears to be safe and well tolerated, but only limited data supports this early initiation of parenteral administration of lipids.[48,59] Data on early administration of lipid emulsions remains controversial due to their possible adverse effects on chronic lung disease (CLD), bilirubin toxicity, sepsis and free radical stress, and increased mortality.[48,59] Guidelines suggest avoidance of high dosages of IVLE and to adjust the delivery of IV lipids to plasma triglyceride concentrations.[59]

PN bags available in South Africa for preterm infants contain standard 20% lipid emulsions with a lower phospholipid emulsifier-triglyceride ratio than a 10% lipid emulsion, allowing more efficient clearance of triglycerides even at high triglyceride intakes.[48,59]

Early initiation of parenteral lipids of 1–2 g/kg/day from birth appears to be safe and well-tolerated when infused simultaneously with similar doses of AA, even with high protein dosages of 2–3 g/kg/day within the first few days of life.[59] Early supply of lipids has been associated with improved neurodevelopmental outcomes and adequate energy intakes in VLBW infants.[3] The goal dose of PN lipids is 3–4 g/kg/day with a minimum of 0.25 g/kg/day of linoleic acid to prevent EFA deficiency.[3,59] The quality of lipids intake is important as increased intake of omega-3 long-chain polyunsaturated fatty acids has been shown to reduce the risk of retinopathy of prematurity.[3]

Preterm infants are not able to fully digest fats in the gut due to low levels of pancreatic lipase and bile salts.[14] Enteral fat availability is more dependent on the preterm infant's digestion and absorption capability rather than on enteral nutrient content and composition, which can lead to fat malabsorption due to low levels of pancreatic lipase and bile salts.[14]

ESPGHAN recommend enteral fat intakes of 4.8–6.6 g/kg/day (4.4–6.0 g/100 kcal), providing 40–55% of total energy, whereas Tsang guidelines suggest higher fat intakes for ELBW infants of 6.2–8.4 g/kg/day (4.1–6.5 g/100 kcal) and 5.3–7.2 g/kg/day for VLBW infants.[3,29,33,34] Infants who are fluid-restricted will require higher fat intakes to meet their energy needs.[14,33]

1.3.5 Carbohydrates

Carbohydrates (CHO) are a major source of energy, with glucose as the principal source for the body's metabolic processes as well as for the brain and heart in preterm infants.[33,52] Glucose is also an important carbon source for the de novo synthesis of fatty acids and several non-essential AA.[33] Preterm infants produce glucose mainly from glycogenolysis and, to a lesser degree, from gluconeogenesis. Carbohydrate intake requirements are based on the total energy that has been calculated once the minimum requirements for protein and fat have been deducted.[33,52]

Preterm infants are at risk of hypoglycaemia. Intrauterine glucose utilisation during the last trimester is approximately 5 mg/kg/minute.[48] Early postnatal glucose infusions at birth of approximately 4 mg/kg/min are necessary to prevent hypoglycaemia due to the interruption of the materno-foetal glucose transfer and low glycogen stores in preterm infants.[39,56] Preterm infants have impaired glucose metabolism which increases their risk of developing hyperglycaemia if fed too aggressively with excessive intravenous glucose.[39,60] Stressed and unstable preterm infants have high concentrations of catecholamines, inhibiting insulin secretion and action and promoting glycogen breakdown, thus causing hyperglycaemia.[60] High cortisol concentrations seen in stressed infants promote glucose production and protein catabolism, whereas high glucagon concentrations increase glycogen breakdown and gluconeogenesis.[60] The use of insulin infusions to prevent or reduce hyperglycaemia is not recommended or beneficial as it runs the risk of increasing the chances of hypoglycaemia, with fluctuations of insulin delivery and serum glucose concentrations, resulting in higher complications and mortality.[29,52] A more effective way of reducing hyperglycaemia is early initiation and advancement of AA uptakes.[29,52]

Glucose infusion rates of 4.2–4.9 mg/kg/min (6–7 g/kg/day) should be started immediately after birth with gradual increases up to 8.5–11.8 mg/kg/min (12–17 g/kg/day), provided energy intakes are tolerated.[48] Glucose rates of 60–75% of the non-protein energy intakes are required to maintain blood glucose levels at 2.8–6.7 mmol/L (50–120 mg/dL).[5,39,54]

CHO enteral recommendations are based on lower limits of energy requirements needed for the brain and other glucose-dependent organs.[33] ESPGHAN suggests that CHO intakes of 11.6–13.2 g/kg/day for preterm infants will minimise irreversible losses of protein by reducing gluconeogenesis and preventing ketosis.[33]

1.4 GROWTH OF THE PRETERM INFANT

Premature infants are categorised according to their birth weights and gestational ages, which often determines their morbidity and mortality risks.[61] The classification system for newborn infants based on their birth weight and gestational age was first devised by Battaglia and Lubchenco in 1967 and has been redefined by the American Academy of Pediatrics and the World Health Organization.[61]

Preterm infants are also categorised according to their birth weight; LBW is defined as a weight < 2 500 g, VLBW is defined as a weight < 1 500 g and ELBW is defined as a weight < 1 000 g.[3] They are further classified as appropriate for gestation age (AGA; between the 10th and 90th percentile) in weight, small-for-gestational age (SGA; below the 10th percentile) and large-for-gestational age (LGA; above the 90th percentile).[3] Intrauterine growth restriction (IUGR) is defined as “a fetus that fails to reach his potential growth”, characterised by a BW below the 10th percentile.[8] Extrauterine growth restriction (EUGR) is defined as a weight, length and head circumference below the 10th percentile of intrauterine growth expectations based on postmenstrual age (PMA) at the time of hospital discharge. This inadequate weight gain can also be seen during hospitalisation.[5,6] Lima et al. demonstrated that perinatal variables, clinical practices and neonatal morbidities contribute to the development of EUGR in preterm infants.[25]

1.4.1 Growth charts

Intrauterine curves based on birth weight commonly used to monitor the trajectory of preterm infants are derived from cross-sectional data of babies born preterm.[53] The first birth weight growth charts were based on 300 Canadian Caucasian infants born between 1959 and 1963, and gender-specific growth charts were first published in the UK in 1971.[58]

The most commonly used international standard growth charts for assessing preterm infants from 23 weeks PMA and *z*-scores are the UK-WHO, Fenton 2013 and INTERGROWTH-21st.[53] The

Fenton and UK-WHO are based on cross-sectional data of infants born preterm with growth curves linked to World Health Organization (WHO) post-term growth standards.[53]

The Fenton 2013 growth curve is a more recent dataset with a larger sample size and is based on growth references from systematic reviews and meta-analyses from six datasets derived from actual PMA in weeks and days.[53] The Fenton 2013 reference is currently the best available option as the INTERGROWTH-21st does not have data prior to 33 weeks, with small numbers at 33–34 weeks, whereas UK-WHO data is older, also with small numbers at 24 weeks.[53] The Fenton 2013 dataset also has a larger sample size for length and head circumference in comparison to the other two references.[53] It is also possible to calculate percentiles and *z*-scores from the Fenton 2013 curve.[53] *Z*-scores represent the number of standard deviations (SDs) above or below the reference population mean or median value and are the best means of analysing anthropometrical data.[53]

The INTERGROWTH-21st was a multi-centre, multi-ethnic, multi-country population-based prospective study conducted in eight countries, with the aim of producing international prescriptive growth standards, extending to the WHO Multicentre Growth Reference Study (MGRS) to cover foetal and newborn life.[62] The new international growth standards describes the foetal growth assessed by clinical and ultrasound measures, postnatal growth of term and preterm infants up to two years of life, and the relationship between birth weight, length and head circumference, gestational age and perinatal outcomes.[62,63] Healthy cohorts were selected with no obvious risk factors for IUGR, which describes how all foetuses and newborn infants should grow, as opposed to how some have grown as seen with traditional growth charts.[62] These growth patterns helps to identify perinatal risks related to morbidity and mortality.[62]

1.4.2 Weight

Weight is the most frequent anthropometrical measurement used in the NICU and should approximate the same growth rate and weight gain composition for a normal foetus of the same postmenstrual age.[3,29]

Weight gain and growth velocity is a rapid, inexpensive and non-invasive way of measuring preterm infants' nutritional intakes.[3,14,58] Weight gain or loss reflects changes in the total body composition of intracellular and extracellular fluid compartments, lean tissue and fat mass.[14]

In utero, the foetus undergoes body composition changes with decreasing extracellular fluids and increases in fat and lean tissue composition as gestation progresses.[14,58] Postnatal weight loss of 5–10% of total body weight is usually seen in preterm infants, with amounts as high as 16% seen in extremely preterm infants in the first few days of life, which may be caused by dehydration or inadequate nutrition.[3,14,58] Maayen-Metzger et al showed in their observational study of VLBW infants, that excessive weight loss (> 20%) does not protect infants from BPD and lead to caloric deprivation.[64]

Experts recommend foetal growth rates of at least 15–20 g/kg/day between 36 weeks GA and birth, with gains in lean body mass as the gold standard.[3,39,58,65] Foetal weight gain rates usually decrease from 20 g/kg/day at 24–28 weeks GA to 10 g/kg/day at 39–40 weeks GA.[39]

Energy and protein intakes are adjusted to assist with catch-up growth when growth falters.[66] Catch-up growth is defined as an accelerated growth rate to overcome early nutritional deficits.[66] Martin et al. demonstrated in a large, multicentre cohort study of 1 187 extremely preterm infants, that gaining weight at the recommended rate of 15 g/kg/day once the preterm infants had regained their initial loss of birth weight, does not allow the infant to return to their birth weight percentiles.[66,67] These preterm infants required a consistent growth velocity of 20–30 g/kg/day to return to their birth weight percentiles, with higher rates required by the most gestationally immature infants.[66,68] A serious concern with catch-up growth is the increasing rate of accumulated fat mass in comparison to lean body mass (fat-free mass) as this imbalance may have a higher risk of long-term metabolic consequences that may manifest in later childhood.[66] Postnatal growth may be difficult to achieve due to various morbidities and adverse conditions, usually from inadequate nutrition intake.

Postnatal growth curves for preterm infants demonstrates an initial weight loss, followed by a period of weight gain, with BW regains being reached by day 14 of life as seen in ELBW infants.[69] Such data is derived from preterm infants in the NICU.[69] Krishnamurphy et al. showed in their study that it took between 16 to 22 days for the preterm infants to regain their birth weight depending if they were fed slow or fast feeding volumes respectively.[50] Some infants may take up to three weeks to regain their birth weight when adequate enteral nutrient intakes are tolerated at these approximate ages.[70]

1.4.3 Length

Intrauterine linear growth velocity is approximately 0.9–1 cm per week, which is the rate most neonatologists aim for in preterm infants and is associated with better neurodevelopmental outcomes.[5,68] Mean growth rates from the Olsen curves are 1.4 cm/week for length.[67]

Nutritional strategies have been ineffective in preventing linear growth failure, and its associated risk to cognitive development has only recently re-emerged as a topic of importance as it is closely related to organ growth, specifically the brain.[68] Linear growth failure in preterm infants extends beyond 24 months' corrected age for prematurity.[68] Linear growth measurement is invasive and difficult to obtain and research is limited in determining the optimal linear growth velocity in preterm infants for positive neurodevelopmental outcomes as this measurement is not usually performed.[68] Low energy and protein intakes are associated with prolonged suppression of linear growth. Certain nutrients such as protein and, to a lesser extent, but also important, carbohydrates, fats and zinc are known to play a key role in regulating a variety of functions in linear and brain growth. Optimising protein delivery and reducing protein degradation from inflammation could potentially improve neurodevelopmental outcomes in this population.[68] Protein plays an important role in brain development by stimulating neural growth factors such as insulin-like growth factor-1 and brain-derived neurotropic factor (BDNF).[68]

1.4.4 Head circumference

Head growth has also been used as a measure for brain growth.[71] Maximum growth acceleration of the foetus occurs at 24 to 25 weeks GA with the onset of a head growth spurt during the last trimester and three months postnatally. Disturbance in nutritional supply during this period can lead to undesirable neurodevelopmental outcomes which can be improved with early nutritional interventions.[3,71] An adequate growth reference for occipitofrontal circumference is approximately 0.8–1.1 cm/week in accordance with the Olsen HC growth rates of 0.9 cm/week.[5,12,67]

1.5 IMPACT OF EARLY NUTRITION ON GROWTH

The goal of feeding the preterm infant is to provide nutritional support to ensure optimal growth and development similar to intrauterine growth rates, and to prevent nutrition-related morbidity and mortality.[33,60] Extra-uterine growth restriction is defined as measured parameters of weight, length and head circumference below the 10th percentile at the time of hospital discharge.[5] Postnatal growth failure is inversely related to gestational age and can be worsen by nutritional deficits.[67] Recent studies have suggested that early nutrition of the preterm infant can reduce postnatal growth restriction associated with negative long-term neurodevelopmental outcomes. However, the effects on long-term health are unknown.[5,60] Various feeding practices contribute to under-nutrition, especially energy and protein deficits during the first few days of life.[60] The purpose of early nutrition is to reduce the cumulative energy and protein deficits to minimum levels without adverse effects on the preterm infant, to prevent a catabolic state and to ensure appropriate growth later in life.[5,54] EN is often delayed for several days due to clinicians' impression or concern of increased risk of feeding intolerance, specifically NEC, with early enteral feeding in preterm infants.[5] Delaying enteral feeds may not be effective and may be a risk factor for severe disease, as this results in gut atrophy and reduces the production of gut enzymes necessary for substrate digestion and absorption.[49,54]

There are three stages of nutritional support in the preterm infant:[5]

1) Acute stage – Early nutritional support during the first several weeks of life when infants are at their most vulnerable.

2) Growing care stage – Fortified human milk or preterm formula milk during the transitional phase when enteral feeds are slowly advanced to full enteral feeds, where the opportunity for catch-up growth could be achieved.
3) Post-hospital discharge stage – Catch-up growth during the period of 40–48 weeks PMA for optimal neurodevelopment.

Christmann et al. showed that VLBW infants developed energy and protein deficits despite improved energy and protein intakes during the first two weeks of life. This is consistent with previous findings in which protein did not reach optimal levels as per the guidelines for preterm infants.[72]

Senterre and Rigo showed in their observational study that early PN with a high energy-protein ratio achieved optimal nutritional intakes, limiting the cumulative deficits in both extremely preterm and very preterm infants. Infants enrolled into their study showed postnatal weight gains similar to foetal growth and regained their BW at around seven days of life.[73] A single-centre retrospective study conducted by Shakeel et al. showed that early initiation of trophic feeds within 24 hours in VLBW infants resulted in rapid birth weight regain, improved weight gain and early achievement of full enteral feeds.[74]

Ehrenkranz et al. showed in their retrospective secondary analysis of data collected by the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network, that early nutritional support provided to ELBW infants mediates the influence of critical illness on adverse outcomes, and is consistent with previous data.[75] This study demonstrated that early aggressive nutrition of PN and EN is safe to administer to critically ill VLBW infants and is associated with improved growth, without increased risk of clinical outcomes such as NEC.[75] A recent Cochrane review showed no increased risk of NEC in early feeding when compared with delayed feeding in very preterm infants.[42] Olsen et al. found that differences in weight gain velocity could be predicted or determined from early protein intake. Data from Stephens showed that increased energy and protein intakes in the first week was associated with higher mental development index scores and lower risk of length growth restrictions at 18 months in ELBW infants.[67]

1.6 MORBIDITY ASSOCIATED WITH PREMATURITY

Although the risk of adverse consequences declines as GA increases, improved survival has raised concerns about increased rates of short- and long-term morbidities, with considerably high risk of death and disability noted in the extremely premature infant.[21,76]

1.6.1 Bronchopulmonary dysplasia (BPD)

Preterm infants are at risk of infectious and non-infectious respiratory complications, with as many as 40% of survivors having some degree of bronchopulmonary dysplasia (BPD) as either short- or long-term morbidity.[21,76] BPD is a common complication related to lung injury in the management and treatment of respiratory distress syndrome (RDS) in low birth weight infants.[77] Infants born before 30 weeks GA and weighing < 1 500 g have about a 20% risk of being diagnosed with BPD, with increased incidence in survival in VLBW infants of lower GA.[77]

Nutrition and fluid management is vital in the management of BPD by decreasing injury through repair and maintenance.[77] Fluid restriction may improve lung function and decrease oxygen consumption and demand. BPD patients have high caloric needs in order to increase metabolic rate and oxygen consumption with balanced intakes of protein, carbohydrates and fats essential for growth and repair, and prevention of increased carbon dioxide (CO_2) production and ventilatory failure.[77]

1.6.2 Intraventricular haemorrhage (IVH)

Intraventricular haemorrhage (IVH) is a major complication of prematurity. IVH originates in the periventricular germinal matrix, the source of neuronal and glial precursor cells in the immature brain.[78] The aetiology is multifactorial and is attributed primarily to the fragility of the germinal matrix vasculature and disturbance in cerebral blood flow.[78]

Optimal early nutrition influences growth and brain development in preterm infants, which may exert neuroprotective effects.[79] Postnatal growth impairment has been linked to a decrease in microstructural development or maturation of the cerebral cortex, which could be the result of inadequate nutritional support.[79] Thus nutritional deficits may impede brain growth and maturation.[79] Exposure to extrauterine life may be harmful to the preterm's developing brain, increasing the chances of developing cerebral palsy (CP), a group of non-progressive motor impairments that results in movement disorders that could have an impact on nutrition intake.[76,80,81] An indication of CP is used as an overall neurologic outcome associated with prematurity.[76]

1.6.3 Retinopathy of prematurity

Increased survival of premature infants increases the chance of retinopathy of prematurity (ROP),[82] a complication of prematurity associated with visual impairment and the second leading cause of blindness in children.[82] Numerous studies conclude that children with visual impairment are susceptible to neurodevelopmental disabilities such as CP, seizures, autism and mental retardation.[82] Poor weight gain is a risk factor for the development of ROP during the first weeks of life, suggesting that early adequate nutritional support and sufficient polyunsaturated fatty acids may play an important role in the prevention of ROP.[3]

1.6.4 Neonatal jaundice

Neonatal jaundice (NNJ) is derived from elevated levels of total serum bilirubin, and affects 80% of preterm infants who are at higher risk of bilirubin toxicity.[83,84] Suboptimal feeding in the first few days of life may lead to dehydration which can result in NNJ and an increase in the enterohepatic circulation related to the re-uptake of excreted bilirubin by the intestines. NNJ can also be seen with decreased food intake and stooling, and reduced blood supply to the liver associated with patent ductus arteriosus (PDA).[83,85]

Clinical jaundice is more difficult to diagnose in infants with dark skin tones, and close examination of the sclera, gums and blanched skin needs to considered.[84] Management of NNJ involves support for early feeding and adequate hydration, treatments that may include phototherapy, blood exchange transfusion and administration of pharmacological agents of intravenous immunoglobulin.[84] Kernicterus or bilirubin encephalopathy can lead to acute or chronic conditions such as lethargy, poor feeding, abnormal tone, seizures, choreoathetoid CP, hearing loss, dental dysplasia and oculomotor palsies.[83]

1.6.5 Neonatal sepsis

Preterm birth is a major risk factor for neonatal sepsis (NNS), a systematic infection that occurs in infants at $\leq$ 28 days of life and is a major cause of neonatal death and chronic morbidity.[86,87] "Suspected sepsis" is a common diagnosis made in the NICU; the signs are non-specific with inflammatory syndromes of non-infectious origin masquerading as those of neonatal sepsis.[88]

NNS is categorised as either early-onset or late-onset sepsis. Early-onset sepsis occurs within 72 hours of life due to transmission of bacterial pathogens from mother to infant before or during delivery, and is inversely related to infant birth weight.[86–88] Late-onset sepsis occurs after 72 hours of life and is caused either by vertically or horizontally acquired pathogens associated with procedures and contamination present in the NICU, or by indirect human contact with the contaminated environment.[86]

Premature infants have an increased risk of infection due to their immature skin and mucous barriers and an underdeveloped defence mechanism.[86] Early enteral feeding initiated within the first 24 hours of life has shown benefits in the prevention of nosocomial infection, without increasing the risk of intestinal complications such as NEC.[89] Feeding human milk within 72 hours after birth reduces the risk of late-onset sepsis about threefold.[89] Preterm delivery may place the newborn in a hypercatabolic state that may be worsened by sepsis, causing the body to provide amino acids for the synthesis of elements essential for the inflammatory response and activation of the immune system.[90] This leads to a negative nitrogen balance, which is poorly corrected by inadequate introduction of exogenous nitrogen.[90]

1.6.6 Patent ductus arteriosus

Patent ductus arteriosus (PDA) is a common congenital heart anomaly in preterm infants and is inversely proportionate to GA at birth.[91] Two-thirds of ELBW infants are diagnosed with persistent PDA, with 75% of those born < 28 weeks GA.[91] The ductus arteriosus is a blood vessel that connects the pulmonary artery to the descending aorta, which carries blood away from the heart of the developing foetus.[3] Spontaneous ductus closure is often delayed in preterm infants, with closure rates declining in lower GAs.[3] The open ductus results in excessive blood flow from the aorta through the lungs, increasing the risk of pulmonary congestion, pulmonary oedema and escalating respiratory distress.[92] Prolonged patency is associated with adverse outcomes of BPD, IVH, periventricular haemorrhage, NEC, CP, prolonged assisted ventilation and higher rates of mortality.[92] Conservative treatment with fluid restriction during the first days of life is associated with a decreased incidence and risk of PDA, as well as of BPD and NEC.[47]

1.6.7 Feeding intolerance

Feeding intolerance, an undefined and uncertain problem, refers to a combination of several clinical features, and is defined as "the inability to digest enteral feedings presented as gastric residual volume of more than 50%, abdominal distension or emesis or both, and the disruption of the patient's feeding plan".[93]

Other clinical manifestations and symptoms associated with feeding intolerance include bloody stools, apnoea, bradycardia, hypotension and temperature instability.[94] The incidence of feeding intolerance is estimated at 16–29% in preterm infants depending on the subjective definition used.[94] Preterm infants often experience feeding difficulties due to functional immaturity of the gastrointestinal tract, placing them at risk of NEC.[95]

Feeding intolerance often results in suboptimal nutrition as a result of fasting or reduced enteral nutrition, delay in achieving full enteral feeds, and increased risk of sepsis due to prolonged usage of parenteral nutrition, all of which are influenced by the clinician's personal judgement.[93,95]

A Cochrane systematic review showed that early enteral feeding does not significantly affect the incidence of feeding intolerance when compared with delayed feeding (starving). However, delayed introduction of enteral feeds does not protect VLBW infants from feeding intolerance, NEC and all-cause mortality, and it significantly increases the duration of hospital stay.[3,43,93]

1.6.8 Necrotising enterocolitis

Necrotising enterocolitis (NEC) is a condition affecting mainly preterm infants, and is characterised by intestinal necrosis of the bowel ranging from mucosal injury to full thickness necrosis and perforation.[15] In the least severe cases, the infant will present with mild abdominal distension and minimal systemic upset. Severe cases result in respiratory and cardiovascular collapse, multi-organ failure and, in some cases, death.[96] Reported incidence is about 7% in VLBW infants, with an estimated 15–30% mortality risk and long-term morbidity among survivors, with the highest risk at 29–33 weeks' corrected GA.[15,97,98]

The aetiology or pathogenesis of NEC is not fully understood, but the main contributing factors are intestinal immaturity, enteral feeds, the intestinal microbiome, inflammation, local inflammation and/or reperfusion injury.[97] Current treatment practices have not changed from those used in the past. They include bowel rest, broad-spectrum antibiotics, parenteral nutrition, ventilatory support, blood pressure measurement, peritoneal drainage and, in severe cases, resection of the necrotic bowel.[98]

A widespread opinion among clinicians is that NEC occurs in preterm infants who are fed enterally with high caloric feeds aimed at boosting growth rates.[96,97] These increased feeds may result in mucosal injury to an existing immature gut, further amplifying the risk of developing of NEC. However, the association between the type of feed and the development of NEC is not completely understood.[96,97] Breastmilk offers dose-related protection against NEC, probably due to its immunologically active components comprising of immunoglobins, cytokines and complement proteins.[96] NEC has negative neurological outcomes that trigger bowel injuries and may promote systemic inflammation, thus possibly affecting brain development.[99]

1.7 FEEDING PRESCRIPTIONS AND NUTRIENT INTAKES

The amount of nutrient intakes takes time to establish in preterm infants during the first days of life but are commonly interrupted for clinical reasons.[100] A number of factors can contribute towards these clinical reasons, including either parenteral or enteral feeds being withheld due to intolerance, blood transfusions, administering medications incompatible with PN, and changes in ventilatory support machines or provision of IV fluids to correct glucose or electrolyte imbalances.[67] Data by Embleton et al showed that infants developed large deficits of energy and protein by day seven, which still had not been recovered by the time of discharge.[100,101] Embleton et al. further points out that infants are fed recommended intakes that are designed for maintenance and normal growth, and not the provision needed for catch-up growth.[101] Clinicians should be mindful of such feeding interruptions, the consequences of inadequate intakes and the impact nutritional deficits seen. As much as a 10–20% difference can be found between feeding prescriptions and intakes which could contribute to cumulative deficits.[67] A better understanding is also needed on how PN prescriptions and intakes are adjusted and reduced when EN is advanced, to determine if preterm infants receive adequate nutrient intakes from suboptimal prescriptions.

Despite medical advances and expert opinion on nutrition for premature infants over the past 20 years, this vulnerable group is still at high risk of postnatal growth restriction due to inadequate nutritional intakes.[102] Abel conducted an observational study in 40 VLBW infants, which showed that delivered nutrient intakes were consistently lower than 15% of prescriptions, with 30–50% of infants having extrauterine growth restriction at 36 weeks PMA.[102]

Nutritional intakes are inadequate due to:[102]

1) Medical and nutritional practices as clinicians are concerned about feeding intolerances, medical complications and NEC.
2) Feeding prescriptions are suboptimal to sustain growth rates and actual nutrient intakes are not being achieved as prescribed.
3) Feeding prescriptions are inconsistent with current recommendations as prescriptions are based mainly on fluids.

Although experts recommend growth rates for preterm infants, these do not account for the accumulated nutritional deficits that occur during the early days of life.[102] Clinicians habitually assume that the preterm infant receives the same amount as they have been prescribed, often not taking into consideration feed interruptions due to intolerances, medical procedures or venous inaccessibility. However, the clinician's main concern is to ensure that the preterm's medical state is stable and not necessarily to focus on the provision of nutrition during the first days of life. Growth rates are not necessarily related to feeding prescriptions, but more likely due to the preterm infant's nutritional intake.[102]

Abel suggests that nutrition and fluid management protocols may need to be revised to meet the nutrient needs of preterm infants during the transition phase from PN to EN.[102] Focusing on enteral and parenteral nutrition rather than on fluid primarily may assist in meeting nutrient needs or recommendations. Providing nutritional support to ELBW and VLBW infants is challenging, especially in resource-constrained conditions.

A recent survey conducted in South Africa by Raban et al. looked at the enteral feeding practices of paediatricians in preterm infants.[103] The survey examined the advancement of enteral feeds and investigated whether the units had feeding policies or strategies, but did not look at specific nutrient intakes.[103] This survey showed that preterm infants commenced enteral feeds within 48 hours and that trophic feeds were defined as volumes between 0.5 and 20 ml/kg/day.[103] These feeding volumes were maintained for four to five days before increasing feeds on a daily basis.[103] The survey had a low response rate as it was web-based, as is commonly observed with such study designs. [103]

The ability of clinicians to know actual nutrient intakes in relation to feeding prescriptions is challenging and often difficult to determine when using different feeding routes or regimens. However, the ability to determine the nutrient intakes and their impact on preterm infants' growth will assist in developing and implementing appropriate feeding protocols.

Studies conducted on premature infants are usually well-resourced, with many having feeding protocols in place, unlike in South Africa where healthcare systems are still under-developed and lack data. Research conducted on actual intakes is time-consuming for a number of reasons such as multiple products used with various nutrient compositions, numerous interruptions, or changes in feeding prescriptions made throughout the day based on decisions relating to the medical care of the patient. Limited resources in South Africa may contribute to poor postnatal growth and the inadequate nutrient intakes of premature infants. CHBAH does not following a feeding protocol for enteral or parenteral nutrition which can lead to poor adherence of prescribing nutrient requirements for premature infants.

This study looked at both parenteral and enteral nutrition, and other non-nutritional fluids such as intravenous (IV) fluids that contribute towards energy and carbohydrates. The study also considered whether intakes and prescriptions are in line with recommended nutritional guidelines and their association with growth outcomes, specifically percentage weight loss and whether birth weight had been regained on particular study days.

1.8 MOTIVATION FOR THE STUDY

Growing advances in the neonatal care has seen increased chances of survival among infants born premature at lower gestational ages and birth weights.[25] Despite these advances, premature birth is the leading cause of child death globally.[7] Although, not listed as one of the top ten countries with the highest preterm birth rates, South Africa reported 7 800 deaths in 2010.[7]

Can optimal nutrition in premature infants can reduce the risk of morbidity and mortality particularly with adequate provision during the first weeks of life? The paucity of studies in South Africa on preterm feeding practises are limited and whether these nutritional recommendations are met in the clinical setting is unknown.

The aim of this literature review and scope of the study is specific to the fluid, energy and macronutrient (protein, carbohydrate and fat) needs of the preterm infant. It does not include further analysis into the micronutrient requirements of preterm infants. Findings may provide baseline information to clinicians on whether nutrient requirements are attained in premature infants born in South Africa, according to international guidelines. This study will help gain insight on existing feeding practises and maybe useful in compiling a feeding protocol to meet nutrient requirements fit for a South African setting. CHBAH will benefit from this study by drawing attention on a implementing such a feeding protocol. This study will also help clinicians to play a more active role in nutrition support to preterm infants, ultimately decreasing nutrient deficits and growth retardation over the short and long term.

CHAPTER 2

RESEARCH DESIGN AND METHODOLOGY

CHAPTER 2: RESEARCH DESIGN AND METHODOLOGY

2.1 AIM

To compare the feeding prescriptions and the actual nutrient intakes to the recommended nutritional guidelines of premature, low birth weight infants admitted to a tertiary hospital.

2.2 SPECIFIC OBJECTIVES

i. To determine the feeding prescriptions of low birth weight (LBW) infants.
ii. To determine the actual nutrient intakes of LBW infants.
iii. To compare feeding prescriptions with recommended guidelines.
iv. To determine the difference between feeding prescriptions and actual nutrient intakes among birth weight categories.
v. To determine the advancement of enteral feeds until full feeds are reached independently of parenteral nutrition.
vi. To determine the impact of nutrient intakes on the regaining of birth weight.

2.3 RESEARCH QUESTION

Are feeding prescriptions and actual nutrient intakes in premature, LBW infants comparable to recommended nutritional guidelines?

2.4 NULL HYPOTHESIS

i. H_0: there is no difference in actual nutrient intakes to feeding prescriptions.
ii. H_0: there is no difference in feeding prescriptions to recommended nutritional guidelines.
iii. H_0: nutrient intakes have no effect on the regaining of birth weight.

2.5 STUDY DESIGN

An observational, descriptive (with an analytical component), prospective cohort study was conducted.

2.6 STUDY POPULATION AND SAMPLING

2.6.1 Study population

All preterm (< 37 weeks GA) and LBW (< 2 500 g) infants born and admitted to the neonatal unit at Chris Hani Baragwanath Academic Hospital (CHBAH), for whom written consent was obtained, were included in the study. The study population was further stratified according to their birth weight (BW) groups, i.e. LBW, VLBW or ELBW.

2.6.2 Sampling method

Non-random sampling was used to select subjects and participants were selected and stratified according to BW groups. Consecutive patients meeting the inclusion criteria were enrolled in the study until the required sample size based on the inclusion criteria was obtained. The data collection period commenced on 5 April 2015 and was completed on 6 September 2015.

2.6.3 Inclusion and exclusion criteria

Inclusion criteria

- Preterm infants born less than 37 weeks GA.
- LBW infants with a birth weight less than 2 500 g.
- Preterm infants born and admitted on day one of life into the neonatal intensive care unit (NICU) and transitional intensive care unit (TICU) of CHBAH.
- Preterm infants who survive longer than 24 hours of life.
- Infants who were receiving majority (more than 50 %) of their mother's breastmilk as expressed breastmilk in order to quantify amounts received.

Exclusion criteria

- Premature infants not born at CHBAH (transfers from other institutions after day one of life).
- Premature infants with a birth weight less than 500 g.
- Infants with congenital, gastrointestinal or chromosomal abnormalities and hydrocephalus.
- Infants who were on fully breastfeeding or majority of feeds (more than 50 %) received via the breast and not expressed breastmilk. These infants were excluded as it would be impossible to quantify the amount of nutrition received.
- Infants seen by the PI who is the dietitian responsible for the nutritional care of patients in the unit. To avoid bias or confounding results, all patients referred for nutritional support were seen by a dietitian not working in the unit.

2.6.4 Sample size and selection

Sample size was confirmed with the help of a statistician. The level of significance was set at $\alpha = 0.05$ to detect statistical significance. The power of the study was set at $\beta = 0.1$, with a 90% power to detect any difference. Confidence Intervals of 95% were used to estimate the true population.

A minimum of $n = 26$ subjects was needed to perform a one-sample t-test between the sample value and the hypothesis value, in order to detect the difference that occurs outside of the hypothesis range for the first two hypotheses. The total sample size was increased to a minimum of 150 subjects to ensure an adequate power for the third and fourth analytical hypotheses. A minimum of 150 subjects was taken into account for limitations such as time, budget and availability of subjects. Equal numbers of subjects, a minimum of $n = 50$ subjects in each BW category were observed to ensure that comparisons could be made for stratification analysis. A larger sample size was used to produce more precise results about the population. A total of one hundred and fifty six patients ($n = 156$) were included in the final sample size.

2.7 METHODS OF DATA COLLECTION

Data collection was carried out in the 12-bed neonatal intensive care unit (NICU) and the approximately 50-bed transitional intensive care unit (TICU) of CHBAH. All patients born and admitted to the unit were screened daily for eligibility for the study based on their presence in the unit and the unit's admission records (Appendix A).

Subjects meeting the inclusion criteria were enrolled into the study and data was collected on day one (day of birth), two, three, seven and day 14 of life. All relevant data was recorded on the data collection sheets (Appendix B).

2.7.1 Subject data

The study subjects' ICU charts, fluid charts and hospital files were reviewed to obtain the following baseline data:

a. ***Patient information***:

   Gender, gestational age, birth weight, length and head circumference, date and time of birth, date of admission and APGAR scores.

b. ***Medical information***:

   Primary diagnosis and other co-morbidities during the study period were recorded. Additional medical information relevant to the study was also recorded on the data collection sheet, such as reasons why the study participant is nil per os; intubation/ extubation or any surgery planned, feeding intolerances (vomiting, gastric aspirations, etc.) or fluid restrictions.

c. ***Maternal information***:

   Date of birth, age, number of pregnancies and deliveries, mode of delivery and HIV status, steroid use and reason for premature delivery.

d. ***Anthropometry***:

Baseline anthropometry included weight, length and head circumference measurements. Weekly anthropometry were also recorded.

2.7.2 Feeding prescription and actual nutrient intakes

The type and route of nutrition, parenteral nutrition (PN), enteral nutrition (EN) and type of intravenous (IV) fluids were recorded in each subject's hospital file as prescribed by the clinician. The feeding and IV fluids received by the subject as recorded by the nursing staff on the feeding chart were recorded as well.

2.8 ANTHROPOMETRY

The summary of anthropometry performed during the study period is presented in Table 2.1.

Table 2.1: Description of anthropometrical measurements: summary

	Weight	**Length**	**Head Circumference**
Days	1, 7, 14	1, 7, 14	1, 7, 14
Description	Naked No diaper No CPAP* cap	Naked No diaper No CPAP cap	Naked No diaper No CPAP cap
Measurement instrument	Baby scale	Length Board	Measuring tape
Measurements taken by	Nursing staff and/or PI	Nursing staff and/or PI	Nursing staff and/or PI
Position	Supine	Supine	-

**CPAP: continuous positive airway pressure*

2.8.1 Weight

Nursing staff in the labour ward routinely weighed the subject after delivery (day one of life) and follow-up measurements were done by the nursing staff and/or PI on a weekly basis (day seven and 14 of life).

Weight was measured with a digital infant scale (Seca 334) on a flat hard surface to the nearest 0.1 kg (100 grams) according to standard weighing procedures.[104] The infant scale was calibrated using 1kg dumbbells during the pilot study. The participant was measured naked, with no clothing or diaper and in a supine position. Weight was measured twice; if the first two weights differed by more than 0.5 kg, a third weight was taken and an average of the three weights was used. Subjects who were placed in incubators without any instruments, such as ventilation tubes, connected to their body were measured for weight by removing them briefly from the incubator and placing them on the scale. Pads or tubes connected to the subject for monitoring their vital signs were removed briefly while anthropometry was being measured.

Subjects whose condition was too critical (minimal handling requested by the medical staff) to be moved due to intubation or other tubing connections, such as CPAP, were measured at the earliest possible opportunity, unless permission had been granted by medical staff to weigh them without compromising their airway passage.

2.8.2 Length

Nursing staff in the labour ward routinely measured the subjects' recumbent length after delivery, and follow-up measurements were done by the PI on a weekly basis (days seven and 14 of life). Inaccurate measures performed by nursing staff were observed and corrected by the PI. Recumbent length was measured with a length board (Seca 417, a measuring device with an integrated headpiece and a separate foot positioner that moves along the slightly raised guide rail) on a flat, hard surface to the nearest 0.1 cm according to standard measuring procedures. The subject was measured naked with no clothing or diaper. The subject was measured in the supine position, the head touching the board firmly with the Frankfort plane perpendicular to the headboard, and the legs were gently straightened and pressed slightly down alongside the (length) board. The foot positioner was placed against the soles of the study subject's feet, touching the heels and toes. The length was measured twice; a third length was taken if the first two lengths differed by more than 0.5 cm and the mean of the three lengths was used.

Subjects who were too critical (minimal handling requested by the medical staff) to be moved due to intubation or other tubing connections, such as the CPAP device, were measured at the earliest possible opportunity, unless permission had been granted by medical staff to measure the subject's length without compromising the subject's airway passage. The length board was inserted under the subject's body when ventilated or on a CPAP machine while in the incubator/radiant warmer. CPAP caps were removed briefly while measuring length.

2.8.3 Head circumference (HC)

Nursing staff in the labour ward measured the subjects' HC after delivery and follow-up measurements were done by the PI on a weekly basis (days seven and 14 of life). HC was measured using a standard, non-stretch measuring tape to the nearest 0.1 cm. The measuring tape was placed around the widest part of the subject's head i.e. occipitofrontal (OF) circumference. Subjects who were placed in incubators without any machines connected to their bodies were measured inside the incubator. Subjects who had any bandages covering their heads or peripheral IV drips obstructing access for accurate measurements were excluded from measuring the HC until the OF area became accessible.

Subjects who were too critical (minimal handling requested by the medical staff) to be moved due to intubation or other tubing connections, such as receiving CPAP, were measured at the earliest possible opportunity, unless permission had been granted by medical staff to measure the subject's HC without compromising the subject's airway passage. CPAP caps were removed briefly while measuring HC, while maintaining CPAP delivery to the subject.

2.9 TRAINING AND STANDARDISATION

General information regarding the research was given to nursing staff working in the NICU, in their staff tea room, in the form of an information sheet addressing the importance of accurate record keeping (Appendix C) before and during the commencement of the study. New staff rotating through the unit were informed verbally of the research being conducted. A standard of practice (SOP) was developed to ensure consistency (Appendix D).

2.10 VALIDITY AND RELIABILITY

Validity and reliability was tested during the pilot study to ensure accurate measurements by using appropriate equipment; a baby scale that measures in weight in kilograms (kg), a length board and a non-stretch measuring tape that measures in centimetres (cm). The pilot study was conducted to ensure that all procedures and data collection forms were readable and consistent throughout the study period. The data collected for the feeding prescriptions by the clinicians is reflective of the feeding guidelines specific to the facility's guidelines for its unit. Data collected is only from a single centre and can thus only be generalised to this unit's population.

