The impact of malnutrition in premature infants on hospital length of stay: A retrospective study in a metropolitan neonatal intensive care unit

by

Karen Glover

B.S., Middle Tennessee State University, 1987

A THESIS

submitted in partial fulfillment of the requirements for the degree

MASTER OF SCIENCE

Department of Food, Nutrition, Dietetics and Health
College of Health and Human Sciences

KANSAS STATE UNIVERSITY
Manhattan, Kansas

2025

Approved by:

Major Professor
Dr. Mark Haub

Copyright

The impact of malnutrition in premature infants on hospital length of stay: A retrospective study in a metropolitan neonatal intensive care unit

Thesis Approved: Dr. Mark Haub
Thesis Advisor

Hospital Approved: Melissa Brooks, MS, RD, LDN
Clinical Dietitian Manager

Karen Ambrose, MHA
Administrative approval, Vice President of Operations

Abstract

Background: The importance of nutrition for the preterm infant is clear, as providing both the appropriate quality and quantity of nutrition to premature infants has been shown to influence infant growth, morbidity, and neurodevelopment outcomes. Nutrition is a lifesaving and life-sustaining intervention in the neonatal intensive care unit (NICU). Therefore, identifying, preventing, and resolving malnutrition in the NICU are all necessary to provide optimal care to the preterm infant. Identifying malnutrition within the first 28 days of life can discern infants struggling to maintain adequate growth and development and having a higher-than-average risk of a longer length of stay (LOS). Addressing malnutrition in the NICU and reducing LOS for these infants dramatically impacts their health outcomes, family distress and decreases the financial burdens of a lengthy stay in the NICU. This study aimed to identify the impact of a malnutrition diagnosis on the 28th day of life on the overall LOS of the subjects.

Methods: The records of 53 patients with birth weight > 600 grams < 2500 grams, 24 weeks to < 37 weeks gestational age (GA), > 27-day LOS admitted to the NICU from July 2024 to December 2024 were included in the retrospective chart review. The charts for preterm malnutrition were reviewed for the six malnutrition indicators, including decline in weight for age z score, weight gain velocity, nutrient intake, days to regain birth weight, linear growth velocity, and decline in length for age z score. A final summary malnutrition category was assigned to each patient: no malnutrition, mild malnutrition, moderate malnutrition, or severe malnutrition. The summary was further defined as not having malnutrition or having malnutrition for the final statistical review. Analysis of not having malnutrition and having malnutrition with mean LOS was analyzed using a t-test: two samples assuming unequal variances for statistical significance.

Results: Using the malnutrition classification criteria, the overall prevalence of malnutrition was (*n*=28, 53%) in the population (*n*=53), mild malnutrition was (*n*=19, 36%) and moderate malnutrition was (*n*=9, 17%). No subjects met the criteria for severe malnutrition. The mean LOS was 49.6 ±18.1 days for no malnutrition (*n*=25, 43%), 57.1±24.2 days for mild malnutrition and 92.3 ± 27.4 days for moderate malnutrition. The mean LOS of the total number of patients that met the malnutrition criteria was 68.4 ± 29.9 days. The mean GA= 29.76 ± 2.8 weeks and the mean birth weight = 1321 ± 472.61 grams. Racial disparities noted in the literature were comparable to the results of this study, the Black/African American (AA) babies were born at smaller birth weights and had a longer LOS. Birth weight class and gestational age in this study followed the literature trends for a longer LOS with the infants having smaller birth weight and born at < 28 weeks gestation. The highest risk of a longer LOS with prenatal risks included chronic hypertension with 61±17.2 days LOS, advanced maternal age with 59±19.9 days LOS, and pregnancies with multiples (twins) with 77.5±52.2 days LOS. The highest risk of complications during pregnancy included problems of the uterus, cervix, or placenta, with 89.3±38.6 days LOS with malnutrition, infections of amniotic fluid or lower genital tract with 80.5±31.5 days LOS with malnutrition, and hypertension developed during pregnancy with 57.6±26.3 days LOS with malnutrition. Preterm complications with the highest LOS included bronchopulmonary dysplasia (BPD) at 90.6±19.6 days LOS, necrotizing enterocolitis (NEC) with 88 days LOS and congenital heart disease (CHD) with 85.8±33.4 days LOS. Statistically comparing the LOS of infants with BPD and malnutrition to all subjects without BPD and with malnutrition, infants with BPD and malnutrition resulted in a higher LOS using the t-test: two-sample assuming unequal variances, (M=90.6±19.6), t(19)= 3.28, p =0.002. The main objective is to determine if malnutrition affects LOS using the t-test: two sample, assuming unequal variances. The t-test results (M=68.4 ± 29.9), t (45) =-2.8, p=0.003 indicate a statistically significant difference in LOS between infants with malnutrition and those without malnutrition. The results suggest that malnutrition affects the length of stay in the NICU.

Conclusion: The findings of this small retrospective study indicate that the presence of malnutrition does increase the probability of a longer overall length of stay. Many factors drive the need for a longer stay in the NICU, such as feeding intolerance and other diagnoses mentioned in the research. Many intertwined factors go along with malnutrition in affecting LOS, such as the diagnosis of BPD, which may play a role in increasing LOS and in the development of malnutrition. This research emphasizes the critical role of an interdisciplinary approach in neonatal care. Cumulatively, this work identifies the need for malnutrition assessments to identify neonatal malnutrition within the NICU to guide the multidisciplinary team in meeting the infants' needs for growth and development with reduced required length of stay in the NICU. Malnutrition can impact the bottom-line dollar costs for hospitals and parents, and the social and behavior well-being of the infants' caretakers. If ignored, that decision will affect the child throughout their life.

Keywords: preterm birth, malnutrition, hospital length of stay, neonatal intensive care unit, racial disparity, bronchopulmonary dysplasia

Table of Contents

List of Figures viii

List of Tables ix

Key Abbreviations and Definitions x

Dedication xiii

Chapter 1 - Introduction 1

Statement of Purpose 2

Chapter 2 - Review of Literature 3

Preterm Birth 3

Malnutrition Indicators and Growth 12

Financial Concerns 22

Length of Stay 23

Chapter 3 - Methodology 25

Chapter 4 - Results 30

Chapter 5 - Statistical Analyses 44

Chapter 6 - Conclusions, Discussion and Future Research 47

References 51

List of Figures

Figure 2.1 Preterm Birth Rate in the United States 2013-2023 9
Figure 2.2 United States Preterm Birth Rate by State 2023 10
Figure 2.3 United States Preterm Birth Rates by Race/Ethnicity 2021-2023 11
Figure 2.4 Tennessee Preterm Birth Rates by Race/Ethnicity 2021-2023 12
Figure 4.1 Average Length of Stay with and without Malnutrition 32
Figure 4.2 Average Length of Stay, Moderate Malnutrition Mild Malnutrition, and No Malnutrition 33
Figure 4.3 Brown Study Compared to Current Study on Birth Weight 35
Figure 4.4 Brown Study Compared to Current Study, Length of Stay 36
Figure 4.5 Race/Ethnicity, Malnutrition and Length of Stay 37
Figure 4.6 Birth Weight Class with Malnutrition and Length of Stay 38
Figure 4.7 Gestational Age with Malnutrition and Length of Stay 39
Figure 4.8 Prenatal Risks, Malnutrition and Length of Stay 40
Figure 4.9 Complications of Pregnancy, Malnutrition and Length of Stay 41
Figure 4.10 Preterm Complications, Malnutrition and Length of Stay 43

List of Tables

Table 2.1 Prematurity Classification of Gestational Age 3
Table 2.2 Weight Classification on Birth Weight.. 4
Table 2.3 Gestational Weight for Age Classification 4
Table 2.4 Malnutrition Indicators in Preterm and Neonates.. 14
Table 2.5 Average Growth Velocity by Age Group 15
Table 2.6 Energy Needs... 16
Table 2.7 Protein Needs... 17
Table 2.8 Fluid Needs.. 18
Table 2.9 Vitamin/Mineral Enteral Recommendations 21
Table 4.1 Characteristics of the Total Study Population (N=53)... 30
Table 4.2 Average Length of Stay, No Malnutrition, Mild Malnutrition, and Moderate Malnutrition 33
Table 4.3 Mean and Standard Deviation of Selected Values... 34
Table 5.1 t-Test for Malnutrition with BPD Compared to without BPD..................................... 44
Table 5.2 Descriptive Statistics for Malnutrition with BPD Compared to without BPD 45
Table 5.3 t-Test for Malnutrition and No Malnutrition 46
Table 5.4 Descriptive Statistics for Malnutrition and No Malnutrition....................................... 46

Key Abbreviations and Definitions

AGA *Appropriate for gestational age* is a birth weight percentile of 10^{th} percentile to 90^{th} percentile, weight for age.(Casirati et al., 2022)

ASPEN *American society of parenteral and enteral nutrition*(Goldberg et al., 2018)

BW *Birth weight* is the first weight of the baby just after birth.(Texas Children's Hospital, 2022)

BMI *Body mass index* is a measure that relates body weight to height.(Texas Children's Hospital, 2022)

BPD *Bronchopulmonary dysplasia* is a chronic lung disease, generally in preterm infants. Also known as chronic lung disease of prematurity.(Rocha et al., 2021)

CHD *Congenital heart disease is* a heart disease or defect present at birth, a term used to describe several different conditions at birth.(Mills et al., 2022)

CHF *Congestive heart failure* is a clinical state of systemic and pulmonary congestion resulting from inability of the heart to pump as much blood as required for the adequate metabolism of the body.(Mills et al., 2022)

CHTN *Chronic hypertension* is hypertension that was present before the pregnancy.(Gidi et al., 2020)

DM *Diabetes mellitus* is a condition characterized by high blood sugar. It is preexisting if it occurs before the pregnancy. It is called gestational diabetes if it is diagnosed during pregnancy.(Preda et al., 2023)

DOL *Day of life.* The birthday is considered day 0. Number of days the infant has been alive.(Koletzko et al., 2021)

EMR *Electronic medical record* is a digital version of the patient's medical record.(Ambinder, 2005)

ELBW *Extremely low birth weight* is less than 1000 grams or 2.2 pounds.(Casirati et al., 2022)

GA *Gestational Age* estimates an infant's age in weeks from conception.(Texas Children's Hospital, 2022)

GV *Growth velocity* The rate at which the infant's weight or length increases over time.(Goldberg et al., 2018)

HCUP *Healthcare Cost and Utilization Project* The Healthcare Cost and Utilization Project is a family of healthcare databases and software tools developed through a Federal-State-Industry partnership and sponsored by the Agency for Healthcare Research and Quality (AHRQ).(Kowlessar et al., 2011)

HTN *Hypertension* is blood pressure that is higher than usual, it can be chronic, existing before pregnancy, or develop in pregnancy. HTN in pregnancy can lead to a condition called preeclampsia.(Koletzko et al., 2021)

IDF *Infant-driven feeding is* a feeding method that focuses on the infant's cues and developmental state rather than feeding volume.(Ilahi et al., 2023)

IVH *Intraventricular hemorrhage* is the most common brain injury, bleeding in the brain in the neonate. IVH is graded 1-4 based on the amount of bleeding in the ventricles, one being the least problematic and four being the most serious.(Skinner & Narchi, 2021; Zheng et al., 2023)

LGA *Large for gestational age* is a birth weight percentile of more than the 90th percentile, weight for age.(Damhuis et al., 2021)

LOS *Length of stay* is the duration of time a patient stays in the hospital from admission to discharge.(Mehretie et al., 2024)

LBW *Low birth weight* is a birth weight of less than 2500 grams or 5.5 pounds.(Casirati et al., 2022)

NEC *Necrotizing enterocolitis* is an intestinal disease in which portions of the bowel are damaged or destroyed because of poor blood flow, inflammation, or infection.(Shulhan et al., 2017)

NICU *Neonatal intensive care unit* is the neonatal intensive care unit that provides care to the premature, sick, or fragile newborns.(Texas Children's Hospital, 2022)

PTD *Preterm delivery* an infant born before 37 weeks gestational age.(*World Health Organization Fact Sheet on Preterm Birth*, 2023)

ROP *Retinopathy of prematurity* is an eye disease of premature infants in which new blood vessels grow abnormally near the retina, causing temporary or permanent damage.(Hellström et al., 2024)

SGA *Small for gestational age* is a birth weight percentile of less than the 10th percentile, weight for age.(Damhuis et al., 2021)

VLBW *Very low birth weight*, a birth weight of less than 1500 grams or 3.3 pounds.(Casirati et al., 2022)

WHO *World Health Organization* is a United Nations agency that focuses on global health and safety.(*World Health Organization Fact Sheet on Preterm Birth*, 2023)

Dedication

The author would like to express their appreciation to the Kansas State University professors who played a crucial role in assisting with completing this thesis and the Master of Science in Dietetics program. Their guidance and expertise, particularly the supervisory committee, Dr. Mark Haub, Dr. Linda Yarrow, and Dr. Weiqun Wang, and the previous supervising professors who assisted with the initial planning of the research were Dr. Richard Rosenkranz and Dr. Tandalayo Kidd.

The author would like to thank previous preceptors in dietetics who have been enormous mentors in training dietetic students and impressing others with the importance of supporting dietetic education and precepting the future students of dietetics, including Alicia Mandel, Faye House (in memory), and Phyllis Goodwin (in memory).

The author would like to thank the medical center for allowing the retrospective data collection obtained for quality improvement of hospital malnutrition. This data was crucial in understanding the prevalence and impact of malnutrition in the neonatal population. The clinical nutrition manager of the hospital, Melissa Brooks, deserves recognition for her support and listening ear during this process.

The time away from family needed during a graduate program means less time to focus on family activities. The author profoundly appreciates her family, who have supported her and understood the time and effort needed to complete this Master of Science in Dietetics. Their unwavering support has been a source of strength and motivation throughout this journey.

Chapter 1 - Introduction

Preterm infants are more susceptible to nutrition deficits than at any other time in the life cycle, contributing to growth failure and poor neurocognitive development.(Goldberg et al., 2018) Nutrition during infancy and development is recognized as a key determinant for health outcomes, performance and disease risks later in life.(Koletzko et al., 2021) However, nutrition is not just a key determinant in the neonatal intensive care unit (NICU); it is a lifesaving and life-sustaining intervention needed for the appropriate growth and development of premature infants. The diagnosis of malnutrition identifies preterm infants at the highest risk of poor growth and neurodevelopmental outcomes, alerting the care team to infants in need of close monitoring.(Goldberg & Becker, 2022; Koletzko et al., 2021) An increased length of stay (LOS) in a NICU contributes to increased financial costs and emotional concerns for the parents.

Recommended indicators for preterm and neonatal malnutrition were published in the *Journal of the Academy of Nutrition and Dietetics*, based on the 2018 article "Identifying Malnutrition in Preterm and Neonatal Populations.(Goldberg et al., 2018) It was designed for neonates, preterm infants < 37 weeks and term infants < 30 days old.(Goldberg et al., 2018) The malnutrition diagnosis identifies preterm infants at highest risk of needing intensive interdisciplinary team nutrition interventions to support growth and neurodevelopment.(Goldberg et al., 2018) The number of days to regain birth weight appears to be a strong indicator in the quality of nutrition received by the neonate and one of the strong indicators in the diagnosis of malnutrition, according to the American Society of Parenteral and Enteral Nutrition (ASPEN) malnutrition indicators in preterm and neonatal populations.(Gao et al., 2020; Goldberg & Becker, 2022; Wang et al., 2021) The quality and quantity of preterm nutrition are associated with immediate outcomes such as risks of infections, necrotizing enterocolitis, bronchopulmonary dysplasia, and retinopathy of prematurity.(Koletzko et al., 2021) It is also linked to other morbidity and mortality outcomes later in life and long-term quality of life such as lung function, visual and neurodevelopment, the risk of glucose intolerance and metabolic syndrome.(Koletzko et al., 2021)

The nutrition guidelines for preterm infants are designed to support the growth and development to be similar to the growth rate and composition of weight gain for a normal fetus until birth.(Casirati et al., 2022; Hay, 2018) There are challenges of under and over nutrition at critical stages of development that may have negative consequences in the preterm infant.(Casirati et al., 2022) Rapid catch-up growth during infancy and childhood characterized by an increase in fat storage or increase in body mass index (BMI) and/or increase in weight for length, leads to the development of higher blood pressure, insulin resistance, metabolic syndrome, cardiovascular disease risk, and metabolic syndrome later in life.(Casirati et al., 2022) In assessing weight status, weight for length is recommended for children under 2 years of age and BMI is used for children over 2 years of age.(Corkins, 2017; Goldberg et al., 2018) Preterm infants grow very fast; they can double and triple their birth weight in 2-3 months compared to term infants, who will double their birth weight in 4-6 months.(Koletzko et al., 2021)

Statement of Purpose

This study is designed to examine the impact of a diagnosis of malnutrition utilizing the malnutrition criteria established by the American Society of Enteral and Parenteral Nutrition on the length of stay of preterm infants in a 60-bed, level III neonatal intensive care unit. The findings of this study may lead to improved care practices and outcomes for preterm infants.