Measurements were performed according to the standard measuring procedures described earlier in this chapter. Measurements on day one were also performed by the PI when discrepancies were noted during the pilot study of differences between lengths measured using measuring tapes instead of a length board despite length board given to measure accurately.

Standard measuring techniques as stated by the manufacturer's measuring instrument were carried out. The measuring scale was set to a 0.00 kg reading before weighing subjects, to ensure accurate and reliable results. Either the same measuring scale, or a different scale of the same model, was used to perform measurements to ensure reliable readings. This method ensured the improved validity of the study. The time of day and whether the infant had been fed before measurements could have potentially affected the measurements and therefore influenced the validity. To improve reliability of the measurements, weights were taken at least twice and the average of the two measurements was used to ensure accurate readings.

2.11 PILOT STUDY

A pilot study was conducted in the NICU/TICU of CHBAH over a period of seven days in order to determine the completeness and accuracy of the following:

- Increase the validity of the study
- Data collection of relevant information needed for study purposes.
- Data entry procedure for day one, two, three and seven of life.
- Data coding procedure.

Ten subjects were included in the pilot study and they were subsequently exempted and excluded from the main study.

Minor adjustments were made to the data collection sheet by including the mother's contact details, hospital number, reason for premature delivery, gravida and parity, steroid usage and inclusion of IV fluid calculations.

2.12 DATA MANAGEMENT AND ANALYSIS

Data was captured on Microsoft Excel (2013)® and exported to IBM SPSS version 23 (StatSoft Inc. [2015] STATISTICA [data analysis program software system], www.statsoft.com) for data analysis. The Peditools™[105] application was used to calculate anthropometrical *z*-scores and GA classifications using the Fenton 2013 growth chart calculator for preterm infants.

2.12.1 Absolute value

The absolute value is the statistical value in which the analysis was calculated and compared to the recommendations. The absolute values were selected on the basis of commonly used values in the hospital or according to reference values based on current literature, when calculating feeding prescriptions.

Fluid values of 150 ml/kg/day and 180 ml/kg/day for PN and EN respectively is commonly aimed values used in the hospital setting and seen as full feeds achieved.

Energy values of 100 kcal/kg/day and 130 kcal/kg/day for PN and EN respectively. The PN value for energy was selected as standard TPN bags provides an estimated amount of 100 kcal/kg/day, whereas the energy value for EN was based on the upper range of recommendations noted in Table 1.2.

Protein targets of 3.5 g/kg/day were selected for both PN and EN. Lower protein values were chosen as achieving high protein targets are challenging as previous documented. The target value chosen was based on similar study outcomes and design, looking into nutrient intakes.[102,107]

Fat targets of 3.5 g/kg/day and 7 g/kg/day for PN and EN were selected as absolute values. PN fat values was based on the standard TPN formulation providing the same amount of protein as fat per bag. Lipid intakes of 25 – 40% of non-protein calories is recommended according to Koletzko.[48] A higher fat value for EN was selected on the basis of ESPGHAN recommending fat intakes or 40 – 55% total energy. Preterm breastmilk fat content is of a higher composition compared to term breastmilk, hence higher values for EN used.[106]

Carbohydrate values of 9 mg/kg/day and 12 g/kg/day for PN and EN respectively were selected. These values provide safe infusions of CHO without the detrimental effects on the infants health seen with either low or high values.[33,48]

These values should give insight into whether guidelines are met as they fall within the reference values of ESPGHAN, currently the best standard references for enteral nutrition. Absolute values used for the first three days of life were calculated on different recommended values by the same authors mentioned in Table 1.1 and 1.2.

2.12.2 A clinical significance

A clinical significance is defined as a small difference found between the feeding prescriptions or nutrient intakes that is of clinical benefit to the infant. There is not set standard of clinical significance.

2.12.3 Feeding prescriptions and nutrient intakes

FP were calculated based on the type of feed (EN and/or PN) and/or IV and the volume prescribed by the clinician. Where two or more prescriptions were made within 24 hours, an average of the prescriptions was used to calculate the total FP for the day. NI was based on the type of feed the subject received (fed by either the mother or the nurse). Total fluid, energy and macronutrients (protein, fat and CHO) were determined and calculated based on prescriptions and intakes. Nutrient analysis of breastmilk was calculated according to gestation age as determined by Bauer and Gerss and formula milk according to the manufacturer's nutritional analysis.[106] The contribution of energy and glucose from the IV was also calculated based on content analysis from the manufacturer's details.

2.12.4 Feed advancements

Feed advancements were calculated based on the fluid increments derived from enteral nutrition, expressed in millilitres per kilogram per day (ml/kg/day). Comparisons of the feed advancements were made between days one, two and three for the prescriptions and intakes, and whether full feeds were reached independently of PN on day seven or 14 of life.

2.12.5 Impact of nutrient intakes on birth weight regain

Correlations between the subjects' NI and their current weights were performed for days seven and 14. These associations served to determine whether NIs had any impact on subjects regaining their BW on day seven and/or 14 of life.

2.12.6 Anthropometry

Anthropometrical measurements were analysed according to the revised Fenton 2013 growth charts, using the Peditools™[105] application for the interpretation of *z*-scores and the appropriateness of their weight (SGA, AGA or LGA). Refer to Table 2.2 for classification of anthropometry.

Table 2.2: Classification of anthropometry

Classification	**Definition of Classification**
IUGR	WAZ < 1.28 *z*-score
Symmetrical	Wt, Lt and HC< 10^{th} percentile
Asymmetrical	Wt < 10^{th} percentile, Lt, HC > 10^{th} percentile
AGA	> 10^{th} percentile
SGA	< 10^{th} percentile
LGA	> 90^{th} percentile
Weight gain	
Poor	< 15 g/kg/day
Adequate	> 15 g/kg/day
WAZ: weight for age *z*-score; Wt: weight; Lt: length; HC: head circumference	

Source: Fenton, Peditools™ application, AAP

2.12.7 Statistical analysis

Summary statistics were used to describe the variables and/or to determine outliers. Distributions of variables were presented with histograms and frequency tables. Medians and means were used as the measure of central tendency for ordinal and continuous responses if data was skewed or normally distributed and standard deviations and quartiles as indicators of spread.

Relationships between two continuous variables were analysed with regression analysis and the strength of the relationship was measured with Pearson correlations, or with Spearman correlations when continuous variables were not normally distributed. Where one continuous response variable was related to several other continuous input variables, multiple regression analysis was used to quantify the relationships. The relationships between continuous response variables and nominal input variables was analysed using appropriate analysis of variance (ANOVA) and appropriate repeated measures analysis of variance (RMANOVA) when data was measured at specific time intervals. The relationship between two nominal variables was investigated with contingency tables and likelihood ratio chi-square tests. The Friedman non-parametric test was used to assess differences among repeated measures of the same ordinal variable. The Mann-Whitney non-parametric test was used to determine if significant differences existed between two ordinal variables.

A p-value of $p < 0.05$ represented statistical significance in hypothesis testing and 95% confidence intervals were used to describe the estimation of unknown parameters.

2.13 ETHICAL AND LEGAL ASPECTS

The study was approved by the University of Stellenbosch Health Research and Ethics Committee (S14/10/248) and the University of Witwatersrand Health Research and Ethics Committee (M150132) through the Chris Hani Baragwanath Academic Hospital's Medical Advisory Committee (MAC). The protocol was adjusted and finalised after being reviewed by the Ethics Committee before conducting the pilot study and main study.

Written permission letters were granted by the following respective people at CHBAH:

1. Chief Executive Officer, Dr. S Mfeyane.
2. Head of Department of Neonatal ICU, Dr R Thomas (Acting Head of Department).

Informed consent was obtained and granted by the subject's parent, in most cases by the mother, as study subjects were minors (Appendix E). Informed consent was obtained by an underage mother's parent as she was still under parental supervision, as well as assent from the mother herself (Appendix F). Consent was also obtained to ensure compliance with the Ethics Committee and translated in the Zulu language for those who could not understand English. All caregivers of the study subjects were informed regarding the purpose of the study, and potential risks and/or benefits were explained to all caregivers present at the time of obtaining consent. Participation into the study was voluntary and caregivers were not coerced into participating. No incentives were offered for participation. The subjects' parents had the right to withdraw from the study if they wished to. Information was communicated in a language that was suitable for the parents to understand the scope of the study, and nursing staff assisted with interpretation of the consent form. Consent was obtained within 24 hours after identification of eligible subjects, allowing the mother to make an informed decision regarding consent. Telephonic consent was not needed during the study (Appendix G).

Data was handled in a confidential manner. A screening sheet containing each subject's name and hospital details admitted to the NICU/TICU was kept separately from the data collection sheets and was only accessible by the PI. The screening sheet was used to trace any information needed by the PI during the study period or for obtaining data that was unavailable on the data collection sheet. Patients who were eligible and met the inclusion criteria were enrolled sequentially into the study and each received a unique research code. All data collection sheets were kept anonymous and only included the research codes. All personal information of the subjects was kept separate from the data collection sheets. Data on subjects' personal information was also kept anonymous from the statistician for analysis.

CHAPTER 3

RESULTS

CHAPTER 3:RESULTS

The results of this study will be represented in the following sequence:

I. Demographic information of the mother-infant dyad.
II. The feeding prescriptions and actual intakes compared with parenteral and enteral recommended guidelines for parenteral nutrition, enteral nutrition and IV fluids.
III. A comparison between the actual nutrient intakes and the feeding prescriptions.
IV. The advancement of enteral feeds and a description of the time of achievement of full enteral feeds.

3.1 BASELINE CHARACTERISTICS

Of the 215 premature infants screened, 165 met the inclusion criteria and were enrolled after parental consent had been obtained. Data analysis was performed on 156 of these included infants. Figure 3.1 shows a detailed flow chart of the included participants. Reasons for not obtaining parental consent includes patients having been discharged before obtaining consent, mothers not being available to give consent, mothers having died, and one case where the mother was underage (< 18 years) and had social issues at home.

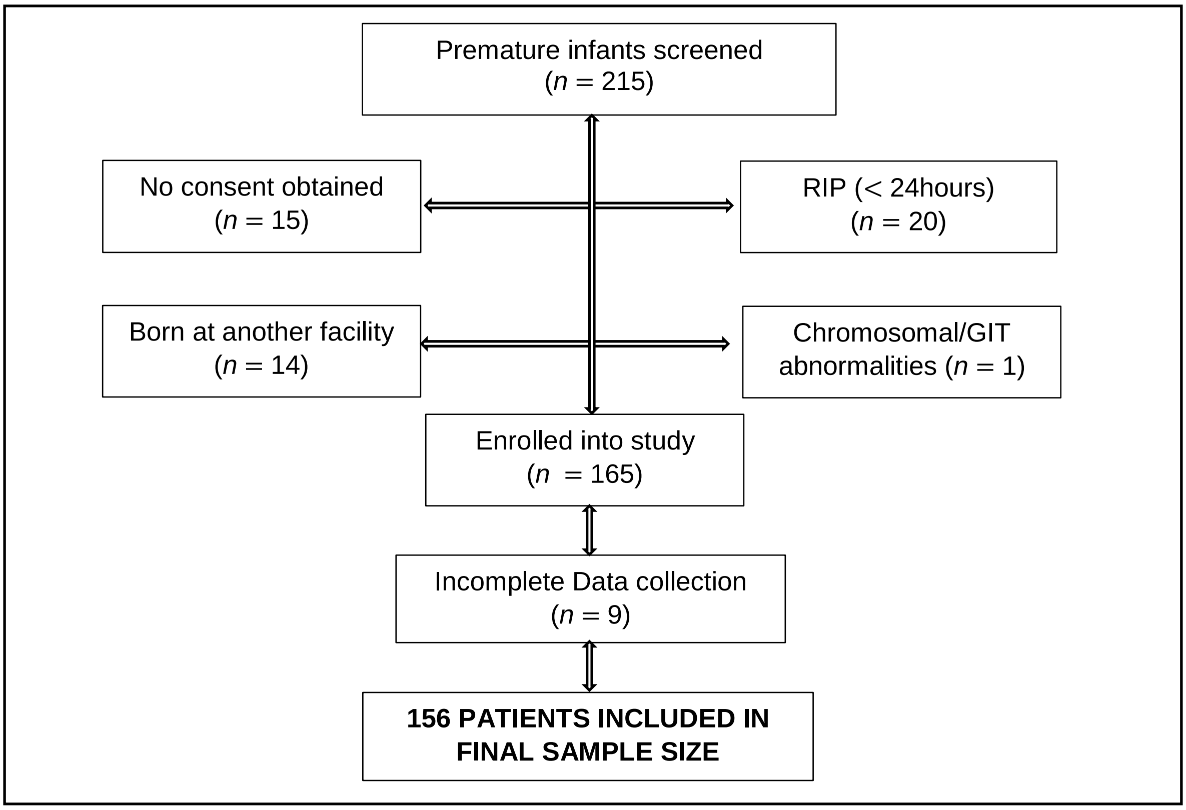


Figure 3.1: Flow chart for inclusion of subjects

A total of 156 subjects were enrolled into the study, the majority of whom were black ($n = 151$, 96.8%), with five (3.2%) being coloured. No Caucasians or Indians were enrolled into the study. The gender distribution was 69 males (44.2%) and 87 females (55.8%) with a mean gestational age of 30 weeks (±2 weeks). The mean birth weight was 1 352g (± 457 g), and the mean length and head circumference at birth was 38.5 cm (± 4.4cm) and 28 cm (±3.1 cm), respectively. The most common complications documented during the study period were respiratory distress syndrome, neonatal jaundice and birth asphyxia (94.9%, 67.9% and 30.8%, respectively). A small percentage of subjects had feeding intolerances, NEC and ileus as diagnosed by the attending clinician (5.8%, 4.5% and 3.2%, respectively). Study subjects' characteristics are reported in Table 3.1.

Table 3.1: Characteristics of study subjects according to BW category

	ELBW	VLBW	LBW	Total
Total – *n* (%)	47 (30.1%)	54 (34.6%)	55 (35.3%)	156
Male – *n* (%)	17 (36.2%)	22 (40.7%)	30 (54.5%)	69 (44.2%)
Female – *n* (%)	30 (63.8%)	32 (59.2%)	25 (45.5%)	87 (55.8%)
GA (weeks) – mean (±SD)	28 (±2)	30 (±2)	33 (±2)	30 (±2)
AGA – *n* (%)	35 (74.5%)	42 (79.2%)	46 (83.6%)	123 (79.4%)
SGA – *n* (%)	11 (23.4%)	5 (9.4%)	4 (7.3%)	20 (12.9%)
LGA – *n* (%)	2 (4.3%)	6 (11.3%)	5 (9.1%)	13 (8.4%)
IUGR – *n* (%)	5 (10.6%)	2 (3.7%)	2 (3.6%)	9 (5.8%)
Birth weight (g) – mean (±SD)	863 (±108)	1 251 (±130)	1 868 (±287)	1 352 (±457)
Birth length (cm) – mean (±SD)	33.8 (±2.1)	38.3 (±3.2)	42.5 (±2.5)	38.5 (±4.4)
Birth HC (cm) – mean (±SD)	25.0 (±2.3)	27.8 (±2.0)	30.7 (±1.8)	28 (±3.1)
Morbidities – *n* (%)				
RDS/HMD*	47 (100%)	53 (98.1%)	48 (87.3%)	148 (94.9%)
NNJ	35 (74.5%)	44 (81.5%)	27 (49.1%)	106 (67.9%)
Sepsis	8 (17%)	16 (29.6%)	6 (10.6%)	30 (19.2%)
NEC*	12 (25.5%)	14 (25.9%)	4 (7.3%)	30 (19.2%)
A.Baumanii sepsis	6 (12.8%)	2 (3.7%)	2 (3.6%)	10 (6.4%)
PDA*	3 (6.4%)	3 (5.6%)	4 (7.3%)	10 (6.4%)
Ileus	4 (8.5%)	3 (5.6%)	0 (0%)	7 (4.5%)
Feed intolerance	2 (4.3%)	3 (5.6%)	0 (0%)	5 (3.2%)

Data is presented as *n* (%) and mean ± SD (standard deviations) according to BW category and total study population.
Abbreviations: ELBW: Extremely low birth weight; VLBW: Very low birth weight; LBW: Low birth weight, GA: Gestational age; AGA: Appropriate for gestational age; SGA: Small for gestational age; LGA: Large for gestational age; IUGR: Intrauterine growth restriction; HC: Head circumference; g: grams; cm: centimetre; RDS/HMD: Respiratory distress syndrome/hyaline membrane disease; NNJ: Neonatal jaundice; NEC: Necrotising enterocolitis; PDA: Patent ductus arteriosus

Table 3.2 describes the number of subjects at each study point for PN, EN and IV prescribed and received. Differences were noted between the number of subjects prescribed feeds and those receiving feeds. These differences were attributed to subjects receiving feeds based on the previous day's prescriptions or prescription changes made only later in the day. The number of patients described in Table 3.2 indicates that patients might've been prescribed or received one, both or all three median of feed on the different study days.

Table 3.2: Number of subjects at each study point for parenteral and enteral nutrition, and IV fluids

Study day	PARENTERAL		ENTERAL		INTRAVENOUS	
	FP	NI	FP	NI	FP	NI
1	6	6	48	48	149	149
2	54	55	141	142	145	154
3	68	73	140	143	127	145
7	54	59	111	119	77	89
14	31	35	88	92	34	38

FP: feeding prescription; NI: nutritional intake

3.2 MATERNAL BASELINE CHARACTERISTICS

The mean maternal age of the mothers was 27 years (±6 years), with a median gravida and parity of two respectively. There was a high prevalence of caesarean sections noted in this study (n = 106, 67.9%). The majority of mothers were HIV-uninfected (n = 105, 66.9.3%) and 48 (30.6%) had a positive HIV status with 2 mothers with unknown status. The mean birth weights of infants born to HIV-infected mothers was 1 451 g (± 457 g), compared with infants born to HIV-negative women at 1 330 g (± 457 g) (data not available in the table). Pregnancy-related hypertension complications were the major cause of preterm delivery with pre-eclampsia as the most common cause (26.9%). Baseline characteristics of mothers are reported in Table 3.3.

3.3 FEEDING PRESCRIPTIONS AND ACTUAL NUTRIENT INTAKES OF LBW INFANTS COMPARED WITH RECOMMENDED GUIDELINES

The parenteral and enteral nutritional prescriptions and actual nutrient intakes was compared with the recommended guidelines for the total study population and according to birth weight group. Data are represented in Appendix H and Appendix I for all study days respectively. The prescriptions and actual nutrient intakes for IV fluids are represented in Appendix J.

3.3.1 Parenteral nutrition

3.3.1.1 Feeding prescriptions for parenteral nutrition

Parenteral feeding prescriptions for the total study population

Data revealed that the total study population met the fluid prescription for PN of 49.94 ml/kg/day (IQR: 47.82–50.61 ml/kg/day; p = 0.917) on day one and glucose oxidation rate (GOR) prescription of 7.83 mg/kg/min (IQR: 6.18–9.41 mg/kg/min, $p = 0.057$) on day 14. Both the fluid and GOR for PN on these study days were clinically comparable to recommendations. For all other study days, a

Table 3.3: Maternal baseline characteristics

	ELBW	VLBW	LBW	TOTAL
Age – mean (±SD)	28 (±6)	28 (±6)	26 (±6)	27 (±6)
Singleton pregnancy – *n* (%)	37 (78.7%)	40 (74.1%)	50 (90.9%)	127 (81.4%)
Multiple pregnancy				
• **Twins – *n* (%)**	7 (29.2%)	12 (50.0%)	5 (20.8%)	24 (15.4%)
• **Triplets – *n* (%)**	3 (60.0%)	2 (40.0%)	0 (0.0%)	5 (3.2%)
HIV Status – *n* (%)				
Positive	12 (25.5%)	17 (31.5%)	18 (32.7%)	47 (30.1%)
Negative	32 (68.1%)	36 (66.7%)	37 (67.3%)	105 (67.3%)
Unknown	3 (6.4%)	1 (1.9%)	0 (0.0%)	4 (2.6%)
Complications related to preterm delivery – *n* (%)				
Foetal distress	10 (21.3%)	12 (22.2%)	21 (38.2%)	43 (27.6%)
PET/Pre-eclampsia	19 (40.4%)	16 (29.6%)	7 (12.7%)	42 (26.9%)
PIH	3 (6.4%)	4 (7.4%)	4 (7.3%)	11 (7.1%)
Failed tocolysis	1 (2.1%)	1 (1.9%)	0 (0.0%)	2 (1.3%)
APH	3 (6.4%)	5 (9.3%)	7 (12.7%)	15 (9.6%)
Abruptio placenta	2 (4.3%)	2 (3.7%)	2 (3.6%)	6 (3.8%)
Oligohydramnios	1 (2.1%)	0 (0.0%)	1 (1.8%)	2 (1.3%)
Preterm labour	0 (0.0%)	5 (9.3%)	6 (10.9%)	11 (7.1%)
PROM	2 (4.2%)	2 (3.8%)	1 (1.8%)	5 (3.2%)
HELLP Syndrome	2 (4.3%)	1 (1.9%)	1 (1.8%)	4 (2.6%)

Data is presented as mean ± SD (standard deviations) and *n* (%) according to BW category and total study population.
Abbreviations: NVD: Normal vaginal delivery; HIV: Human immunodeficiency virus; PIH: Pregnancy-induced hypertension; APH: Antepartum haemorrhage; PROM: Premature rupture of membranes; HELLP: Hemolysis, elevated liver enzymes, low platelet count

significant difference ($p < 0.05$) was observed between parenteral nutrition prescriptions and recommendations for fluid, energy and all macronutrients. This study's data highlights that recommendations were not met by the feeding prescriptions, let alone the nutrient intakes even by day 14 of life. It is very sobering to note, for example, that feeding prescriptions had only met a third of the infants' requirements on day one, and only two-thirds by day 14. Refer to Appendix H for the parenteral nutrition prescriptions and Figures 3.2–3.6 for fluid, energy, protein, fat and GOR prescriptions from parenteral nutrition respectively.

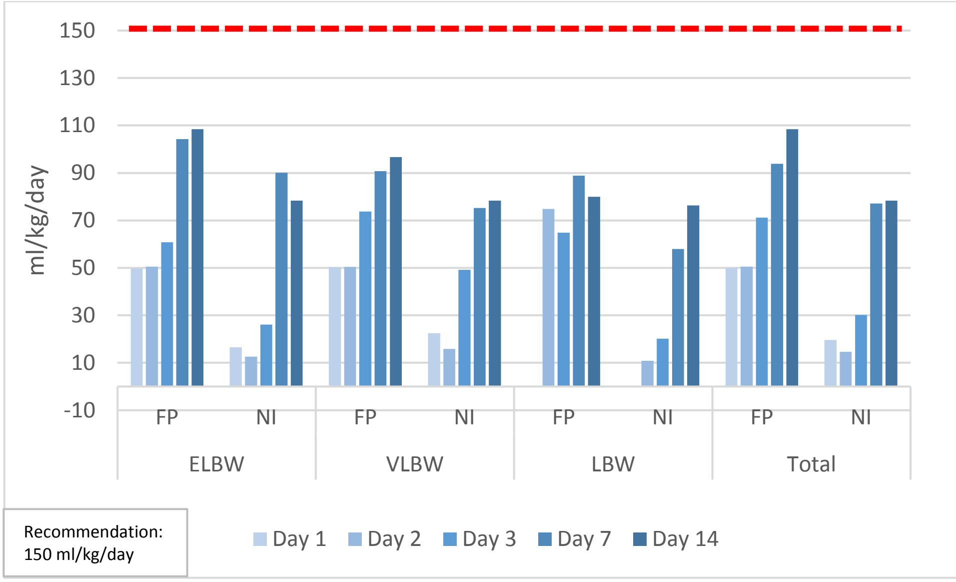


Figure 3.2: Fluid from PN per BW categories: prescriptions and actual intakes compared to recommendations

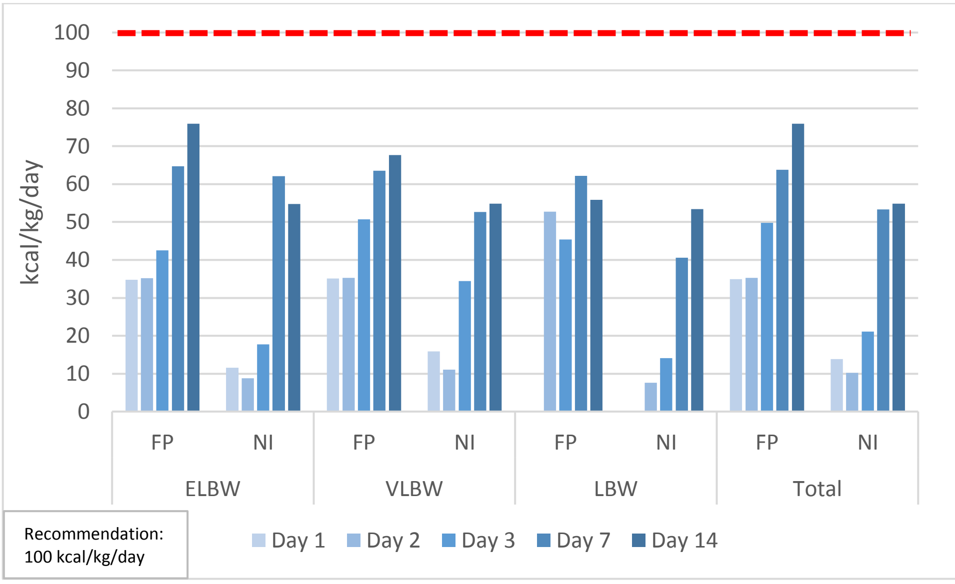


Figure 3.3: Energy from PN per BW categories: prescriptions and actual intakes compared to recommendations

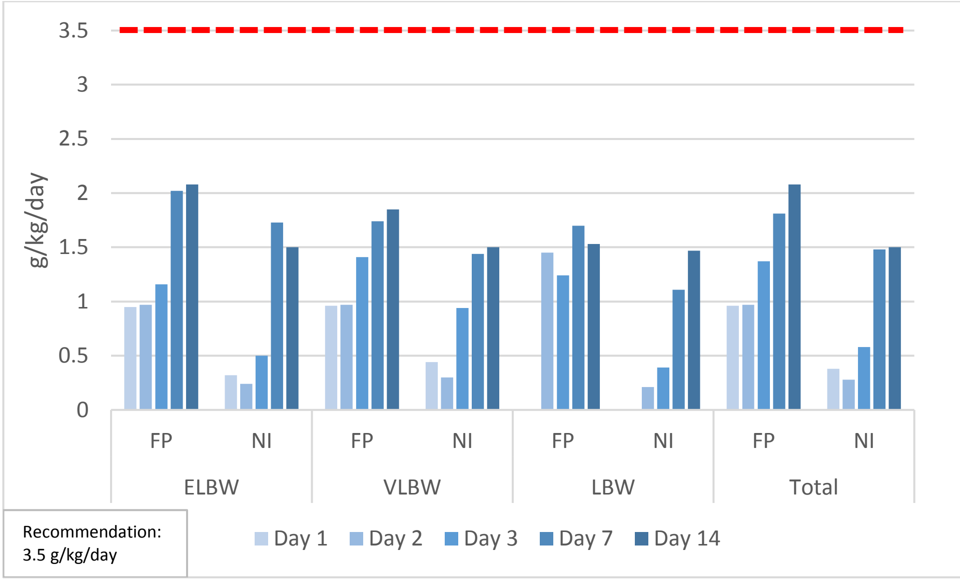


Figure 3.4: Protein from PN per BW categories: prescriptions and actual intakes compared to recommendations

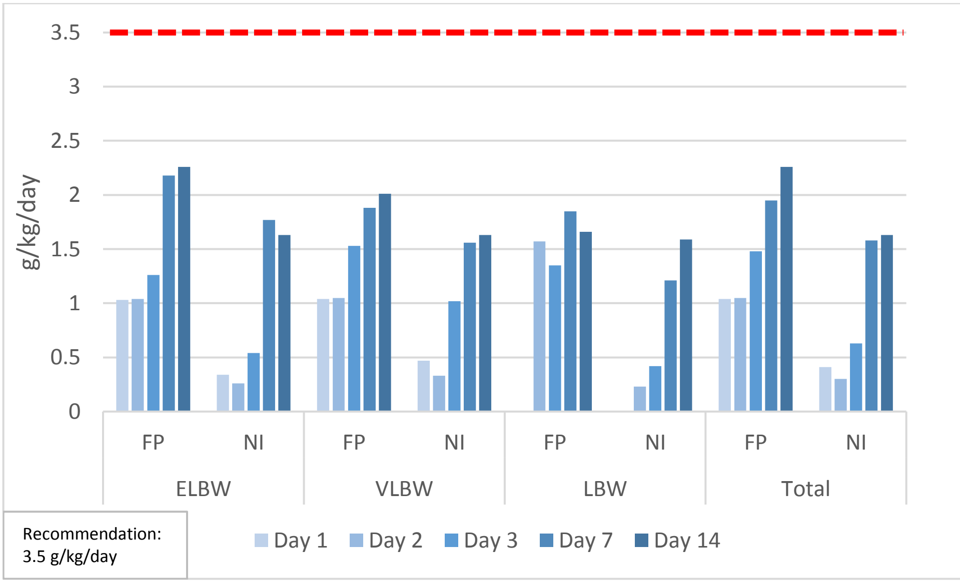


Figure 3.5: Fat from PN per BW categories: prescriptions and actual intakes compared to recommendations

Parenteral feeding prescriptions per birth weight category

When observing the data according to the BW categories, on day one, parenteral prescriptions for ELBW infants were comparable (p = 0.317) to recommendations of 49.66 ml/kg/day for fluid, 34.75 kcal/kg/day for energy and 0.95 g/kg/day for protein, 1.03 g/kg/day for fat and 3.58 mg/kg/min for GOR. Parenteral nutrition prescriptions for fluid, energy and GOR were significantly lower than recommendations ($p < 0.05$) on study days two, three and seven, including prescriptions for protein and fat on study days two, three, seven and 14 of life for the ELBW group. Even though inadequate

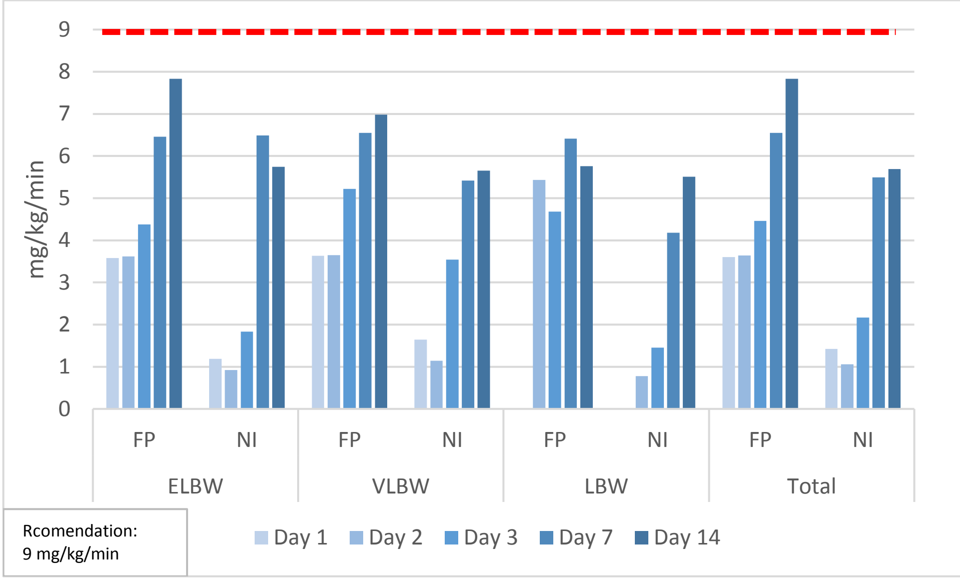


Figure 3.6: GOR from PN per BW categories: prescriptions and actual intakes compared to recommendations

amounts were prescribed, values were not significantly different from the recommendations on day 14 of 108.47 ml/kg/day for fluid (p = 0.056), 75.93 kcal/kg/day for energy (p: 0.056) and 7.83 mg/kg/min for GOR (p = 0.756) when compared with the recommendations. The same trend was seen in the VLBW group. Feeding prescriptions for the VLBW groups were significantly lower than the recommendations ($p < 0.05$) for fluid, energy and all macronutrients on all the study days except on day one of life where 50.21 ml/kg/day for fluid (p = 0.893) was prescribed. It was only in the higher weight category, the LBW group, where no significant differences could be found between the FP and recommendations on study days two, three, seven and 14 of life, respectively (refer to Appendix H for p-values) for PN. None of the LBW infants received PN prescriptions on day one of life. Refer to Appendix H for the parenteral nutrition prescriptions and to Figures 3.2–3.6 for fluid, energy, protein, fat and GOR prescriptions from parenteral nutrition.

3.3.1.2 Actual nutrient intake derived from parenteral nutrition.

Actual parenteral intake for the total study population

Data on actual nutrient intakes for PN revealed that fluid, energy and macronutrients for the total study population were significantly different ($p < 0.05$) compared with recommendations on all the study days, indicating subjects received inadequate intakes. This study's results on nutrient intakes are even more inferior that those seen with the feeding prescriptions, which has an even greater concern and discrepancy when compared to recommendations. Data for the total study population showed that PN intakes for fluid and energy met about half of the recommendations on day 14, protein and fat met less than half of the recommendations by day 14 except for the GOR intakes.

Refer to Appendix H for the parenteral nutrition actual intakes and to Figures 3.2–3.6 for fluid, energy, protein, fat and GOR intakes from parenteral nutrition.

Parenteral nutrition actual nutrient intakes per birth weight category

Data revealed that the actual PN intakes were non-significant ($p = 0.317$) for the ELBW infants when compared with recommendations on day one of life of 16.55 ml/kg/day for fluid, 11.58 kcal/kg/day for energy, 0.32 g/kg/day for protein, 0.34 g/kg/day for fat and 1.19 mg/kg/min for GOR. Even though these intakes were non-significant they were still clinically low compared with recommendations. For the remaining study days, the PN actual intakes were found to be statistically significant ($p < 0.05$) and clinically lower compared with recommendations for fluid, energy and all macronutrients in the ELBW group.

Data on PN intakes for the VLBW group revealed that fluid, energy and all macronutrients were significantly lower ($p < 0.05$) than recommendations on all study days. PN intakes in the VLBW group were inadequate and did not meet recommendations. As before, the LBW group met recommendations ($p > 0.05$) when observing the data on actual intakes from PN for fluid, energy and all macronutrients on all study days except day one of life where no prescriptions were made, thus no intakes of PN were received. However, the actual intakes from PN in the LBW group were not clinically comparable to recommendations on all study days observed despite data showing statistical non-significance (refer to Table 1.1 for the absolute value used for statistical analysis). Refer to Appendix H for the parenteral nutrition actual intakes and to Figures 3.2–3.6 for fluid, energy, protein, fat and GOR intakes from parenteral nutrition.

Conclusion: It is evident that the prescriptions for parenteral nutrition truly met recommendations only on day one of life. However, all other study days showed shortfalls of the PN feeding prescriptions meeting half to two-thirds of recommendations for fluid, energy, protein, fat and GOR. In addition to prescriptions, nutrient intakes fell even further short, meeting half of the recommendations or less on day seven and 14. Furthermore, PN actual intakes did not meet prescriptions for all nutrients investigated on all study days except day one of life.

3.3.2 Enteral nutrition

3.3.2.1 Feeding prescriptions for enteral nutrition

Enteral nutrition prescriptions for the total study population

On day one, a third of study subjects were prescribed trophic enteral feeds ($n = 48$, 30.8%). Enteral prescriptions were increased from 24.13 ml/kg/day for fluid on day one of life to 168.23 ml/kg/day for fluid by day 14 of life for the total study population. For all study days the enteral volume prescribed was significantly less than recommended for fluids ($p < 0.001$). Coinciding with low volumes, the prescriptions were started at 18.13 kcal/kg/day on day one and increased to 122.09 kcal/kg/day for energy ($p < 0.001$), meeting 93.8% of the recommendation (130 kcal/kg/day) by day 14. Feeding prescriptions were low throughout the study period with 0.47 g/kg/day on day one and maximum prescriptions of 3.17 g/kg/day for protein on day 14, showing significant differences ($p < 0.001$) compared with recommendations on all study days. Enteral fat and CHO prescriptions for all study days were significantly lower than recommendations except for day 14 ($p = 0.115$, $p = 0.055$, respectively) when 7.1 g/kg/day of fat and 11.92 g/kg/day of CHO had met recommendations. Refer to Appendix I for the enteral nutrition prescriptions and Figures 3.7–3.11 for fluid, energy, protein, fat and carbohydrate prescriptions from enteral nutrition respectively.

Enteral nutrition prescriptions per birth weight category

Day one showed that all BW groups were prescribed minimal enteral fluid of 22.6 ml/kg/day, 21.13 ml/kg/day and 30.85 ml/kg/day for ELBW, VLBW and LBW infants respectively, which only began increasing from day three onwards. Enteral fluid prescriptions on day 14 of life were 145.38 ml/kg/day, 167.30 ml/kg/day and 171.03 ml/kg/day for ELBW, VLBW and LBW infants respectively. As reflected in the results from the total study population, when stratified for BW category, they too had enteral prescriptions on day 14 of life that were significantly lower than the 180 ml/kg/day recommendation for all study days ($p < 0.05$).

On day one, the ELBW and VLBW groups had prescriptions of 17.88 kcal/kg/day and 16.39 kcal/kg/day for energy, respectively, unlike energy prescribed for the LBW group which was higher (23.67 kcal/kg/day). Enteral prescriptions of 119.81 kcal/kg/day for energy were similar (92%) to recommendations on day 14 of life in the LBW group ($p = 0.156$). Results show that the lower birth weight groups had energy prescriptions significantly lower than the recommendations (VLBW infants: 122.80 kcal/kg/day; $p = 0.020$ and ELBW infants: 106.51 kcal/kg/day; $p = 0.028$).

Similar results are reflected for all macronutrients within the BW groups, where prescriptions did not meet recommendations during the first three days of life and on day seven. Only by day 14 of life did feeding prescriptions begin to meet nutrient recommendations, mainly evident with the fat and CHO prescriptions in the VLBW and LBW groups. No significant differences were seen for enteral fat prescriptions in the ELBW group compared with recommendations on day 14 of life (p = 0.053). Similar results were found in the VLBW and LBW groups for enteral fat prescriptions (p = 0.251 and p = 0.355, respectively) and CHO (p = 0.272 and p = 0.881, respectively) when compared with the recommendations. Refer to Appendix I for the enteral nutrition prescriptions and Figures 3.7–3.11 for fluid, energy, protein, fat and carbohydrates prescriptions from enteral nutrition respectively.

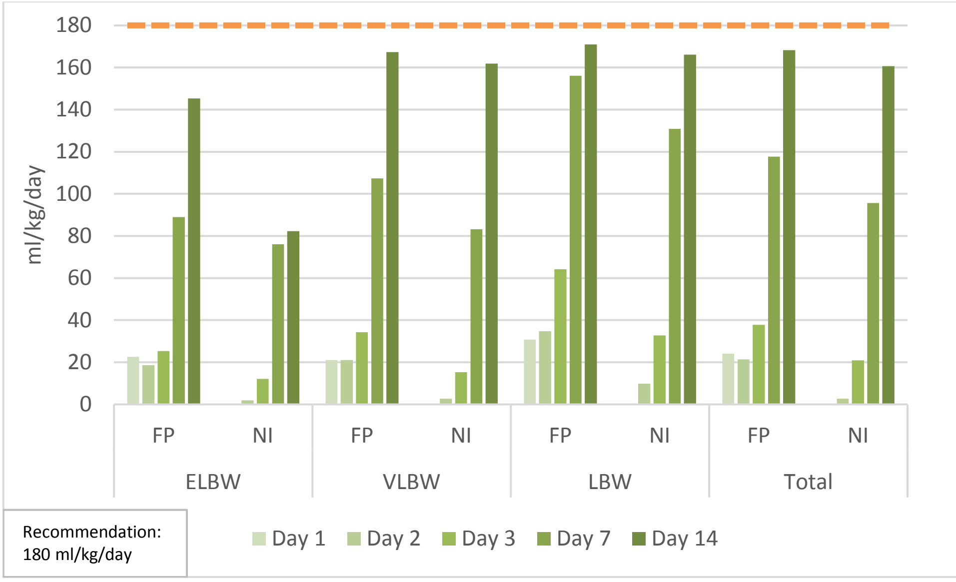


Figure 3.7: Fluid from EN per BW categories: prescriptions and actual intakes compared to recommendations

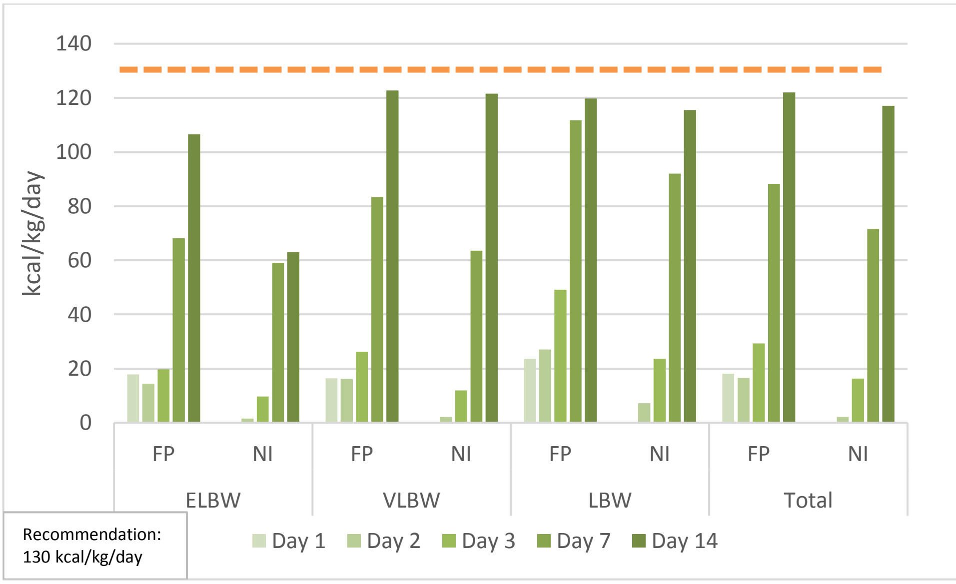


Figure 3.8: Energy from EN per BW categories: prescriptions and actual intakes compared to recommendations

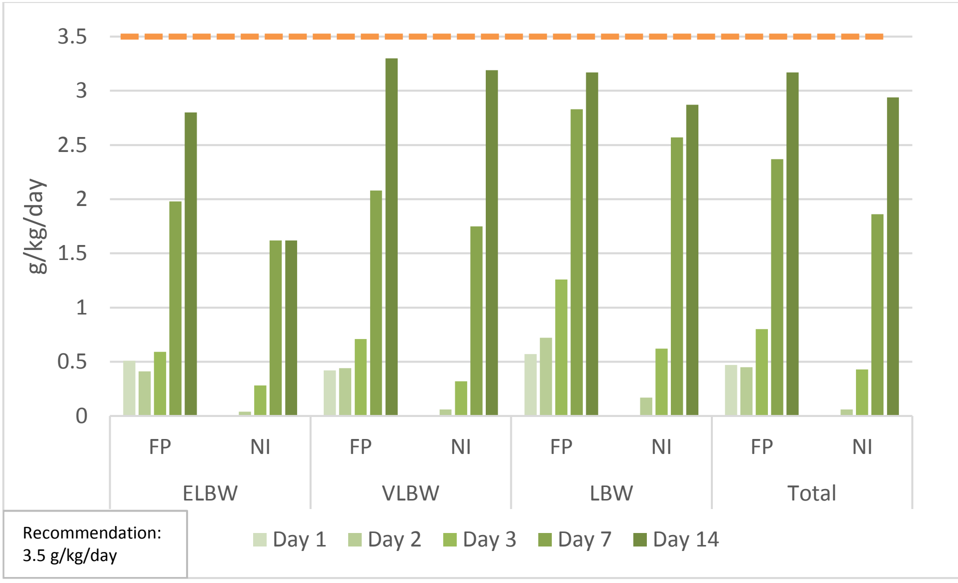


Figure 3.9: Protein from EN per BW categories: prescriptions and actual intakes compared to recommendations

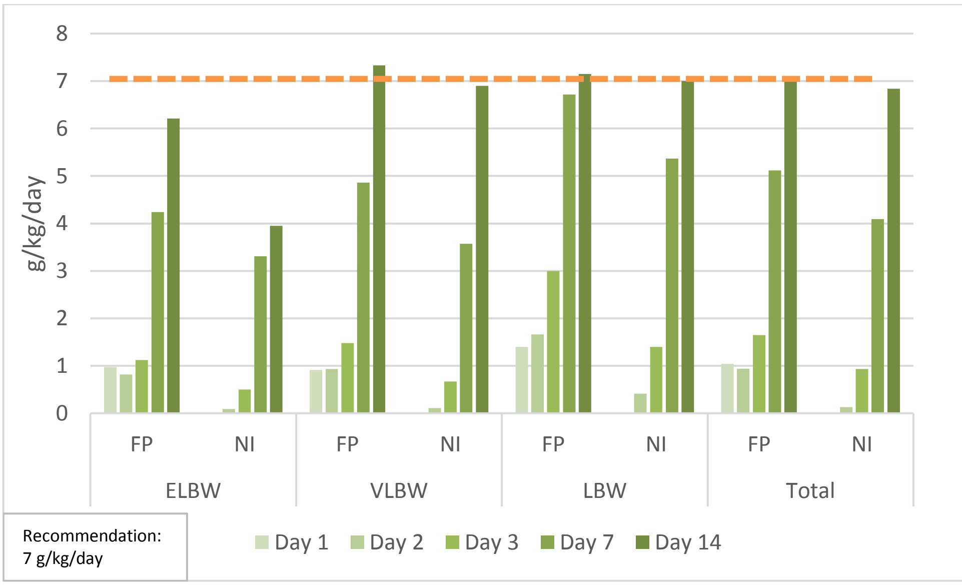


Figure 3.10: Fat from EN per BW categories: prescriptions and actual intakes compared to recommendations

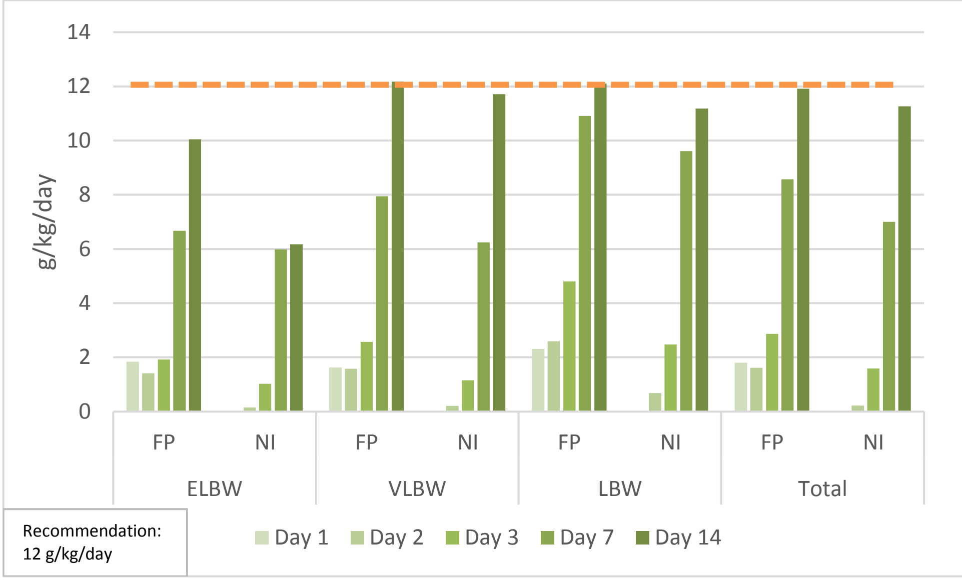


Figure 3.11: Carbohydrates from EN per BW categories: prescriptions and actual intakes compared to recommendations

3.3.2.2 Actual nutrient intakes derived from enteral nutrition

Enteral nutrition actual nutrient intakes for the total study population

Two-thirds of the study population (n = 108, 69.2%) did not receive any enteral nutrition (EN) on day one of life. Study subjects (n = 142, 91.0%) only received minimal enteral intakes on day two of life for fluid, energy and all macronutrients, protein, fat and CHO (refer to Appendix I for actual values). Actual EN intakes were significantly lower than the recommended amounts for fluid, energy and all macronutrients on all observed study days ($p < 0.05$). However, by day 14 of life, enteral intakes had increased and were clinically comparable with recommendations even though statistically non-significant. On day 14 of life, the actual intakes of 117.11 kcal/kg/day for energy (90% similarity), 11.27 g/kg/day for CHO (93.9% similarity) and 6.84 g/kg/day for fat (98% similarity) were clinically significant when compared with the recommendations. Refer to Appendix I for the actual enteral nutrition intakes and Figures 3.7–3.11 for fluid, energy, protein, fat and carbohydrates intakes from enteral nutrition respectively.

Enteral nutrition actual nutrient intakes per birth weight category

Enteral nutrition intakes were significantly lower for fluid, energy and all macronutrients on all study days when compared with recommendations for all birth weight categories. Actual enteral intakes only started to increase by day seven of life for fluid, energy and all macronutrients. These intakes on day seven were significantly lower in comparison to recommendations even by day 14, across all birth weight groups ($p < 0.05$).

The energy-contributing macronutrients namely; fat and CHO met recommendations only by day 14 of life. This is evident in the VLBW group which received 11.71 g/kg/day for CHO (p = 0.140), and in the LBW group which received 7.00 g/kg/day for fat (p = 0.852) and 11.18 g/kg/day for CHO (p = 0.455) on day 14 of life. Refer to Appendix I for the enteral nutrition actual intakes and Figures 3.7–3.11 for fluid, energy, protein, fat and carbohydrates intakes from enteral nutrition respectively.

Conclusion:

It is evident that enteral feeding prescriptions did not rise in increments that meet international recommendations.

Actual EN intakes were significantly lower than the recommended amounts for fluid, energy and all macronutrients on all observed study days.

There was a direct association within BW categories between the quantity and quality of the feeding prescription and intakes. The smaller the infant, the more likely they were to receive suboptimal prescriptions and intakes.

3.3.3 Intravenous fluids

Descriptive statistics were performed for the feeding prescriptions of the intravenous (IV) fluids. Appendix J shows the IV fluid prescriptions for the total study population and BW categories on all the study days.

3.3.3.1 Feeding prescriptions for intravenous fluids

Intravenous fluid prescriptions for the total study population

The majority of the fluids prescribed on day one of life were derived from IV fluids at a mean rate of 79.1 ml/kg/day. The FP of fluids did not differ much between the other study days in comparison to day one as seen in Figure 3.12.

The number of subjects prescribed IV fluids decreased as the days progressed, whereas the number of subjects prescribed fluids from enteral and parenteral nutrition increased (Table 3.2). Data on IV FP for energy and CHO is similar to that described for prescriptions of IV fluids in that minimal differences were seen in FP on the study days. Refer to Figures 3.13 and 3.14 for the energy and CHO prescriptions respectively from IV fluids.

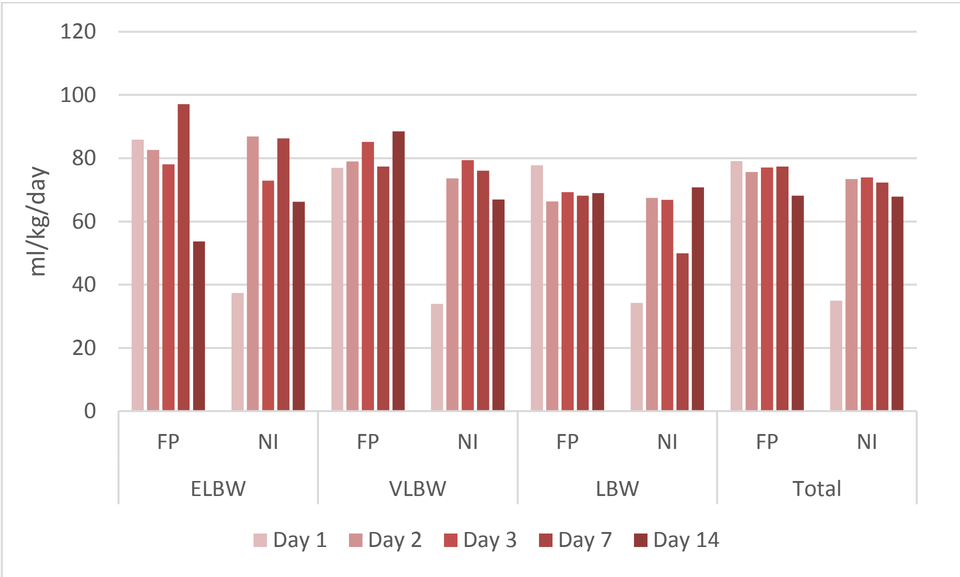


Figure 3.12: Fluid from IV infusions per BW categories: prescriptions and actual intakes

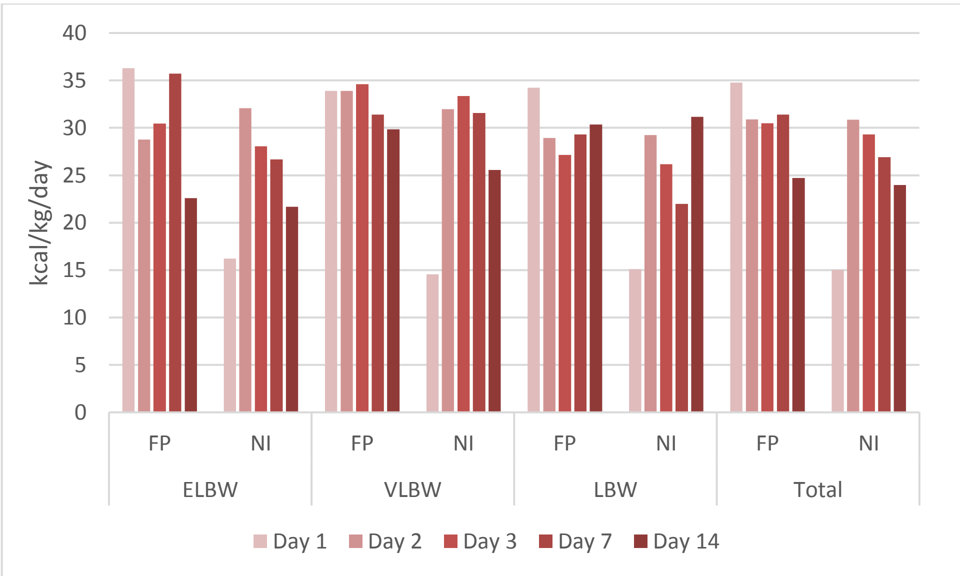


Figure 3.13: Energy from IV infusions per BW categories: prescriptions and actual intakes

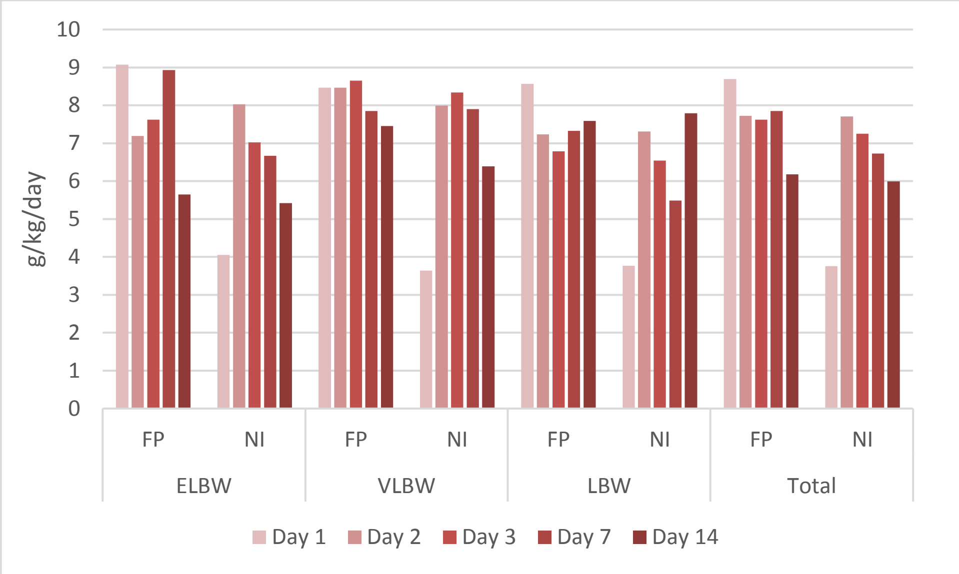


Figure 3.14: Carbohydrates from IV infusions per BW categories: prescriptions and actual intakes

Intravenous fluid prescriptions per birth weight category

Similar results can be seen for the IV fluids prescribed for the birth weight categories across the study days. The majority of fluids prescribed were derived from IV fluids for the first three days of life and had decreased slightly by day seven. Although, infants should be weaned off IV fluids by day 14, lower volumes for IV fluids were, surprisingly, still prescribed when compared with enteral fluid prescriptions for all birth weight groups. ELBW infants were prescribed higher volumes of fluid compared with the VLBW and LBW infants on days one, two and seven of life. On days three and 14, the VLBW group had IV fluid prescriptions greater than the ELBW and LBW groups. As expected, the results show that IV prescriptions on days one and two of life in the ELBW and VLBW groups contributed more towards energy than from enteral nutrition prescriptions. This was also true on day three of life for the both weight groups. However, in the LBW group, IV fluids were observed to have greater energy prescriptions than EN. IV data on the FP for IV-CHO revealed higher prescriptions for all the BW groups on the first three days of life as well as on day seven for the ELBW group when compared with CHO derived from EN. Refer to Figures 3.12–3.14 for fluid, energy and carbohydrate prescriptions from IV fluids respectively.

3.3.3.2 Actual nutrient intakes from intravenous fluids

Intravenous fluid actual intakes for the total study population

Data on the actual intakes from IV fluids on day one of life showed that subjects received their fluids, energy and CHO intakes mainly from IV, compared with enteral and parenteral nutrition during the first three days of life.

The actual nutrient intakes received from fluid, energy and CHO for study days seven and 14 decreased slightly and did not differ much between the two days. The main contribution of fluids, energy and CHO were derived from enteral and parenteral nutrition. Refer to Figures 3.12–3.14 for fluid, energy and carbohydrate intakes from IV fluids respectively.

Intravenous fluid actual intakes per birth weight category

Similar results for the total study population were observed within the birth weight groups; the main contribution for the fluid, energy and CHO intakes were derived from IV compared to enteral and parenteral nutrition for the first three days of life. The actual intakes of fluid, energy and CHO gradually decreased on days seven and 14, but did not differ much between the two days.

Surprisingly, the LBW group received more fluid, energy and CHO intakes from IV fluids on day 14 of life compared with the ELBW and VLBW groups; the ELBW group also received lower amounts than the VLBW group. Refer to Figures 3.12–3.14 for fluid, energy and carbohydrate intakes from IV fluids respectively.

Conclusion:
Evident from the results, IV fluids prescribed and received made the highest contribution to the daily volume of fluid, energy and CHO intake for the first three days of life when compared with enteral and parenteral nutrition.

3.4 COMPARISONS BETWEEN FEEDING PRESCRIPTIONS AND ACTUAL NUTRIENT INTAKES

Comparisons between feeding prescriptions and actual nutrient intakes refer to fluid, energy and macronutrients for parenteral and enteral nutrition and IV fluids for the total study population and birth weight categories.

3.4.1 Fluid

Comparison between feeding prescriptions and actual nutrient intakes for the total study population for fluid

Fluid prescribed and received from PN showed a statistical difference ($p < 0.05$) and were clinically non-significant, i.e. large differences were noted on all the study days. Similar results can be seen with EN prescriptions and intakes ($p < 0.05$), except on day 14 of life where fluid intakes met 95% of the volume prescribed. Refer to Figure 3.15 (a) and (b) which illustrate the differences between fluid prescriptions and intakes from parenteral and enteral nutrition respectively.

Comparison between feeding prescriptions and actual nutrient intakes per birth weight group for fluid

No statistical differences were found between the feeding prescriptions and actual fluid intakes for parenteral and enteral nutrition in the ELBW group. However, clinical differences between FP and NI were found on day one (p = 0.317) and day seven (p = 0.317) for fluids from PN in the ELBW group. The VLBW group showed similar results between PN and EN fluids prescribed and received on day seven (p = 0.058). All other study days showed statistical significance ($p < 0.05$) and clinical differences between fluids prescribed and received for the VLBW group, except day 14 where enteral fluids were of clinical benefit to the study subjects. The PN fluid received met the PN prescriptions on all the study days in the LBW group ($p > 0.05$). This was, however, not true for enteral fluids received and prescribed in this birth weight group ($p < 0.05$). Only on day 14 of life were the feeding prescriptions for fluid clinically comparable to the actual fluid received in the LBW group for both parenteral and enteral nutrition. No PN feeding prescriptions were made or intakes received on day one of life in the LBW group. Significant differences ($p < 0.05$) were found between the feeding prescriptions and actual nutrient intakes for enteral fluids in all the birth weight groups on all the study days. Enteral fluids prescribed were clinically significant compared with actual intakes for the VLBW ($p < 0.05$) and LBW groups ($p < 0.05$) on day 14 of life, even though statistical significance was found. Refer to Figure 3.16 (a) and (b) which illustrate the differences between fluid prescriptions and intakes from parenteral and enteral nutrition respectively.

3.4.2 Energy

Comparison between feeding prescriptions and actual nutrient intakes for the total study population for energy

In accordance with previously described fluids, the daily energy received from PN was significantly less than the prescriptions ($p < 0.05$) on all the study days. No clinical significance was observed between parenteral energy prescriptions and intakes. Similar results ($p < 0.05$) were found between the enteral feeding prescriptions and actual intakes for energy. Although statistically different, enteral energy intakes were clinically comparable to the prescription on day 14 of life. Refer to Figure 3.17 (a) and (b) which illustrate the differences between energy prescriptions and intakes from parenteral and enteral nutrition respectively.

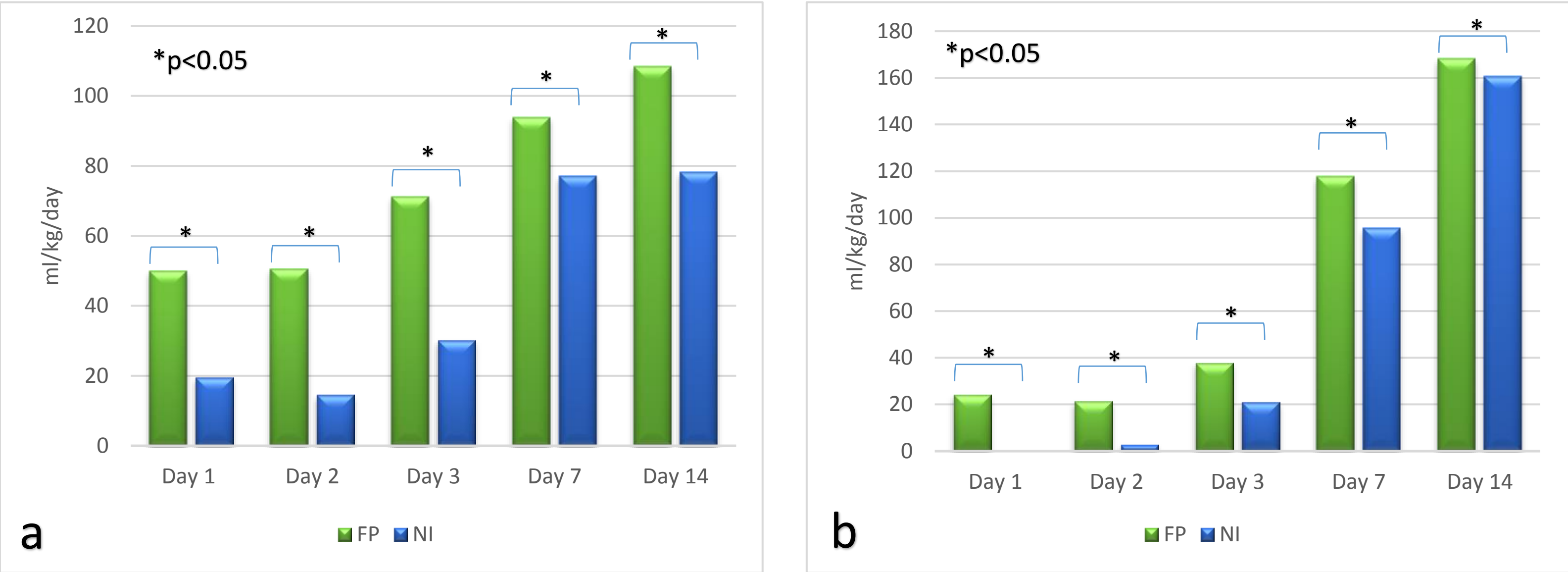


Figure 3.15 (a) and (b): Feeding prescriptions compared with actual nutrient intakes of fluid from parenteral and enteral nutrition for the total study population

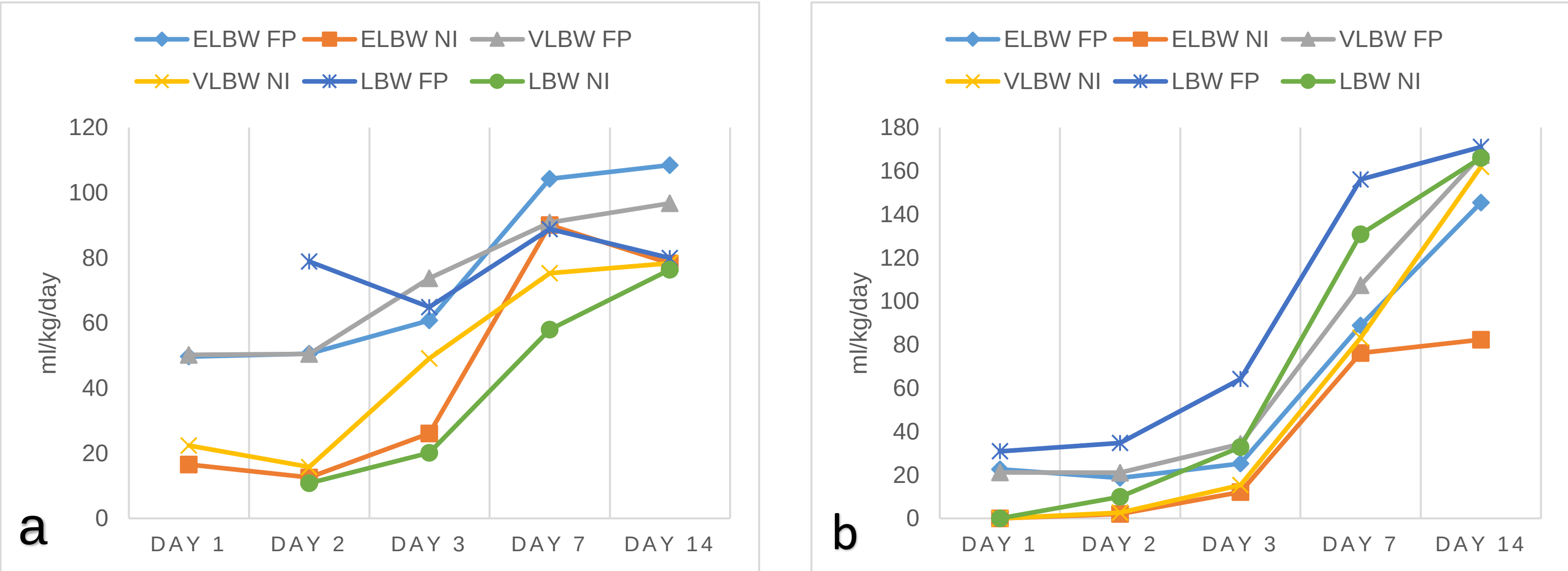
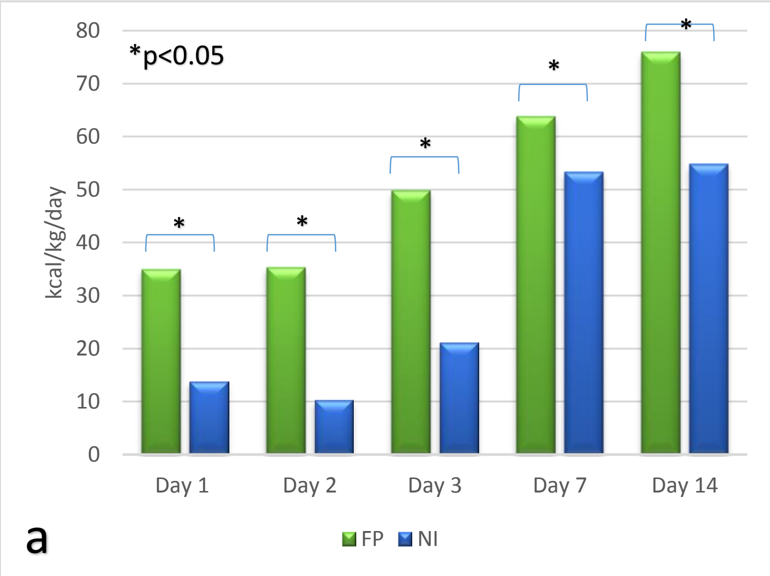


Figure 3.16 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for fluid from parenteral and enteral nutrition for the birth weight groups

Comparison between feeding prescriptions and actual nutrient intakes per birth weight group for energy

No differences were found between the feeding prescriptions and actual nutrient intakes for energy from PN in the ELBW group on day one (p = 0.317) and day seven (p = 0.913), the VLBW group on day seven (p = 0.062) and the LBW group on all study days (refer to Appendix I for p values). Large differences (>15%) were observed between PN prescriptions and intakes for all birth weight groups for energy. These differences were not found on day seven for the ELBW group (97% similarity) and day 14 for the LBW group (96% similarity) when comparing prescriptions and intakes. The enteral energy intakes were significantly lower ($p < 0.05$) than the prescriptions in all the birth weight groups for all study days. The VLBW and LBW groups had clinically comparable energy intakes to the prescriptions for EN on day 14 of life. Refer to Figure 3.18 (a) and (b) which illustrate the differences between energy prescriptions and intakes from parenteral and enteral nutrition respectively.



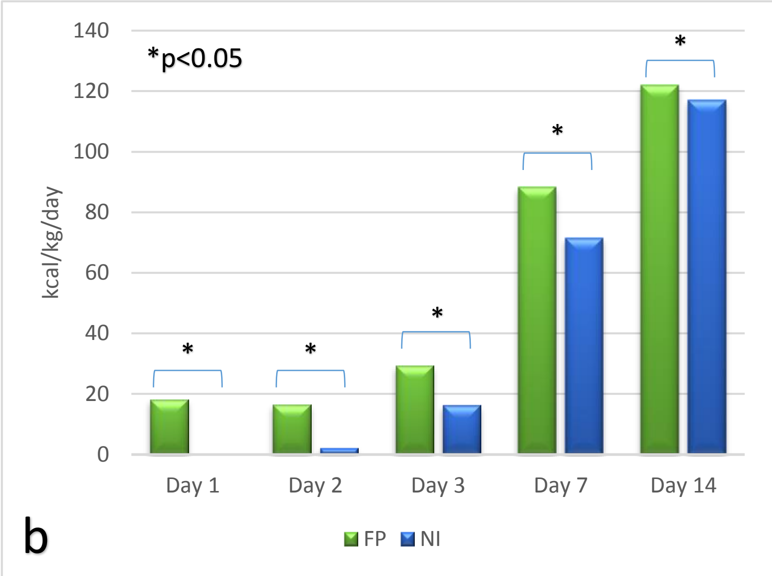
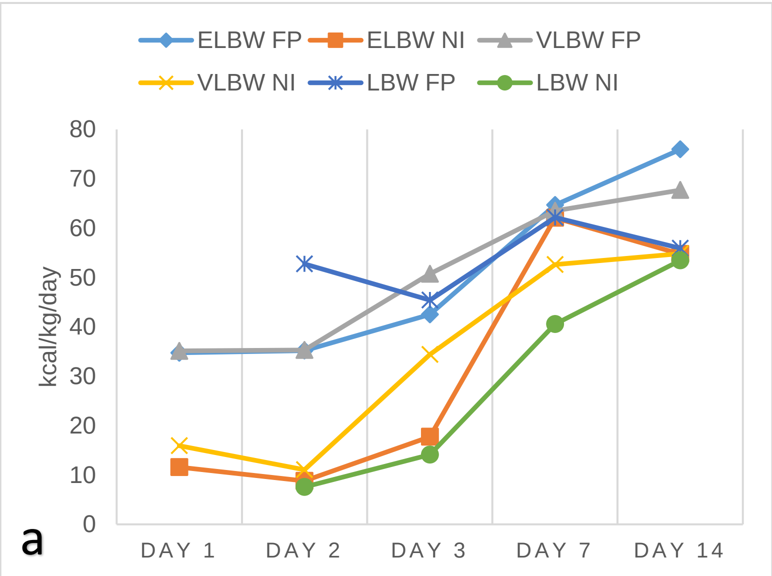


Figure 3.17 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for energy from parenteral and enteral nutrition for the total study population



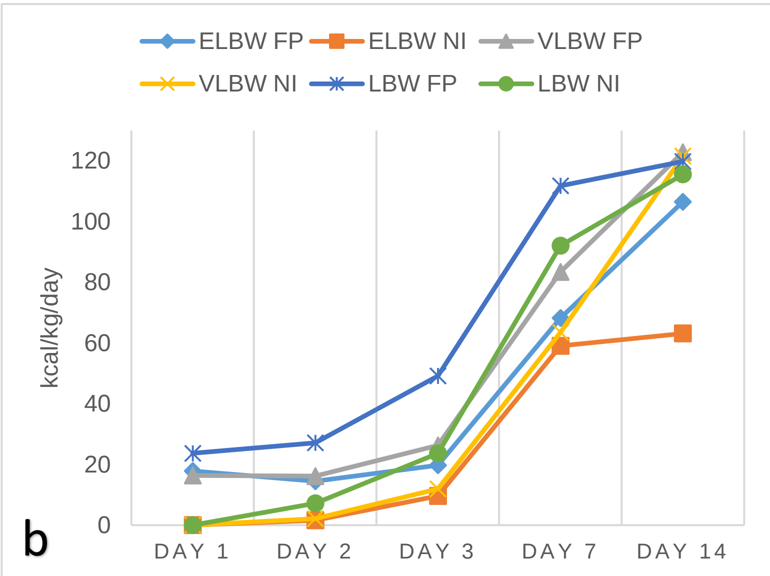


Figure 3.18 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for energy from parenteral and enteral nutrition for the birth weight groups

3.4.3 Protein

Comparison between feeding prescriptions and actual nutrient intakes for the total study population for protein

Actual protein intakes from parenteral nutrition were significantly lower ($p < 0.05$) compared to the feeding prescriptions on all study days. Protein intakes from PN met less than 50% of prescriptions for the first 3 days of life. Parenteral protein intakes increased by day seven and 14 of life, but were still not clinically comparable (81.8% and 72.1% similarity respectively) to prescriptions. Similar results ($p < 0.05$) can be seen for EN protein intakes compared with feeding prescriptions for all study days. Protein intakes were clinically comparable (92.7% similarity) to enteral prescriptions only on day 14 of life. Refer to Figure 3.19 (a) and (b) which illustrate the differences between protein prescriptions and intakes from parenteral and enteral nutrition respectively.

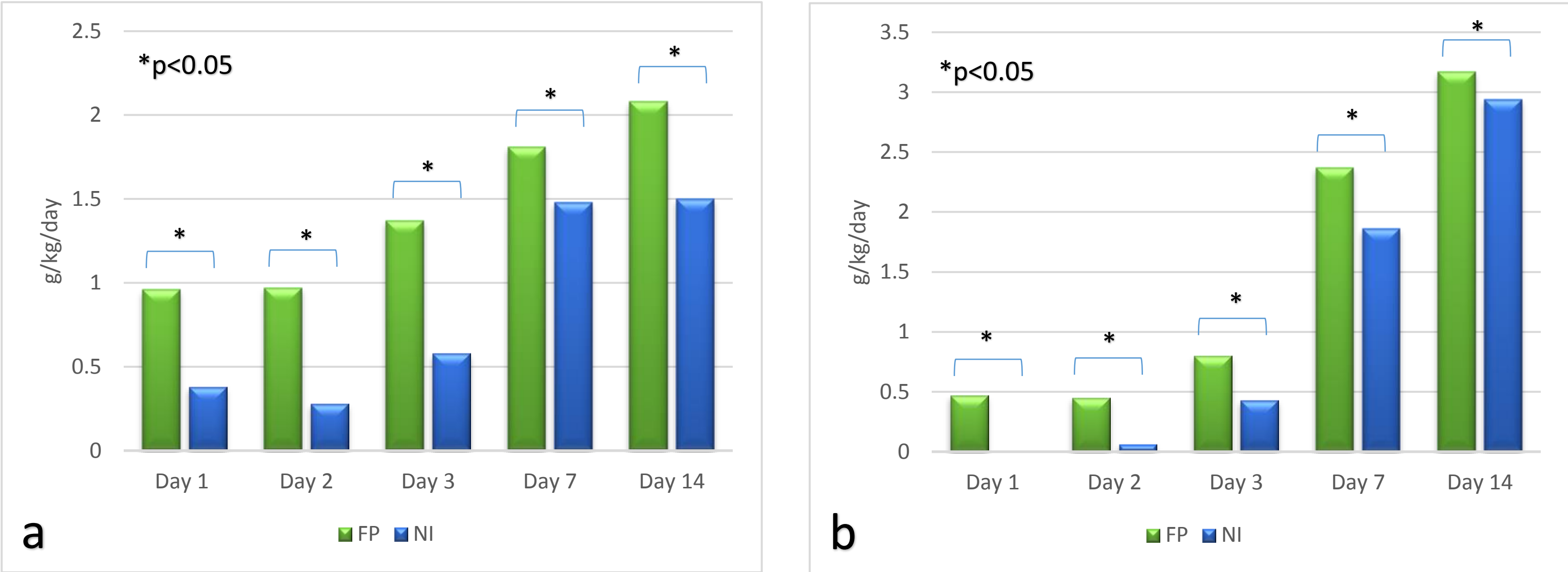


Figure 3.19 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for protein from parenteral and enteral nutrition for the total study population

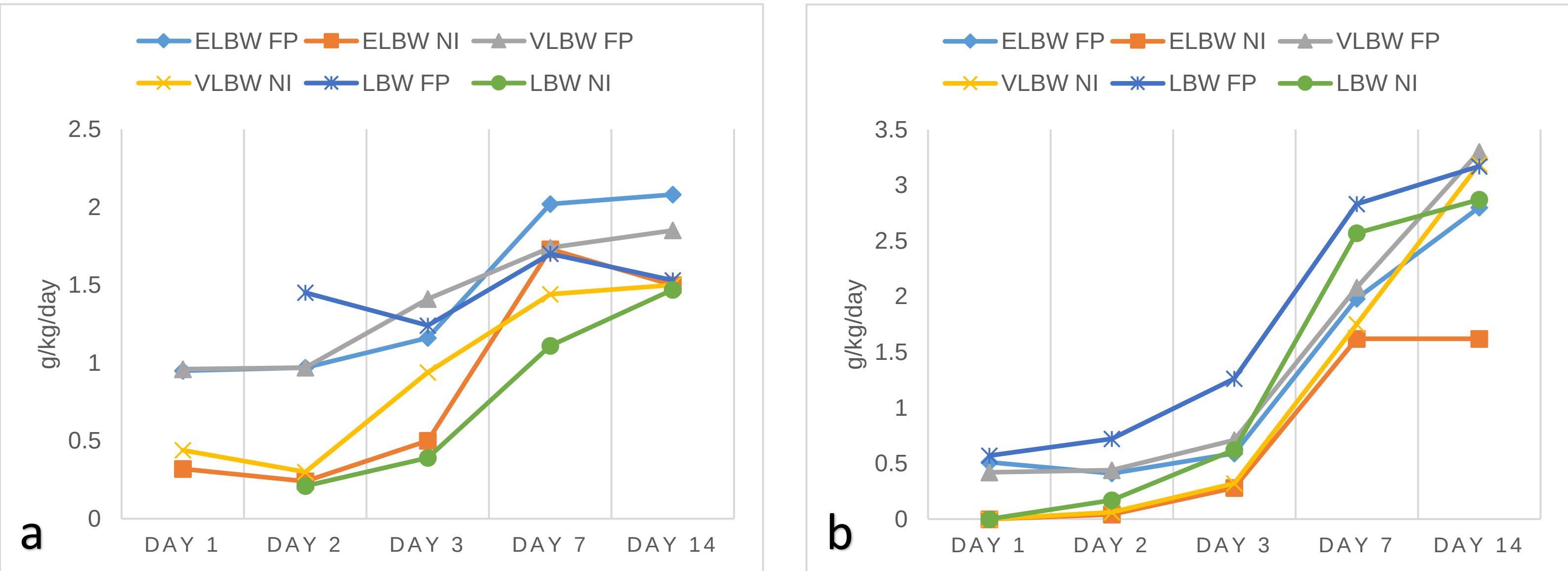


Figure 3.20 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for protein from parenteral and enteral nutrition for the birth weight groups

Comparison between feeding prescriptions and actual nutrient intakes per birth weight group for protein

The actual protein intakes from PN were not significantly different from the prescriptions in the ELBW group on day one (p = 0.317) and seven (p = 0.313). Similar results can be found in the VLBW group on day seven (p = 0.058) and for all study days in the LBW group when prescriptions and intakes are compared (see Appendix J for all p-values). Protein intakes from PN were only clinically comparable to prescriptions in the LBW group on day 14 of life. It is evident from figure 3.17 that large differences are seen between prescriptions and intakes. These findings ($p < 0.05$) can also be found with the enteral protein intakes when compared with the feeding prescriptions in all the birth weight groups on all study days. Refer to Figure 3.20 (a) and (b) which illustrate the differences between protein prescriptions and intakes from parenteral and enteral nutrition respectively.