Chapter 2 - Review of Literature

Preterm Birth

Preterm birth is defined as a birth before 37 weeks of pregnancy with subcategories based on gestational age according to the World Health Organization (WHO), **Table 2.1**.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a; *World Health Organization Fact Sheet on Preterm Birth*, 2023)

Table 2.1 Prematurity Classification of Gestational Age

Classification of Prematurity	Gestational Age of Infant
Extremely Preterm	< 28-week gestation
Very Preterm	28- <32 weeks gestation
Moderate to late preterm	32- < 37 weeks gestation

(*World Health Organization Fact Sheet on Preterm Birth*, 2023)

A term newborn's average birth weight (BW) is 3500 grams.(Casirati et al., 2022) They are classified in subcategories based on the infant's weight, **Table 2.2**.(Casirati et al., 2022) The smaller the birth weight class of the infant, the more likely it is for complications related to prematurity and an increased possibility of longer length of stay.(Fu et al., 2023)

Table 2.2 Weight Classification on Birth Weight

Birth Weight Classification	**Weight of Infant**
Term infant	3500 grams average
Low birth weight (LBW)	< 2500 grams
Very low birth weight (VLBW)	< 1500 grams
Extremely low birth weight (ELBW)	< 1000 grams
Micropreemie	< 750 grams

(Casirati et al., 2022)

Size for gestational age classification can help guide and anticipate the clinical care needs of the neonate, **Table 2.3**.(Casirati et al., 2022; Damhuis et al., 2021) Gestational age classification gives an understanding based on gestation and comparisons to the norm if the child is at the normal percentile, smaller, or larger than average.

Table 2.3 Gestational Weight for Age Classification

Weight for Age Classification	**Percentile Defined**
Appropriate for gestational age (AGA)	10-90th Percentile weight for age
Small for gestational age (SGA)	< 10th Percentile weight for age
Large for gestational age (LGA)	>90th Percentile weight for age

(Casirati et al., 2022; Damhuis et al., 2021)

Appropriate for gestational age (AGA) classification means that the infants' weight for age percentile is between the 10th and the 90th percentile for their gestational age.(*World Health Organization Fact Sheet on Preterm Birth*, 2023) Approximately 10-20 % of preterm infants' birth weight fall in the AGA classification.(*World Health Organization Fact Sheet on Preterm Birth*, 2023) Small for gestational age (SGA) preterm infants without subsequent recovery growth are likelier to have poor long-term developmental outcomes than infants with growth recovery.(Goldberg & Becker, 2022) SGA infants have significantly less fat mass at birth. (Goldberg & Becker, 2022) The SGA population is expected to have a weight gain velocity above the norm and subsequently should quickly regain their birth weight by day 14.(Goldberg & Becker, 2022)

There is limited data on the expected growth of large for gestational age (LGA) infants. However, reported growth is expected to be slower, creating a downward shift or catch-down trajectory, resulting in weight and length similar to appropriate for gestational age (AGA) infants.(Goldberg & Becker, 2022) The number of days to regain birth weight may not be the best indicator for the diagnosis of malnutrition in the LGA population.(Goldberg & Becker, 2022) The downward trend should be considered when evaluating the weight gain velocity or decline in weight *z*-score that meets the criteria for malnutrition.(Goldberg & Becker, 2022)

Complications of preterm birth are responsible for the most significant proportion of neonatal deaths in the world, accounting for 35% of the world's 3.1 million neonatal deaths per year.(Gidi et al., 2020) Worldwide, 15 million preterm births occur every year, with those less than 32 weeks of gestation at the highest risk of morbidity and mortality.(Gidi et al., 2020) Risk factors for preterm birth include delivering a premature baby in the past, being pregnant with multiples, tobacco use, substance abuse, hypertension, unhealthy weight, diabetes, and short time (less than 18 months) between pregnancies.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) Additionally, pregnancy complications including infections of amniotic fluid and lower genital tract, high blood pressure, diabetes, and problems with the uterus, cervix or placenta can result in preterm birth because the baby must be delivered early.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) An interesting study from 2020 observed lower odds of preterm birth during the Tennessee stay-at-home order issued in response to the COVID-19 compared to the five preceding years.(Harvey et al., 2021) The author suggested that reducing outside-the-home activities may have been associated with less frequent preterm labor.(Harvey et al., 2021)

Undernutrition in preterm infants is associated with serious consequences such as increased mortality and long-term neurodevelopmental, metabolic, and growth disorders.(Gidi et al., 2020) Undernutrition predominantly affects the brain, resulting in poor brain growth and neurodevelopmental delay.(Gidi et al., 2020) Regardless of the degree of prematurity, early postnatal growth (during hospitalization) has been associated with neurological and cognitive outcomes in infancy and preschool-age.(Gidi et al., 2020) Premature infants are prone to nutrient deficiencies due to inadequate stores, inability to feed adequately, and digest due to immaturity of the digestive system . (Gidi et al., 2020) Optimal nutrition of preterm infants is expected to result in growth similar to that of normally growing fetuses of the same gestational age.(Gidi et al., 2020)

Complicating Conditions

Necrotizing Enterocolitis (NEC): NEC is one of the most devastating diseases occurring in neonatal care with a mortality of 20-30%.(Koletzko et al., 2021) It consists of major intestinal dysfunction associated with intestinal ulcerations, particularly in the terminal ileum.(Koletzko et al., 2021) There are detrimental outcomes for survivors including short gut syndrome, cholestatic liver disease and neurological developmental delays.(Koletzko et al., 2021) The management is focused on prevention of disease progression, allowing time for injured bowel to heal and the inflammatory response to subside.(Koletzko et al., 2021) The treatment typically requires bowel rest, parenteral nutrition and slow progression back to enteral feedings.(Koletzko et al., 2021) The length of stay average of preterm infants with NEC was approximately 11.7-15 days longer when compared to infants without NEC.(Shulhan et al., 2017) The financial consequences from a 2011-2012 data evaluation in the United States indicated that the non-surgical cost of NEC is approximately $180,000-$198,000 and it doubles to $313,000 with surgically treated NEC.(Shulhan et al., 2017)

<u>Bronchopulmonary Dysplasia (BPD):</u> BPD remains the most common severe complication of preterm birth and nutrition plays a vital role in lung growth and repair.(Rocha et al., 2021) BPD is a lung disease that causes dependence on oxygen or mechanical ventilation for an extended period.(Rocha et al., 2021) Infants with BPD have an elevated resting energy expenditure, 15-20% higher compared to infants without BPD, which may be responsible for their common growth failure.(Karatza et al., 2022) Respiratory rate is the most critical determinant of energy expenditure.(Bauer et al., 2021)

<u>Congenital Heart Disease: (CHD):</u> Congenital heart disease refers to structural defects that are present at birth, some require surgery, and some are outgrown with age and growth.(Mills et al., 2022) Undernutrition and growth failure are well recognized challenging complications of CHD.(Koletzko et al., 2021) Increased metabolic demand includes increased work of breathing, left-to-right shunts which increase cardiac workload, pulmonary hypertension and increased catecholamine secretion.(Koletzko et al., 2021) Heart failure causes feeding difficulties due to dyspnea and increased fatigue.(Koletzko et al., 2021) Poor cardiac output results in the activation of the renin-aldosterone-angiotensin system, the sympathetic nervous system, cytokine-induced inflammation and possibly signaling cascades that trigger anorexia and malnutrition.(Koletzko et al., 2021) Preoperatively neonates with CHD may have 35-50% above the energy requirement of a normal full–term neonate, 90-120 calories/kilogram/day versus > 150 calories/kilogram/ day.(Koletzko et al., 2021; Mills et al., 2022) Fortifying breastmilk, increasing caloric density of formulas, and providing supplemental tube feedings are common strategies to help meet energy needs.(Koletzko et al., 2021)