3.4.4 Fat

Comparison between feeding prescriptions and actual nutrient intakes for the total study population for fat

The results between parenteral fat intakes and prescriptions were found to be statistically significant for all study days ($p < 0.05$), showing clinical differences between the prescriptions and intakes. Enteral fat intakes showed similar results and were significantly less compared with their prescriptions on all study days ($p < 0.05$). Clinical significance between enteral fat prescriptions and intakes was found only on day 14 of life. Refer to Figure 3.21 (a) and (b) which illustrate the differences between prescriptions and intakes for fat from parenteral and enteral nutrition respectively.

Comparison between feeding prescriptions and actual nutrient intakes per birth Weight Group for fat

No differences were found between parenteral fat intakes and prescriptions in the ELBW group on day one (p = 0.317) and seven (p = 0.135). These results were also found in the VLBW group on day seven (p = 0.060) and all study days in the LBW group. Fat derived from parenteral nutrition showed clinical differences to prescriptions in the LBW group on day 14 of life. Significant differences were found between enteral fat intakes and prescriptions for all BW groups on all study days. Enteral fat intakes were of clinical value when compared with the prescriptions on day 14 of life for the VLBW and LBW groups. Refer to Figure 3.22 (a) and (b) which illustrate the differences between fat prescriptions and intakes from parenteral and enteral nutrition respectively.

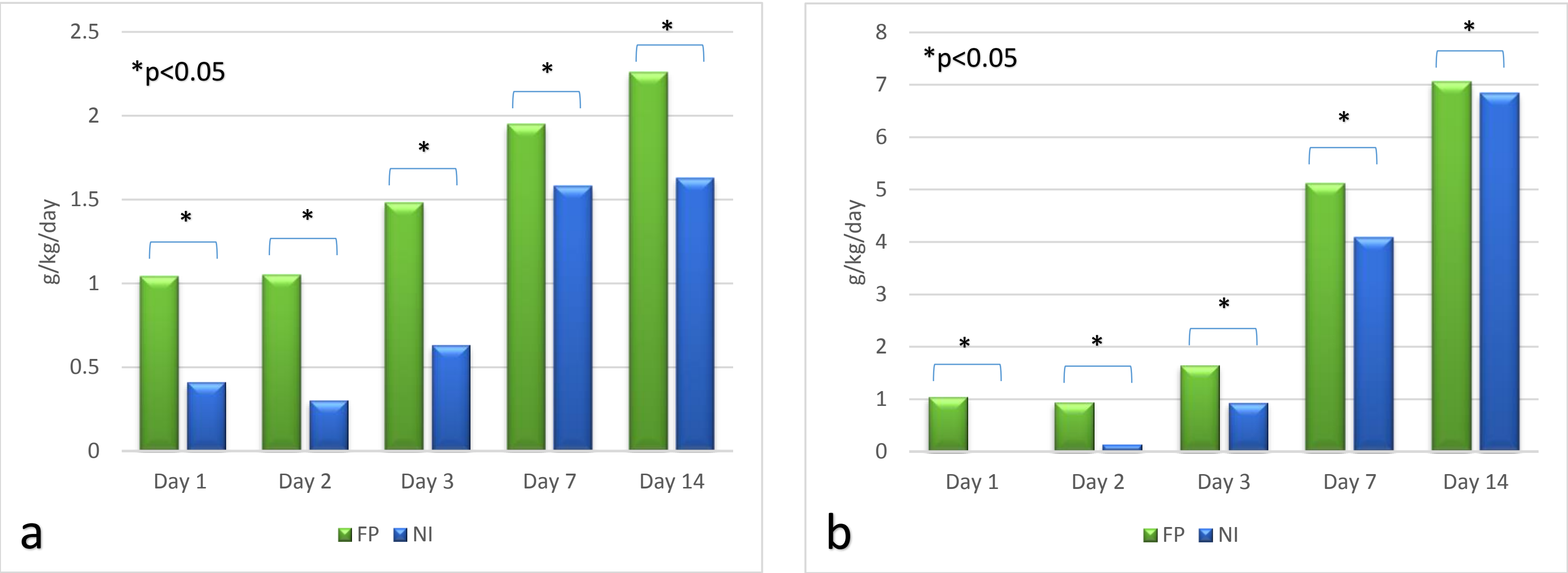


Figure 3.21 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for fat from parenteral and enteral nutrition for the total study population

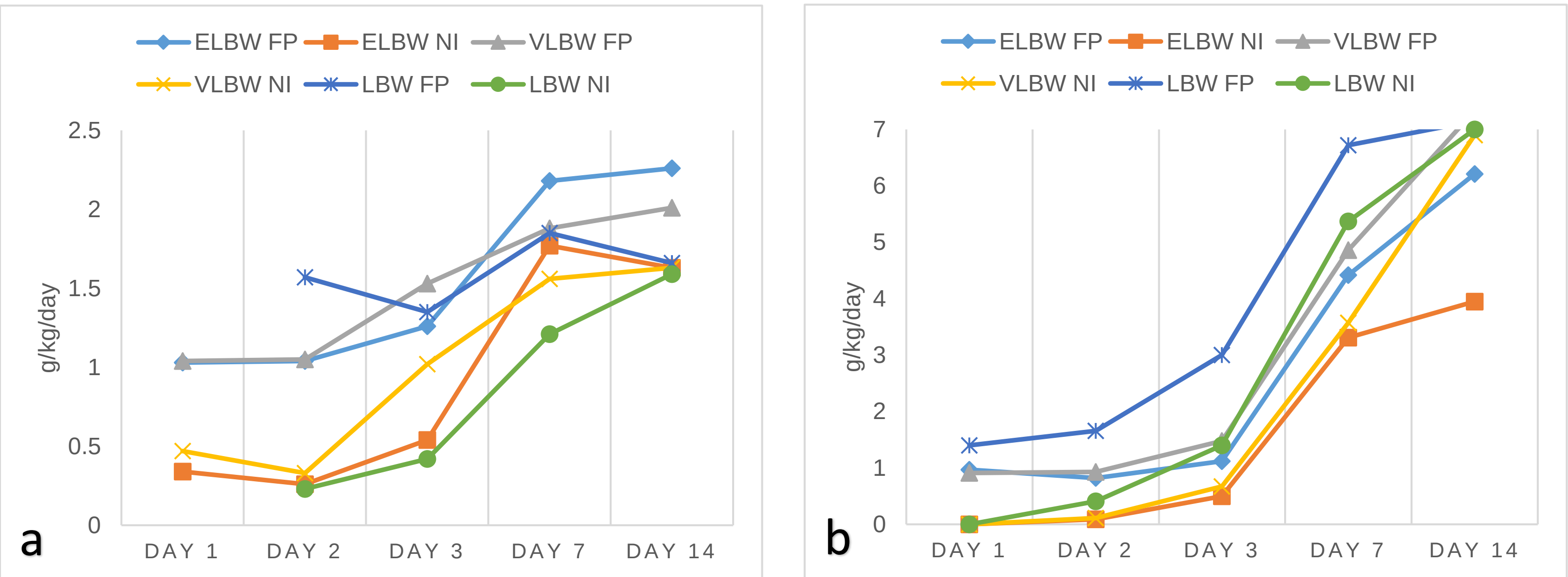


Figure 3.22 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for fat from parenteral and enteral nutrition for the birth weight groups

3.4.5 Carbohydrates

Comparison between feeding prescriptions and actual nutrient intakes for the total study population for carbohydrates

The actual GOR from PN was found to be significantly lower ($p < 0.05$) than the prescriptions on all the study days. The same findings can be seen with the enteral CHO intakes when compared with the prescriptions ($p < 0.05$). Although these results were statistically significant, they also showed clinical differences between FP and NI. Only on day 14 of life were the actual CHO intakes from EN clinically comparable to prescriptions. Refer to Figure 3.23 (a) and (b) which illustrate the differences between CHO prescriptions and intakes from parenteral and enteral nutrition respectively.

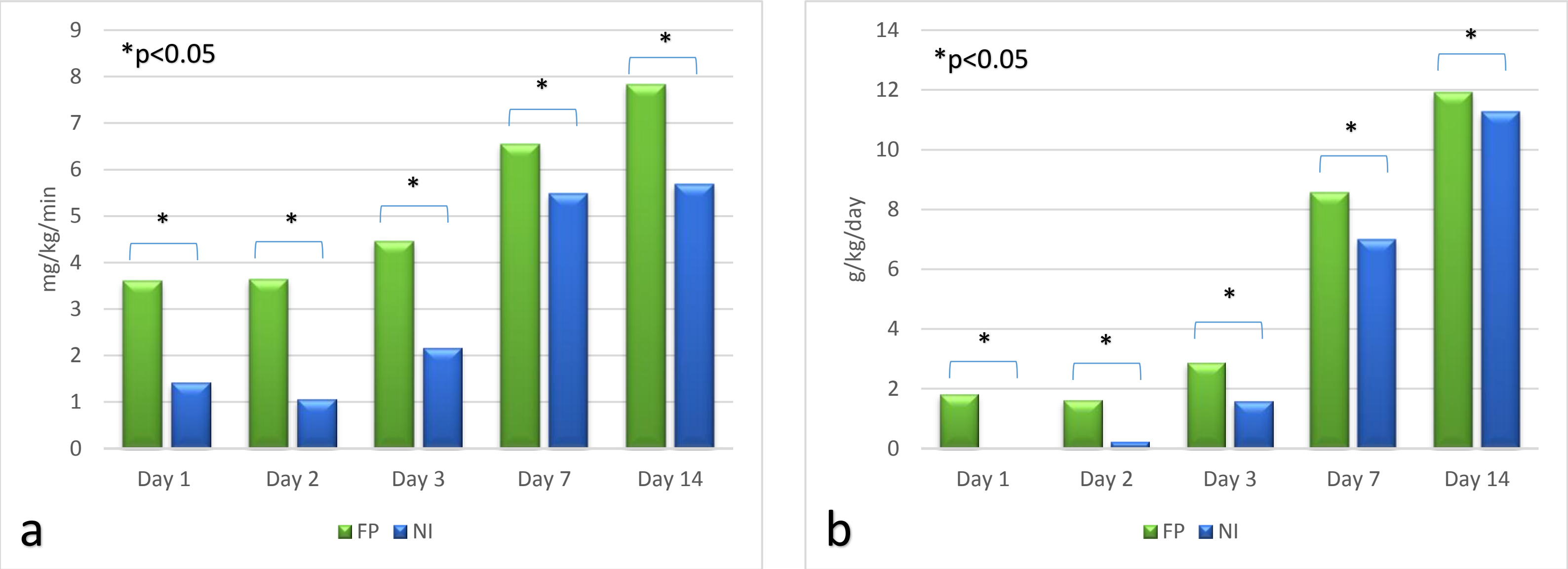


Figure 3.23 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for carbohydrates from parenteral and enteral nutrition for the total study population

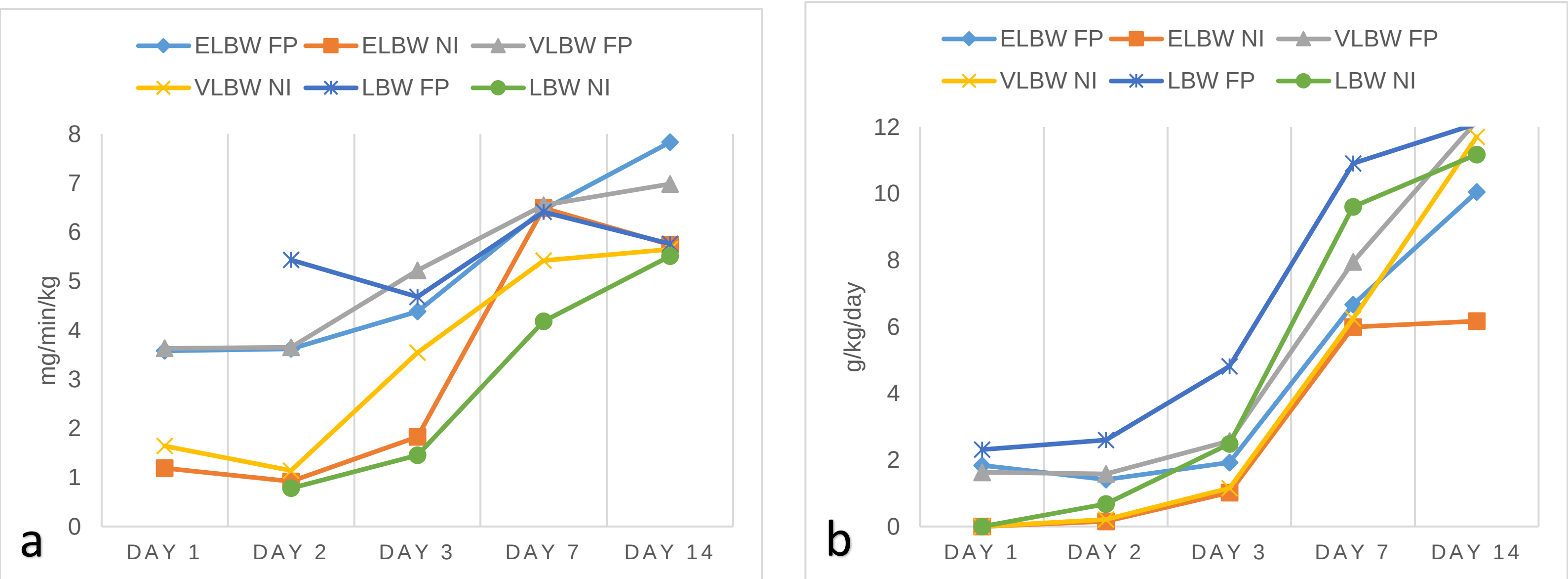


Figure 3.24 (a) and (b): Feeding prescriptions compared with actual nutrient intakes for carbohydrates from parenteral and enteral nutrition for the birth weight groups

Comparison between feeding prescriptions and actual nutrient intakes per birth weight group for carbohydrates

No differences were found between the feeding prescriptions and actual intakes for GOR from PN in the ELBW group on day one (p = 0.317) and seven (p = 0.145), the VLBW group on day seven (p = 0.062) and the LBW group on all the study days (figure 3.19). The actual GOR was clinically significant compared with parenteral prescriptions in the ELBW and LBW group only on day 14 of life. Significant differences were found between the feeding prescriptions and actual intakes for enteral CHO for all birth weight groups on all study days (p < 0.05). The enteral CHO intakes were only clinically significant compared with their prescriptions in the ELBW group on day seven and in both the VLBW and LBW group on day 14 of life. Refer to Figure 3.24 (a) and (b) which illustrate the differences between CHO prescriptions and intakes from parenteral and enteral nutrition respectively.

Conclusion:
It is evident that differences between the prescriptions and actual nutrient intakes for parenteral and enteral nutrition were found for the total study population. Enteral nutrient intakes met prescriptions on day 14 of life.

The ELBW infants showed that PN actual intakes were clinically comparable to prescriptions on day seven of life for energy and GOR. Findings were similar for the LBW group for PN for fluids, energy and macronutrients on day 14 of life.

3.5 FEED ADVANCEMENTS UNTIL FULL FEEDS REACHED INDEPENDENTLY OF PARENTERAL NUTRITION

3.5.1 Enteral feeds independent from PN

On day seven of life, full enteral feeding prescriptions were provided to only 12 infants (10.9%). Of these, only nine infants received feeds (7.6%) independent from PN. The mean enteral prescription from these feeds were 180.37 ml/kg/day and actual intakes reflected a mean volume of 174.68 ml/kg/day on day seven of life. These volumes were, however, within recommendations of 180 ml/kg/day. On day 14 of life, fewer than half the subjects (n = 40, 45.9%) were prescribed a mean enteral feed volume of 179.70 ml/kg/day. Thirty eight percent (n = 35) of these infants received a mean volume of 180.65 ml/kg/day on day 14 of life for enteral nutrition.

3.5.2 Enteral fluid advancement according to study days

The fluid distribution between the prescriptions and intakes was both found to be significantly ($p < 0.05$) different between all the study days. Friedman's two-way analysis of variance was used to detect any significant differences between the fluid prescription and intake advancements of the study days one to 14 of life.

No significant differences ($p = 0.961$) were found between fluids prescribed on day one to day two of life. Similar results are shown between day two and day three of life ($p = 0.057$). Differences ($p < 0.05$) can be found when comparing fluid prescribed on day three (37.75 ml/kg/day) and day seven (117.65 ml/kg/day) of life. No differences ($p = 0.558$) were found between fluid prescribed on day seven and 14 of life. Although not significant, clinical differences between day seven and 14 were observed.

Similar findings are shown between fluid intakes received on day one and two of life ($p = 0.140$) as intakes did not differ much between the two days. Differences ($p < 0.05$) were found between fluid intakes on day two and three of life as feeds began to increase in accordance with recommendations of 20 ml/kg/day. Differences ($p < 0.05$) in feed advancement intakes were also found between days three and seven of life. No statistical differences ($p = 0.074$) were found between feed advancement intakes on day seven and 14 of life, but clinical differences were observed between the two days. Figure 3.25 shows the feed advancements of enteral nutrition.

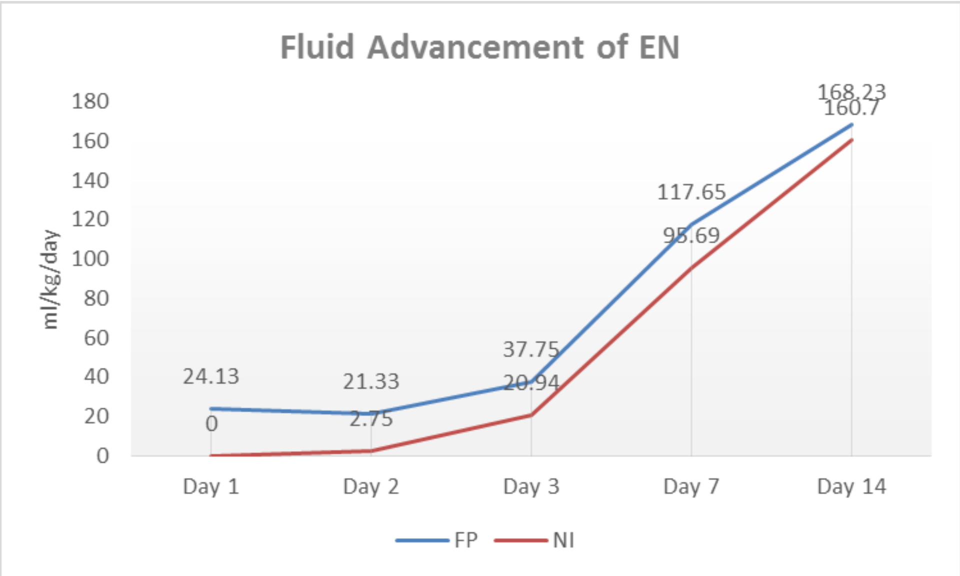


Figure 3.25: Fluid advancement of enteral nutrition

3.6 GROWTH OF THE PREMATURE INFANT

Infants showed postnatal growth failure during the first two weeks of life. Figure 3.26 shows the changes in the *z*-scores on days one, seven and 14 of life for weight, length and head circumference. For the duration of follow-up (14 days), the z-scores had decreased from –0.19SD to –0.25SD, –0.20SD to –0.78SD and 0.41SD to –0.75SD for weight, length and HC, respectively, for the total study population. No catch-up growth was seen in the anthropometric measurements during the study period.

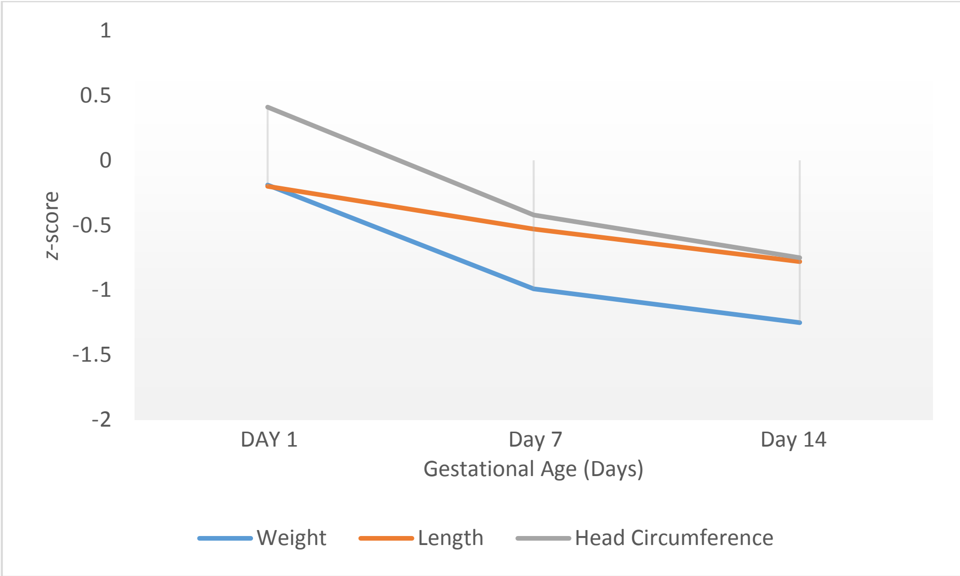


Figure 3.26: Growth of preterm infants from birth to day 14 of life

3.6.1 Weight

The *z*-scores for the different birth weight groups decreased on day one to day 14 of life from –0.63SD to –1.73SD, 0SD to –1.06SD and 0SD to –1.11SD in the ELBW, VLBW and LBW group, respectively (see Figure 3.27). Median weight gains were low in the total study population on day seven (3.99 g/kg/day) and 14 (3.73 g/kg/day) of life. Similar results were seen across the BW groups: ELBW – 2.95 g/kg/day, 4.03 g/kg/day; VLBW – 6.11 g/kg/day, 3.33 g/kg/day and LBW – 4.13 g/kg/day, 3.92 g/kg/day.

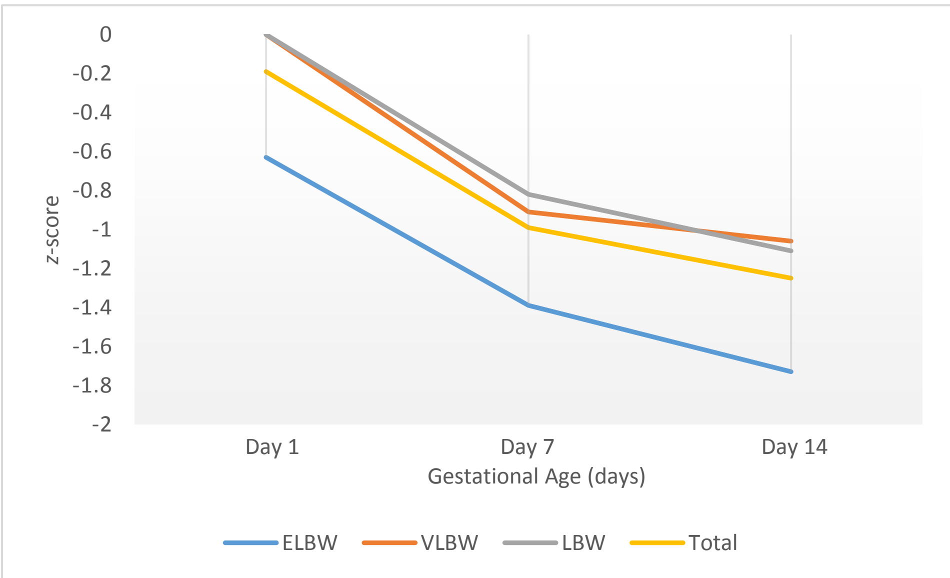


Figure 3.27: Weight-for-age *z*-scores per birth weight category

3.6.2 Length

The *z*-scores for length also decreased from day one to day 14 of life from –0.7SD to –1.44, 0.04SD to –0.65SD and –0.05SD to –0.28SD in the ELBW, VLBW and LBW groups, respectively (see Figure 3.28).

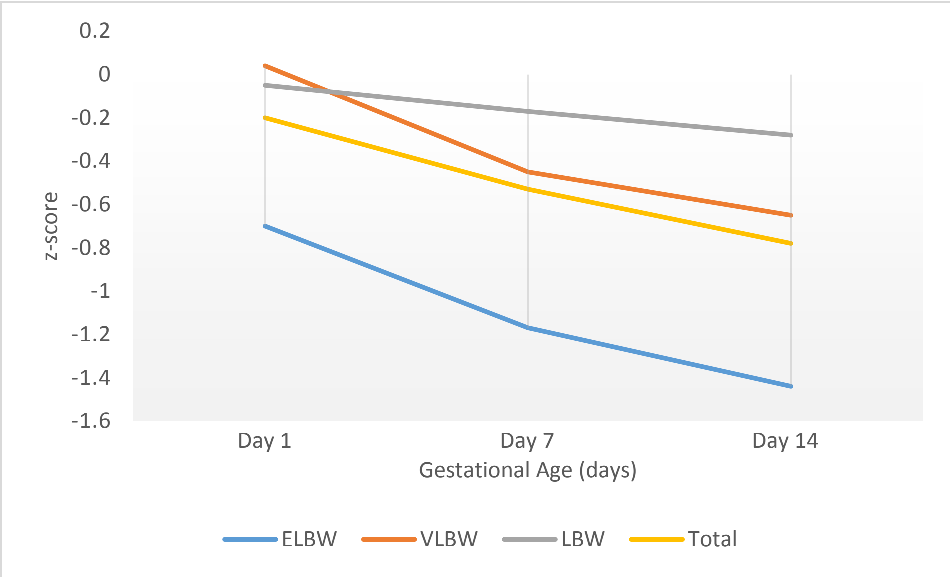


Figure 3.28: Length-for-age *z*-scores per birth weight category.

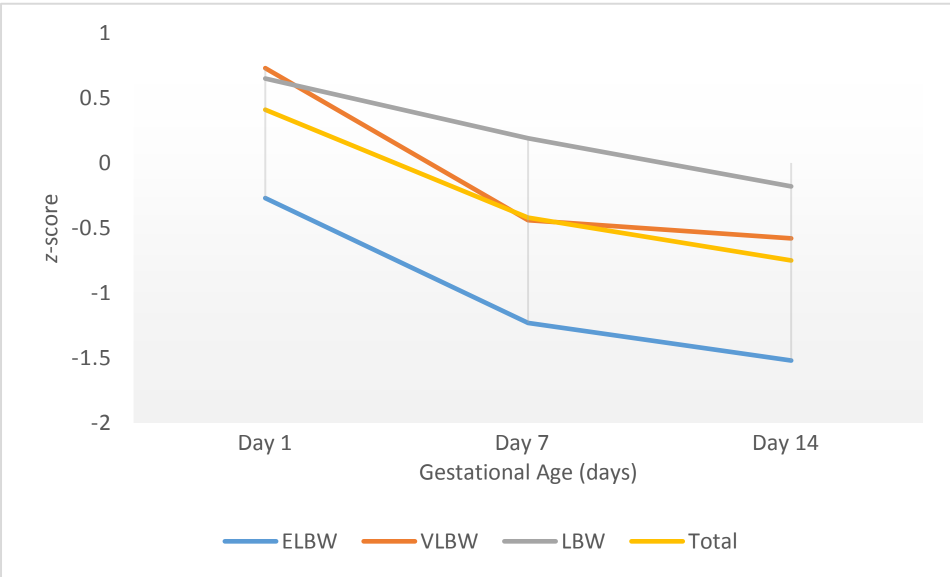


Figure 3.29: Head circumference-for-age *z*-scores per birth weight category

3.6.3 Head circumference

The z-score values for HC showed similar decreases on day one to day 14 of life, from –0.27SD to –1.52SD, 0.73SD to –0.58SD and 0.65SD to –0.18SD in the ELBW, VLBW and LBW groups, respectively (see Figure 3.29).

3.7 IMPACT OF ACTUAL NUTRIENT INTAKES ON PERCENTAGE WEIGHT LOSS ON DAYS SEVEN AND 14 OF LIFE

Spearman pairwise rank-order correlations were used to explore the associations between the actual nutrient intakes of fluid, energy and macronutrients (protein, CHO and fat) and the impact it has on percentage weight loss from birth to day seven and 14 of life for the total study population and BW category (Table 3.4).

Of the total study population, day seven (7.6%, *n*= 99) and 14 (7.3%, *n*= 52) *showed* similar weight loss averages. However, by day 14, a lesser amount of infants had weight loss.

No significant associations were found between actual fluid, energy and macronutrient intakes from PN and percentage weight loss on days seven and 14 of life for the total study population. This data reveals that actual nutrient intakes from PN had no impact on the percentage weight loss of subjects.

The opposite was found when observing the enteral nutrient intakes: significantly negative correlations were found between enteral nutrient intakes for fluid, energy and macronutrients and the impact it had on the percentage weight loss observed on day seven of life. These negative correlations indicates that increases in enteral nutrient intakes were associated with a decrease percentage weight loss. No significant associations were found between actual enteral intakes and percentage weight loss on day 14 of life.

Table 3.4 shows the correlations and *p*-values for the actual parenteral and enteral nutrient intakes for day seven and 14 of life.

3.8 THE EFFECT OF ACTUAL NUTRIENT INTAKES ON THE REGAINING OF BIRTH WEIGHT ON DAY SEVEN AND 14 OF LIFE

The Mann-Whitney test was used to explore the impact between actual nutrient intakes and regaining of the birth weight for the total study population and BW groups on day seven and 14 of life.

On day seven of life, a quarter (24.8%) of the total study population had regained their BW. This data had improved, with just under half (46.9%) of the study population achieving their BW by day 14 of life.

There was no association ($p > 0.05$) between parenteral and enteral intakes for fluid, energy and macronutrients, protein, fat and CHO for study subjects regaining their BW ($p > 0.05$) on day seven and 14 of life for the total study population. Similar results were also found within the BW categories. However, there was an association ($p < 0.05$) between parenteral intakes for fluid, energy and macronutrients and VLBW subjects regaining their birth weight on day 14 of life. Figure 3.28-3.32 shows the parenteral and enteral intakes on day seven and 14 of life between study subjects who regained their BW and those who did not.

Surprisingly, study subjects who did not regain their BW had higher parenteral and enteral nutrient intakes than those who regained their BW by day seven or 14 of life. This is evident in the total study population and BW categories for fluids, energy and macronutrients on day seven and 14 of life. Figures 3.28–3.32 indicate these differences with asterisks.

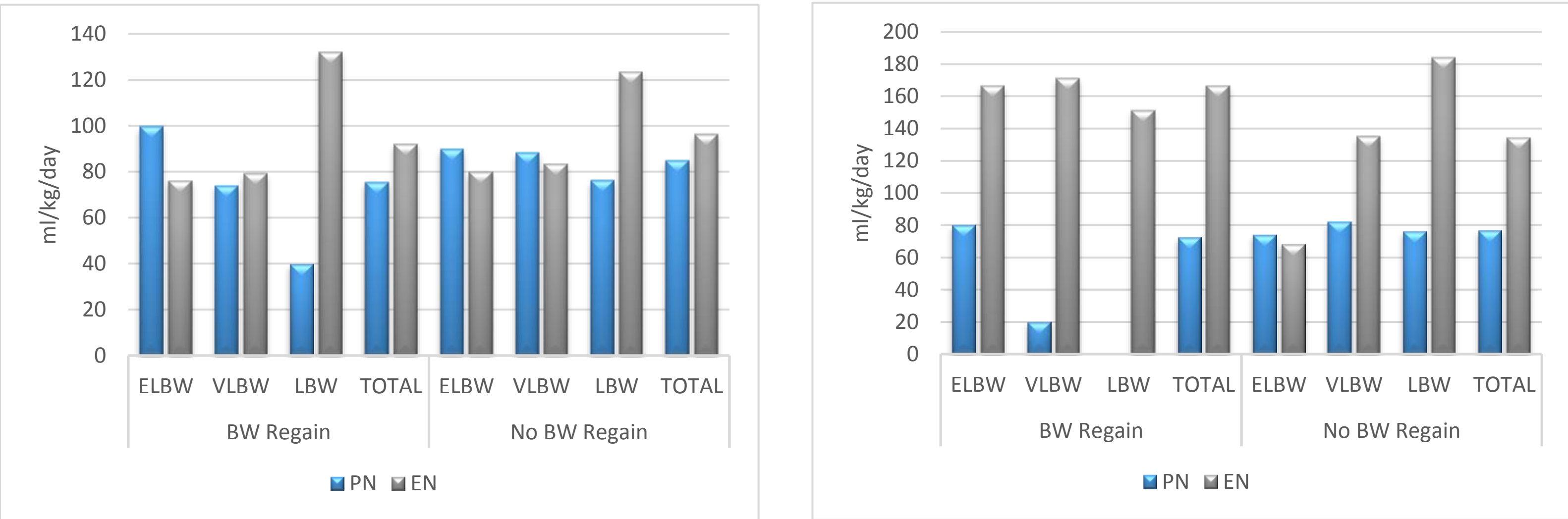


Figure 3.30 (a) and (b): Impact of parenteral and enteral fluid intakes on the regaining of birth weights on days seven and 14 of life

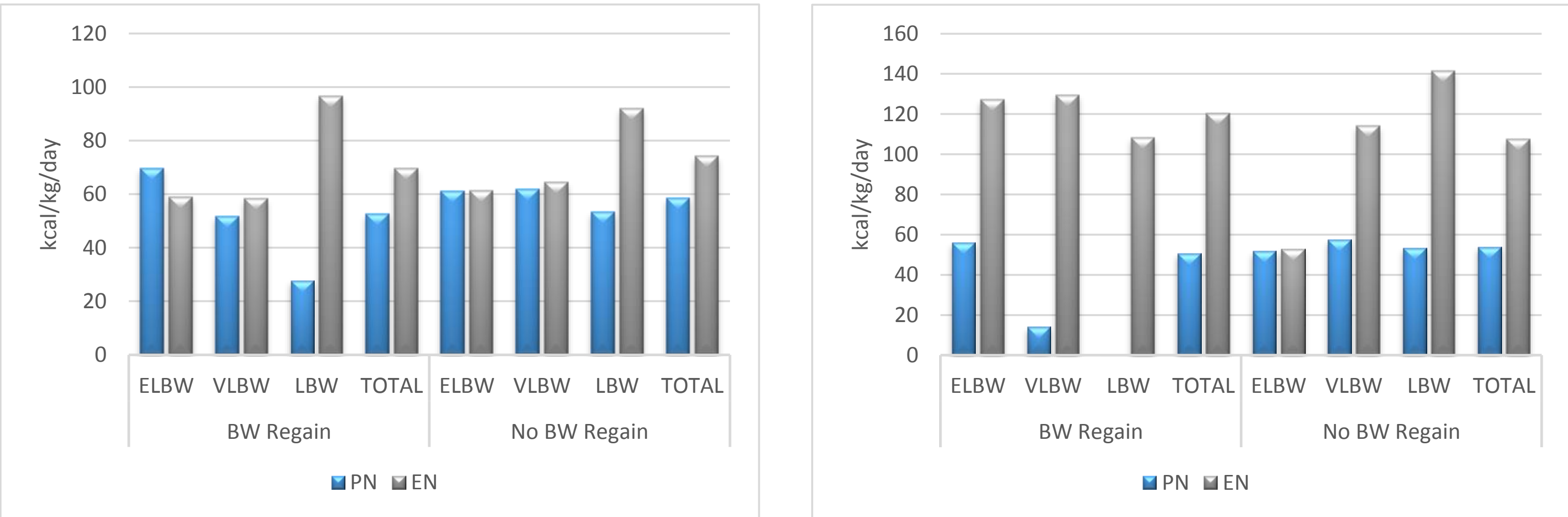


Figure 3.31 (a) and (b): Impact of parenteral and enteral energy intakes on the regaining of birth weights on days seven and 14 of life

Table 3.4: Impact of actual nutrient intakes on percentage weight loss on days 7 and 14 of life

	PN NI CC (*p*-value)	PN NI CC (*p*-value)	EN NI CC (*p*-value)	EN NI CC (*p*-value)
	Day 7	Day 14	Day 7	Day 14
Fluid				
Total	0.106 (0.480)	0.135 (0.530)	–0.309 (0.004)**	–0.104 (0.486)
ELBW	0.167 (0.482)	0.150 (0.659)	0.028 (0.914)	–0.152 (0.676)
VLBW	–0.025 (0.907)	–0.182 (0.593)	–0.111 (0.502)	–0.209 (0.287)
LBW	0.500 (0.667)	1.000 (–)	–0.450 (0.013)*	–0.084 (0.830)
Energy				
Total	0.109 (0.466)	0.135 (0.530)	–0.252 (0.019)	–0.094 (0.532)
ELBW	0.147 (0.536)	0.150 (0.659)	–0.012 (0.963)	–0.152 (0.676)
VLBW	–0.025 (0.907)	–0.182 (0.593)	–0.082 (0.620)	–0.187 (0.342)
LBW	0.500 (0.667)	1.000 (–)	–0.415 (0.023)*	0.084 (0.830)
Protein				
Total	0.107 (0.475)	0.135 (0.530)	–0.236 (0.029)*	–0.116 (0.438)
ELBW	0.167 (0.482)	0.150 (0.659)	0.011 (0.966)	–0.176 (0.627)
VLBW	–0.025 (0.907)	–0.182 (0.593)	–0.060 (0.717)	–0.217 (0.268)
LBW	0.500 (0.667)	1.000 (–)	–0.439 (0.015)*	0.173 (0.656)
GOR/CHO				
Total	0.085 (0.572)	0.146 (0.505)	–0.274 (0.011)*	–0.102 (0.496)
ELBW	0.099 (0.678)	0.267 (0.455)	0.018 (0.944)	–0.152 (0.676)
VLBW	–0.025 (0.907)	–0.182 (0.593)	–0.077 (0.643)	–0.172 (0.382)
LBW	0.500 (0.667)	1.000 (–)	–0.483 (0.007)**	0.143 (0.714)
Fat				
Total	0.121 (0.418)	0.132 (0.538)	–0.299 (0.005)**	–0.136 (0.363)
ELBW	0.154 (0.515)	0.150 (0.659)	–0.012 (0.963)	–0.152 (0.676)
VLBW	–0.020 (0.924)	–0.182 (0.593)	–0.111 (0.501)	–0.224 (0.253)
LBW	0.500 (0.667)	1.000 (–)	–0.434 (0.017)*	–0.261 (0.498)

Abbreviations:PN; parenteral nutrition,NI; nutrient intakes, EN; enteral nutrition, CC; correlations, ELBW; extremely-low-birth-weight, VLBW; very-low-birth-weight, LBW; low-birth-weight, GOR; glucose oxidation rate, CHO; carbohydrates
p-value: * <0.05, **<0.01, ***<0.001

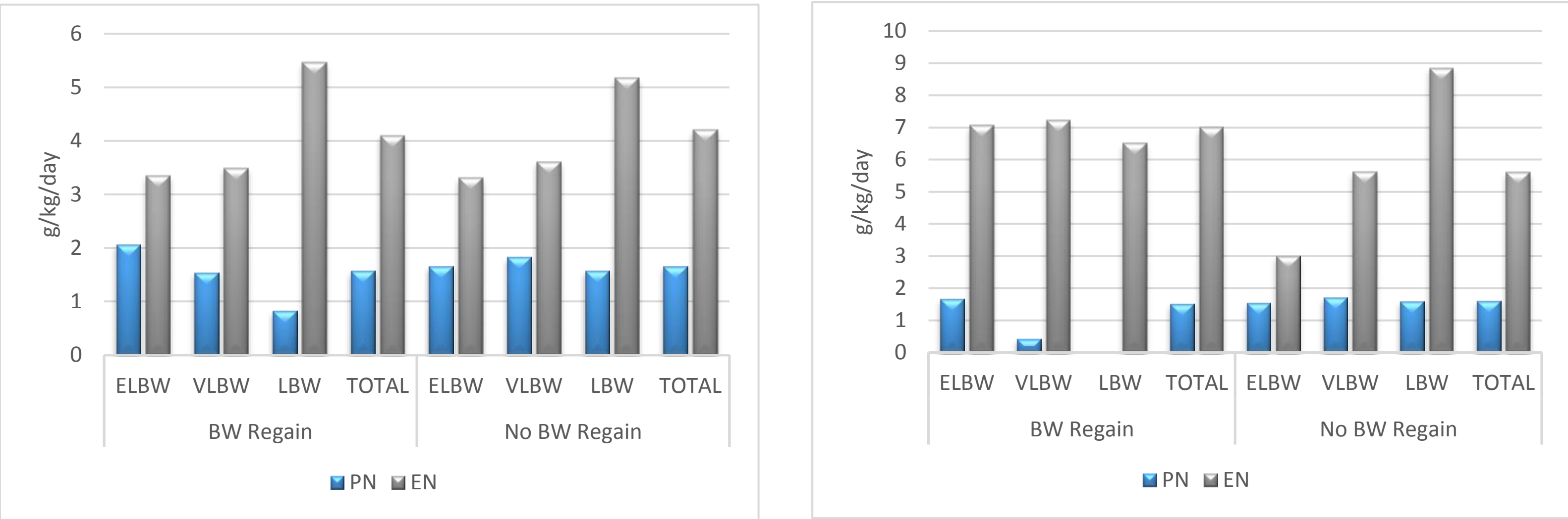


Figure 3.32 (a) and (b): Impact of parenteral and enteral protein intakes on the regaining of birth weights on days seven and 14 of life

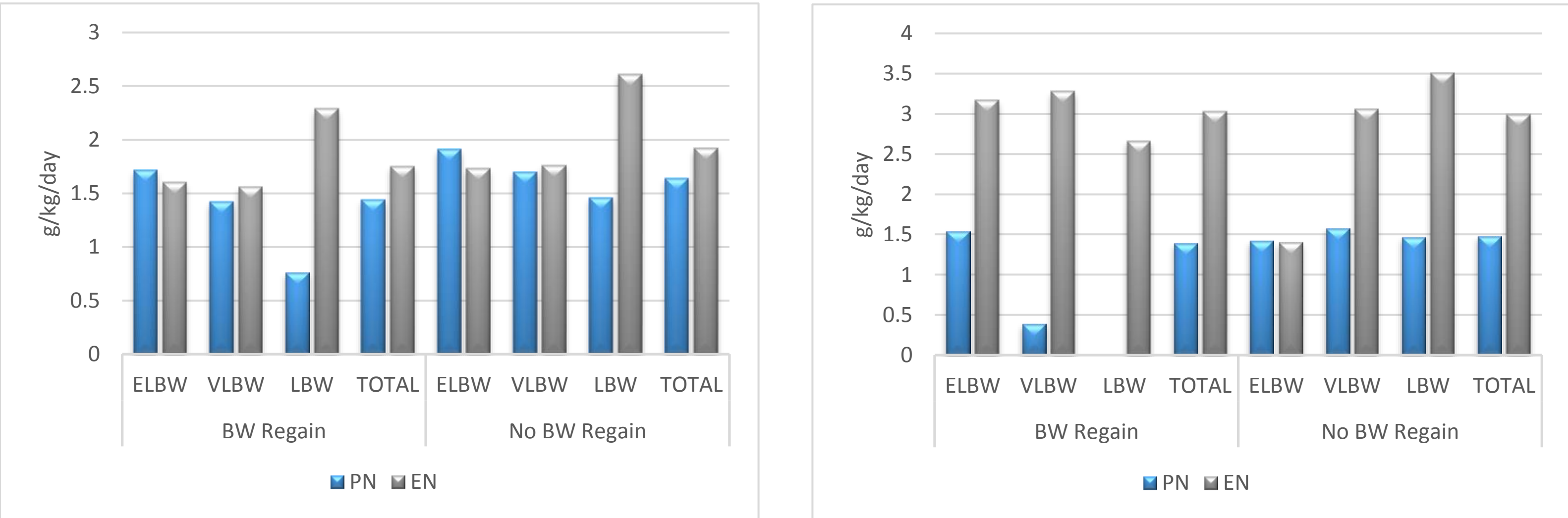


Figure 3.33 (a) and (b): Impact of parenteral and enteral fat intakes on the regaining of birth weights on days seven and 14 of life

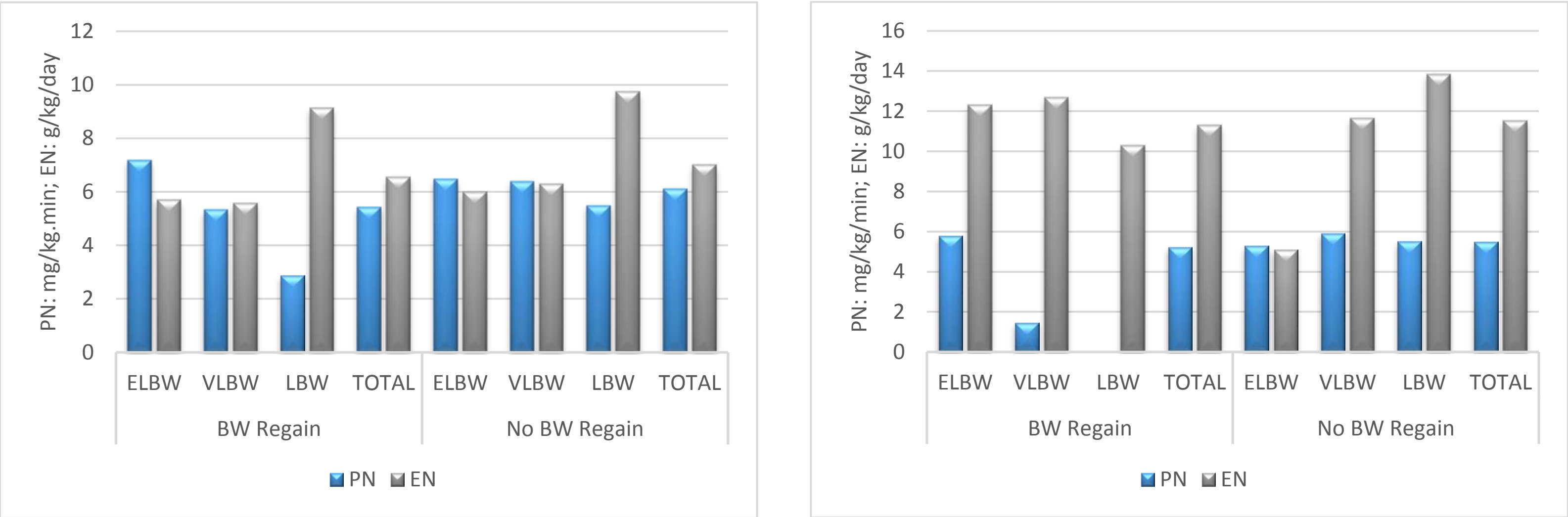


Figure 3.34 (a) and (b): Impact of parenteral and enteral carbohydrate intakes on the regaining of birth weights on days seven and 14 of life

CHAPTER 4

DISCUSSION

CHAPTER 4: DISCUSSION

A prospective, observational cohort study was performed to determine the feeding prescriptions and actual nutrient intakes of low birth weight (LBW), preterm infants born at CHBAH during the first two weeks of life. The feeding prescriptions and nutrient intakes were compared with nutritional recommendations for preterm infants. The anthropometry of the LBW, preterm infants were assessed on a weekly basis.

This study relied on the clinicians' feeding prescriptions for all of the observed study days. Retrospectively, the information recorded by the nursing staff of the actual intakes received in the hospital records were also observed on that particular day.

4.1 STUDY SUBJECTS' CHARACTERISTICS

The study population was fairly distributed between the birth weight (BW) categories (ELBW: 30.1%; VLBW: 34.6%; LBW: 35.3%). The majority of preterm infants were female (55.8%), which is contrary to previous claims of a higher incidence of prematurity amongst male infants.[7] This study showed an inverse relationship between birth weight (BW) and gestational age (GA) with a mean BW and GA of 1 352 g (±457 g) and 30 weeks (± 2), respectively, for the total study population. Numerous studies publishing data on feeding preterm infants focus mainly on VLBW infants.[3,54,102,108–110] There is very limited and reliable data on preterm births in sub-Saharan Africa despite the very high incidence reported globally.[111,112] South Africa is ranked 128th out of 184 countries with eight out of every 100 births being preterm births.[113] Velaphi et al. found that over a three-year period, the majority (81%) of VLBW infants admitted to CHBAH were less than 33 weeks GA with a median BW and GA of 1 180 g and 30 weeks, respectively.[108] This study showed that the majority of infants (42.9%) were born between 28 and 30 weeks GA.

Despite data from Lee et al. showing very high estimates (43.3 million) of preterm or small-for-gestational age (SGA) births from national and regional estimates in low-middle income countries, the majority of infants born in this study were AGA (79.4%).[114] A small percentage (12.9%) of infants born in this study were SGA, most of whom were ELBW infants (23.4%). This study also noted a small number (8.4%) of infant BWs interpreted as LGA, which is similar to findings by Norris et al. concerning the prevalence of LGA in British (9%) and Pakistani (10%) infants.[115] Although SGA and IUGR are used interchangeably and both characterised by adverse outcomes, they are not synonymous.[8] Intrauterine growth restriction (IUGR) had only been reported in 5.8% of the total study population in this study. In developed countries, 3–7% of newborns are classified as having IUGR, with up to 72% of unexplained deaths related to IUGR or SGA.[8]

It has been shown that morbidity and mortality rates are inversely related to a decreased GA and BW, mainly seen among infants born less than 32 weeks GA.[112] This study showed that the majority of subjects (94.9%) were diagnosed with respiratory distress syndrome (RDS). RDS is inversely related to immaturity due to insufficient pulmonary surfactant and gestational age, with increased incidence of 50% at 30 weeks GA, 75% at 28 weeks GA and 90% at 26 weeks GA.[112,116]

This study found a disturbingly high incidence (19.2%) of infants diagnosed with NEC unlike data from literature ranging between 4% and 7%.[21] The incidence of feeding intolerance is approximately 16–29% depending on the definition used.[94] This study had a low occurrence of feeding intolerance (FI) that might also have been diagnosed as NEC. Diagnosing the true incidence of NEC and feeding intolerance can be difficult and tends to be subjective as it is based on clinical assessment of abdominal distension or severity of emesis without specification of volume or colour.[94,117] Diagnostic errors or misdiagnosing can over- or under- represent the true incidence of morbidity seen in this population. Because the criteria used for diagnosing may have differed in this study's unit compared with international standards, it may not correlate well with literature.

4.2 MATERNAL CHARACTERISTICS

The mean age of mothers giving birth to preterm infants was 27 years, with the majority having caesarean deliveries (67.9%) due to foetal distress (27.6%) and pregnancy-related hypertension complications such as pre-eclampsia (26.9%). Velaphi et al. showed that 42% of mothers delivered by caesarean section, which was lower among infants weighing less than 1 000g.[108] Saving Babies 2012–2013 report showed that the majority of mothers have normal vaginal deliveries when compared with caesarean section (n = 992 830 vs 295 386)[23]. Trending analysis from Canada suggests a significant prevalence of increased preterm births is related to more aggressive policies for caesarean sections due to poor foetal growth or distress as seen in the hospital.[112] Other minor complications that resulted in preterm delivery were antepartum haemorrhage (APH) (9.6%), preterm labour (7.1%), abruptio placenta (3.8%) and PROM (3.6%). Preterm birth is multifactorial, and Ofori et al. found a strong risk association between preterm delivery and obstetrical conditions such as placenta previa, placental abruption, abnormalities of the uterus, intestinal infections, diabetes and gestational hypertension/pre-eclampsia, with hypertension as an independent risk factor, whereas Shrestha et al. reported that APH was the common risk factor for preterm birth.[118,119] These complications were found in this study too. The majority of the mothers were HIV-negative (66.9%) at the time of delivery. There has been assumptions that infective morbidity, including HIV infection, is generally responsible for higher rates of preterm delivery in Africa compared with other regions but was not seen in this study.[111] Brits et al. conducted a study to determine the cause of prematurity in the Bloemfontein Academic Hospital Complex.[120] Their study found that teenage mothers and those above 35 years of age are at risk, and that HIV and hypertension were definite risk factors for prematurity.[120] Previous premature labour and multiple pregnancies in their study were also a risk factor, consistent with literature findings. Although, the cause of preterm labour was not known in the majority of cases, conditions such as spontaneous premature rupture of membranes, over-distension of the uterus or infections during pregnancy may be a risk factor for premature delivery.[120]

4.3 FEEDING PRESCRIPTIONS AND ACTUAL NUTRIENT INTAKES

This section will further discuss the feeding prescriptions and actual nutrient intakes for fluid, energy, protein, fat and CHO from parenteral and enteral nutrition and IV fluids on all the study days for the total study population.

4.3.1 Fluid

Feeding prescriptions for fluids on day one in this study were similar to recommendations, starting at 60–80 ml/kg/day mainly derived from IV fluids (79 ml/kg/day).[29,121] Fluid prescriptions and intakes from PN (50 ml/kg/day, 20 ml/kg/day respectively) were below those recommended by Koletzko et al. for day one of 60 ml/kg/day.[48] A small number of subjects (3.8%) in this study received PN within 24 hours, even though early provision has been shown to be safe in preterm infants.[56,122] This study, like Law & Chan's study (5.8%, 60 ml/kg/day), showed only a few subjects received PN on day one, indicating that early provision of PN is not generally practised.[122] Minimal enteral feeds (24 ml/kg/day) were prescribed for a third of the study subjects (n = 48, 30.8%) within 24 hours, in line with recommended values, but insignificant amounts were received.[14,29] Infants were mostly diagnosed with respiratory complications and other co-morbidities, which may have influenced and delayed enteral feeding. RDS is a common cause of death in premature infants which may have influenced the clinicians' decision to either not prescribe or advance enteral feeds as a precautionary measure.[120] Such infants may also be physiologically immature with temperature instability and not sufficiently medically stable to feed, as the focus is on infant survival, hence the delay in feeding.[102]

According to a systematic review of nine trials, trophic feeds of 10–25 ml/kg/day from day one of life are safe without increasing the risk of NEC, although these findings cannot be generalised to extreme preterm, ELBW or growth-restricted infants.[110] This study showed that parenteral and enteral feeds only began advancing according to recommendations, by day three. By day seven, the majority of fluids prescribed were derived from enteral (118 ml/kg/day), with a fair amount of fluids from parenteral (94 ml/kg/day) and IV (77 ml/kg/day). In the study by Abel, PN was the major nutritional contributor compared to EN. Parenteral fluid prescriptions and intakes in this study did not reach recommendations of 150 ml/kg/day.[48] EN fluid prescriptions and intakes (168 ml/kg/day, 161 ml/kg/day respectively) only met ESPGHAN recommendations of 160 ml/kg/day by day 14 of life, but not this study's recommendation of 180 ml/kg/day (absolute value).[33] This study's findings were inconsistent with the randomised control trial by Kristhnamurthy et al. who showed that full enteral feeds of 170 ml/kg/day can be achieved by day seven, with rapid advancement of 30 ml/kg/day in VLBW infants without increasing the risk of apnoea, feed interruptions or intolerances.[50] PN fluid prescriptions and intakes contributed a significant amount on day 14 and study subjects were still being prescribed IV fluids similar to previous study days. Wemhöner et al. found in their study that VLBW infants, regardless of BPD diagnosis, had total fluid administrations of less than 160 ml/kg/day by day 14 while this study showed comparatively higher fluid prescriptions.[123] Results were similar across BW categories, except in the ELBW group which showed lower fluid prescriptions and intakes than expected. There is evidence that careful fluid administration during the first week of life can reduce the risk of PDA, NEC, CLD and death.[124] However, fluid should not be the only factor to consider when ensuring adequate nutrition, as it can influence the quantity of nutrients infants receive, especially if fluid restricted.

4.3.2 Energy

This study revealed that the majority of the energy prescribed and received on day one were from IV and PN, even though IV provided a bigger contribution of fluids than PN. Prescriptions and actual intakes for PN energy in this study were below day one recommendations of 40–60 kcal/kg/day.[39] Previous studies indicate that rapid enteral feed advancement rates greater than 20 kcal/kg/d have been associated with an increase in the incidence of NEC; however, these studies are insufficiently robust.[125,126] Recent studies discuss timing and feed advancement intakes as an optimal strategy for decreasing the risk of NEC by stimulating the gut with enteral feeds.[127,128] In this study, energy prescriptions on day one were prescribed, but study subjects received almost no intakes from EN. Enteral nutrition has been shown to influence the incidence of NEC by providing nutrients to the mucosal epithelial cells, stimulating the secretion of growth factors and hormones for GIT growth and maturation.[129] While Abel's study had higher energy prescriptions and intakes than this study on day one of life, it looked at combined PN, EN and IV dextrose.[102]

No significant changes and advancements were seen in the energy prescriptions and intakes between day two and three for PN, EN and IV fluids compared with day one. Data on energy prescriptions from EN were initiated in this study, but only reached trophic amounts by day three of life, unlike the study by Ng et al. which had median energy intakes above 20 kcal/kg/day by day two.[130] Ng et al.'s study reported data on combine parenteral and enteral nutrition prescriptions and intakes.[130]

Experts recommend 90–100 kcal/kg/day of energy from PN to achieve normal growth rates and adequate protein accretion.[52,60] This study showed that energy from PN prescriptions on day seven and 14 of life were within recommendations, but low intakes were given. Only by day 14 of life were enteral energy prescriptions and intakes in this study comparable to recommendations of 100–135 kcal/kg/day.[33]

Target energy intakes of 90–100 kcal/kg/day for enteral nutrition are recommended within the first week of life.[56] This study showed similar results of low enteral energy prescriptions and intakes compared with recommendations as did the Ng et al. study by day seven.[130]

Studies show that the majority of energy prescriptions and intakes were derived from PN during the first week, decreasing during the second week where EN began increasing.[102,124] The median energy prescriptions and intakes in Abel's study were significantly less when compared with Ziegler's requirements during the first week.[102] Similar trends can be seen in this study, with infants receiving more enteral than parenteral feeds during the second week of life. These inadequate intakes of energy noted during the first two weeks of life can result in high nitrogen losses (cumulative and negative) and poor growth.[56,129] Previous studies showed similar low energy intakes to this study, which have shown the long term adverse consequences of low energy intakes as being a strong predictor of weight gain and neurocognitive development.[102,130,131] Other long term consequences of undernutrition are reduced concentrations of the IGF-1 growth-promoting hormone which is associated with poor HC growth rates.[60] Studies have shown that energy intakes of 115–120 kcal/kg/day support protein intakes of 3.5–4 g/kg/day. Providing higher energy intakes to the preterm infant may contribute more to body fat gain and not to lean body mass.[52,60] Although, this study met energy requirements on day 14 of life, the protein requirements were found to be inadequate and below recommended amounts.

This study's results, like those from Ng et al., showed that infants do not meet their energy requirements during the first week of life.[130] This study's subjects managed to achieve enteral energy prescriptions and intakes according to ESPGHAN (110 – 135 kcal/kg/day) by day 14 of life, unlike Abel's study which showed lower energy prescriptions and intakes throughout the study period for enteral feeds.[102] A clinician's concern is to do no harm, which may result in caution with respect to providing enteral nutrition, due to the perceived risk of feeding intolerance and NEC.

4.3.3 Protein

Recommendations for parenteral protein infusions should be initiated at rates of ≥ 2.0 g/kg/day at birth and increase daily to 3.5–4 g/kg/day.[56,126] This study had low PN AA prescriptions (0.96 g/kg/day) and intakes (0.38 g/kg/day) on day one of life, similar to Ng et al., which had ±1.0 g/kg/day (combined PN and EN calculated estimates).[130] ESPGHAN recommends a minimum of 1.5 g/kg/day of protein to prevent a negative nitrogen balance in parenterally fed preterm infants, and higher intakes for protein accretion and growth.[55]

A study conducted by Law & Chan used standard preterm PN regimens, formulated according to AAP and ESPGHAN recommendations, that provided AA infusions of 2 g/kg/day on day one.[122] Unlike their study which achieved 2.0 g/kg/day of AA in 55% of the sample on day two and 3.5 g/kg/day by day five, in this study, FP and NI were low in comparison at 0.97 g/kg/day and 0.28 g/kg/day, respectively, on day two. Prescriptions (2.08 g/kg/day) and intakes (1.50 g/kg/day) only achieved minimal parenteral AA recommendations on day 14. However, studies demonstrate that earlier infusions of higher amounts of AA are safe.[5,60,130] The intrauterine protein accretion rate is 2 g/kg/day until 32 weeks GA, followed by rates of 1.8 g/kg/day thereafter.[122] Early aggressive PN aims to achieve AA infusions of 4 g/kg/day within the first week of life, which was not found to be the case in this study.[122]

Infants in this study were prescribed and received substantially less protein during the first three days of life (35% less on days one and two and 9% less on day three), compared with initial recommendations of 1.5 g/kg/day and 2 g/kg/day (more than 70% less) of parenteral and enteral, respectively.[3,28,33,37,39,48,55,58] However, a Cochrane review of seven trials showed that early AA administration of 0.5 g/kg/day in various studies (within the first 24 hours of birth) improved nitrogen balance, but had no benefit on mortality, early and late growth, and neurodevelopment. The authors concluded that there is insufficient evidence to practice these guidelines.[132] Clinicians' prescriptions in this study only achieved minimal recommendations of parenteral AA by day seven of life (1.8 g/kg/day) and actual protein intakes of 1.5 g/kg/day were received on day 14. PN protein intakes on day seven (1.48 g/kg/day) were slightly below recommendations. The maximum protein prescribed for PN occurred on day 14 of 2.08 g/kg/day, but was below recommendations of 3–4 g/kg/day needed to avoid negative nitrogen balances.[3,28,37,39,48] By days seven and 14 of life, this study's findings for FP for protein via the enteral route had increased to 2.37 g/kg/day and 3.17 g/kg/day, respectively, but were still below the recommendations of 3.5–4 g/kg/day.[33] Protein intakes from EN did not meet the clinicians' prescriptions or recommendations and study subjects received a maximum protein intake of 2.94 g/kg/day on day 14 of life.

Due to the immature gastrointestinal tract of the preterm infant, minimal nutrient intakes need to be provided to maintain an anabolic state; hence reliance on feeding the infant via the parenteral route is important for providing trophic enteral feeds to aid the maturation of the intestinal tract.[56] Protein requirements should be increased daily to 3.5 g/kg/day within two to four days. This study did not observe these practices.

The current PN bags available in South Africa provide low doses of nitrogen, making it difficult to achieve initial rates of 2 g/kg/day on day one of life within recommended fluid intakes of 60–80 ml/kg/day (without providing fluids above recommendations). Proaño et al. conducted a study on nutrient intakes of protein and energy of VLBW infants during the first month of life and found that protein intakes were also suboptimal during the four weeks.[107] Infants who developed chronic lung disease (CLD) in the Cormack study had lower protein intakes after the first two weeks of life compared with those without CLD reported in previous studies.[133] The Cormack study also observed protein intakes below recommendations during the first week of life.[133] Significantly smaller HC and cognitive development scores are associated with lower protein intakes during the first five days.[102] This study's results are consistent with Proaño et al. and Cormack in that protein goals are not met, indicating that a more aggressive approach is needed to avoid cumulative protein deficits.[107,124,133]

As seen with energy requirements, Abel's study showed that the majority of protein provided during the first week of life was derived mainly from PN and was significantly less than the estimated requirements.[102] However, protein prescriptions and intakes from Abel's study were not significantly different from estimated requirements during the second week of life and showed gradual increases from EN while PN decreased.[102] This study's results were consistent with Abel's study in that they too showed inadequate protein prescriptions and intakes from parenteral and enteral nutrition, primarily in the first week of life, i.e. the first three days and day seven. This study showed that PN protein prescriptions and intakes did not advance to full recommendations as full parenteral feeds were not achieved. It is possible that it was the clinicians' intention to initiate and advance enteral feeds instead of focusing on reaching full parenteral feeds. Studies do demonstrate that providing high levels of early AA of 1.0–3.5 g/kg/day is safe and can reverse a negative nitrogen balance, and that this should be encouraged.[55]

Only by day 14 of life were enteral prescriptions and intakes in this study comparable to recommendations for the total study population, the VLBW and LBW group, whereas all previous study days provided inadequate amounts. This study showed that the smaller infants, i.e. the ELBW group, had inadequate protein prescriptions and intakes during the study period. This emphasises further that the most vulnerable infants are frequently nutritionally neglected, thus often making it difficult to meet protein needs in these smaller weight infants. The varying composition of enteral feeding, particularly breastmilk, which is low in protein can also contributor to study subjects not meeting their protein needs. This further emphasises the importance of early provision of PN to avoid a negative nitrogen balance and promote weight gain, and is associated with neurocognitive benefit.[126]

4.3.4 Fats

Initiating PN lipid infusions on day one at 1–2 g/kg/day recommended by experts are safe and well-tolerated if similar doses of AA are infused.[5,29,56,59,60] TPN bags available in South Africa have been formulated in such a way that advancements of PN over three days can meet the lipid infusion recommendations. Within a few days, lipid infusions can be advanced daily to meet recommendations of 3 g/kg/day.[56] In this study, PN lipid prescriptions (1.04 g/kg/day) met recommendations on day one, but actual intakes were low (0.41 g/kg/day). When cautiously advancing PN, lipid infusions should meet recommendations.

Previous studies showed associations between high and rapidly advancing lipid intakes and adverse outcomes such as sepsis, CLD, lipid intolerance and hyperglycaemia.[130] A systematic review and meta-analysis by Vlaardingerbroek showed that initiation of lipids in the first two days of life in VLBW infants is both safe and well tolerated.[130,134] This study did not observe the advancing of lipid infusions at 0.5–1 g/kg/day increments as suggested for study days one, two and three for PN.[5,122] The prescriptions for parenteral lipids on days seven and 14 were below the recommendations of 3–4 g/kg/day, as seen with the actual lipid intakes as well.[3,48] Similar findings were seen in the parenteral lipids on all the study days, where neither prescriptions or intakes met recommendations. The greatest parenteral lipid intake of 1.63 g/kg/day was achieved on day 14. Providing sufficient lipid infusions supports a positive nitrogen balance and improved weight gains.[122] ESPGHAN recommends minimum fat intakes of 3.8–4.8 g/kg/day for enteral nutrition.[33] However, these values could not have been met during the first three study days as these infants were not on full enteral feeds to warrant reaching such high amounts. Data from this study showed that enteral prescriptions (5.12 g/kg/day) and intakes (4.09 g/kg/day) had met minimum recommendations by day seven of life.

Tsang guidelines suggest higher fat intakes of 7.2-8.4 g/kg/day for VLBW and ELBW infants, respectively.[3,29,33] This study showed that by day 14 of life, maximum fat prescriptions and actual intakes were 7.06 g/kg/day and 6.84 g/kg/day respectively. This study’s results were comparable to ESPGHAN, but not to the Tsang guidelines.[33,34]

4.3.5 Carbohydrates

Initiation of glucose infusions of 4 mg/kg/min at birth is needed to maintain euglycemic status (blood glucose concentrations of 6.7 mmol/L, $<$ 120mg/dl).[48,56] Glucose infusions for FP (3.60 mg/kg/min) and NI (1.42 mg/kg/min) on day one were below initial recommendations. However, IV fluids were also prescribed and contributed towards CHOs of 8.69 g/kg/day (≈6.03 mg/min/kg). Caution should be taken when prescribing intravenous fluids and PN to avoid high glucose infusion rates $>$ 10–11 mg/min/kg, which can increase the risk of hyperglycaemia.[52]

The Ng et al. study showed that carbohydrate (CHO) intakes (10.8 g/kg/day) had not met recommendations of 12 g/kg/day by the first week of life.[130] This study showed similar results of low parenteral glucose FP (6.55 mg/kg/min, 7.83 mg/kg/min) and NI (5.49 mg/kg/min, 5.69 mg/kg/min) by day seven and 14 of life, respectively, compared with Tsang’s recommendations.[34] Enteral prescriptions for CHOs were very low in comparison to recommendations and had only met these values by days seven and 14 of life of 8.57 g/kg/day and 11.92 g/kg/day, respectively. The advancement of enteral feeds and, ultimately, increasing CHOs were minimal during the first three study days. CHOs derived from IV fluids met recommendations needed to avoid hypoglycaemic episodes throughout the study period. High CHO values (8.69 g/kg/day) were derived from IV fluid prescriptions on day one, but less than 50% of the prescribed value was actually received by the study subjects for the first day of life. Excluding day one of life, IV fluid intakes met prescriptions between 85% and 100% on all the other study days. Enteral intakes for CHO were very low in the first three days of life and only met recommendations by day seven (7 g/kg/day) and day 14 (11.27 g/kg/day). IV fluids contribute a large amount of glucose per 100 ml in comparison to PN and EN CHOs. Carbohydrates ingested via the enteral route require digestion and absorption, resulting in less glucose in the blood circulation compared with IV and PN solutions.

Summary of this study:

Interrupting foetal nutrient supply at birth should be kept to a minimum. Nutritional management during the first few weeks of life is vital for preterm infants' survival.[56,102] Inadequate nutrient intakes have been shown to lead to negative long-term neurological developmental outcomes as shown in previous studies.[102,130,28] Preterm human milk does not adequately meet the high nutritional needs of preterm infants, thus warranting fortification. Results from this study showed that all nutrients were inadequate by the first week of life, also reported in the study by Ng et al., despite the authors adopting a more aggressive early feeding approach.[130]

Parenteral nutrition should be the major source of nutrition during the first week of life while establishing enteral feeds, thereby avoiding an accumulated nutrient deficit.[126] The preterm infant is reliant on parenteral nutrition as the immature GIT limiting the digestion and absorption of enteral nutrient supply. Achieving nutritional recommendations during the first week of life in preterm infants is vital to reduce nutrient deficits, especially protein, which correlates with growth and neurodevelopmental outcomes.[1,102] Meeting energy and protein needs is imperative for AA utilisation as these deficits can negatively affect protein metabolism and lean mass accretion.[130] Alternatively, providing lipid infusions as a non-carbohydrate source of energy may be considered and seems to be safe when initiated within two days of life.[59,135] It has been documented that early lipid provision can positively affect nitrogen balance, despite some concerns of adverse outcomes such as CLD.[59] Another factor to take into consideration is clinicians' prescriptions of IV fluids, which can disrupt and compromise achieving nutrient goals from parenteral and enteral feeds.

4.4 COMPARISONS BETWEEN FEEDING PRESCRIPTIONS AND NUTRIENT INTAKES

It has been shown that actual intakes are 10–20% lower than prescriptions during the first weeks of life.[102] This study had similar results, with large differences noted during the first week of life between feeding prescriptions and nutrient intakes for fluid, energy and macronutrients for the total study population on all study days. These differences were seen mainly between the FP and NI of enteral feeds, unlike some data on parenteral feeds from the BW groups that showed similarity. The greatest deficits in this study, between enteral prescriptions and intakes were noted during the first week, i.e. the first three days and day seven, except for the ELBW group and data on PN which varied. Abel's study also showed similar findings to this study, with deficits of approximately 15% found between energy and protein prescriptions and intakes during the first week of life.[102] Despite improved intakes during the second week of life, similar differences were still seen between prescriptions and intakes in Abel's study.[102]

Cormack et al. showed in their prospective, observational study that energy (97%), protein (98%) and lipid (94%) intakes met most of their prescriptions, unlike the findings of this study.[133] This study did not focus on obstacles that might have resulted in large differences between prescriptions and intakes, but causes of feed interruptions have been documented. Prescriptions and intakes are not always achieved due to medical complications, such as an immature GIT with decreased enzymes, malabsorption, respiratory issues, PDA or NEC.[102] Other barriers that may affect feeding goals also include electrolyte and fluid imbalances, impaired renal function, blood transfusions, and difficulty in accessing peripheral catheters to administer nutrition.[102] Cormack showed in their study that the median actual energy intakes met 75 % of the prescriptions, a few of the babies met their lipid and energy prescriptions (75 and 88 % respectively).[133] The author highlighted that PN was stopped due to administration of antibiotics over two hours, whereas PN prescriptions were calculated over 24 hours.[133] This study showed large differences between FP and NI, were noted in the smallest infants (ELBW group) as these infants have a more immature GIT. Another dilemma often contributing to large variances noted between FP and NI, is that there is sometimes no human milk (mother's own milk) and/or donor milk available to start feeding. This is either due to the mother not being available or experiencing difficulty in producing milk. Mothers of preterm infants often experience difficulty in initiating and maintaining lactation for multiple reasons such as deficient mammary development, poor hormonal responses, separation from the infant, stress, anxiety or fatigue, and inadequate milk expressing equipment or technique.[136,137] A review by Dutta et al. recommends preterm formula milk after 24–48 hours if no maternal or donor milk is available.[110] Countries like South Africa are regarded as a high HIV prevalent area and the recommendation by Dutta et al. should be considered with caution. According to the infant feeding policy adopted by the World Health Organisation, the promotion of exclusively breastfeeding or expressed breastmilk is recommended.[138] If no such milk is available, consent should be obtained from the mother for either donor milk, if available, or preterm formula milk as a replacement. Implementation of the Mother and Baby Friendly Initiative (MBFI) in South African health facilities emphasises the importance of breastfeeding for overall health.[139] Unfortunately, CHBAH is not MBFI accredited, and showed differences in the type of feed i.e. breastmilk or formula milk. This study's focus was on feeding prescriptions and nutrient intakes and not on the type of feed per se. However, it is an important aspect to consider as it does influence the amount of energy and macronutrients and possible shortfalls on nutritional recommendations as seen in this study.

This section highlights the importance of evaluating nutritional prescriptions and actual intakes, showing that large differences do still occur despite recommendations advocating for early nutritional support. More focus should be given on minimising barriers to achieve intakes parallel to prescriptions and having these prescriptions mirroring international recommendations. It is also recommended that the source of nutritional guidelines used to calculate nutritional value be based on sound scientific evidence .[53]

4.5 FEED ADVANCEMENT UNTIL INDEPENDENT FROM PARENTERAL NUTRITION

The study by Ng et al. study showed that the median time for reaching full enteral feeds of 150 ml/kg/day was 17 days.[130] The study found that the likelihood of reaching full enteral feeds was greater when protein intakes were increased with every 1 g/kg/day.[130] This was also seen with lipid intake increases, but not energy and CHO intakes.[130] This study observed whether study subjects achieved full feeds regarded as 180 ml/kg/day on study days seven and 14. When reviewing the data on day seven, only a few study subjects (7.6%, n = 9) achieved full enteral feeds. A slight improvement of this outcome was seen on day 14 when 38% (n = 35) of study subjects achieved full enteral feeds. MEF has been shown to have a clinical benefit in reducing the time infants achieve full enteral feeds compared with those with delayed feeding.[54,60] As reported in the results section, study subjects barely received any enteral feeds during the first three days, which may be why only few subjects achieved full feeds on day seven and 14 of life. Cormack's study reached full enteral feeds (150–180ml/kg/day) by day eight of life.[53] MEF has been shown to reduce hospital stay and serious infections despite controversy pertaining to the risk of NEC.[53]

Berseth et al. conducted a study to determine NEC incidence with prolonged, small and increased feeds. The latter study was stopped due to seven infants developing NEC in the advanced feeding volume group and one infant in the slow feeding group. Berseth et al. showed that maturation of intestinal motor patterns, incidence of late-onset sepsis and feeding intolerance was similar in both groups despite feeding volumes given. Many studies support the view and have shown that early enteral feeding with daily advancements does not increase the incidence of NEC.[43,53,140] These studies also show faster attainment of full enteral feeds. This study showed significant differences between fluids prescribed on day three and seven, as well as for fluid intakes received between day two and three, and between day three and seven.

Abel's study showed that early energy intakes and BWs are significantly associated with reaching full enteral feeds. This study, however, did not stratify this outcome according to BW.[102]

Delayed full feeds may be related to feeding intolerances or suspected NEC where feeds are stopped for a few days.[102] Delaying enteral feeds or small increases results in a longer time taken to regain BW and reach full feeds.[60] Krishnamurthy et al. showed in their study that VLBW infants fed rapid feed advancements (30 ml/kg/day) achieved full enteral feeds earlier than those who had slow advancements, i.e. 20 ml/kg/day. This study showed that advancements of enteral feeds were slow, especially during the first week of life. Clinicians should ensure that attention be given to early enteral feeds that would, in due course, result in faster attainment of full feeds. The findings from this study, further emphasises the need of having a feeding protocol in place, in order to address the impact of delayed enteral feeds often seen amongst this group on infants. By having such a feeding protocol, issues such as non-adherence and poor nutrient supply to infants can be addressed and restricted in the clinical setting.