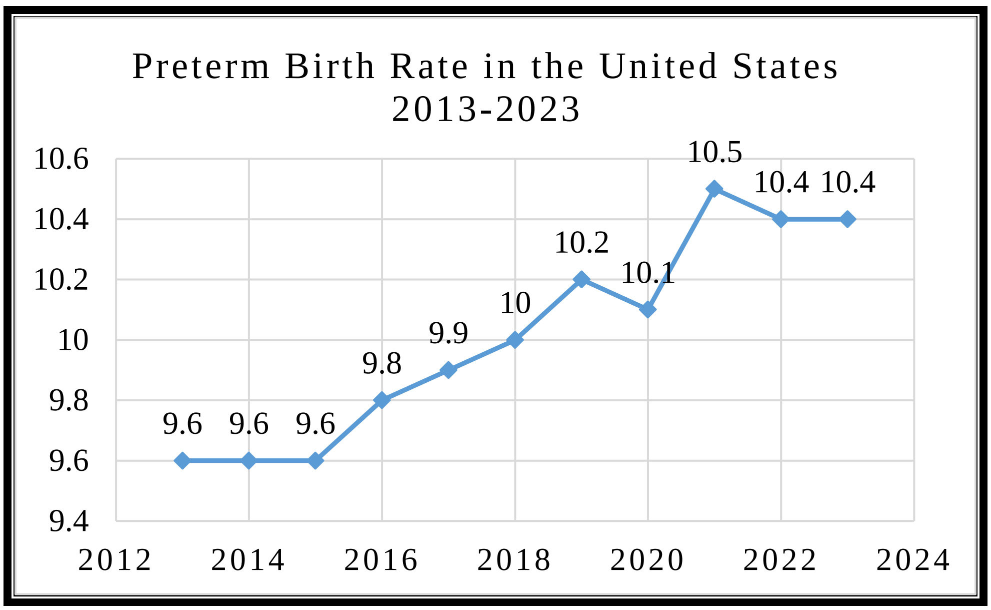
Retinopathy of Prematurity (ROP): Retinopathy of prematurity is an eye condition that primarily affects premature infants, it occurs from atypical blood vessel formation in the retina and, if not taken seriously, often ends in vision impairment and even blindness.(Mandala et al., 2023) Early nutrition interventions, both orally and intravenously, significantly impact the severity and progression of ROP.(Hellström et al., 2024; Mandala et al., 2023) A systemic review by Mandala, et al, 2023, highlights the value of enteral and parenteral nutrition in meeting the nutritional needs of preterm newborns.(Mandala et al., 2023) As the infant's immune system and general health develop, good nutrition protects against ROP.(Mandala et al., 2023)

Intraventricular Hemorrhage (IVH): IVH is bleeding within the brain's ventricles, the fluid-filled spaces that nourish and protect the brain.(Zheng et al., 2023) Very preterm infants have immature nervous systems and are vulnerable to brain injury due to hypoxia, ischemia, infection and other factors.(Zheng et al., 2023) Intraventricular hemorrhage (IVH) is the most common type of brain injury and is associated with death, neurodevelopment delay and cerebral.(Zheng et al., 2023) IVH is graded 1-4 based on the amount of bleeding in the brain's ventricles.(Skinner & Narchi, 2021) In the preterm neonate, the brain is the most metabolically demanding organ, consuming the most significant proportions of energy and nutrient intake for its function and programmed growth and maturation.(Skinner & Narchi, 2021) Weight gain, linear growth and head circumference growth are all markers of nutrition status and are independently associated with long-term neurodevelopment.(Skinner & Narchi, 2021; Zheng et al., 2023) Various bioactive factors contained in breastmilk, particularly colostrum, may have protective effects for IVH in preterm infants.(Skinner & Narchi, 2021)

Prevalence and Incidence of Preterm Birth

Reducing preterm birth is a national public health priority.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) The preterm United States (U.S.) birth rate was 10.4% (380,000 preterm births) in 2022 and 2023, following an increase of 4% from 2020-2021, **Figure 2.1**.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a)

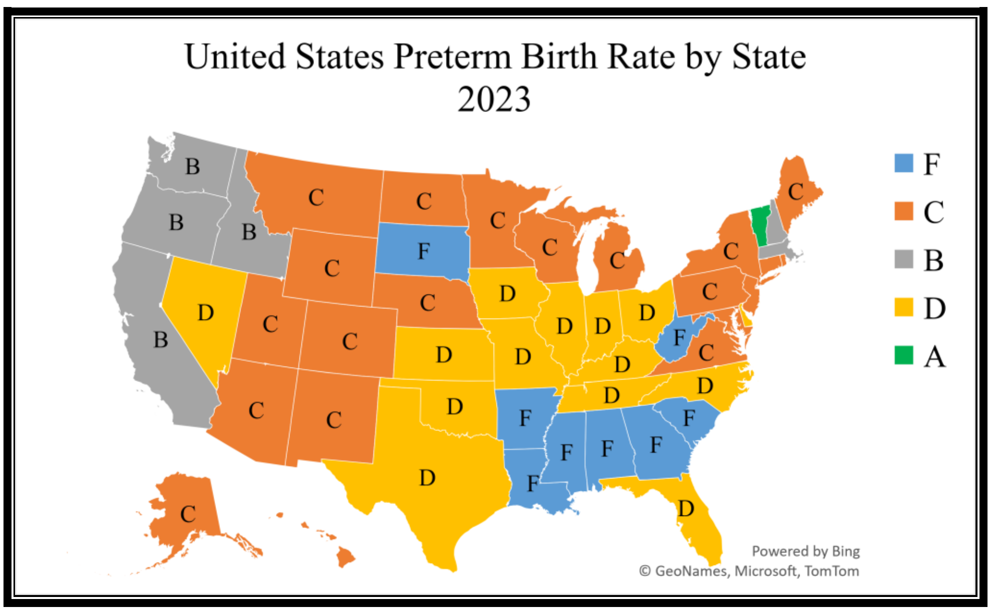
Figure 2.1 Preterm Birth Rate in the United States 2013-2023



(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a)

Meanwhile, eight states and one territory have preterm birth rates that received an F grade: South Carolina 11.6%; Georgia 11.8%, Arkansas 12.1%, Puerto Rico 12.2%, South Dakota 12.5% Alabama 12.9%, West Virginia 13.1%; Louisiana 13.4% and Mississippi with the highest preterm birth rate of all states at 15.0%.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) Overall, the United States received a D+ birth grade and the worst grades occurred in the southern region of the United States.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) Vermont and New Hampshire have the lowest rates of preterm birth in the United States.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) Vermont gets an A grade of 7.7%, and New Hampshire receives a B+ of 8.3%.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) Other states with a B to B- grades were Washington 8.7%, Idaho 8.7%, Oregon 9.0%, Massachusetts 9.1% and California 9.2%.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) **Figure 2.4** gives an overview of the birth grades in each state in the United States.

Figure 2.2 United States Preterm Birth Rate by State 2023



(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a).

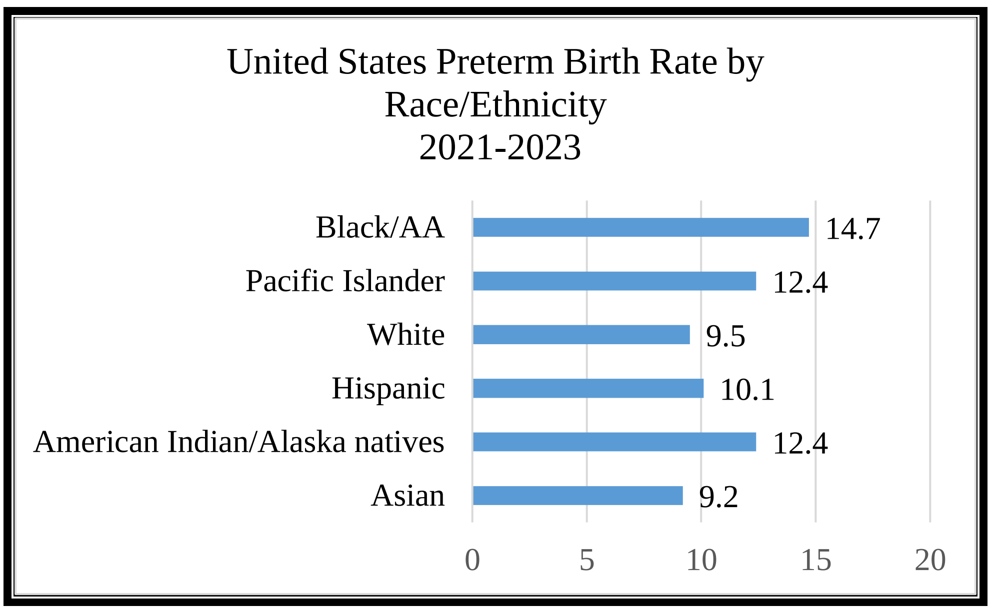
Legend: A= <7.7 to 8.1 B= 8.6-9.2 C= 9.3-10.3 D=10.4-11.4 F 11.5 or greater