4.6 PRETERM GROWTH

Energy and nutrient intakes in the first week of life were not associated with weight, length and head circumference (HC) *z*-scores at discharge in the Ng et al. study.[130]

ELBW infants in the Law & Chan study showed highest growth rates with high urea concentrations. These high values not only reflect intolerances to AA infusions, but also appropriate AA utilisation for energy and lean muscle production.[122] The ELBW infants in the Law & Chan study showed higher weight gains than the LBW infants; however, this was not shown for HC growth velocity.[122] Such high weight gains could be a result of smaller infants having higher percentage weight loss compared with bigger infants where catch-up growth is not major. The results from the Law & Chan study showed that growth velocities for weight, length and HC, which included term infants, were 14.3 g/kg/day, 1.2 cm/week and 1 cm/week, respectively, and preterm infants' weight gains were 15.3 g/kg/day, similar to intrauterine growth.[122] Their growth parameters had increased in all the BW groups after the first week of PN therapy[122] Cormack's study showed a decrease in weight SDS of –1 from birth to 36 weeks postmenstrual age. Weight gains observed were 16–17 g/kg/day in infants <1 200 g or 30 weeks GA during the first month of life, which were in line with recommendations in the latter study.[124] Unlike Law & Chan and Cormack's studies, this study showed postnatal growth failure during the first two weeks of life, with 4.0 g/kg/day and 3.7 g/kg/day weight gains between day one and seven, and seven and 14, respectively. Recommended growth rates are estimated at 15–20 g/kg/day, but do not take into account nutritional deficits that accrue in the early weeks of life.[102]

This study showed decreases in growth measurements for weight, length and HC over the first two weeks of life. However, this study observed growth from birth to day 14 of life, whereas the majority of research data on preterm infants' growth extends beyond week two or three of life.[53,107] Therefore, data from this study should be interpreted with caution as it does not give a true reflection of growth outcomes extending beyond the 14 days of life where improvements might be seen. It has been reported that growth usually illustrates a downward trend, with estimates of 10–20% body weight during the first week of life, with a BW recovery between the second and third week, followed by intermittent weight gains thereafter.[70,141]This study showed that weight loss were below 10% on day seven and 14 of life.

A study by Proaño et al. found that BW *z*-scores were an important predicator of neonatal death or extrauterine growth restriction.[107] Their study also showed BW z-scores lower than reported in other studies as seen in this study.[107] This study observed infants growth parameters during the study period, but made no associations with morbidities.

Supporting appropriate growth with adequate nutrition in these vulnerable infants will help to bring about positive neurodevelopmental outcomes and reduced risk of co-morbidities and mortality.

International consensus groups have provided energy and protein recommendations based on research studies to avoid nutritional deficits that may impair lean body mass accretion and linear growth.[53] Despite literature showing a relationship between nutritional intakes and growth outcomes, observation studies do not demonstrate clear cause and effect.[1] Growth parameters including length and HC measurements should be considered, and not only weight gain, as an indication of a preterm infant's growth, as additional energy may only contribute towards fat mass rather than increasing lean mass.

4.7 IMPACT OF NUTRIENT INTAKES ON PERCENTAGE WEIGHT LOSS

Most feeding recommendations suggest early aggressive and increased energy and protein intakes for preterm infants, as early as possible after birth.[60] The systematic review and meta-analysis by Moyses et al. showed that early PN had significant reductions in the maximum weight loss in the studies included.[36] This study showed that NI derived from PN showed no significant association with the percentage weight loss of study subjects on days seven and 14 of life except for data on the VLBW group. NI derived from EN showed a significant impact on the percentage weight loss on day seven, but not on day 14 of life, although data showed negative correlations on day 14. Maayan-Metzger et al. showed a mean weight loss of 15.6% and 10.5% for AGA and SGA infants, espectively.[64] This study showed lower percentage weight losses of 7.6% (±4.5%) for the total study population compared with the latter study. It would be more beneficial to look at the preterm infant's weight gain and not necessarily the weight loss per se. Preterm infants tend to lose weight during the first two weeks of life due to water imbalances and the percentage weight loss might not be a good indicator of a preterm infant's growth rates, as would be the case with weight gain trajectory.[58] A lack of optimal nutrition received during the first week of life may further amplify a preterm infant's weight loss. A better indication of thriving infants is perhaps to view their body composition and not just their weight gains.

4.8 IMPACT OF NUTRIENT INTAKES ON BIRTH WEIGHT REGAIN

The systematic review and meta-analysis by Moyses et al., which consisted of observational studies and RCTs, showed that early PN reduced the time taken to regain BW.[36] Fenton et al. showed faster birth weight regains of 10–12 days in the Preterm Infant Multicentre Growth Study (PreMGS) cohorts compared with the NICHD cohorts of 13–17 days. This study showed that by day seven of life, a quarter of study subjects had reached their birth weights (24.8%), whereas the majority had not. This was more common in the heavier infants (LBW, $n = 15$). By day 14 of life, just half of the study population (46.9%) had reached their birth weights. This study showed that study subjects who reached their birth weight on day seven had lower NI for parenteral and enteral nutrition than those who did not reach their BWs. Intakes derived from enteral nutrition for fluid, energy, protein and fat were greater in the study subjects who regained their BWs compared with those who did not.

Cormack's study showed that weight gains were significantly associated with energy and protein intakes, but associations were weak.[133] This is an indication that despite adequate intakes within recommendations, it may not be possible to avoid post-natal growth failure as seen in this study. This study's findings differed from Ng's study which showed that, by the first week, BWs were correlated with energy and lipid intakes, but not protein or CHO.[130] The VLBW infants in Abel's study took an average of 10 days (±4 days) to return to their BWs, with the SGA infants reaching their BWs faster than the AGA infants.[102] Abel's study showed that actual energy and protein intakes during the first week of life were not significantly correlated with the time to regain BW, which was similar to this study's observations.[102]

Krishnamurthy et al.'s study showed furthermore that infants who had rapid feed advancements regained their BWs much sooner than those in the slow feed advancement group (16 vs 22 days respectively, $p < 0.001$).[50]

Anchieta et al. showed that weight loss occurred during the first week of life, with infants regaining their birth weights between the second and third week.[141] This was followed by a period of weight gain.[141] Their study also showed that mean daily weight gain velocities were proportional to the infant's BW.[141] Valentine et al. found an association between early AA administration and less growth failure at term, compared with infants who received AA later.[142]

4.9 HYPOTHESES

i. Highly significant differences were detected between feeding prescriptions and actual nutrient intakes received by LBW, preterm infants. Thus, the null hypothesis is partially rejected as some intakes met prescriptions on day 14 of life.
ii. Actual nutrient intakes significantly differed from the recommended guidelines. The null hypothesis is partially rejected as some intakes were similar to prescriptions and
iii. Nutrient intakes affected the regaining of birth weight. The null Hypothesis is rejected.

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

CHAPTER 5:CONCLUSION AND RECOMMENDATIONS

Prematurity is the leading cause of neonatal morbidity and mortality despite increased chances of survival with improved advances in the medical care.[7,120] The PIPP database on premature births in South Africa illustrates majority of premature births being born in the Gauteng province.[23] Data by Velaphi et al showed overall improved survival rates of 72 – 74% in VLBW infants born or admitted admitted to CHBAH.[108] Optimal care during the neonatal period has the prospective of reducing short and long term adverse outcomes with a major concern to provide adequate nutrition.[109] Adequate parenteral and enteral nutrition is associated with optimal neurodevelopment and growth outcomes in preterm infants as short periods of inadequacies can have consequences later in life.[53,130] A South African survey conducted by Raban examined the enteral feeding practices of paediatricians in preterm infants showing slow feeding advancements.[103] No studies on premature nutrient intakes have been investigated at the time of conducting this study. This is the first study in South Africa to determine the feeding prescriptions and actual nutrient intakes of fluid, energy and macronutrients from intravenous fluids, parenteral and enteral nutrition in preterm, LBW infants. Comparisons between prescriptions and intakes to recommendations were made. The nutrient analysis of breastmilk was based on Bauer's study showing the difference in composition according to GA.[106] This study used the Fenton 2013 growth reference when plotting and analysing growth, which is currently the best growth chart available.

The objectives of this study were:

i. To determine the feeding prescriptions of LBW infants.
ii. To determine the actual nutrient intakes of LBW infants.
iii. To compare feeding prescriptions with recommended guidelines.
iv. To determine differences of feeding prescriptions and actual nutrient intakes between birth weight categories.
v. To determine the advancement of enteral feeds until full feeds are reached independently of parenteral nutrition.
vi. To determine the impact of nutrient intakes on birth weight regain.

Following basic principles by starting PN immediately after birth to provide adequate energy and protein intakes with minimal enteral feeds is recommended, especially in units where PN is not always accessible such as in low-middle income countries.[121] These basic principles assist in providing preterm infants with optimal nutrition. PN in this study were only prescribed and received in a small amount of subjects on day one of life. This was also seen with enteral feeds being prescribed with minimal amounts received.

Limited studies report the achievement of recommended energy and protein intakes in very preterm infants during the first few weeks of life.[53,102,107,130,133] A more aggressive approach by initiation and advancement of MEF with PN reduces the accumulative energy and protein deficits seen with inadequate intakes, with significant reductions in the days to regain BW, days to reached full enteral feeds, improved anthropometry, incidence of NEC, unchanged or reduced risk of late-onset sepsis and overall shorter length of hospital stay.[28,60] However, an aggressive approach to nutrition is not advisable to unstable infants with severe morbidity.[33,130] As premature infants are vulnerable and unstable due to severe morbidity, it is often difficult to achieve optimal nutritional support. The feeding prescriptions and nutrient intakes for parenteral and enteral nutrition were inadequate during the first week of life and had only met some estimated requirements by day 14 of life in this study, similar to studies.[3,102,107,130,133] An aggressive approach was not adopted in this study as recommended.

This study also reported numerous discrepancies between FP and NI for fluid, energy and macronutrients. Large differences between prescriptions and intakes were found in this study as seen by Abel's study, where differences of 15% were found for energy and protein.[102] These findings highlights the importance of monitoring actual intakes compared with prescriptions and that these prescriptions meet nutrient goals. Studies like Abel, Ng et al and Sjöström looked at combined PN and EN prescriptions and intakes and showed inadequate nutrition.[102,130,143] This study; however, compared PN and EN separately to the indicated nutrient references made for each feeding route as recommended by Cormack et al.[53] Separate PN and EN prescriptions and intakes were investigates as different digestion and absorption process eminent between the two feeding routes, as well as the unknown actual bioavailability.[53] However, combined PN, EN and IV prescriptions and intakes for nutrients may provide more value to the clinician.

It has been reported that early enteral feeds of mother's own milk and the use of antenatal administration of steroids reduces gut permeability of small molecules to penetrate the GI mucosa, decreasing intestinal injury and possibly the incidence of NEC.[133] This study showed that of the infants prescribed enteral feeds, half (56%) of the infants were prescribed expressed breastmilk (EBM), but only one (5.9%) infant actually received EBM on day one of life. Enteral feeds in this study were not increased as recommended, with minimal intakes of 20 ml/kg/day received by day three which would be considered late feeding according to literature.[140] A small number of infants received full feeds on days seven (10.9%) and less than half (45.9%) of the study population had achieved full feeds by day 14 of life, which could be related to delayed trophic feeds seen in the earlier days of this study.

Postnatal growth failure is a burden impacting on associated health costs with longer hospital stays.[60,109] Similar to other findings, all anthropometrical measurements in this study declined over the two week study period.[3,102] Weight loss in this study were within normal ranges of 5 – 10%

reported in the literature. Weight loss during the first few weeks can be attributable to fluid shifts due to dehydration or inadequate nutrition, which is to be expected. Drawing conclusions based on calculating z-scores based on these weights that are sensitive to change, need to be interpreted with caution. Prescriptions based on these weights, can also influence the amount of nutrients, especially with large differences of 20% losses described in the literature. Having said so, it is also shown in the literature that BW regain can also be achieved if full enteral feeds are met within the first two to three weeks of life.[70,73,74] Even though this study showed no correlation between nutrients and growth outcomes and the regain of birth weight, other studies have documented that nutrient intakes of energy and protein are independently correlated with growth outcomes, i.e. weight, length and HC.[28,143]

Priority is given to saving the infant's life and assisting with breathing, often overlooking and underestimating early nutrient provision.[102] Focus should also be given to infants during the first week of life where prescriptions and intakes are inadequate. Health care costs can be reduced when careful evaluation and implementation of early nutrition is achieved. Developing trends on nutrition and growth will provide insight into the resources needed to achieve these goals and further identify flaws in current practises.

Due to the interruption of nutrients to the foetus when the infant is born, it is imperative to restore these nutrients as soon as possible in adequate amounts to ensure optimal growth and development. It is important to provide adequate energy intakes for protein metabolism and accretion. Although fluid management is attained, it does not provide the recommended energy and nutrients needed to achieve optimal growth similar to that of the foetus in the intrauterine environment. Achieving PN recommendations may assist in achieving optimal growth rates, as bypassing the gut makes nutrients readily available. Clinicians should take cognizance on providing optimal nutrition when transitioning from parenteral to enteral nutrition. Despite clinicians prescriptions and actual intakes received, it has been theorized that meeting recommendations does not guarantee to equate to growth rates seen in utero.[133]

5.1 LIMITATIONS

Limitations of the study included:

i. The retrospective collection of nutritional data from hospital records provided by nursing staff rely on their accuracy and honesty of the charted information.
ii. A lack of standardisation of anthropometric measurements performed by nursing staff could have had an impact on growth differences found during the study days.

iii. Feeding prescriptions may have varied between clinicians due to rotation and possibly result in inconsistent neonatal feeding practices. Such differences in feeding practises were also seen in an international survey conducted by Klingenberg et al.[26]

iv. Feeding prescriptions were calculated over 24 hours and not at the exact time these prescriptions were made by clinicians, as not all times of prescriptions were recorded. Unlike the FP, the calculations of the actual nutrient intakes were based on the actual time charted on the feeding charts. This, however, does have an impact on the discrepancy seen between the FP and NI noted during the study period, but still illustrates the inadequate nutritional intakes seen in this group of infants during the first two weeks of life.

v. Analysis of feeding prescriptions and nutrient intakes were performed on specific days, and there could have been variations between days that were excluded and not analysed where recommendations could have been met. However, observations of prescriptions and intakes had not met recommendations by day 14. Although FP and NI were not collected on days eight to 13 in this study, data collected in the Abel study showed that energy and protein intakes were significantly less compared with the prescriptions during the first 15 days of life.[102]

vi. Some prescriptions made by the clinician were either based on the infants' birth weight or previous weight and not the most recent weight. The weight used to calculate the feeding prescriptions could have had an impact on prescriptions that did not meet recommendations.

vii. This study was limited to 14 days. Longer-term studies are need to provide better insight on infants' nutritional intakes and their effect on weight gains and losses.

5.2 RECOMMENDATIONS

Recommendations based on this study are:

i. Ongoing in-service training is necessary for all healthcare professionals working with preterm, LBW infants on the latest research on providing nutrition for optimal growth and health.

ii. Clinicians should aim to reduce nutrient interruption to a minimum and with attempts at restoring an optimal nutrient supply with provision of deficits encountered as soon as feasible. Medical procedures that do not warrant discontinuing parenteral or enteral nutrition should be restricted.

iii. Parenteral nutrition should be initiated immediately after birth to all stable preterm infants when unable to tolerate sufficient enteral nutrition due to an immature GIT. PN should also be given in adequate amounts as recommended for longer periods until a sufficient supply of enteral nutrition is received. When enteral feeds reach 120 – 140 ml/kg/day, can PN be stopped.

iv. Prescriptions based on a feeding protocol for the unit should be in incorporated as part of managing the premature infant. The feeding protocol should be based on international recommendations. Prescriptions should be communicated to the nursing staff for implementation. A feeding protocol in the unit will help ensure that parenteral and enteral nutritional goals are met with less deficits.

v. Identifying inadequacies in current practise that may impede achieving nutrient goals, especially when transitioning from parenteral to enteral feeds.

vi. Feeding prescriptions calculations should not only be based on fluid, but also calculate the energy and macronutrient prescriptions and intakes from all feeding routes and other infusions.

vii. Early provision of adequate energy (40 – 60 kcal/kg/day kcal/kg/day for PN, goal rate of 110 – 135 kcal/kg/day for EN) and protein intakes (1.5 – 3 g/kg/day and 2 – 2.5 g/kg/day for PN and EN respectively) in the first week of life is recommended for the very vulnerable and high nutritional risk infants which may prevent postnatal growth failure later in life.

viii. Trophic feeds of either, the mother’s own milk or donated breastmilk should be given as the first choice of feed to stable premature infants. Minimal enteral feeds of 20 – 30 ml/kg/day is considered safe and does not increase the risk of NEC.

ix. Nursing staff should encourage mothers to start expressing immediately after birth so as to not delay initiation of feeds. Support by a qualified lactation nurse should be given to mothers experiencing difficulty in expressing their breastmilk.

5.3 FURTHER AREAS OF RESEARCH

Recommendations for further research include the following;

i. Assessing the barriers in achieving nutritional goals need to be investigated, including clinicians’ concerns about aggressive feeding in relation to glucose or lipid intolerance, feeding intolerance and NEC.

ii. Larger sized studies are needed to observe daily intakes during the first week of life, extended to 28 days to give a clearer indication of intakes and growth. These studies may provide insight and data on early nutrition that is safe, to ensure optimal growth outcomes.

iii. More studies are needed to assess the barriers and discrepancies in nutrition prescriptions and intakes and how feeding protocols can be better implemented to address such problems in South Africa.

iv. To ascertain why feeding protocols are not adhered to and why changes in practises exist amongst clinicians.

v. More studies are needed on nutritional intakes, especially protein quality on body composition of lean muscle mass and fat mass.

vi. Long-term studies are needed to determine the impact of early nutrition and the metabolic alterations of preterm infants later on in life.

REFERENCES

1. Ehrenkranz RA. Nutrition, Growth and Clinical Outcomes. In: Koletzko B, Poindexter B UR, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.* Vol 110. Switzerland: Karger; 2014:11-26.

2. Gibbins S, Wong SE, Unger S, O'Connor D. Donor human milk for preterm infants: Practice considerations. *J Neonatal Nurs*. 2013;19(4):175-181.

3. Sjöström ES. The impact of early nutrition on extremely preterm infants. 2014.

4. Bankhead R, Boullata J, Brantley S, et al. Enteral nutrition practice recommendations. *J Parenter Enter Nutr*. 2009;33(2):122-167.

5. Su BH. Optimizing nutrition in preterm infants. *Pediatr Neonatol*. 2014;55(1):5-13.

6. Ehrenkranz RA. EUGR is it preventable? *J Paediatr Rio J*. 2014;90(1):1-3.

7. Blencowe H, Cousens S, Chou D, et al. Born too soon: the global epidemiology of 15 million preterm births. *Reprod Health*. 2013;10 Suppl 1(Suppl 1):S2.

8. Bozzetti V, Tagliabue PE, Visser GHA, van Bel F, Gazzolo D. Feeding issues in IUGR preterm infants. *Early Hum Dev*. 2013;89:S21-S23.

9. Salama GSA, Kaabneh MAF, Almasaeed MN, Alquran MIA. Clinical Medicine Insights: Pediatrics Intravenous Lipids for Preterm Infants: A Review. *Paediatrics*. 2015;9:25-36.

10. Li Z, Wang YA, Ledger W, Sullivan EA. Birthweight percentiles by gestational age for births following assisted reproductive technology in Australia and New Zealand, 2002-2010. *Hum Reprod*. 2014;29(8):1787-1800.

11. Williams AF. Early enteral feeding of the preterm infant. *Arch Dis Child Fetal Neonatal Ed*. 2000:219-221.

12. Örs R. The practical aspects of enteral nutrition in preterm infants. *J Pediatr Neonatal Individ Med*. 2013;22(11):2281-69235.

13. Prince A, Groh-Wargo S. Nutrition management for the promotion of growth in very low birth weight premature infants. *Nutr Clin Pract*. 2013;28(6):659-668.

14. Terrin G, Senterre T, Rigo J DCM. Enteral Nutrition in Preterm Neonates. In: Guandalini S, Dhawan A BD, ed. *Textbook of Pediatric Gastroenterology, Hepatology and Nutrition*. 1st ed. Springer International Publishing; 2016:53-69.

15. Chen Y, Chang KTE, Lian DWQ, et al. The role of ischemia in necrotizing enterocolitis. *J Pediatr Surg*. 2015.

16. Muti M, Tshimanga M, Notion GT, Bangure D, Chonzi P. Prevalence of pregnancy induced hypertension and pregnancy outcomes among women seeking maternity services in Harare, Zimbabwe. *BMC Cardiovasc Disord*. 2015;15(1):111.

17. American Academy of Pediatrics. Age Terminology During the Perinatal Period. *Pediatrics*. 2004;114(5):1362-1364.

18. Chowdary KVR, Reddy PN. Parenteral nutrition: Revisited. *Indian J Anaesth*. 2010;54(2):95-103.

19. Siervo M, Bertoli S, Battezzati A, et al. Accuracy of predictive equations for the measurement of resting energy expenditure in older subjects. *Clin Nutr*. 2014;33(4):613-619.

20. Ding G, Tian Y, Zhang Y, Pang Y, Zhang JS, Zhang J. Application of A global reference for fetal-weight and birthweight percentiles in predicting infant mortality. *BJOG An Int J Obstet*

Gynaecol. 2013;120(13):1613-1621.

21. Platt MJ. Outcomes in preterm infants. *Public Health*. 2014;128(5):399-403.

22. Lawn JE, Davidge R, Paul VK, et al. Born Too Soon: Care for the preterm baby. *Reprod Health*. 2013;10(Suppl 1):S5.

23. Pattinson R, Rhoda N. *Saving Babies 2012-2013: Ninth Report on Perinatal Care in South Africa*.; 2014.

24. Liu L, Johnson HL, Cousens S, et al. Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000. *Lancet*. 2012;379(9832):2151-2161.

25. Lima PAT, De Carvalho M, Da Costa ACC, Moreira MEL. Variables associated with extra uterine growth restriction in very low birth weight infants. *J Pediatr (Rio J)*. 2014;90(1):22-27.

26. Klingenberg C, Embleton ND, Jacobs SE, O'Connell L a. F, Kuschel C a. Enteral feeding practices in very preterm infants: an international survey. *Arch Dis Child - Fetal Neonatal Ed*. 2012;97(1):F56-F61.

27. Puntis JWL. Nutritional support in the premature newborn. *Postgrad Med J*. 2006;82(965):192-198.

28. Ehrenkranz RA. Early nutritional support and outcomes in ELBW infants. *Early Hum Dev*. 2010;86:S21-S25.

29. Kleinman RE GF, ed. Nutritional Needs of the Preterm Infant. In: *Pediatric Nutrition*. 7th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:83-121.

30. Ayede AI. Achieving optimal feeds for preterm babies, recommendations and realities in practice: Nigerian perspective. *Ann Ibadan Postgrad Med*. 2011;9(1):1-7.

31. Underwood M. Human milk for prepature infant. 2014;60(1):189-207. doi:10.1016/j.pcl.2012.09.008.Human.

32. Daniels L, Jackson D. Knowledge , attitudes and practices of nursing staff regarding the Baby-Friendly Hospital Initiative in non-accredited obstetric units in Cape Town. *South African J Clin Nutr*. 2011;24(1):32-38. http://www.ajol.info/index.php/sajcn/article/view/65389.

33. Agostoni C, Buonocore G, Carnielli VP, et al. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. *J Pediatr Gastroenterol Nutr*. 2010;50(1):85-91.

34. Tsang R. *Nutrition of the Premature Infant: Scientific Basis and Practice Guidelines*. 2nd ed. Cincinnati, OH: Digital Educational Publishing Inc; 2005.

35. Nutrition Committee (Canadian Paediatric Society). Full-Text. *Can Med Assoc J*. 1995;152(11):1765-1785.

36. Moyses HE, Johnson MJ, Leaf A, Cornelius VR. Early parenteral nutrition and growth outcomes in preterm infants : a systematic review and meta-analysis 1 – 4. *Am J Clin Nutr*. 2013;(3):816-826.

37. Turpin RS, Liu FX, Prinz M, Macahilig C, Malinoski F. Parenteral Nutrition Prescribing Pattern: A Medical Chart Review of 191 Preterm Infants. *Nutr Clin Pract*. 2013;28(2):242-246.

38. Stewart J, Mason D, Smith N, Protopapa K, Mason N. A Mixed Bag. An enquiry into the care of hospital patients receiving parenteral nutrition. *WwwNcepodOrgUk*. 2010;14:1-100.

39. Senterre T, Terrin G, De Curtis M RJ. Parenteral Nutrition in Premature Infants. In: Guandalini S, Dhawan A BD, ed. *Textbook of Pediatric Gastroenterology, Hepatology and*

Nutrition. 1st ed. Springer International Publishing; 2016:73-86.

40. Velaphi S. Nutritional requirements and parenteral nutrition in preterm infants. *South African J Clin Nutr*. 2011;24(3):S27-S31.

41. ElHassan NO, Kaiser JR. Parenteral Nutrition in the Neonatal Intensive Care Unit. *Neoreviews*. 2011;12(3):e130-e140.

42. Morgan J, Bombell S, McGuire W. Early trophic feeding versus enteral fasting for very preterm or very low birth weight infants. *Cochrane database Syst Rev*. 2013;(3).

43. Morgan J, Young L, McGuire W. Delayed introduction of progressive enteral feeds to prevent necrotising enterocolitis in very low birth weight infants. *Cochrane database Syst Rev*. 2014;(12).

44. Moya F. Preterm Nutrition and the Lung. In: Koletzko B, poindexter B UR, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.2*. Switzerland: Karger; 2014:239-252.

45. Modi N. Management of fluid balance in the very immature neonate. *Arch Dis Child Fetal Neonatal Ed*. 2004;89(2):F108-11.

46. Bhatia J. Fluid and electrolyte management in the very low birth weight neonate. *J Perinatol*. 2006;26 Suppl 1:S19-S21. doi:10.1038/sj.jp.7211466.

47. Bell EF, Acarregui MJ. Restricted versus liberal water intake for preventing morbidity and mortality in preterm infants (Review) Restricted versus liberal water intake for preventing morbidity and mortality in preterm infants. *Cochrane Database Syst Rev*. 2014;(12):1-9.

48. Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R. 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 Paedia. *J Pediatr Gastroenterol Nutr*. 2005;41 Suppl 2(November 2005):S1-S87.

49. Leaf A. Introducing enteral feeds in the high-risk preterm infant. *Semin Fetal Neonatal Med*. 2013;18(3):150-154.

50. Krishnamurthy S, Gupta P, Debnath S, Gomber S. Slow versus rapid enteral feeding advancement in preterm newborn infants 1000-1499 g: A randomized controlled trial. *Acta Paediatr Int J Paediatr*. 2010;99(1):42-46.

51. Hamilton E, Massey C, Ross J, Taylor S. Early enteral feeding in very low birth weight infants. *Early Hum Dev*. 2014;90(5):227-230.

52. Hay Jr, Brown LD DS. Energy Requirements, Protein-Energy Metabolism and Balance, and Carbohydrates in Preterm Infants. In: Koletzko B, Poindexter B UR, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.2*. Switzerland: Karger; 2014:64-81.

53. Cormack BE, Embleton ND, van Goudoever JB, Hay WW, Bloomfield FH. Comparing apples with apples: It is time for standardized reporting of neonatal nutrition and growth studies. *Pediatr Res*. 2016;79(October 2015):1-11.

54. De Curtis M, Rigo J. The nutrition of preterm infants. *Early Hum Dev*. 2012;88:S5-S7.

55. van Goudoever JB, Vlaardingerbroek H, van den Akker CH, de Groof F van der SS. Amino Acids and Proteins. In: Koletzko B, Pointdexter B UR, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.* Switzerland: Karger; 2014:49-63.

56. Ziegler EE. Meeting the nutritional needs of the low-birth-weight infant. *Ann Nutr Metab*. 2011;58(suppl 1):8-18.

57. Embleton ND. Optimal nutrition for preterm infants: Putting the ESPGHAN guidelines into practice. *J Neonatal Nurs*. 2013;19(4):130-133.

58. Tudehope D, Gibbons K, Cormack B, Bloomfield F. Growth monitoring of low birthweight infants: What references to use? *J Paediatr Child Health*. 2012;48(9):759-767.

59. Lapillonne A. Enteral and Pareneral Lipid Requirement of Preterm Infants. In: Koletzko B, Poindexter B UR, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.2*. Switzerland: Karger; 2014:82-98.

60. Hay WW. Aggressive Nutrition of the Preterm Infant. *Curr Pediatr Rep*. 2013;1(4):1-17.

61. Engle WA. A recommendation for the definition of “late preterm” (near-term) and the birth weight-gestational age classification system. *Semin Perinatol*. 2006;30(1):2-7.

62. Villar J, Altman DG, Purwar M, et al. The objectives, design and implementation of the INTERGROWTH-21st Project. *BJOG An Int J Obstet Gynaecol*. 2013;120(SUPPL. 2):9-26.

63. Silveira MF, Barros FC, Sclowitz IKT, et al. Implementation of the INTERGROWTH-21st project in Brazil. *BJOG An Int J Obstet Gynaecol*. 2013;120(SUPPL. 2):81-86.

64. Maayan-Metzger A, Mazkereth R, Kuint J. Weight Loss and Bronchopulmonary Dysplasia in Very Low Birth Weight Infants. *Fetal Pediatr Pathol*. 2008;27(4-5):215-222.

65. Fenton TR, Nasser R, Eliasziw M, Kim JH, Bilan D, Sauve R. Validating the weight gain of preterm infants between the reference growth curve of the fetus and the term infant. *BMC Pediatr*. 2013;13(1):1-10.

66. Steward DK. Growth Outcomes of Preterm Infants in the Neonatal Intensive Care Unit: Long-term Considerations. *Newborn Infant Nurs Rev*. 2012;12(4):214-220.

67. Poindexter B. Approaches to Growth Faltering. In: Koletzko B, Poindexter B UR, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.2*. Switzerland: Karger; 2014:228-238.

68. Pfister KM, Ramel SE. Linear Growth and Neurodevelopmental Outcomes. *Clin Perinatol*. 2014;41(2):309-321.

69. Ehrenkranz RA. Nutrition, Growth and Clinical Outcomes. In: Koletzko B, Poindexter B UR, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.* Switzerland: Karger; 2014:11-26.

70. Heird WC. Nutritional Management of Preterm Infants Postdischarge. In: Duggan C et al, ed. *Nutrition in Pediatrics 4*. 4th ed. Ontario: BC Decker Inc; 2008:395-402.

71. Morgan C, McGowan P, Herwitker S, Hart AE, Turner MA. Postnatal head growth in preterm infants: a randomized controlled parenteral nutrition study. *Pediatrics*. 2014;133(1):e120-8.

72. Christmann V, Visser R, Engelkes M, De Grauw AM, Van Goudoever JB, Van Heijst AFJ. The enigma to achieve normal postnatal growth in preterm infants - Using parenteral or enteral nutrition? *Acta Paediatr Int J Paediatr*. 2013;102(5):471-479.

73. Senterre T, Rigo J. Optimizing early nutritional support based on recent recommendations in VLBW infants and postnatal growth restriction. *J Pediatr Gastroenterol Nutr*. 2011;53(5):536-542.

74. Shakeel F, Napolitano A, Newkirk M, Harris JE, Ghazarian SR. Improving Clinical Outcomes of Very Low Birth Weight Infants by Early Standardized Nutritional Management. *ICAN*. 2015;(December):328-337.

75. Ehrenkranz RA, Das A, Wrage LA, et al. Early Nutrition Mediates the Influence of Severity of Illness on Extremely Low Birth Weight Infants. *Pedaitr Res*. 2011;69(6):522-529.

76. Glass HC, Costarino AT, Stayer SA, Brett CM, Cladis F, Davis PJ. Outcomes for extremely

premature infants. *Anesth Analg*. 2015;120(6):1337-1351.

77. Deakins KM. Bronchopulmonary dysplasia. *Respir Care*. 2009;54(9):1252-1262.

78. Ballabh P. Intraventricular Hemorrhage in Premature Infants: Mechanism of Disease. *Pediatr Res*. 2010;67(1):1-8.

79. Keunen K, van Elburg RM, van Bel F, Benders MJNL. Impact of nutrition on brain development and its neuroprotective implications following preterm birth. *Pediatr Res*. 2015;77(1-2):148-155.

80. Trønnes H, Wilcox AJ, Lie RT MD. Risk of cerebral palsy in relation to pregnancy disorders and preterm birth: a national cohort study. *Dev Med CHild Neurol*. 2014;56(8):779-785.

81. Gupta R, Appleton RE. Cerebral palsy: not always what it seems. *Arch Dis Child*. 2001;85:356-360.

82. Beligere N, Perumalswamy V, Tandon M, et al. Retinopathy of prematurity and neurodevelopmental disabilities in premature infants. *Semin Fetal Neonatal Med*. 2015;20(5):346-353.

83. Ramachandran A. Neonatal hyperbilirubinaemia. *Paediatr Child Heal (United Kingdom)*. 2016;26(4):162-168.

84. Ives NK. Management of neonatal jaundice. *Paediatr Child Health (Oxford)*. 2011;21(6):270-276.

85. Cohen RS, Wong RJ, Stevenson DK. Understanding neonatal jaundice: A perspective on causation. *Pediatr Neonatol*. 2010;51(3):143-148.

86. Silva SMR, da Motta G de CP, Nunes CR, Schardosim JM, da Cunha MLC. Late-onset neonatal sepsis in preterm infants with birth weight under 1.500 g. *Rev Gaúcha Enferm*. 2015;36(4):84-89.

87. Simonsen KA, Anderson-Berry AL, Delair SF, Dele Davies H. Early-onset neonatal sepsis. *Clin Microbiol Rev*. 2014;27(1):21-47.

88. Polin RA. Management of Neonates With Suspected or Proven Early-Onset Bacterial Sepsis. *Pediatrics*. 2012;129(5):1006-1015.

89. Dong Y, Speer CP. Late-onset neonatal sepsis: recent developments. *Arch Dis Child Fetal Neonatal Ed*. 2015;100(3):F257-63.

90. Chagas de Freitas BA, Leão RT, Gomes AP, Siqueira-Batista R. Nutrition therapy and neonatal sepsis. *Lipids*. 2011;23(4):492-498.

91. Rolland A, Shankar-Aguilera S, Diomandé D, Zupan-Simunek V, Boileau P. Natural evolution of patent ductus arteriosus in the extremely preterm infant. *Arch Dis Child Fetal Neonatal Ed*. 2015;100(1):F55-8.

92. Benitz WE. Patent Ductus Arteriosus in Preterm Infants. *Pediatrics*. 2016;137(1):1-6.

93. Fanaro S. Feeding intolerance in the preterm infant. *Early Hum Dev*. 2013;89(SUPPL2):S13-S20.

94. Moore TA, Pickler RH. Evaluating the precision of clinical assessments for feeding intolerance. *Newborn Infant Nurs Rev*. 2013;13(4):184-188.

95. Tekgündüz KŞ, Gürol A, Apay SE, Caner I. Effect of abdomen massage for prevention of feeding intolerance in preterm infants. *Ital J Pediatr*. 2014;40:89.

96. Hall NJ, Eaton S, Pierro A. Necrotizing enterocolitis: Prevention, treatment, and outcome. *J Pediatr Surg*. 2013;48(12):2359-2367.

97. Eaton S, Rees CM, Hall NJ. Current research in necrotizing enterocolitis. *Early Hum Dev*. 2016;97:33-39.

98. Vongbhavit K, Underwood MA. Prevention of Necrotizing Enterocolitis Through Manipulation of the Intestinal Microbiota of the Premature Infant. *Clin Ther*. 2016;38(4):716-732.

99. Meyer S, Gortner L, Lindner U, Dahmen K, Butte M. Fast food versus slow food in very and extremely low-birthweight infants: Speed of feeds is a little more than a gut feeling. *Acta Paediatr Int J Paediatr*. 2016;(1):1-3.

100. Cooke RJ, Embleton ND. Feeding issues in preterm infants. *Arch Dis Child Fetal Neonatal Ed*. 2000;83(3):F215-8. doi:10.1136/fn.83.3.F215.

101. Embleton NE, Pang N, Cooke RJ. Postnatal malnutrition and growth retardation: an inevitable consequence of current recommendations in preterm infants? *Pediatrics*. 2001;107(2):270-273. doi:10.1542/peds.107.2.270.

102. Abel DM. Actual and prescribed energy and protein intakes for very low birth weight infants: An observational study. 2012;(June).

103. Raban MS, Joolay Y, Horn a R, Harrison MC. Enteral feeding practices in preterm infants in South Africa. *South African J Child Heal*. 2013;7(1):8-12.

104. Lee R, Nieman D. Nutritional Assessment. In: Lee R, Nieman D, eds. *Nutritional Assessment*. 5th ed. Boston: McGraw Hill International Edition; 2010:160-213.

105. http://peditools.org/fenton2013/. http://peditools.org/fenton2013/. Accessed February 8, 2016.

106. Bauer J, Gerss J. Longitudinal analysis of macronutrients and minerals in human milk produced by mothers of preterm infants. *Clin Nutr*. 2011;30(2):215-220. doi:10.1016/j.clnu.2010.08.003.

107. Proaño A, Aragón RE, Rivera F, Zegarra J. Nutritional intake and weight z-scores in very low birth weight infants in Peru. *Medwave*. 2016;16(2):e6414-e6414.

108. Velaphi SC, Mokhachane M, Mphahlele RM, Beckh-Arnold E, Kuwanda ML, Cooper PA. Survival of very-low-birth-weight infants according to birth weight and gestational age in a public hospital. *S Afr Med J*. 2005;95(7):504-509.

109. Corvaglia L, Fantini MP, Aceti A, et al. Predictors of full enteral feeding achievement in very low birth weight infants. *PLoS One*. 2014;9(3).

110. Dutta S, Singh B, Chessell L, et al. Guidelines for feeding very low birthweight infants. *Nutrients*. 2015;7(1):423-442.

111. Van Den Broek NR, Jean-Baptiste R, Neilson JP. Factors associated with preterm, early preterm and late preterm birth in Malawi. *PLoS One*. 2014;9(3).

112. Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C. Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. *BMC Pregnancy Childbirth*. 2010;10(S1):1-22.

113. Linked to “Born too Soon: The Global Action Report on Preterm Birth.” Country data and rankings for preterm birth EMBARGO UNTIL MAY 2ND 2012. *“Born too Soon Glob Action Rep Preterm Birth.”* 2012:6-9. http://www.who.int/pmnch/media/news/2012/201204_borntoosoon_countryranking.pdf.

114. Lee ACC, Katz J, Blencowe H, et al. National and regional estimates of term and preterm babies born small for gestational age in 138 low-income and middle-income countries in 2010. *Lancet Glob Heal*. 2013;1(1). doi:10.1016/S2214-109X(13)70006-8.

115. Norris T, Johnson W, Farrar D, Tuffnell D, Wright J, Cameron N. Small-for-gestational age

and large-for-gestational age thresholds to predict infants at risk of adverse delivery and neonatal outcomes: are current charts adequate? An observational study from the Born in Bradford cohort. *BMJ Open*. 2015;5(3):e006743.

116. Morris I, Adappa R. Minimizing the risk of respiratory distress syndrome. *Paediatr Child Health (Oxford)*. 2012;22(12):513-517.

117. Zani A, Pierro A. Necrotizing enterocolitis: controversies and challenges. *F1000Research*. 2015;4:1373.

118. Ofori BD, Le Tiec M BA. Risk factors associated with preterm birth according to gestational age at birth. *Pharmacoepidemiol Drug Saf*. 2008;17:556-564.

119. Shrestha S, Dangol SS, Shrestha M SR. Outcome of preterm babies and associated risk factors in a hospital. *J Nepal Med Assoc*. 2010;50(180).

120. Brits H, Adriaanse M, Rall D-M, et al. Causes of prematurity in the Bloemfontein Academic Complex. *South African Fam Pract*. 2015;57(3):223-226.

121. Slusher T, Vaucher Y, Zamora T, Curtis B. Feeding and Fluids in the Premature and Sick Newborn in the Low-Middle Income Countries. *Contemp Paediatr*. 2012:27-57.

122. Law KS, Chan LG. Early Aggressive Total Parenteral Nutrition To Premature Infants in Neonatal Intensive Care Unit. *J Pediatr Sci*. 2015;7.

123. Wemhoner A, Ortner D, Tschirch E, Strasak A, Rudiger M. Nutrition of preterm infants in relation to bronchopulmonary dysplasia. *BMC Pulm Med*. 2011;11(1):7.

124. Cormack BE, Bloomfield FH, Dezoete A, Kuschel CA. Does more protein in the first week of life change outcomes for very low birthweight babies? *J Paediatr Child Health*. 2011;47(12):898-903.

125. Neu J, Weiss MD. Necrotizing Enterocolitis: Pathophysiology and Prevention. *Parenter Enter Nutr*. 1999;23(5):S13-17.

126. Embleton ND SK. Practice of Parenteral Nutrition in VLBW and ELBW Infants. In: Koltezko B, Poindexter B UR, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.2*. Switzerland: Karger; 2014:177-189.

127. Good M, Sodhi CP, Hackam DJ. Evidence-based feeding strategies before and after the development of necrotizing enterocolitis. *Expert Rev Clin Immunol*. 2014;10(7):875-884.

128. Ramani M, N. Ambalavanan. Feeding Practices and NEC. *Clin Perinatol*. 2013;40(1):1-10.

129. Thibault Senterre. Practice of Enteral Nutrition in Very Low Birth Weight and Extremely Low Birth Weight Infants. In: Koletzko, B, Pointdexter, B, Uauy R, ed. *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.* Switzerland: Karger; 2014:201-214.

130. Ng D, Brennan-Donnan J, Unger Sharon, Bando N, Gibbins S, Nash A, Kiss A OD. How Close Are We to Achieving Energy and Nutrient Goals for Very Low Birth Weight Infants in the First Week? *J Parenter Enter Nutr*. 2015.

131. Ziegler EE. Protein requirements of very low birth weight infants. *J Pediatr Gastroenterol Nutr*. 2007;45 Suppl 3:S170-4.

132. Trivedi A, Sinn JKH. Early versus late administration of amino acids in preterm infants receiving parenteral nutrition. *Cochrane database Syst Rev*. 2013;7(7):CD008771.

133. Cormack BE, Bloomfield FH. Audit of feeding practices in babies < 1200 g or 30 weeks gestation during the first month of life. *J Paediatr Child Health*. 2006;42:458-463.

134. Vlaardingerbroek H, Spronk S, Goudoever JB Van. Parenteral lipid administration to very-low-birth-weight infants — early introduction of lipids and use of new lipid emulsions : a systematic. *Am J Clin Nutr*. 2012;96(4):255-268.

135. Vlaardingerbroek H, van Goudoever JB, van den Akker CHP. Initial nutritional management of the preterm infant. *Early Hum Dev*. 2009;85(11):691-695.

136. Jones E, Spencer SA. Why is preterm milk expression so difficult? *Infant*. 2005;1(3):77-80.

137. Post EDM, Stam G, Tromp E. Milk production after preterm, late preterm and term delivery; effects of different breast pump suction patterns. *J Perinatol*. 2016;36(1):47-51.

138. Republic of South Africa: Department of Health. *National Consolidated Guidelines for the Prevention of Mother-to-Child Transmission of HIV (PMTCT) and the Management of HIV in Children, Adolescents and Adults*.; 2014.

139. du Plessis L, Peer N, Honikman S, English R. Breastfeeding in South Africa: are we making progress? *Sahr*. 2016:109-123. doi:10.1093/heapol/czq021.

140. Morgan J, Bombell S, McGuire W. Early trophic feeding versus enteral fasting for very preterm or very low birth weight infants. *Cochrane database Syst Rev*. 2013;(3):CD000504.

141. Anchieta LM, Xavier CC, Colosimo EA, Souza MF. Weight of preterm newborns during the first twelve weeks of life. *Brazilian J Med Biol Res*. 2003;36(6):761-770.

142. Valentine CJ, Fernandez S, Rogers LK, et al. Early amino-acid administration improves preterm infant weight. *J Perinatol*. 2009;29(6):428-432.

143. Stoltz Sjöström E, Öhlund I, Ahlsson F, et al. Nutrient intakes independently affect growth in extremely preterm infants: results from a population-based study. *Acta Paediatr*. 2013;102(11):1067-1074.

APPENDIX A:

SCREENING SHEET

SCREENING LOG SHEET

Screening number	Date of screening	Patient name	GT (hospital) number	Born at CHBAH	Date of Admission	Date of Birth	Gestational Age	Birth Weight	No chromosomal abnormalities	Seen by Dietitian	Patient Eligible	Research number
1												
2												
3												
4												
5												
6												
7												
8												
9												
10												
11												
12												
13												
14												
15												
16												
17												
18												
19												
20												
TOTAL ELIGIBLE:												

APPENDIX B:

DATA COLLECTION SHEET

BASELINE INFORMATION SHEET

Patient Hospital No.: ____________________	Research No.: __________________________

PATIENT INFORMATION

Sex: Male ☐ Female ☐

Date of Birth (dd/mm/yyyy): ____

Date of Admission (dd/mm/yyyy): ____________________________________

Time of Birth (HR:Min): ____

Gestational Age (weeks): ______________________ Birth Weight (grams): _______________

Birth Length (cm): ___________________________ Birth Head Circumference (cm): __________

Single: ☐ Twins: ☐ Triplets/more: ☐

APGAR Scores: ____(1min) ____(5min)

Primary Diagnosis: ____

____

____

Co-morbidities/Medical or Nutritional Problems: _____________________________________

____

____

____

MATERNAL INFORMATION

Hospital No.: ________________________	Contact No.: ______________________________

Age (year & months): ________________

Gravida: ______________________________ Paravida: ____________________________

Steroids: Antibiotics:

Reason for premature birth:

Mode of Delivery:

vertex		breech		vacuum		forceps		caesar	

HIV Status: positive ☐ negative ☐

BASELINE ANTHROPOMETRY ASSESSMENT

W/A *z*-score:

-3		-2		-1		0		+1		+2		+3	

L/A *z*-score:

-3		-2		-1		0		+1		+2		+3	

HC/A *z*-score:

-3		-2		-1		0		+1		+2		+3	

Interpretation: AGA ☐ SGA ☐

IUGR ☐ N/A ☐

W/A: Weigth-for-Age, L/A: Length-for-Age, HC/A: Head Circumference-for-Age, AGA: Appropriate-for-Gestational-Age, SGA: Small-for-Gestational-Age, IUGR: Intra-Uterine Growth Restriction, EUGR: Extra-Uterine Growth restriction.

Research No. / Code:________________________ Date of Birth:________________________

	Day 1 Date:		Day 2 Date:		Day 3 Date:		Day 7 Date:		Day 14 Date:	
	Ward/Cubicle:		Ward/Cubicle:		Ward/Cubicle:		Ward/Cubicle:		Ward/Cubicle:	
Enteral	Prescription	Intake	Prescription	Intake	Prescription	Intake	Prescription	Intake	Prescription	Intake
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Type										
Comments										
Rate Volume/24h (ml)										
Time										
Fluid (ml/kg/d)										
Fluid Increments (ml/kg/d)										
Energy (kcal/kg/d)										
Protein (g/kg/d)										
Cho (g/kg/d)										
Fat (g/kg/d)										
Parenteral	Prescription	Intake	Prescription	Intake	Prescription	Intake	Prescription	Intake	Prescription	Intake
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Type										
Comments										
Rate Volume/24h (ml)										
Time										
Fluid (ml/kg/d)										
Fluid increments (ml/kg/d)										
Energy (kcal/kg/d)										
Protein (g/kg/d)										
Cho (g/kg/d)										

Fat (g/kg/d)										
Other (specify)	Prescription	Intake	Prescription	Intake	Prescription	Intake	Prescription	Intake	Prescription	Intake
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Type										
Rate Volume/24h (ml)										
Comments										
Time										
Other (specify)	Prescription	Intake	Prescription	Intake	Prescription	Intake	Prescription	Intake	Prescription	Intake
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Type										
Rate Volume/24h (ml)										
Comments										
Time										
Anthropometry		z-score						z-score		z-score
	Yes	No					Yes	No	Yes	No
Comments										
Weight (grams)										
Weight gain (g/kg/day)										
Length (cm)										
Length (cm/week)										
Head circumference (cm)										
Head Circumference(cm/week)										

APPENDIX C:

INFORMATION SHEET

CLINICAL NUTRITION RESEARCH

GENERAL INFORMATION TO HEALTH PROFESSIONALS IN THE NEONATAL UNIT AT CHBAH

INVESTIGATOR: Renette Reeding

CO-INVESTIGATORS: Evette van Niekerk

Hannelie Kemp

CONTACT DETAILS: renettereeding@gmail.com

(011) 933 9068 / 071 871 6114

AIM: To compare actual nutrient intakes and feeding prescriptions of low birth weight infants to recommended guidelines.

OBJECTIVES:

i. To determine actual nutrient intakes of Low Birth Weight (LBW) infants.

ii. To ascertain feeding prescriptions of LBW infants.

iii. To compare feeding prescriptions to recommended guidelines.

iv. To determine the advancement of feeds until full feeds are reached independently of parenteral nutrition.

v. To determine the impact of feeding prescriptions and actual nutrient intakes on percentage weight loss.

vi. To determine the impact of feeding prescriptions and actual nutrient intakes on the number of days to regain birth weight.

DATA COLLECTION:

Data will be collected **prospectively** from the patient's hospital file for the feeding prescription of the doctor and fluid balance chart for the actual nutrient intakes received from the day of birth and admission into the Neonatal unit.

Data for nutrient intakes and feeding prescriptions will be collected on day 1, 2, 3, 7 and 14 of life. Data for anthropometry i.e. weight, length and head circumference will be collected and when necessary be performed on day 1, 7 and 14 of life.

ENTERAL NUTRITION

All nutrient intakes or feeding prescriptions fed via the enteral route i.e. orogastric or nasogastric tube to be recorded accurately on the days specified as above.

Accurately record type of EN i.e. breastmilk, expressed breastmilk (EBM) or the type of formula milk e.g. prenan and the feeding volume or rate of administration (40ml x 8 or 13ml/hr).

If the nutrient intake differs to the feeding prescription or only half of the feeding prescription/type of feed was given, please record accurately e.g.

Feeding prescription: EBM 9ml x 8

Nutrient Intake: EBM 6ml x 4 and prenan 9ml x 4

If any feeds were omitted, please record time and number of feeds omitted and reason why feed/s was omitted.

PARENTERAL NUTRITION

All nutrient intakes and feeding prescriptions fed via intravenous route to be recorded on the days specified.

To record on the fluid chart:

- The type/regimen of ITN/TPN bag prescribed and type of ITN/TPN bag given e.g.
    - *Prescribed- ITN baby 104*
    - *Delivered- ITN baby 102*
- The volume rate of infusion prescribed and delivered e.g.
    - *at 11h30, ITN baby 104 at 12ml/hr x 24hours was prescribed*
    - *at 15h00, ITN baby 102 at 12ml/hr x 24 hours was infused*
- The time a bag was started and when a new/second bag of TPN was given/hung up.

The time PN and/or EN was prescribed e.g. 10h00 and the time PN and/or EN was actually started e.g. 11h00, as well as the duration e.g. 11h00-24h00

ANTHROPOMETRY

Measurement of the study subjects weight (in grams), length (in centimeters) and head circumference (in centimeters) to be done on day 1, 7 and 14 of life according to standard measurements as described in the standard operating procedure.

SUMMARY OF DATA COLLECTION:

The following information to be collected from the day of admission into the unit which will also be day 1 of life until day 14 of life;

- Day 1- anthropometry, feeding prescriptions and nutrient intakes
- Day 2- feeding prescriptions and nutrient intakes
- Day 3- feeding prescriptions and nutrient intakes
- Day 7- anthropometry, feeding prescriptions and nutrient intakes
- Day 14- anthropometry, feeding prescriptions and nutrient intakes
- Type, volume and time of EN and PN prescribed and delivered to the patient
- Type, volume and time of IV fluids that contain any nutrient substrates e.g. dextrose

APPENDIX D:

STANDARD OPERATING PROCEDURE

CLINICAL NUTRITION RESEARCH: THE NUTRIENT INTAKES AND FEEDING PRESCRIPTIONS OF LOW BIRTH WEIGHT INFANTS AT CHBAH.

STANDARD OPERATING PROCEDURE

Purpose

This Standard Operating Procedure (SOP) explains the necessary steps for collecting data for the clinical nutrition research, "The Nutrient Intakes and Feeding Prescriptions of Low Birth Weight (LBW) infants at CHBAH". Accurate records of all intakes and prescriptions is vital for the success of the research as stipulated in the protocol.

Scope and Duties/Responsibilities

The scope of this SOP is to:

- Screen all patients admitted in the NICU.
- Identify all eligible patients for participation into the study according to inclusion and exclusion criteria as per protocol (addendum I).
- Allocate screening numbers to all patients admitted into the unit (addendum I).
- Allocate research numbers to those participants who qualify from the screening log sheet (addendum I).
- Obtain consent and where applicable assent for participation of the patient into the study/research (addendum II, III, IV and V).
- Record information on the study participant and mothers details (addendum VI).
- Record all patients enrolled into the study and monitor daily recordings of data collection(addendum VII)
- Collect and record data on all feeding prescriptions as documented by the prescribing doctor on day 1, 2, 3, 7 and 14 of life from the study participants' fluid balance chart and/or hospital file (addendum VIII).
- Record time when feeds were prescribed and when received for EN and PN (addendum VIII).
- Collect and record data on all nutrient intakes as documented by the nursing staff on day 1, 2, 3, 7 and 14 of life from the participants' fluid balance chart and/or hospital file (addendum VIII).
- Collect and record data on study participants' anthropometry i.e. weight, length and head circumference, and when applicable perform measurements accurately and accordingly on day 1, 7 and 14 of life (addendum VIII).
- Report and submit all data collected to primary investigator on daily basis.
- Identify reasons why patient is not receiving any nutrition (addendum VII).

Procedure

- To record all data on the appropriate addendum sheets (see Section on Documents and Attachment).
- To perform anthropometric measurements when applicable (i.e. days when data needs to be collected which may not be the same day as the Units routine measurement days i.e. Mondays and Thursdays):
    - Weight[1]
        - Scale to be placed on a hard, flat surface.
        - Scale to be calibrated before weighing.
        - Infant to be naked, with no diaper/nappy.
        - Infant to lie in supine position.
        - Weight to be performed twice, take a third weight if the first two weights differ by more than 0.5kg.
        - Record weight to the nearest 0.1kg (1 gram).
    - Length[1]
        - Measuring mat/Length board to be placed on a hard, flat surface.
        - Infant to be naked or with minimal clothing (vest) but no diaper/nappy.
        - Infant to lie in supine position.
        - Head to touch the board firmly and legs to be straightened and pressed down alongside the mat.
        - Place the shift board (other side of the measuring mat) up against the infants' feet, touching the heel and toes.
        - Length to be performed twice, take a third length if the first two lengths differ by more than 0.5cm
        - Record the length to the nearest 0.1cm (1 millimetre).
    - Head Circumference[1]
        - A non-stretch measuring tape to be used.
        - Infant to be seated in an upright position.
        - Place measuring tape around the infants widest part of the head i.e. occipital-frontal.
        - Head circumference to be performed twice, take a third head circumference if the first two measurements differ by more than 0.5cm.
        - Record head circumference to the nearest 0.1cm (1 millimetre).
- To record any possible reasons why study participant might be NPO or when feeds have been stopped on the appropriate addendum sheet.
- Calibration of scale:
    - Scale to be calibrated before every measurement to be done i.e. before weighing every infant.

- Place a standard 5kg object onto the scale to determine weight before weighing infant.
- Weigh infant and then calibrate scale again before next measurement.

- Collecting information about the feeds i.e. EN or PN or both:
    - Record whether study participant is receiving EN, PN or both.
    - Record whether study participant is receiving neonatalyte (NNL).
    - Record the time when feeds/NNL was prescribed and when the feeds/NNL was received.
    - Record the type, volume and frequency (no. of feeds) in 24 hours of feeds prescribed by the doctor and the actual intake received for EN. Example:

Enteral		
	Intake	Prescript
Type	EBM	EBM
Volume/24h (ml)	3ml x 5	3ml x 8
Time	12:00	11:00

Enteral		
	Intake	Prescript
Type	Prenan	EBM
Volume/24h (ml)	12ml x 8	15ml x 8
Time	15:00	13:30

- Record the type, volume and frequency/infusion rate (no. of hours) in 24 hours of feeds prescribed by the doctor and the actual infusion received by PN.

Example:

Parenteral		
	Intake	Prescript
Type	ITN Baby102	ITN Baby102
Volume/24h (ml)	3ml x 20 hrs	3ml x 24hrs
Time	12:30	12:00

Parenteral		
	Intake	Prescript
Type	ITN Baby102	ITN Baby102
Volume/24h (ml)	3ml x 20 hrs	3ml x 24hrs
Time	12:30	12:00

- Record the volume and infusion rate (no. of hours) prescribed by the doctor and actual infusion received by NNL.

IV-NNL		
	Intake	Prescript
Type	NNL 5%	NNL 5%
Volume/24h (ml)	3ml x 20 hrs	3ml x 24hrs
Time	09:15	09:00

Review and Revision

The SOP will be reviewed and revised by the primary investigator successively after:

- Ethics approval from Stellenbosch HREC for any adjustments in terms of duties/responsibilities or procedures to be performed.
- Pilot study is completed to resolve and correct any issues with data collection and procedures to be performed

Contingencies: Corrective Actions/safety and quality control

The research is observational, therefore no intervention by the primary investigator or fieldworker will occur and thus there is no corrective action or contingency planned for if any adverse events occur.

Quality control of collecting information by the fieldworker will be cross-checked and verified by the primary investigator by selecting every 10th study participant's data collection sheets to ensure correct entry of information.

If any errors occur during data collection (including the pilot study), the fieldworker should report this information immediately to the primary investigator. All errors and corrective measures to be documented.

The fieldworker to ensure sufficient amount of copies of all data collection sheets are available at all times- this can be obtained by the primary investigator.

The fieldworker to practice infection control by washing hands upon entering the unit, as well as before and in between data collection from study participant's hospital file or measuring study participant.

Working Conditions of Fieldworker:

- To communicate daily with primary investigator with regards to:
  - Number of participants enrolled
  - Any issues encountered with staff or data collection
- If ill or absent, to inform primary investigator immediately; who will thus have to collect information.

History of Change

To be included once any change/s to be made to the SOP suggested from the Stellenbosch Health and Research Ethics Committee.

Compiled by: **Date:**___________________

____

Renette Andrea Reeding
Primary Investigator

Reviewed and approved by: **Date:**___________________

____

Evette van Niekerk
Supervisor

References

1. Lee RD and Nieman Dc. *Nutritional Assessment*. 5th Edition. McGraw Hill International Edition. Boston. 2010

APPENDIX E:

CONSENT FORMS (ENGLISH/ZULU)

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT: The Nutrient Intakes and Feeding Prescriptions of Low Birth Weight Infants at Chris Hani Baragwanath Academic Hospital

REFERENCE NUMBER: S14/10/248
M150132

PRINCIPAL INVESTIGATOR: Renette Andrea Reeding

ADDRESS: 52A King Street
Berario
Johannesburg
2195

CONTACT NUMBER: 071 871 6114 / (011) 933-9068
renettereeding@gmail.com

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the fieldworker or investigator any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved.

This study has been approved by the **Health Research Ethics Committee at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

- The study will take place in the neonatal and transitional unit (NICU and TICU) of Chris Hani Baragwanath Academic Hospital. The participants to join and take part will consist of low birth weight infants (<2500grams) who are born too small for their age.
- The project will be looking at what milk the doctors are prescribing to feed your baby and what your baby is actually receiving, as well as what the nurses is giving and what the baby is receiving, including what the nurses is giving and comparing the milk to what research says is best for infants so that they grow nicely and that the milk won't affect the baby's brain and growth development long term, also how the feeding affects the baby's weight, length and head growth.
- The investigator will record what the doctors prescribe, what the baby was actually fed and the baby's growth (weight, length and head size) on the following days; 1, 2, 3, 7 and 14 of life. The investigator will get this information from the patients file and fluid chart.
- There will be no specific pattern in choosing participants, every infant that meets the inclusion criteria will take part in the project.
- The project will not interfere with the normal medical treatment provided by the hospital.

Why have you been invited to participate?

- Your baby meets the condition and situation to participate into the project because they weigh less than 2500grams and was born too small for the age.

What will your responsibilities be?

- You can help by telling the investigator the number of cups you fed your baby and the type of milk that was given; either breastmilk, formula or the total parenteral nutrition (TPN; the drip with the white liquid). Information will be taken from the hospital file but you can also assist by confirming what is recorded in the file.

Will you benefit from taking part in this research?

There will be no direct benefit from you taking part in this research. By taking part in this research, you will be helping to improve our knowledge of infant feeding.

Are there any risks involved in you taking part in this research?

- No risks will be involved if your baby takes part in the research. The research will only observe what the baby is getting and there will be no changes of how things are being done in the hospital.

If you do not agree to take part, what alternatives do you have?

- It is your decision whether you would like to take part or not. If you decide not to take part in the study it will not affect the care given to your baby. You are free to pull out of the study at any point without explanation or any negative consequences. You and your baby's routine health care will not be negatively affected.

Who will have access to your medical records?

- Only the investigator and persons directly linked with the study will have access to your medical records. All information will always be kept private.
  The researcher will treat all information gathered as strictly confidential and no information that can identify you or your baby will be released to any person who is not directly linked with the study.
  The information collected will be handled with complete confidentiality and privacy, but will be published on Stellenbosch University's website and possibly in "peer-reviewed" scientific journal/s and presented at congresses. Under no situations will you or your baby's name be revealed.
  Information will be accessible to mainly to health care professionals, but also to non-health care professionals including journalists.

Will you be paid to take part in this study and are there any costs involved?

No you will not be paid to take part in the study. The researcher will pay back costs e.g. transport money if the parents come to the hospital only to sign permission for the baby to take part in the research. No costs will be paid if the parents are visiting the baby.

Is there anything else that you should know or do?

- You can contact Renette Reeding at telephone numbers: 0718716114/ 011-933 9068 for any further queries or problems.
- You can contact the Health Research Ethics Committee at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by the investigator.
- You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I, the parent/caregiver of (insert research code) ………………………….………… agree to take part in a research study entitled *"The Nutrient Intakes and Feeding Prescriptions of Low Birth Weight Infants at Chris Hani Baragwanath Academic Hospital"*.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*) ....…........…………….. on (*date*) …………....……….. 2015.

....	....
Signature of parent/caregiver	**Signature of witness**

Declaration by investigator

I *(name)* ……………………………………………..……… declare that:

- I explained the information in this document to …………………………………..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.*

Signed at (*place*) ....…........…………….. on (*date*) …………....……….. 2005.

....	....
Signature of investigator	**Signature of witness**

Declaration by interpreter

I *(name)* ……………………………………………..……… declare that:

- I assisted the investigator (*name*) ………………………………………. to explain the information in this document to (*name of participant*) ……………..……………………………….. using the language medium of Zulu.
- We encouraged him/her to ask questions and took adequate time to answer them.
- I conveyed a factually correct version of what was related to me.
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

Signed at (*place*) ....…........…………….. on (*date*) …………....………………..

....	....
Signature of interpreter	**Signature of witness**

INCWAJANA EHLINZEKA NGOLWAZI KUBANTU ABAZOBAMBA IQHAZA OCWANINGWENI KANYE NEFOMU LEMVUME

ISIHLOKO SOCWANINGO: Izinga Lezondlamzimba Ezitholwa Ngabantwana Abazalwe Benesisindo Esingaphansi Kwaleso Esilindelekile e-Chris Hani Baragwanath Academic Hospital kanye neMiyalelo Ekhishwa Ngodokotela Yokudla Okumele Kuphakelwe Abantwana Abakuleso simo

INOMBOLO EYIREFERENSI YOCWANINGO: S14/10/248
M150132

UMCWANINGI OYINHLOKO: Renette Andrea Reeding

IKHELI: 52A King Street
Berario
Johannesburg
2195

INOMBOLO YOCINGO: 071 871 6114 / (011) 933-9068
renettereeding@gmail.com

Uyamenywa ukuthi ubambe iqhaza kulolu cwaningo. Ngicela ukuthi uzinikeze isikhathi ufunde ulwazi oluhlinzekwe lapha, olukuchazela ngemininingwane ephathelene nocwaningo. Uma kukhona ingxenye yalolu cwaningo ongayiqondisisi kahle uyacelwa ukuthi ubuze kwisisebenzi socwaningo noma kumcwaningi ukuze ucaciseleke kahle. Kusemqoka kakhulu ukuthi uzigculise ngokuphelele ukuthi uyaqondisisa ukuthi luphathelene nani lolu cwaningo kanye nendlela ongazibandakanya ngayo kulona.

Lolu cwaningo lwamukelwe **yiKomidi Lokuziphatha Ngendlela Efanele Kwezocwaningo Lwezempilo eNyuvesi yase-Stellenbosch** futhi luzokwenziwa ngokulandela imihlahlandlela kanye nemigomo yokuziphatha ngokwenkambiso efanele Yesitatimende Somhlaba saseHelsinki, Imihlahlandlela yaseNingizimu Afrika Yokuziphatha Ngendlela Efanele Kwezokwelapha kanye Nemihlahlandlela Yokuziphatha Ngokwenkambiso Efanele Kwezocwaningo yoMkhandlu Wocwaningo Lwokwelapha (MRC).

Ngabe luphathelene nani lolu cwaningo?

- Lolu cwaningo luzokwenzelwa ophikweni lwezokubeletha kanye nolokunakekelwa kweziguli ngenkathi zilungiselelwa ukuyolulamela ekhaya (i-NICU kanye ne-TICU). Abantwana abazobamba iqhaza kulolu cwaningo babandakanya izinsana ezinesisindo esincane kakhulu uma kuqhathaniswa nesisindo sontanga yabo (amagramu angaphansi kuka-2500).
- Lolu cwaningo luzobheka uhlobo lobisi odokotela abayalele ukuthi lunikezwe umntwana wakho bese kubhekwa ukuthi umntwana wakho uyalunikezwa yini uhlobo lobisi oluyalelwe ngodokotela noma unikezwa olunye uhlobo, kubandakanya nokubheka uhlobo lobisi olunikezwa ngabahlengikazi uma kuqhathaniswa nobisi okuyilona olulungele umntwana ngokusho kocwaningo, ukuze bakhule kahle, futhi kuzobhekwa nokuthi ubisi ngeke yini lube nomthelela ongemuhle ngokuqhubeka kwesikhathi emqondweni womntwana kanye nasekukhuleni kwakhe futhi kubhekwe ukuthi lolu bisi lunomthelela onjani kwisisindo somntwana, ubude bakhe kanye nokukhula kwekhanda lakhe.
- Umcwaningi uzoqopha phansi lokho okuyalelwe ngodokotela, kanye nalokho okuyikonakona okunikezwa umntwana futhi aqophe phansi nokukhula komntwana (isisindo, ubude kanye nobukhulu bekhanda) ngalezi zinsuku ezilandelayo; usuku 1, 2, 3, 7 kanye nosuku-14

umntwana ezaliwe. Lolu lwazi, umcwaningi uzoluthola kwifayela lesiguli kanye neshadi loketshezi (*fluid chart*).

- Ayikho indlela eqokiwe ezolandelwa ekukhethweni kwabantwana abazobamba iqhaza, bonke abantwana abasesimweni esifanelekile esidingwa wucwaningo bazobandakanywa kulolu cwaningo.
- Lolu cwaningo ngeke luphazamise ukwelashwa okwejwayelekile okunikezwa umntwana esibhedlela.

Kungani umenyiwe ukuthi ubambe iqhaza?

- Umntwana wakho kutholakale ukuthi usesimweni esifanelekile sabantwana okuzokwenziwa kubona ucwaningo, esimvumela ukuthi abandakanywe kulolu cwaningo ngoba unesisindo esingaphansi kwesisindo esingamagramu angu-2500 futhi uzalwe enesisindo esincane kakhulu uma kuqhathaniswa nontanga yakhe.

Yiziphi izinto okumele zenziwe nguwena?

- Wena ungalekelela ngokuthi utshele umcwaningi ukuthi umntwana wakho umncelisa izinkomishi ezingaki futhi umncelisa nhloboni yobisi; lokhu kungaba wubisi lwebele, ubisi oluyimpuphu noma isondlamzimba esiphelele esifakwa ngqo egazini (TPN; idriphu enoketshezi olumhlophe oluyisondlamzimba). Ulwazi luzothathwa kwifayela yasesibhedlela kodwa futhi nawe ungalekelela ngokuqinisekisa ukuthi lokho okubhalwe kwifayela ngempela kuyiqinisio.

Ngabe ukhona umhlomulo ozowuthola ngokubamba kwakho iqhaza kulolu cwaningo?

Awukho umhlomulo ozowuthola oqondene nawe ngqo kulolu cwaningo. Ngokubamba iqhaza kulolu cwaningo, uzolekelela emzamweni wethu wokwenza ngcono ulwazi lwethu mayelana nokuphakelwa kanye nokunceliswa kosana.

Ngabe bukhona ubungozi mayelana nokubamba kwakho iqhaza kulolu cwaningo?

- Abukho ubungozi azongena kubona umntwana wakho ngokubamba iqhaza kulolu cwaningo. Ucwaningo luzobuka kuphela ukudla okunikezwa umntwana wakho futhi alukho uguquko oluzokwenzeka kwindlela okwenziwa ngayo izinto esibhedlela.

Uma ungavumi ukubamba iqhaza, yikuphi okunye ongakwenza?

- Nguwena ozothatha isinqumo sokuthi uyavuma noma cha ukubamba iqhaza ocwaningweni. Uma ungavumi ukubamba iqhaza, lokho ngeke kube nomthelela ongemuhle ekwelashweni okunikezwa umntwana wakho. Uma uthanda, ungahoxa noma nini ocwaningweni, ngaphandle kokusizikeza isizathu futhi lokho ngeke kube nomthelela omubi kuwena. Ngeke kube nomthelela ongemuhle kwindlela wena nomntwana wakho enihlinzekwa ngayo ngosizo lokwelashwa olwejwayelekile.

Ngubani ozovunyelwa ukubona amarekhodi akho okwelashwa?

- Amarekhodi akho okwelashwa azobonwa kuphela ngumcwaningi kanye nabantu abaxhumene ngqo nocwaningo. Lonke ulwazi luzogcinwa luyimfihlo ngaso sonke isikhathi.
  Umcwaningi uzolugcina luyimfihlo lonke ulwazi oluqoqiwe futhi alukho ulwazi olungakuveza ukuthi wena ungubani noma luveze umntwana wakho oluzonikezwa noma yimuphi umuntu ongaqondene ngqo nocwaningo.
  Ulwazi oluqoqiwe luzogcinwa luyimfihlo ngokuphelele kodwa luzoshicilelwa kwiwebsayithi yeNyuvesi yase-Stellenbosch kungenzeka "lubuyekezwe ngabanye abacwaningi" kumajenali ezesayensi futhi lwethulwe nakwizingqungquthela. Ngeke nakancane lidalulwe igama lomntwana wakho.

Ulwazi luzobonwa ikakhulu ngabantu abangochwepheshe bezokwelapha, kepha kungenzeka lubonwe ngabanye ochwepheshe abangekho ngaphansi komkhakha wezokwelapha, kubandakanya nezintatheli.

Ngabe uzokhokhelwa ngokubamba kwakho iqhaza kulolu cwaningo futhi ngabe kukhona izindleko ozongena kuzona?

Ayikho inkokhelo ozoyithola ngokubamba kwakho iqhaza kulolu cwaningo. Umcwaningi uzokubuyisela izindleko ongene kuzona, isib. imali yokugibela uma abazali bomntwana kumele bafike esibhedlela kuphela ukuzosayinda imvume yokuthi umntwana abambe iqhaza ocwaningweni. Azikho izindleko abazobuyiselwa zona abazali uma beya esibhedlela ngoba beyovakashela umntwana.

Ngabe kukhona okunye okumele ukwazi noma ukwenze?

- Uma unemibuzo noma izinkinga ungaxhumana no-Renette Reeding kulezi zinombolo zocingo ezilandelayo: 0718716114/011-933 9068.
- Uma unokukhathazeka okuthile noma isikhalo esingaxazululwanga ngokugculisayo ngumcwaningi ungaxhumana neKomidi Lokuziphatha Ngokwenkambiso Efanele Kwezocwaningo Lokwelapha kule nombolo 021-938 9207.
- Uzohlinzekwa ngekhophi yalolu lwazi kanye neyefomu lokunikeza imvume ukuze uzigcinele lona njengerekhodi lakho lokubamba iqhaza ocwaningweni.

Isifungo somuntu obambe iqhaza ocwaningweni

Ngokusayinda lapha ngezansi, mina, umzali/umnakekeli ka- (faka ikhodi yocwaningo)…………………….……………… ngiyavuma ukubamba iqhaza ocwaningweni olunesihloko esithi *"Izinga Lezondlamzimba Ezitholwa Ngabantwana Abazalwe Benesisindo Esingaphansi Kwaleso Esilindelekile e-Chris Hani Baragwanath Academic Hospital kanye neMiyalelo Ekhishwa Ngodokotela Yokudla Okumele Kuphakelwe Abantwana Abakuleso simo"*.

Mina ngiyaqinisekisa ukuthi:

- Ngilufundile noma ngilufundeliwe lolu lwazi kanye nefomu lokunikeza imvume futhi lokhu kubhalwe ngolimi engilwaziyo, engiluqondayo futhi engingenankinga nalo.
- Nginikeziwe ithuba lokubuza imibuzo futhi yonke imibuzo yami iphendulwe ngendlela egculisayo.
- Ngiyaqonda ukuthi ukubamba iqhaza kulolu cwaningo **yinto engiyenza ngentando yami** futhi akekho ongiphoqelelile ukuthi ngibambe iqhaza.
- Nginelungelo lokuhoxa kulolu cwaningo noma nini futhi lokho ngeke kuholele ekutheni ngihlawuliswe noma ngilahlekelwe ngamalungelo ami nganoma iyiphi indlela.
- Kungenzeka ngicelwe ukuthi ngiphume kulolu cwaningo ngaphambi kokuthi luphothulwe, uma umcwaningi ebona ukuthi lokho kungaba wusizo kimina, noma uma ngingalulandeli uhlelo locwaningo okuvunyelwane ngalo.

Sisayindwe e-(*indawo*) ....….......…………….. mhlaka(*usuku*) …………...……….. 2015.

....	....
Isiginesha yomzali/yomnakekeli womntwana	**Isiginesha kafakazi**

Isifungo somcwaningi

Mina *(igama)* …………………………………………………..……… ngiyaqinisekisa ukuthi:

- Ngimchazelile ulwazi oluqukethwe kule ncwajana u- …………………………………..
- Ngimkhuthazile ukuthi abuze imibuzo futhi ngizinikile isikhathi esanele sokuphendula imibuzo yakhe.
- Ngigculisekile ukuthi uyakuqonda konke okuphathelene nalolu cwaningo, njengoba kuchaziwe lapha ngenhla.
- Ngisebenzise/angisebenzisanga utolika. (*Uma kusetshenziswe utolika kumele asayinde lesi sifungo esibhalwe lapha ngezansi.)*

Sisayindwe e-(*indawo*) ....….......…………….. mhlaka (*usuku*) …………...……….. 2015.

....	....
Isiginesha yomcwaningi	**Isiginesha kafakazi**

Isifungo sikatolika

Mina *(igama)* …………………………………………………..……… ngiyaqinisekisa ukuthi:

- Ngimlekelelile umcwaningi u-(*igama*) ………………………………………. ukuchazela u-(*igama lomuntu obambe iqhaza*) ……………..……………………………….. ulwazi oluqukethwe kule ncwajana ngolimi lwesiZulu.
- Simkhuthazile ukuthi abuze imibuzo futhi sizinikeze isikhathi esanele sokuphendula imibuzo yakhe.
- Ngimnikeze ulwazi oluyiqiniso futhi oluqondile mayelana nalokho engitshelwe kona.
- Ngigculisekile ukuthi umuntu obambe iqhaza ukuqonda kahle lokho okuqukethwe kule ncwajana yokunikeza imvume futhi yonke imibuzo yakhe iphendulwe ngendlela egculisayo.

Sisayindwe e-(*indawo*) ....….......…………….. mhlaka (*usuku*) …………...………………..

....	....
Isiginesha katolika	**Isiginesha kafakazi**

APPENDIX F:

ASSENT FORMS (ENGLISH/ZULU)

STELLENBOSCH UNIVERSITY

FACULTY OF HEALTH SCIENCES

PARTICIPANT INFORMATION LEAFLET AND ASSENT FORM

TITLE OF THE RESEARCH PROJECT: Nutrition Intakes and Feeding Prescriptions of Low Birth Weight Infants at Chris Hani Baragwanath Academic Hospital.

RESEARCHERS NAME(S): Renette Andrea Reeding

ETHICS REFERENCE NUMBER: S14/10/248
M150132

ADDRESS: 52A King Street, Berario, Johannesburg, 2195

CONTACT NUMBER: 071 871 6114 / 011-933 9068

What is RESEARCH?

Research is something we do to find new knowledge about the way things (and people) work. We use research projects or studies to help us find out more about disease or illness. Research also helps us to find better ways of helping, or treating children who are sick.

What is this research project all about?

The research will be done in the neonatal and transitional unit (NICU and TICU) of Chris Hani Baragwanath Academic Hospital. The participants will consist of low birth weight (<2500grams) who are born too small for their age. The project will be looking at what milk the doctors are prescribing to feed your baby and what your baby is actually receiving, including what the nurses is giving and comparing the milk to what research says is best for infants so that they grow nicely and that the milk won't affect the baby's brain and growth development long term, also how feeding affects the baby's weight, length and head growth. The investigator will record what the doctors prescribe, what the baby was actually fed and the baby's growth (weight, length and head circumference; size of head) on the following days; 1, 2, 3, 7 and 14 of life. The investigator will get this information from the patients file and fluid chart. There will be no specific pattern in choosing participants, every infant that meets the inclusion criteria will take part in the project. The project will not interfere with the normal medical treatment provided by the hospital.

Why have I been invited to take part in this research project?

Your baby meets the condition and situation to take part in the project because they weigh less than 2500grams and was born small for the age.

Who is doing the research?

I, the investigator will be doing the research. To observe the food your baby is getting is what the doctors are prescribing and if this is according to guidelines of what the baby should get from what other studies suggest is good for them and also to look at if the food they getting is enough to help them to grow nicely.

What will happen to me in this study?

You can help by telling the investigator the number of cups you fed your baby and the type of milk that was given; either breastmilk, formula or total parenteral nutrition (TPN; the drip with the white liquid). Information will be taken from the hospital file but you can also assist confirming what is recorded in the file.

Can anything bad happen to me?

The study will only observe what is being given to the baby. If anything happens to your baby you must tell the investigator.

Can anything good happen to me?

By taking part in this research, you will be helping to improve knowledge on infant feeding.

Will anyone know I am in the study?

No one will know that your baby is participating in the study. All information about your baby will be kept secret and only the people linked to the study will have the information about your baby. The information collected will be used in scientific journals and presented at workshops.

Who can I talk to about the study?

If you have any questions or problems about the study you can contact the investigator by phoning the cellphone number (0718716114) or work office number (0119339068). You can also send me an email to renettereeding@gmail.com

What if I do not want to do this?

If you don't want your baby to take part in the study you can refuse and won't be forced to take part. Even if you decide to take part in the study in the beginning but afterwards decide you do not want to, then it will be fine and you won't get into trouble for not taking part anymore.

Do you understand this research study and are you willing to take part in it?

YES NO

Has the researcher answered all your questions? YES NO

Do you understand that you can pull out of the study at any time? YES NO

________________________ ____________________

Signature of parent/caregiver Date
(<18 years of age) of (Research Code)
…………………………………………………………………….

(Hospital Number)……………………………………..