Racial and ethnic disparities in preterm birth rates are complex and likely stem from a combination of factors including socioeconomic disparities, chronic stress, access to healthcare, and environmental exposure in Tennessee.(Braveman et al., 2021; National Institutes of Health

(NIH) Office of Dietary Supplements, n.d.-a) Black/AA women in reproductive years have elevated rates of a variety of health conditions that can increase the risk of preterm birth.(Braveman et al., 2021) Adding the reduced access, the health care services, including contraception, control of chronic disease, and preventive services, adds to the risk of preterm births.(Braveman et al., 2021)

There is still a significant difference in racial and ethnic populations' preterm birth rates in the United States (US). In 2023, the rate of preterm birth among non-Hispanic black women (14.7%) was about 50% higher than the rate of preterm birth among non-Hispanic white women (9.5%) or Hispanic women (10.1%), **Figure 2.3**.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) In the United States, the preterm birth rate among babies born to black birthing people is 1.4x higher than the rate among all other babies.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a)

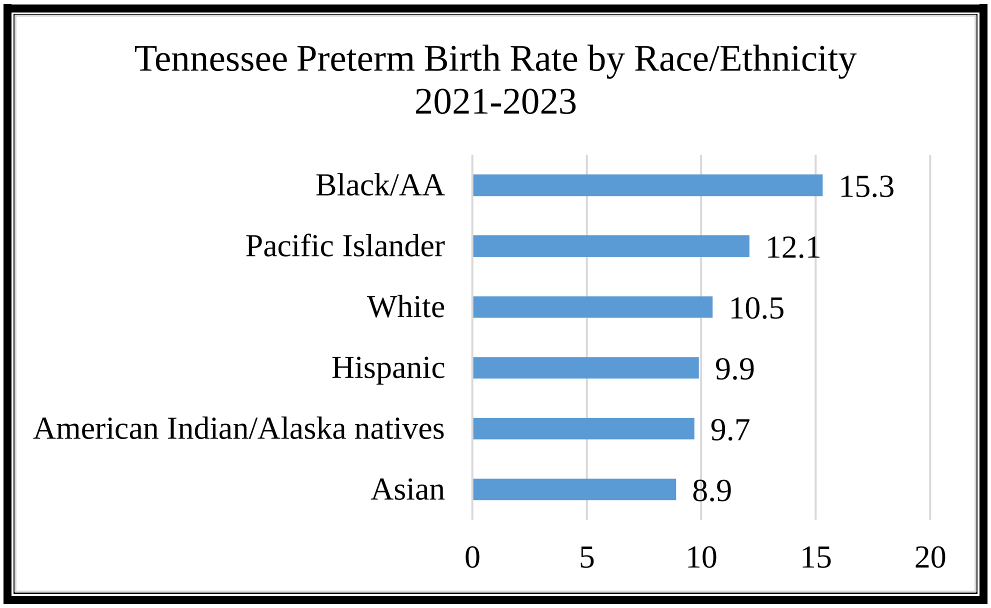
Figure 2.3 United States Preterm Birth Rates by Race/Ethnicity 2021-2023



(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a).

In 2023, 9,078 preterm births or 11.3% of all live births were born preterm in Tennessee.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) The rate of preterm birth in Tennessee is highest for Black/African American (AA) infants (15.3%), followed by Asian/Pacific islanders (12.1%), whites (10.5%), Hispanics (9.9%), and American Indian/Alaska natives (9.7%), **Figure 2.2**.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a)

Figure 2.4 Tennessee Preterm Birth Rates by Race/Ethnicity 2021-2023



(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a)

Malnutrition Indicators and Growth

Special growth charts are used in the NICU to assess growth in preterm infants. The Fenton growth chart is from 22 weeks to 50 weeks gestation and was updated in 2013, to support an improved transition of preterm infant growth monitoring to the WHO charts.(Fenton & Kim, 2013) The World Health Organization (WHO) updated their multicenter growth reference study in 2006, which is considered superior to previous growth surveys.(Fenton & Kim, 2013) These WHO charts are recommended for preterm infants after the infants reach term age, 40 weeks gestation.(Fenton & Kim, 2013) This study will utilize the revised 2013 Fenton preterm growth charts.

Defining Malnutrition in Preterm and Neonates < 30 Days of Life

The diagnosis of malnutrition identifies preterm infants at highest risk of poor growth and neurodevelopmental outcomes.(Goldberg et al., 2018; Goldberg & Becker, 2022) The preferred indicator during the first 2 weeks of life is based on the nutrient intake of the neonate.(Goldberg et al., 2018; Goldberg & Becker, 2022) Once they reach 2 weeks of life, other indicators become useful in diagnosing malnutrition.(Goldberg et al., 2018; Goldberg & Becker, 2022) Primary indicators only require one indicator to diagnose malnutrition, including a weight decline for age z score, weight gain velocity, and nutrition intake.(Goldberg et al., 2018; Goldberg & Becker, 2022) Primary indicators requiring two or more indicators include number of days to regain birth weight, linear growth velocity, and decline in length for age z score.(Goldberg et al., 2018; Goldberg & Becker, 2022) The malnutrition indicators in **Table 2.4** were created using the pediatric consensus statements and a selected literature review and experience of the committee to determine the recommended indicators and cutoffs for mild, moderate and severe malnutrition.(Goldberg et al., 2018)

Table 2.4 Malnutrition Indicators in Preterm and Neonates

Primary Indicators Requiring One Indicator				
Indicator	**Mild Malnutrition**	**Moderate Malnutrition**	**Severe Malnutrition**	**Use of Indicator**
Decline in weight for age z score	Decline of 0.8-1.2 SD	Decline of > 1.2-2.0 SD	Decline of > 2.0 SD	Not appropriate the first 2 weeks of life.
Weight gain velocity	< 75% of expected rate of weight gain to maintain growth	< 50% of expected rate of weight gain to maintain growth	< 25% of expected rate of weight gain to maintain growth	Not appropriate the first 2 weeks of life.
Nutrient Intake	≥ 3-5 consecutive days protein/energy intake ≤75% of estimated needs	≥ 5-7 consecutive days protein/energy intake ≤75% of estimated needs	≥ 7 consecutive days of protein/energy intake ≤75% of estimated needs	Preferred indicator during the first 2 weeks of life.

Primary Indicators Requiring Two or More Indicators				
Indicator	**Mild Malnutrition**	**Moderate Malnutrition**	**Severe Malnutrition**	**Use of Indicator**
Days to regain birth weight	15-18	19-21	>21	Use in conjunction with nutrient intake
Linear growth velocity	< 75% of expected rate of linear gain to maintain expected growth rate	< 50% of expected rate of linear gain to maintain expected growth rate	< 25% of expected rate of linear gain to maintain expected growth rate	Not appropriate for the first 2 weeks of life. May be deferred in critically ill, unstable infants. **
Decline in length for age z score	Decline of 0.8-1.2 SD	Decline of > 1.2-2.0 SD	Decline of > 2.0 SD	Not appropriate for the first 2 weeks of life. May be deferred in critically ill, unstable infants. **

******** *Use in conjunction with another indicator when accurate length measurement is available.*
Abbreviations: SS, Standard deviation
(Goldberg et al., 2018)

Primary Indicators Requiring One Indicator

Decline in Weight for Age *z*-score: Measurement of decline in weight for age *z*-score should compare a weight gain rate consistent with their birth *z*-score and not with the z-score that occurs after their post-natal diuresis.(Goldberg et al., 2018) Therefore, the birth weight should be used as the initial point in the calculations.(Goldberg et al., 2018) This indicator is inappropriate for the first 2 weeks of life related to the postnatal diuresis.(Goldberg et al., 2018)