INYUVESI YASE-STELLENBOSCH

UPHIKO LWEZOKWELAPHA KANYE NAMASAYENSI EZEMPILO

INCWAJANA EHLINZEKA NGOLWAZI KUBANTU ABAZOBAMBA IQHAZA OCWANINGWENI KANYE NEFOMU LEMVUME

ISIHLOKO SOCWANINGO: Izinga Lezondlamzimba Ezitholwa Ngabantwana Abazalwe Benesisindo Esingaphansi Kwaleso Esilindelekile e-Chris Hani Baragwanath Academic Hospital kanye neMiyalelo Ekhishwa Ngodokotela Yokudla Okumele Kuphakelwe Abantwana Abakuleso simo.

IGAMA LOMCWANINGI/AMAGAMA ABACWANINGI: Renette Andrea Reeding

INOMBOLO EYIREFERENSI YOCWANINGO: S14/10/248
M150132

IKHELI: 52A King Street, Berario, Johannesburg, 2195

INOMBOLO YOCINGO: 071 871 6114 / 011-933 9068

Yini UCWANINGO?

Ucwaningo yilokho esikwenzayo ukuze sithole ulwazi olusha mayelana nendlela izinto ezisebenza ngayo (noma mayelana nabantu). Sisebenzisa ucwaningo ukuze sikwazi ukuthola ulwazi oluthe xaxa mayelana nezifo noma ukugula. Ucwaningo luyasilekelela futhi ukuthi sikwazi ukuthola izindlela ezingcono zokusiza, noma zokwelapha izingane ezigulayo.

Ngabe luphathelene nani lolu cwaningo?

- Lolu cwaningo luzokwenzelwa ophikweni lwezokubeletha kanye nolokunakekelwa kweziguli ngenkathi zilungiselelwa ukuyolulamela ekhaya (i-NICU kanye ne-TICU). Abantwana abazobamba iqhaza kulolu cwaningo babandakanya izinsana ezinesisindo esincane (<amagramu angaphansi kwangu-2500) kakhulu uma kuqhathaniswa nesisindo sontanga yabo. Lolu cwaningo luzobheka uhlobo lobisi odokotela abayalele ukuthi lunikezwe umntwana wakho bese kubhekwa ukuthi umntwana wakho uyalunikezwa yini uhlobo lobisi oluyalelwe ngodokotela noma unikezwa olunye uhlobo, kubandakanya nokubheka uhlobo lobisi olunikezwa ngabahlengikazi uma kuqhathaniswa nobisi okuyilona olulungele umntwana ngokusho kocwaningo, ukuze bakhule kahle futhi kuzobhekwa nokuthi ubisi ngeke yini lube nomthelela ongemuhle ngokuqhubeka kwesikhathi emqondweni womntwana kanye nasekukhuleni kwakhe futhi kubhekwe ukuthi lolu bisi lunomthelela onjani kwisisindo somntwana, ubude bakhe kanye nokukhula kwekhanda lakhe. Isisebenzi socwaningo sizoqopha phansi lokho okuyalelwe ngodokotela, kanye nalokho okuyikonakona okunikezwa umntwana futhi baqophe phansi nokukhula komntwana (isisindo, ubude kanye nobukhulu bekhanda) ngalezi zinsuku ezilandelayo; usuku 1, 2, 3, 7 kanye nosuku-14 umntwana ezaliwe. Lolu lwazi isisebenzi socwaningo sizoluthola kwifayela lesiguli kanye neshadi loketshezi (fluid chart). Ayikho indlela eqokiwe ezolandelwa ekukhethweni kwabantwana abazobamba iqhaza, bonke abantwana abasesimweni esifanelekile esidingwa wucwaningo bazobandakanywa kulolu cwaningo. Lolu cwaningo ngeke luphazamise ukwelashwa okwejwayelekile okunikezwa umntwana esibhedlela.

Kungani ngimenyiwe ukuthi ngibambe iqhaza kulolu cwaningo?

Umntwana wakho kutholakale ukuthi usesimweni esifanelekile sabantwana okuzokwenziwa kubona ucwaningo, esimvumela ukuthi abandakanywe kulolu cwaningo ngoba unesisindo esingaphansi kwesisindo esingamagramu angu-2500 futhi uzalwe enesisindo esincane kakhulu uma eqhathaniswa nontanga yakhe.

Ngubani ozokwenza ucwaningo?

Mina, umcwaningi yimina engizokwenza ucwaningo. Ucwaningo luzobuka ukuthi ukudla okutholwa ngumntwana wakho yilokho okuyalelwe ngodokotela futhi luzobheka ukuthi lokhu kwenziwa ngokwemihlahlandlela yokudla okumele kutholwe ngumntwana wakho, okuwukudla okubonwa wucwaningo njengokudla okulungele umntwana futhi kuzobhekwa ukuthi ukudla okutholwa ngumntwana wakho kwanele yini ukulekelela umntwana ukuthi akhule kahle.

Yini ezokwenzeka kulolu cwaningo?

Wena ungalekelela ngokuthi utshele isisebenzi socwaningo ukuthi umntwana wakho umncelisa izinkomishi ezingaki futhi umncelisa nhloboni yobisi; lokhu kungaba wubisi lwebele, ubisi oluyimpuphu noma isondlamzimba esiphelele esifakwa ngqo egazini (TPN; idriphu enoketshezi olumhlophe oluyisondlamzimba). Ulwazi luzothathwa kwifayela yasesibhedlela kodwa futhi nawe ungalekelela ngokuqinisekisa ukuthi lokho okubhalwe kwifayela ngempela kuyiqinisio.

Ngabe kukhona okubi okungenzeka kimina?

Ucwaningo luzobuka kuphela ukuthi umntwana unikwa ukudla okunjani. Uma kukhona okwenzekayo kumntwana wakho kumele utshele umcwaningi.

Ngabe kukhona okuhle okuzokwenzeka kimina?

Ngokubamba iqhaza kulolu cwaningo, uzolekelela emzamweni wethu wokwenza ngcono ulwazi lwethu mayelana nokuphakelwa kanye nokunceliswa kosana.

Ngabe ukhona omunye umuntu ozokwazi ukuthi mina ngiyingxenye yocwaningo?

Akekho ozokwazi ukuthi umntwana wakho ubambe iqhaza ocwaningweni. Lonke ulwazi oluphathelene nomntwana wakho luzogcinwa luyimfihlo futhi ngabantu abaxhumene nocwaningo kuphela abazoba nolwazi oluphathelene nomntwana wakho. Ulwazi oluqoqiwe luzosetshenziswa kumajenali ezesayensi kanye nakuma-workshop (izigcawu zokucobelelana ngolwazi).

Ngubani engingakhuluma naye mayelana nocwaningo?

Uma unemibuzo noma izinkinga mayelana nocwaningo ungaxhumana nomcwaningi ngokufonela le nombolo yeselula (0718716114) noma inombolo yasemsebenzini ethi (0119339068). Ungangithumelela futhi i-imeyili kuleli kheli-renettereeding@gmail.com

Uma ngingafuni ukubamba iqhaza ocwaningweni?

Uma ungafuni ukubamba iqhaza ocwaningweni unelungelo lokwenqaba, usho ukuthi awufuni ukubandakanywa futhi ngeke uphoqelelwe ukuthi ubambe iqhaza. Nakuba uvumile ukubamba iqhaza ekuqaleni, kodwa uma emva kwalokho uthatha isinqumo sokuthi awusafuni ukuqhubeka, akunankinga nakancane lokho futhi ayikho inkinga ozongena kuyona uma ungasafuni ukuqhubeka nocwaningo.

Ngabe uyaqonda ukuthi luphathelene nani lolu cwaningo futhi ngabe uyathanda ukubamba iqhaza ocwaningweni?

YEBO CHA

Ngabe umcwaningi uyiphendule yonke imibuzo yakho?

YEBO CHA

Ngabe uyaqonda ukuthi unelungelo lokuhoxa noma nini ocwaningweni?

YEBO CHA

______________________ __________________

Isiginesha yomzali/yomnakekeli womntwana Usuku

(uma umntwana eneminyaka yobudala engaphansi kweyi-18) (Faka Ikhodi Yocwaningo)

……………………………………………………………………

(Inombolo Yasesibhedlela)……………………………………..

APPENDIX G:

TELEPHONIC CONSENT

TELEPHONIC CONSENT FORM

TITLE OF THE RESEARCH PROJECT: The Nutrient Intakes and Feeding Prescriptions of Low Birth Weight Infants at Chris Hani Baragwanath Academic Hospital

ETHICS REFERENCE NUMBER: S14/10/248
M150132

PRINCIPAL INVESTIGATOR: Renette Andrea Reeding

ADDRESS: 52A King Street
Berario
Johannesburg
2195

CONTACT NUMBER: 071 871 6114 / (011) 933-9068 / renettereeding@gmail.com

The below information will be discussed with the parents during the telephonic consent:

"Your baby has been invited to take part in a study that will take place in the Neonatal and Transitional Intensive Care Unit of Chris Hani Baragwanath Academic Hospital. The study will involve all low birth weight babies that weigh less than 2500grams and are born too small for their age. The study will look at the doctor's prescription of feed and what the nursing staff are feeding the baby during the first 14 days of life. This information will be compared to what research says is best for babies to ensure good growth and brain development."

"A fieldworker will gather information about the feeding from the participants hospital file, and will also be collecting information about the baby's weight, length and head circumference (size of the head)."

"The project will not interfere with the normal medical treatment provided by the hospital. There will be no direct benefit to you or your baby but taking part in the study will help to improve knowledge on infant feeding. There will be no risks involved in taking part and you are free to pull out of the study at any time without any reason."

"Only people directly linked to the study with have access to your baby's information, and the information collected will be published in scientific journals and be presented at congresses. It does not cost money to take part in the study, but you will be paid for transport costs if you come only to the hospital to sign permission for your baby to take part in the study- not if you will be visiting your baby."

This document serves as proof that consent to participate in the above research was given telephonically by the participants parents. When possible, a follow-up appointment to be made with mother/parents to obtain a written and signed consent form. In cases where no written consent form is obtained i.e. mother/parents refuse a follow-up appointment, the telephonic consent form will be appropriate and acceptable for involving participant in the research.

Hospital Number	
Research Code	
Maternal Contact Number	
Maternal Alternative Number	
Maternal Next of Kin	
Maternal Residential Address	
Maternal Email Address	
Date of Telephonic Consent	
Date of Follow-up Appointment	
Paternal Contact Number	
Paternal Alternative Number	
Paternal Next of Kin	
Paternal Residential Address	
Paternal Email Address	
Date of Telephonic Consent	
Date of Follow-up Appointment	
Fieldworker Name	
Fieldworker Signature	
Witness Name	
Witness Signature	

APPENDIX H:

FEEDING PRESCRIPTIONS AND ACTUAL NUTRIENT INTAKES OF PARENTERAL NUTRITION

FEEDING PRESCRIPTIONS AND ACTUAL NUTRIENT INTAKES OF PARENTERAL NUTRITION COMPARED WITH RECOMMENDED GUIDELINES

BW Category	**Feeding Prescription (PN) median (IQR)**	***p*-value**	**Nutrient Intakes (PN) median (IQR)**	***p*-value**	***p*-value (FP vs NI)**
TOTAL STUDY POPULATION					
Fluid (ml/kg/day)					
Day 1	49.94 (47.82-50.61)	0.917	19.57 (15.92-24.38)	0.028	0.028
Day 2	50.59 (48.98-60.22)	0.000	14.64 (0.00-23.15)	0.000	0.000
Day 3	71.19 (50.51-95.50)	0.000	30.15 (20.00-61.06)	0.000	0.000
Day 7	93.88 (62.86-120.66)	0.000	77.11 (41.30-120.86)	0.000	0.018
Day 14	108.46 (85.71-130.43)	0.000	78.34 (48.50-102.81)	0.000	0.000
Energy (kcal/kg/day)					
Day 1	34.95 (33.47-35.42)	0.028	13.81 (10.58-17.06)	0.028	0.028
Day 2	35.29 (34.23-37.75)	0.000	10.25 (0.00-17.11)	0.000	0.000
Day 3	49.82 (34.69-60.19)	0.000	21.10 (14.00-41.88)	0.000	0.000
Day 7	63.79 (43.99-83.98)	0.000	53.32 (28.91-84.35)	0.000	0.005
Day 14	75.92 (59.99-91.29)	0.000	54.83 (33.94-71.95)	0.000	0.000
Protein (g/kg/day)					
Day 1	0.96 (0.92-0.97)	0.028	0.38 (0.31-0.46)	0.027	0.028
Day 2	0.97 (0.94-1.15)	0.000	0.28 (0.00-0.47)	0.000	0.000
Day 3	1.37 (0.96-1.85)	0.000	0.58 (0.38-1.17)	0.000	0.000
Day 7	1.81 (1.20-2.31)	0.000	1.48 (0.79-2.32)	0.000	0.018
Day 14	2.08 (1.67-2.50)	0.000	1.50 (0.93-1.97)	0.000	0.000
GOR (mg/kg/min)					
Day 1	3.60 (3.45-3.65)	0.028	1.42 (1.05-1.76)	0.028	0.028
Day 2	3.64 (3.52-4.06)	0.000	1.06 (0.00-1.79)	0.000	0.000
Day 3	4.46 (3.61-6.20)	0.000	2.17 (1.40-3.91)	0.000	0.000

Day 7	6.55 (4.36-8.65)	0.000	5.49 (2.98-8.32)	0.000	0.008
Day 14	7.83 (6.18-9.41)	0.057	5.69 (3.41-7.45)	0.000	0.000
Fat (g/kg/day)					
Day 1	1.04 (0.99-1.05)	0.028	0.41 (0.33-0.51)	0.028	0.027
Day 2	1.05 (1.02-1.15)	0.000	0.30 (0.00-0.51)	0.000	0.000
Day 3	1.48 (1.04-1.99)	0.000	0.63 (0.42-1.27)	0.000	0.000
Day 7	1.95 (1.31-2.51)	0.000	1.58 (0.86-2.51)	0.000	0.007
Day 14	2.26 (1.79-2.71)	0.000	1.63 (1.01-2.14)	0.000	0.000
ELBW					
Fluid (ml/kg/day)					
Day 1	49.66 (49.66–49.66)	0.317	16.55 (16.55–16.55)	0.317	0.317
Day 2	50.53 (48.98–52.75)	0.000	12.57 (0.00–25.97)	0.000	0.000
Day 3	60.76 (50.23–96.00)	0.000	26.05 (14.40–47.05	0.000	0.000
Day 7	104.23 (72.94–143.16)	0.001	90.04 (63.10–137.11)	0.000	0.313
Day 14	108.47 (91.41–156.04),	0.056	78.28 (69.46–102.81)	0.000	0.004
Energy (kcal/kg/day)					
Day 1	34.75 (34.75–34.75)	0.317	11.58 (11.58–11.58)	0.317	0.317
Day 2	35.16 (34.11–36.51)	0.000	8.79 (0.00–18.30)	0.000	0.000
Day 3	42.52 (34.02–66.49)	0.000	17.74 (9.95–32.93)	0.000	0.000
Day 7	64.70 (47.21–100.19)	0.002	62.07 (44.16–88.40)	0.000	0.093
Day 14	75.93 (63.97–109.21)	0.056	54.78 (48.61–71.95)	0.000	0.000
Protein (g/kg/day)					
Day 1	0.95 (0.95–0.95)	0.317	0.32 (0.32–0.32)	0.317	0.317
Day 2	0.97 (0.94–1.01)	0.000	0.24 (0.00–0.50)	0.000	0.000
Day 3	1.16 (0.95–1.88)	0.000	0.50 (0.28–0.90)	0.000	0.000
Day 7	2.02 (1.40–2.75)	0.000	1.73 (1.21–2.52)	0.000	0.341
Day 14	2.08 (1.77–2.99)	0.001	1.50 (1.33–1.97)	0.000	0.004
GOR (mg/kg/min)					
Day 1	3.58 (3.58–3.58)	0.317	1.19 (1.19–1.19)	0.317	0.317

Day 2	3.62 (3.51–3.78)	0.000	0.92 (0.00–1.89)	0.000	0.000
Day 3	4.38 (3.56–6.85)	0.000	1.83 (1.03–3.39)	0.000	0.000
Day 7	6.46 (4.49–10.33)	0.032	6.49 (4.34–8.98	0.005	0.145
Day 14	7.83 (6.59–11.25)	0.756	5.74 (5.01–7.42)	0.002	0.008
Fat (g/kg/day)					
Day 1	1.03 (1.03–1.03)	0.317	0.34 (0.34–0.34)	0.317	0.317
Day 2	1.04 (1.01–1.09)	0.000	0.26 (0.00–0.54)	0.000	0.000
Day 3	1.26 (1.03–2.02)	0.000	0.54 (0.30–0.98)	0.000	0.000
Day 7	2.18 (1.52–2.98)	0.000	1.77 (1.04–2.63)	0.000	0.135
Day 14	2.26 (1.91–3.25)	0.003	1.63 (1.44–2.14)	0.000	0.004
VLBW					
Fluid (ml/kg/day)					
Day 1	50.21 (47.82–50.61)	0.893	22.40 (16.74–23.20)	0.043	0.043
Day 2	50.43 (48.98–60.22)	0.000	15.78 (12.66–22.47)	0.000	0.000
Day 3	73.69 (53.33–96.81)	0.000	49.13 (31.47–74.62)	0.000	0.000
Day 7	90.79 (60.50–112.06)	0.000	75.22 (41.30–114.47)	0.000	0.058
Day 14	96.73 (88.80–128.00)	0.002	78.34 (43.75–99.92)	0.001	0.015
Energy (kcal/kg/day)					
Day 1	35.14 (33.47–35.42)	0.043	15.90 (11.71–16.24)	0.043	0.043
Day 2	35.29 (34.23–42.14)	0.000	11.05 (8.86–15.95)	0.000	0.000
Day 3	50.72 (34.86–58.17)	0.000	34.39 (22.02–50.90)	0.000	0.000
Day 7	63.53 (42.34–78.43)	0.000	52.64 (28.91–80.12)	0.000	0.062
Day 14	67.70 (62.15–89.58)	0.003	54.83 (30.62–69.93)	0.001	0.015
Protein (g/kg/day)					
Day 1	0.96 (0.92–0.97)	0.043	0.44 (0.32–0.44)	0.042	0.043
Day 2	0.97 (0.94–1.15)	0.000	0.30 (0.24–0.44)	0.000	0.000
Day 3	1.41 (1.02–1.86)	0.000	0.94 (0.60–1.43)	0.000	0.000
Day 7	1.74 (1.16–2.15)	0.000	1.44 (0.79–2.19)	0.000	0.058
Day 14	1.85 (1.70–2.45)	0.001	1.50 (0.84–1.92)	0.001	0.015

GOR (mg/kg/min)					
Day 1	3.63 (3.45–3.65)	0.043	1.64 (1.21–1.67)	0.043	0.043
Day 2	3.65 (3.50–4.34)	0.000	1.14 (0.92–1.64)	0.000	0.000
Day 3	5.22 (3.78–5.99)	0.000	3.54 (2.27–5.24)	0.000	0.000
Day 7	6.55 (4.36–8.08)	0.000	5.42 (2.98–8.26)	0.000	0.062
Day 14	6.98 (6.40–9.23)	0.033	5.65 (3.15–7.21)	0.001	0.015
Fat (g/kg/day)					
Day 1	1.04 (0.99–1.05)	0.043	0.47 (0.35–0.48)	0.043	0.043
Day 2	1.05 (1.02–1.25)	0.000	0.33 (0.26–0.47)	0.000	0.000
Day 3	1.53 (1.04–2.01)	0.000	1.02 (0.65–1.55)	0.000	0.000
Day 7	1.88 (1.26–2.33)	0.000	1.56 (0.86–2.38)	0.000	0.060
Day 14	2.01 (1.85–2.66	0.001	1.63 (0.91–2.08)	0.001	0.015
LBW					
Fluid (ml/kg/day)					
Day 1	–	-	–	-	-
Day 2	74.84 (74.07–75.61)	0.180	10.80 (0.00–21.60)	0.180	0.180
Day 3	64.88 (49.76–80.00)	0.180	20.13 (18.66–21.60)	0.180	0.180
Day 7	88.83 (48.75–136.73)	0.144	57.97 (27.11–120.28)	0.144	0.285
Day 14	79.94 (35.73–124.14)	0.180	76.36 (41.23–111.49)	0.180	0.655
Energy (kcal/kg/day)					
Day 1	–	-	–	-	-
Day 2	52.74 (51.84–53.64)	0.180	7.56 (0.00–15.12)	0.180	0.180
Day 3	45.41 (34.82–55.99)	0.180	14.09 (13.06–15.12)	0.180	0.180
Day 7	62.17 (34.12–96.51)	0.144	40.58 (18.97–84.99)	0.144	0.285
Day 14	55.90 (25.00–86.80)	0.180	53.45 (28.86–78.03)	0.180	0.655
Protein (g/kg/day)					
Day 1	–	-	–	-	-
Day 2	1.45 (1.42–1.48)	0.180	0.21 (0.00–0.41)	0.180	0.180
Day 3	1.24 (0.95–1.53)	0.180	0.39 (0.36–0.41)	0.180	0.180

Day 7	1.70 (0.93–2.66)	0.068	1.11 (0.52–2.34)	0.068	0.285
Day 14	1.53 (0.68–2.38)	0.180	1.47 (0.79–2.14)	0.180	0.655
GOR (mg/kg/min)					
Day 1	–	-	-	-	-
Day 2	5.43 (5.34–5.52)	0.180	0.78 (0.00–1.56)	0.180	0.180
.Day 3	4.68 (3.59–5.77)	0.180	1.45 (1.35–1.56)	0.180	0.180
Day 7	6.41 (3.51–9.94)	0.273	4.18 (1.95–8.75)	0.144	0.285
Day 14	5.76 (2.58–8.95)	0.180	5.51 (2.97–8.04)	0.180	0.655
Fat (g/kg/day)					
Day 1	–	-	–	-	-
Day 2	1.57 (1.54–1.59)	0.180	0.23 (0.00–0.45)	0.180	0.180
Day 3	1.35 (1.03–1.66)	0.180	0.42 (0.39–0.45)	0.180	0.180
Day 7	1.85 (1.02–2.87)	0.068	1.21 (0.57–2.52)	0.068	0.285
Day 14	1.66 (0.74–2.58)	0.180	1.59 (0.86–2.32)	0.180	0.655

APPENDIX I:

FEEDING PRESCRIPTIONS AND ACTUAL NUTRIENT INTAKES OF ENTERAL NUTRITION

FEEDING PRESCRIPTIONS AND ACTUAL NUTRIENT INTAKES OF ENTERAL NUTRITION COMPARED WITH RECOMMENDED GUIDELINES

BW Category	Feeding Prescription (EN) median (IQR)	*p*-value	Nutrient Intakes (EN) median (IQR)	*p*-value	*p*-value (FP vs NI)
TOTAL STUDY POPULATION					
Fluid (ml/kg/day)					
Day 1	24.13 (19.67–40.10)	0.000	0.00 (0.00–8.88)	0.000	0.000
Day 2	21.33 (18.60–34.67)	0.000	2.75 (0.00–10.14)	0.000	0.000
Day 3	37.75 (21.46–57.49)	0.000	20.94 (9.30–32.37)	0.000	0.000
Day 7	117.65 (87.80–144.97)	0.000	95.69 (67.76–126.06)	0.000	0.000
Day 14	168.23 (104.41–178.67)	0.000	160.70 (82.87–176.44)	0.000	0.000
Energy (kcal/kg/day)					
Day 1	18.13 (15.14–30.87)	0.000	0.00 90.00–6.93)	0.000	0.000
Day 2	16.55 (14.32–27.09)	0.000	2.14 (0.00–7.66)	0.000	0.000
Day 3	29.36 (16.52–44.28)	0.000	16.28 (6.75–24.44)	0.000	0.000
Day 7	88.27 (67.93–110.34)	0.000	71.56 (51.4–93.66)	0.000	0.000
Day 14	122.09 (80.44–138.64)	0.000	117.11 (62.66–135.62)	0.000	0.000
Protein (g/kg/day)					
Day 1	0.47 (0.40–0.81)	0.000	0.00 (0.00–0.18)	0.000	0.000
Day 2	0.45 (0.39–0.73)	0.000	0.06 (0.00–0.22)	0.000	0.000
Day 3	0.80 (0.45–1.19)	0.000	0.43 (0.18–0.70)	0.000	0.000
Day 7	2.37 (1.76–2.83)	0.000	1.86 (1.37–2.57)	0.000	0.000
Day 14	3.17 (2.08–3.65)	0.000	2.94 (1.58–3.66)	0.000	0.000
CHO (g/kg/day)					
Day 1	1.81 (1.46–3.01)	0.000	0.00 (0.00–0.71)	0.000	0.000
Day 2	1.61 (1.40–2.60)	0.000	0.22 (0.00–0.76)	0.000	0.000
Day 3	2.87 (1.65–4.30)	0.000	1.59 (0.70–2.61)	0.000	0.000
Day 7	8.57 (6.53–10.71)	0.000	7.00 (5.08–9.61)	0.000	0.000

Day 14	11.92 (7.83–13.94)	0.055	11.27 (6.13–13.98)	0.004	0.000
Fat (g/kg/day)					
Day 1	1.04 (0.86–1.86)	0.000	0.00 (0.00–0.37)	0.000	0.000
Day 2	0.94 (0.82–1.55)	0.000	0.13 (0.00–0.44)	0.000	0.000
Day 3	1.7 (1.0–2.6)	0.000	0.93 (0.41–1.40)	0.000	0.000
Day 7	5.1 (4.0–6.4)	0.000	4.09 (2.91–5.37)	0.000	0.000
Day 14	7.1 (4.9–8.1)	0.115	6.84 (3.82–7.85)	0.002	0.000
ELBW					
Fluid (ml/kg/day)					
Day 1	22.66 (17.99–39.04)	0.000	0.00 (0.00–0.00)	0.000	0.012
Day 2	18.60 (16.93–20.78)	0.000	1.56 (0.00–5.19)	0.000	0.000
Day 3	25.30 (18.29–37.65)	0.000	12.06 (6.40-21.48)	0.000	0.000
Day 7	88.89 (56.14–120.23)	0.000	76.09 (40.99-102.96)	0.000	0.000
Day 14	145.38 (29.09–173.91)	0.001	82.29 (14.55-169.59)	0.000	0.004
Energy (kcal/kg/day)					
Day 1	17.88 (13.98–30.33)	0.000	0.00 (0.00–0.00)	0.000	0.012
Day 2	14.47 (13.14–16.20)	0.000	1.56 (0.00–5.19)	0.000	0.000
Day 3	19.69 (14.19–29.46)	0.000	9.65 (4.98-16.71)	0.000	0.000
Day 7	68.18 (43.56–93.30)	0.000	59.04 (31.81-79.90)	0.000	0.000
Day 14	106.51 (22.63–135.38)	0.028	63.12 (11.32-131.98)	0.003	0.004
Protein (g/kg/day)					
Day 1	0.51 (0.40–0.86)	0.000	0.00 (0.00–0.00)	0.000	0.025
Day 2	0.41 (0.36–0.46)	0.000	0.04 (0.00–0.15)	0.000	0.000
Day 3	0.59 (0.39–0.85)	0.000	0.28 (0.15-0.49)	0.000	0.000
Day 7	1.98 (1.18–2.52)	0.000	1.62 (0.86-2.16)	0.000	0.000
Day 14	2.80 (0.66–3.65)	0.019	1.62 (0.33-3.47)	0.003	0.004
CHO (g/kg/day)					
Day 1	1.84 (1.36–2.95)	0.000	0.00 (0.00–0.00)	0.000	0.012
Day 2	1.41 (1.27–1.60)	0.000	0.15 (0.00–0.51)	0.000	0.000

Day 3	1.92 (1.38–2.86)	0.000	1.02 (0.49-1.64)	0.000	0.000
Day 7	6.67 (4.21–9.02)	0.000	5.99 (3.07-7.72)	0.000	0.000
Day 14	10.05 (2.21–13.41)	0.049	6.17 (1.11-12.90)	0.011	0.004
Fat (g/kg/day)					
Day 1	0.97 (0.81–1.72)	0.000	0.00 (0.00–0.00)	0.000	0.012
Day 2	0.82 (0.74–0.91)	0.000	0.09 (0.00–0.29)	0.000	0.000
Day 3	1.12 (0.8–1.7)	0.000	0.50 (0.28-0.96)	0.000	0.000
Day 7	4.24 (2.5–5.1)	0.000	3.31 (1.24-4.41)	0.000	0.000
Day 14	6.21 (1.3–7.7)	0.053	3.95 (0.64-7.24)	0.012	0.004
VLBW					
Fluid (ml/kg/day)					
Day 1	21.13 (19.12–22.33)	0.000	0.00 (0.00–7.20)	0.000	0.000
Day 2	21.05 (17.91–22.84)	0.000	2.67 (0.00–8.33)	0.000	0.000
Day 3	34.26 (21.15–43.84)	0.000	15.33 (8.60-30.00)	0.000	0.000
Day 7	107.40 (85.41–125.76)	0.000	83.19 (61.80-107.59)	0.000	0.000
Day 14	167.30 (107.62–179.31)	0.000	161.91 (95.13-178.51)	0.000	0.000
Energy (kcal/kg/day)					
Day 1	16.39 (14.84–17.86)	0.000	0.00 (0.00–5.76)	0.000	0.000
Day 2	16.17 (14.22–17.78)	0.000	2.09 (0.00–6.67)	0.000	0.000
Day 3	26.28 (16.34–34.02)	0.000	11.89 (6.60-23.70)	0.000	0.000
Day 7	83.35 (66.28–95.23)	0.000	63.51 (48.08-82.52)	0.000	0.000
Day 14	122.80 (82.55–139.14)	0.020	121.52 (73.57-137.31)	0.005	0.001
Protein (g/kg/day)					
Day 1	0.42 (0.41–0.51)	0.000	0.00 (0.00–0.17)	0.000	0.000
Day 2	0.44 (0.40–0.52)	0.000	0.06 (0.00–0.19)	0.000	0.000
Day 3	0.71 (0.44–0.92)	0.000	0.32 (0.17-0.65)	0.000	0.000
Day 7	2.08 (1.79–2.46)	0.000	1.75 (1.27-2.10)	0.000	0.000
Day 14	3.30 (2.12–3.77)	0.004	3.19 (1.92-3.77)	0.003	0.012
CHO (g/kg/day)					

Day 1	1.63 (1.43–1.88)	0.000	0.00 (0.00–0.62)	0.000	0.000
Day 2	1.58 (1.38–1.90)	0.000	0.21 (0.00–0.71)	0.000	0.000
Day 3	2.57 (1.58–3.36)	0.000	1.15 (0.65-2.40)	0.000	0.000
Day 7	7.95 (6.43–9.30)	0.000	6.24 (4.70-8.07)	0.000	0.000
Day 14	12.18 (8.07–14.01)	0.272	11.71 (7.20-14.06)	0.140	0.015
Fat (g/kg/day)					
Day 1	0.91 (0.84–1.04)	0.000	0.00 (0.00–0.30)	0.000	0.000
Day 2	0.93 (0.78–1.10)	0.000	0.11 (0.00–0.35)	0.000	0.000
Day 3	1.5 (1.0–1.9)	0.000	0.67 (0.41-1.27)	0.000	0.000
Day 7	4.9 (4.0–5.5)	0.000	3.57 (2.68-4.77)	0.000	0.000
Day 14	7.3 (5.0–8.1)	0.251	6.90 (4.04-7.91)	0.033	0.000
LBW					
Fluid (ml/kg/day)					
Day 1	30.85 (20.58–46.65)	0.000	0.00 (0.00–10.84)	0.000	0.000
Day 2	34.67 (26.30–50.79)	0.000	9.87 (0.00–22.37)	0.000	0.000
Day 3	64.14 (42.55–102.33)	0.000	32.80 (20.65-57.99)	0.000	0.000
Day 7	156.11 (132.46–176.80)	0.000	130.86 (99.77-165.26)	0.000	0.000
Day 14	171.03 (148.31–184.59)	0.028	166.04 (138.90-184.24)	0.006	0.004
Energy (kcal/kg/day)					
Day 1	23.67 (15.62–36.20)	0.000	0.00 (0.00–8.02)	0.000	0.000
Day 2	27.09 (19.34–39.42)	0.000	7.20 (0.00–17.25)	0.000	0.000
Day 3	49.19 (30.30–77.37)	0.000	23.61 (16.02-43.79)	0.000	0.000
Day 7	111.74 (96.80–129.14)	0.000	92.06 (71.56-119.79)	0.000	0.000
Day 14	119.81 (102.52–141.58)	0.156	115.51 (100.92-141.64)	0.042	0.005
Protein (g/kg/day)					
Day 1	0.57 (0.39–0.98)	0.000	0.00 (0.00–0.20)	0.000	0.000
Day 2	0.72 (0.46–1.05)	0.000	0.17 (0.00–0.41)	0.000	0.000
Day 3	1.26 (0.75–1.90)	0.000	0.62 (0.35-1.09)	0.000	0.000
Day 7	2.83 (2.34–3.24)	0.000	2.57 (1.75-3.09)	0.000	0.000

Day 14	3.17 (2.46–3.53)	0.023	2.87 (2.39-3.51)	0.014	0.023
CHO (g/kg/day)					
Day 1	2.31 (1.51–3.50)	0.000	0.00 (0.00–0.86)	0.000	0.000
Day 2	2.60 (1.77–4.18)	0.000	0.68 (0.00–1.58)	0.000	0.000
Day 3	4.81 (2.96–7.37)	0.000	2.48 (1.50-4.62)	0.000	0.000
Day 7	10.91 (9.12–12.24)	0.004	9.61 (6.99-11.99)	0.000	0.000
Day 14	12.10 (9.62–13.94)	0.881	11.18 (9.24-13.87)	0.455	0.015
Fat (g/kg/day)					
Day 1	1.40 (0.95–2.05)	0.000	0.00 (0.00–0.42)	0.000	0.000
Day 2	1.66 (1.17–2.23)	0.000	0.41 (0.00–0.93)	0.000	0.000
Day 3	3.0 (1.8–4.7)	0.000	1.40 (0.91-2.36)	0.000	0.000
Day 7	6.7 (5.8–7.5)	0.048	5.37 (4.48-7.13)	0.000	0.000
Day 14	7.2 (6.2–8.8)	0.355	7.00 (5.70-8.13)	0.852	0.002

APPENDIX J:

FEEDING PRESCRIPTIONS AND NUTRIENT INTAKES OF INTRAVENOUS FLUIDS IN LBW INFANTS

Birth Weight Category	Feeding Prescription median (IQR)	Nutrient Intakes median (IQR)
TOTAL STUDY POPULATION		
Fluid (ml/kg/day)		
Day 1	79.10 (70.40–83.72)	34.93 (13.30–49.87)
Day 2	75.61 (54.79–89.60)	73.46 (62.79–86.90)
Day 3	77.04 (59.18–99.38)	73.88 (48.31–91.28)
Day 7	77.42 (53.08–116.42)	72.35 (38.00–109.94)
Day 14	68.16 (42.67–121.66)	67.88 (31.51–95.52)
Energy (kcal/kg/day)		
Day 1	34.77 (30.86–36.41)	15.04 (5.85–21.82)
Day 2	30.88 (22.81–36.54)	30.85 (25.23–36.56)
Day 3	30.50 (22.54–42.09)	29.31 (19.60–36.75)
Day 7	31.41 (19.47–43.10)	26.92 (15.12–41.16)
Day 14	24.71 (15.99-53.53)	23.96 (12.77-38.26)
CHO (g/kg/day)		
Day 1	8.69 (7.72–9.09)	3.76 (1.46–5.36)
Day 2	7.72 (5.70–9.13)	7.71 (6.31–9.14)
Day 3	7.62 (5.63–10.52)	7.25 (4.87–9.19)
Day 7	7.85 (4.87–10.78)	6.73 (3.78–10.29)
Day 14	6.18 (4.00–13.38)	5.99 (3.19–9.57)
ELBW		

Fluid (ml/kg/day)		
Day 1	85.85 (80.00–99.41)	37.35 (13.49–53.61)
Day 2	82.65 (58.75–98.74)	86.90 (67.06–97.49)
Day 3	78.03 (55.81–102.34)	72.89 (45.61–99.41)
Day 7	97.07 (65.91–143.77)	86.24 (40.45–155.21)
Day 14	53.63 (31.37–77.69)	66.23 (24.24–97.53)
Energy (kcal/kg/day)		
Day 1	36.29 (33.52–42.52)	16.20 (5.93–23.02)
Day 2	28.75 (22.81–37.71)	32.08 (24.14–39.55)
Day 3	30.46 (21.12–39.16)	28.06 (17.22–36.78)
Day 7	35.72 (20.36–58.14)	26.68 (17.16–44.05)
Day 14	22.59 (13.80–34.18)	21.69 (10.35–42.91)
CHO (g/kg/day)		
Day 1	9.07 (8.38–10.63)	4.05 (1.48–5.68)
Day 2	7.19 (5.70–9.43)	8.03 (6.04–9.89)
Day 3	7.62 (5.28–9.79)	7.02 (4.30–9.20)
Day 7	8.93 (5.09–14.54)	6.67 (4.29–11.01)
Day 14	5.65 (3.45–8.55)	5.42 (2.59–10.73)
VLBW		
Fluid (ml/kg/day)		
Day 1	77.01 (70.14–7.67)	33.89 (19.74–45.28)
Day 2	79.01 (53.93–86.33)	73.66 (62.96–81.39)

Day 3	85.20 (59.27–111.68)	79.35 (51.95–92.99)
Day 7	77.42 (53.08–94.43)	76.07 (41.45–121.28)
Day 14	88.48 (58.06–125.81)	66.95 (40.82–89.13)
Energy (kcal/kg/day)		
Day 1	33.89 (30.28–35.07)	14.56 (8.69–19.92)
Day 2	33.89 (23.58–36.57)	31.97 (26.40–35.81)
Day 3	34.60 (24.95–43.77)	33.35 (18.99–39.15)
Day 7	31.41 (20.77–36.98)	31.56 (18.24–39.08)
Day 14	29.85 (17.22–55.35)	25.55 (12.77–38.26)
CHO (g/kg/day)		
Day 1	8.47(7.57–8.76)	3.64(2.17–4.98)
Day 2	8.47 (5.89–9.14)	7.99 (6.60–8.95)
Day 3	8.65 (6.23–10.94)	8.34 (4.42–9.79)
Day 7	7.85 (5.19–9.25)	7.90 (4.56–9.77)
Day 14	7.45 (4.30–13.84)	6.39 (3.19–9.57)
LBW		
Fluid (ml/kg/day)		
Day 1	77.82 (61.40–80.23)	34.28 (13.24–49.67)
Day 2	66.32 (51.74-–81.85)	67.41 (56.79–78.14)
Day 3	69.31 (59.02–89.36)	66.88 (49.09–84.03)
Day 7	68.16 (41.48–94.78)	49.95 (17.30–85.09)
Day 14	68.97 (37.62–107.69)	70.83 (37.62–81.61)

nergy (kcal/kg/day)		
Day 1	34.24 (27.01–35.30)	15.09 (5.83–21.85)
Day 2	28.93 (22.76–35.20)	29.24 (24.86–34.35)
Day 3	27.16 (22.82–36.48)	26.15 (20.85–34.12)
Day 7	29.30 (18.21–41.70)	21.98 (6.53–37.44)
Day 14	30.34 (16.55–47.38)	31.17 (16.55–35.91)
CHO (g/kg/day)		
Day 1	8.57 (6.75–8.83)	3.77 (1.46–5.46)
Day 2	7.23 (5.69–8.80)	7.31 (6.22–8.59)
Day 3	6.79 (5.70–9.12)	6.54 (5.21–8.53)
Day 7	7.33 (4.55–10.43)	5.49 (1.63–9.36)
Day 14	7.59 (4.14–11.85)	7.79 (4.14–8.98)