Growth Velocity: Infant weight loss in the first week of life ranges from 8-15% with more significant losses in smaller and premature infants related to water losses.(Koletzko et al., 2021; Texas Children's Hospital, 2022) The expectation is to maintain < 10% of weight loss and that the infant will regain birth weight by the 14th day of life.(Koletzko et al., 2021) In most NICU's the infants are weighed daily and the length and head circumference are measured weekly.(Koletzko et al., 2021) When presenting growth data as weight gain velocity over a set number of days, the optimum period seems to be a time interval of 5-7 or more days, shorter periods are less precise and include excessive variations.(Fenton et al., 2019)

Table 2.5 Average Growth Velocity by Age Group

Age	Weight (grams)	Height (cm/week)
Preemie < 2 kg	15-20 g/kg/day	0.8-1.1 cm/week
Preemie > 2 kg	20-30 g/day	0.8-1.1 cm/week
0-4 months	23-34 g/day	0.8-0.93 cm/week

Abbreviations: kg, kilograms; g/kg/day, grams per kilogram per day; g/day, grams per day
cm/week= centimeters per week
(Texas Children's Hospital, 2022)

,

The published growth goal in **Table 2.5** is based on attaining growth comparable to fetal growth. (Texas Children's Hospital, 2022) This growth rate may underestimate growth velocity needed and maybe insufficient to prevent postnatal growth retardation.(Goldberg et al., 2018) Some NICUs may express weight gain in grams per kilogram per day, it is recommended that grams per day be used to identify malnutrition.(Goldberg & Becker, 2022) It is best to establish individual weight gain goals based on an online preterm growth calculator, such as www. Peditools.org, that provides the weekly weight gain needed to maintain current growth metrics.(Chou et al., 2020; Goldberg & Becker, 2022)

Nutrient Needs

Energy Needs: A minimum energy intake must be provided to prevent breakdown of endogenous stores while accounting for energy expenditure and growth.(Koletzko et al., 2021) Calorie intake should be individualized based on clinical status and growth.(Koletzko et al., 2021) Depending on a patient's energy expenditure, calorie needs may be increased or decreased.(Koletzko et al., 2021) Infants with diagnosed BPD generally have a higher energy need of 120-150 calories per kilogram per day (calories/kg).(Karatza et al., 2022) Preoperatively some neonates with diagnosed CHD may require > 150 calories/kg for optimal growth.(Koletzko et al., 2021; Mills et al., 2022) **Table 2.6** defines the general expected calories per kilogram of weight based on gestational age.

Table 2.6 Energy Needs

ASPEN	Calories per kilogram per day
Preterm < 34 weeks	85-130 calories per kilogram per day
Late Preterm 34-<37 weeks	100-135 calories per kilogram per day
Term > 37 weeks	90-120 calories per kilogram per day

Abbreviations: ASPEN- American society of enteral and parenteral nutrition
(Goldberg et al., 2018)

Protein Needs: Parenteral amino acid supply for very preterm infants can start directly from birth at a rate of 1.5-2.5 g/kg/day safely and can be increased to 3.5 g/kg/day in the next few days.(Koletzko et al., 2021) Enterally fed very preterm infants should receive at least 3.5-4.0 g protein/kg/day and sufficient macronutrients and micronutrients.(Koletzko et al., 2021) Infants with BPD may have protein needs of 3.5-4.0 g/kg/day for infants weighing 1000-1800 grams and 4.0-4.5 g/kg/day for those weighing less than 1000 grams.(Karatza et al., 2022; Rocha et al., 2021) The general expected grams of protein per kilogram of weight are defined in **Table 2.7** based on gestational age and subcategory for infants with BPD.

Table 2.7 Protein Needs

ASPEN:	**Protein grams per kilogram**
< 34 weeks	3-4.5 grams per kilogram
34-<37 weeks	3-3.5 grams per kilogram
Term > 37 weeks	2.5-3.0 grams per kilogram
BPD: < 1000 grams weight	4.0-4.5 grams per kilogram
BPD: 1000-1800 grams weight	3.5-4.0 grams per kilogram

Abbreviation: ASPEN, American society of parenteral and enteral nutrition
(Goldberg et al., 2018; Koletzko et al., 2021)*0*

Fluid Needs: Term infants can lose up to 10% of their birth weight, and preterm infants can lose up to 15% due to fluid losses.(Chawla et al., 2008) Fluid needs can be variable to maintain an infant's fluid and electrolyte balance.(Chawla et al., 2008) Infants with BPD should receive restricted fluid intake of 135-150 milliliters (mL) per kilogram (kg).(Karatza et al., 2022) Infants with CHD are at risk of congestive heart failure (CHF) and fluid intake in these infants may be restricted to 120-140 mL/kg/day.(Karatza et al., 2022) Fluid needs based on weight and medical condition are defined in **Table 2.8**.

Table 2.8 Fluid Needs

Birth weight	➢ Day 7 of life
< 1000 grams	160 milliliter per kilogram per day
1000 to >1500 grams	150 milliliter per kilogram per day
BPD	135-150 milliliter per kilogram per day
CHD	120-140 milliliter per kilogram per day

Abbreviations: BPD, Bronchopulmonary dysplasia; CHD, Congenital heart disease
(Karatza et al., 2022; Koletzko et al., 2021; Rocha et al., 2021)

Primary Indicators Requiring Two or More Indicators

Days to Regain Birth weight: Following birth, water loss occurs with a resulting physiological decrease in body weight.(Koletzko et al., 2021) The general expectation is that the difference in body weight remains less than 10% and is regained by 14 postnatal days.(Koletzko et al., 2021) It is a strong indicator of malnutrition in combination with another appropriate indicator such as inadequate nutrient intake.(Goldberg & Becker, 2022)

Linear Growth Velocity: The relationship between length, brain development, and neurodevelopmental outcome is well established.(Goldberg et al., 2018) The association of faltering linear growth and stunting with a similar fat mass suggests that a decline of length z score obtained from accurate length measurements is a valuable indicator of malnutrition in preterm infants.(Goldberg et al., 2018) Linear growth depends on fat-free mass accretion and adequate protein and micronutrient intake.(Koletzko et al., 2021) The linear growth assessment may be used with nutrient intake to identify malnutrition.(Goldberg et al., 2018) The expert committee agreed that linear measurements reflecting lean body mass accretion were necessary and recommended using them with another indicator when accurate length measurements are available.(Goldberg et al., 2018)

Decline in length for age *z*-score: Measurement of decline in length for age *z*-score should compare a linear growth rate consistent with their birth *z*-scores and not with the z-score that occurs after their post-natal diuresis.(Goldberg et al., 2018) Therefore, the birth length should be used as the initial point in the calculations.(Goldberg et al., 2018) This indicator is inappropriate for the first 2 weeks of life.(Goldberg et al., 2018)

Micronutrients

Requirements for optimal nutrition, especially micronutrients, are not well defined for premature infants.(Bhatia et al., 2013) It is known that most fetal mineral accretion occurs during the third trimester.(Bhatia et al., 2013; Kleinman & Greer, 2020) Neonatal nutritional disorders can occur, such as metabolic bone disease and neonatal anemias.(Kleinman & Greer, 2020; Koletzko et al., 2021) Important nutrients to consider in the preterm infant include calcium, phosphorus, magnesium, vitamin D, iron, zinc, and copper.(Kleinman & Greer, 2020; Koletzko et al., 2021) The formation of bone matrix requires adequate calcium, phosphorus, magnesium, vitamin D, as well as adequate protein and energy.(Kleinman & Greer, 2020; Koletzko et al., 2021; National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-b, n.d.-e, n.d.-f, 2022)

Calcium, magnesium, and phosphorus are prominently involved in skeletal development, but all three also play a critical role in cellular function, especially metabolism.(Bhatia et al., 2013; Kleinman & Greer, 2020; National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-b, n.d.-e, 2022) Because of the high accretion of calcium and phosphorus in the third trimester of pregnancy, preterm birth is associated with a deficiency of these minerals.(Koletzko et al., 2021; National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-b, n.d.-e) Magnesium has rapid accretion beginning in the fifth month of gestation and therefore has less risk of a deficit in the preterm infant.(Koletzko et al., 2021; National Institutes of Health (NIH) Office of Dietary Supplements, 2022) Vitamin D is critical for infant bone mineralization, supplementation of 400 IU/day and up to 1000 IU/day is recommended in preterm infants.(Koletzko et al., 2021; National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-f)

Iron is a necessary nutrient for brain development and iron deficiency anemia in infants is associated with poor neurodevelopment.(Koletzko et al., 2021; National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-d) There is no mechanism for excretion of iron from the body, making excessive iron supplementation risky because it can contribute to increased risk of infections, cause poor growth, and interact with the absorption and metabolism of other nutrients.(Koletzko et al., 2021)

Copper deficiency is generally associated with copper-free parenteral nutrition support. Copper deficiency can contribute to anemias.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-c) The fetus stores 70% of its body reserve of copper and zinc in the last trimester, indicating that the premature infant has low reserves of copper and zinc at delivery.(Koletzko et al., 2021; National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-c; Sinha et al., 2022) Zinc is an essential nutrient for multiple physiologic functions and plays a vital role in growth and prevention of diarrhea.(National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-g; Sinha et al., 2022) Preterm infants have low body stores of zinc because of reduced time for placental transfer, low intake, and excessive endogenous losses.(Sinha et al., 2022) **Table 2.9** compares the nutrition needs for selected vitamins and minerals between the milligram per kilogram per day for preterm infants, and the milligram per day expected needs for term infants.

Table 2.9 Vitamin/Mineral Enteral Recommendations

Nutrient	Preterm enteral recommended daily intakes	Term infant recommended daily intakes
Calcium	120-220 mg/kg/day	200 mg/day
Phosphorous	70-120 mg/kg/day	100 mg/day
Magnesium	8-15 mg/kg/day	30 mg/day
Vitamin D	400-1000 IU/day	400 IU/day
Iron	1-3 mg /kg/day, dependent on birth weight	0.27 mg/day
Zinc	2-3 mg/kg/day	2 mg/day
Copper	100-230 mg/kg/day	200 mg/day

Abbreviations: mg/kg/day, milligram per kilogram per day; mg/day, milligram per day;
IU, International unit
(Koletzko et al., 2021))

Emotional Concerns for the Parents and Caretakers

Mothers and fathers of infants born very preterm experience elevated levels of depressive, anxiety and post-traumatic stress symptoms compared with parents of term-born babies.(Treyvaud & Brown, 2022) Parents have described their NICU experience as an emotional "roller coaster" because they experience a variety of emotions, including feeling overwhelmed, sad, stressed, tired, relieved, happy, angry and helpless.(Grunberg et al., 2019) One study showed that approximately one third of mothers and fathers experienced post-traumatic stress symptoms in the early months after very preterm birth, with almost one fifth of parents continuing to report post-traumatic stress symptoms two years after the birth.(Gray et al., 2004) Symptoms of depression and anxiety in parents of babies born preterm also appear to remain higher across childhood and adolescence compared with parents of term-born babies.(Treyvaud & Brown, 2022) Parents of infants with lower gestational ages and birth weights reported increased stress, especially within the first three years compared to parents of term and normal birth weight infants.(Grunberg et al., 2019) Factors such as higher socioeconomic disadvantage early in life and severe neonatal brain abnormalities have also been associated with increased risk for later mental health difficulties in these children.(Treyvaud & Brown, 2022) The results suggest that the NICU experience and subsequent stressors are crucial elements that influence family adjustment in the present and the future.(Grunberg et al., 2019) The infants' complex medical needs and families' stress and desire for answers that are yet to come, and pressures on the NICU staff are enormous.(Grunberg et al., 2022) The high rates of NICU admissions (7-15% of US annual births), parenteral distress (40-50%) and staff burnout (30-50%) emphasize the need for effective and sustainable psychosocial services for parents and the staff – the caretakers of these tiny medically complex patients.(Grunberg et al., 2022) Integrating mental health services for families in the NICU as well as screening measures and the provision of resources following discharge are pertinent to ensure optimal development for NICU children and their families.(Grunberg et al., 2019)

Financial Concerns

Preterm birth is the leading cause of neonatal mortality and a significant cause of both short and long term infant morbidity and disability.(Beam et al., 2020) The economic impact of preterm birth is substantial.(Beam et al., 2020) The societal economic burden in the United States was at least 26.2 billion annually, or $51,600 per preterm infant in 2005 based on a 2007 comprehensive study from the Institute of Medicine (IOM).(Behrman et al., 2007) Healthcare spending is an important topic and preterm infants have some of the highest healthcare expenditures of any patient population.(Beam et al., 2020) The financial burden related to the cost of care for a preterm infant is another concern and area of stress for the parents.(Beam et al., 2020) In a retrospective cohort study of insured individuals from 2008-2016, the average 6 month expenditure for a preterm infant was $76,153 compared to the average 6 month expenditure for a normal birth weight infant $

6743.(Beam et al., 2020) In another study 2010-2017, the median cost was $ 77,132.90 per NICU admission.(Rolnitsky et al., 2023) The average first year medical costs, including inpatient and outpatient care, were about 4 times greater for preterm $49,140 than for term infants $13,024 according to an analysis of cost with common preterm diagnoses during a NICU stay.(Waitzman et al., 2021) Malnutrition increases the costs associated with the care of patients.(Corkins, 2017) The 2010 Healthcare cost and Utilization Project (HCUP) found that patients coded as having malnutrition had a longer mean length of stay (9.7 vs 3.8 days).(Abdelhadi et al., 2016) This increased length of stay resulted in a higher mean cost for the stay of $55,255 vs $17,309.(Corkins, 2017) Diagnosing and then treating malnutrition is essential because in the end, it is the best care for the patients, with benefits extending to multiple levels.(Corkins, 2017)

Length of Stay

The most critical factors that affect the length of stay for preterm infants include birth weight, gestational age, sepsis, NEC, BPD, CHD and ROP.(Fu et al., 2023; Mowitz et al., 2019) The analysis of 12,660 infants between 23 and 30 weeks gestational age in 2005-2017, the median LOS was 42 days.(Rolnitsky et al., 2023) In a 2024 analysis of very low birth weight neonates (<1500 grams) the median length of stay was 24 days.(Mehretie et al., 2024) Data from the Healthcare Cost and Utilization Project (HCUP) in the United States in 2011 indicated that the average LOS for all live hospital births of 3.4 days, preterm 14.3 days, low birth weight 17.7 days, weight > 1500 grams 10.9 days, weight < 1500 grams 42.6 days, and respiratory distress syndrome 31.3 days.(Kowlessar et al., 2011)

Influences of Early Nutrition and NICU Feeding Practices

The feeding of preterm infants poses a challenge to the healthcare team with their unique nutritional requirements that make an individual approach tailored to their clinical status and degree of prematurity.(Silveira et al., 2023) The initiation of parenteral nutrition support, including amino acids, is fundamental for all infants that cannot tolerate full enteral feedings.(Hay, 2018) The brain is the most metabolically active organ in premature infants, which demands a substantial supply of nutrients for optimal growth and function development.(Silveira et al., 2023) The infants' nutrition status, including growth, must be monitored daily with the need for fortified breast milk and/or concentrated formulas to meet the high nutrition needs of the infant to promote optimal growth to prevent malnutrition and potentially reduce LOS in the NICU.(Silveira et al., 2023)

Feeding practices in the NICU are critical in determining an infant's readiness for discharge.(Ilahi et al., 2023) Oral feeding is a complex process and the foundation for optimal feeding begins before an infant attempts the first oral feed.(Ilahi et al., 2023) One approach used in the NICU is infant driven feeding (IDF). IDF is a validated, structured and standardized feeding method consisting of three key behavioral assessments: feeding readiness, feeding quality, and caregiver support.(Ilahi et al., 2023) Potential benefits of using the IDF model include faster attainment of full oral feeds and potential impact of LOS. One possible concern is the impact on neonatal weight gain, but the researcher's data on this remain mixed.(Ilahi et al., 2023) Overall, NICU teams are challenged to provide optimal nutrition support tailored to the individualized infant to meet their nutrition needs for health and development within the minimum number of hospital days possible.

Chapter 3 - Methodology

Problem Statement: Does the diagnosis of malnutrition in the preterm infant based on the American Society of Parenteral and Enteral Nutrition malnutrition indicators in preterm populations(Goldberg et al., 2018) impact the length of stay? The included population was infants born at 24 weeks but < 37 weeks gestational age with a length of stay in the NICU > 27 days. The intervention/indicator was the malnutrition indicators in the preterm population, **Table 2.4**. The comparison group consisted of infants who met the criteria for malnutrition, and the control group consisted of infants who did not meet the criteria for malnutrition. The outcome question in this study is, do preterm infants with malnutrition have an increased risk of longer LOS compared to the control group?

Methods: Evaluation of malnutrition indicators was based on the Goldberg indicators of malnutrition for preterm and neonates.(Goldberg et al., 2018) The primary indicators requiring only one indicator for malnutrition include decline in weight for age z-score, weight gain velocity, and nutrition intake. Decline in weight for age z-score was assessed by comparing the weight for age z-score at birth to the weight for age z-score at 28 days after birth. The NICU staff generally weigh the infant at the same time daily and record the amount in grams in the electronic medical record. Weight gain velocity was compared to the weight on the day of life (DOL) which achieved a return to birth weight to the day 28 weight. The daily grams per kilogram (g/kg) was calculated to compute the weight gain velocity average. This was compared to the peditools calculated growth velocity needed to maintain birth *z*-score. Nutrient intake compared to the actual intake in milliliters and calories per kilogram achieved to the goal per physician recommendations from the regain of birth weight day of life through the 28^{th} DOL and assessed. The indicators were < 75%

of estimated nutrient needs for ≥3-5 days consecutively for mild malnutrition, < 50% of estimated nutrient needs for ≥5-7 days consecutively for moderate malnutrition and < 25% of estimated nutrient needs for ≥ 7 consecutively for severe malnutrition.

The primary indicators requiring two indicators for malnutrition include days to regain birth weight, linear growth velocity, and decline in length for age z score.(Goldberg et al., 2018) Days to regain birth weight should be used in conjunction with nutrient intake to indicate level of malnutrition.(Goldberg et al., 2018) Days to regain birth weight is the DOL the patient achieved the return to birth weight.(Goldberg et al., 2018) When accurate length measurement is available, linear growth velocity should be used with another indicator.(Goldberg et al., 2018) Linear growth velocity (GV) compared the length from the birth length to the day 28 length / 4 for the weekly average linear GV. This was compared to the peditools calculated GV needed to maintain birth *z*-score for length. Decline in length for age should be used in conjunction with another indicator when accurate length measurement is available. Decline in length for age *z*-score compared to the birth length *z*-score to the day 28 z-score. Levels of malnutrition were determined based on the measurement outcomes and the Goldberg indicators of malnutrition for preterm and neonates.(Goldberg et al., 2018)

Overview: This retrospective chart review research study in a single center, 60-bed, level III NICU, aims to evaluate the relationship between a diagnosis of malnutrition during the first 28 days of life and the length of stay in the NICU.

Ethics: Kansas State University and the medical center approved retrospectively reviewing the data from admissions to the NICU from July 2024 through December 2024.

Data Source and Subject Criteria: Data used for the study were collected from the electronic medical record (EMR). This study qualifies for a waiver of consent as this project is retrospective and no identifying data were collected. In addition, approval was granted by the Kansas State Institutional Review Board for Research Involving Human Subjects- IRB proposal # 12179.

Measures: Growth parameters, growth velocity, and nutrient intake of the included infants were assessed and classified as having no malnutrition or having malnutrition. Further, the malnutrition was classified as no malnutrition, mild, moderate, or severe using the criteria developed by Goldberg et al.(Goldberg et al., 2018) The results were compiled as having no malnutrition and having malnutrition for the statistical review. The 2013 Fenton growth chart for preterm infants was used through the Peditools electronic growth chart calculator to determine the weight and length *z* score for the infants assessed.(Chou et al., 2020; Fenton & Kim, 2013)

Subject Characteristics: All infants were included if they met the following inclusion criteria: 24 to < 37 weeks gestational age at birth, LOS in the NICU of > 27 days, birth weight > 600 grams and <2500 grams. They were excluded for the following factors: < 24 weeks or =>37-week gestation age at birth, LOS < 28 days, birth weight < 600 grams and > 2500 grams, admission/transfer to institution NICU at > 48 hours past birth, still admitted at the time of evaluation, discharge to higher level of care facility, death. Population characteristics were collected to include: sex, race/ethnicity, prenatal care, gravida, insurance, gestational age according to the WHO, prenatal risks: age, substance abuse, chronic hypertension, preexisting diabetes, unhealthy weight, previous preterm deliveries, multiples, less than 18 months between deliveries, pregnancy complications: pregnancy induced hypertension/preeclampsia, pregnancy induced diabetes, infections of amniotic fluid or lower genital track, problems with uterus, cervix or placenta.(Casirati et al., 2022; National Institutes of Health (NIH) Office of Dietary Supplements, n.d.-a) Complications of the infant post-delivery included: hypoglycemia, BPD, CHD, NEC, IVH stages 3-4, immature retina and ROP stages 3-4. Birth size classification, SGA, AGA, and LGA were determined using the birth percentiles obtained in the Fenton growth charts using the Peditools electronic growth chart calculator.(Casirati et al., 2022; Chou et al., 2020; Damhuis et al., 2021; Fenton & Kim, 2013) Birth class is based on the birth weight of the infant.(Casirati et al., 2022) Birth weight, lowest weight day of life and % weight loss from birth weight were obtained using the hospital electronic health record.

Data Collection and Analysis

Thorough data collection and analysis were conducted using an Excel spreadsheet. Statistical analyses were performed, with a significance level of $p < .05$. Descriptive statistics were calculated to comprehensively describe the characteristics of the total study population, including means, and standard deviations for malnutrition, percent weight loss from birth weight, regain weight day of life, birth weight grams, gestational age, and length of stay. Proportions, percentiles and means were calculated to include gender, race/ethnicity, prenatal care, type of insurance, birth weight class, size class gestational age, gestational age class, prenatal risks, pregnancy complications and preterm complications, ensuring a comprehensive understanding of the data.

A t-test: two-sample assuming unequal variances was used to compare the mean length of stay in infants with malnutrition and infants without malnutrition, two independent groups, assuming that the population has equal variances. The same t-test was used to compare the infant's length of stay of infants with malnutrition and BPD to those infants with malnutrition and not having BPD. Descriptive statistics were also completed in each group to identify the standard deviation and confidence level.

Chapter 4 - Results

Study Population

The study population, consisting of 53 patient records, was carefully selected based on the planned inclusion and exclusion criteria. The characteristics of the 53 patients listed in **Table 4.1** provide significant insights. There was a mean birth gestational age of 29.76±- 2.8 weeks and a mean birth weight of 1321 ± 472.61 grams. The birth weights were classified as follows: 11% of the patients were SGA, 79 % were AGA, and 10% were LGA. Of the study population, 49% were White, 36% were Black/AA, 13% were Hispanic/Latino and 2% were Asian, highlighting the diversity of the sample and the importance of considering racial disparities in neonatal care.

Table 4.1 Characteristics of the Total Study Population (N=53)

Variable	Result %, SD ±	Average LOS days	NO malnutrition, average LOS	Malnutrition, average LOS
Gender				
Male	26 (49%)	56.7±25.3	13, 43.5±11.5	13, 69.8±28.9
Female	27 (51%)	62.3±27.8	12, 56.2±21.8	15, 67.2±31.7
Race/Ethnicity				
White	26 (49%)	52.3	12, 44±11.8	14, 59.4±24.2
Black/AA	19 (36%)	72.2	9, 60.9±23.4	10, 82.3±38.8
Hispanic/Latino	7 (13%)	55.1	3, 42±5.6	4, 65±29.2
Asian	1 (2%)	37	1, 37	0, 0
Prenatal care				
Yes	49 (92%)	58.3	23,49.4±18.6	26, 66.1±29.7
No	3 (6%)	81.7	1, 48	2, 98.5±10.6
Unknown	1 (2%)	55	1, 55	0, 0
Insurance				
Private	29 (55%)	65.6	9, 47.6	15
Medicaid	24 (45%)	54.4	16, 50.8	13
Birth weight class				
LBW < 2500	17 (32%)	40.3	12, 39.1±7.9	5, 43.2±14.6
VLBW < 1500	22 (42%)	52.7	8, 47.5± 10.4	14, 55.6±18
ELBW < 1000	10 (19%)	88	5, 78.2± 15.4	5, 97.8±27.5
Micropremie < 750	4 (7%)	108	----	4, 108±2.94

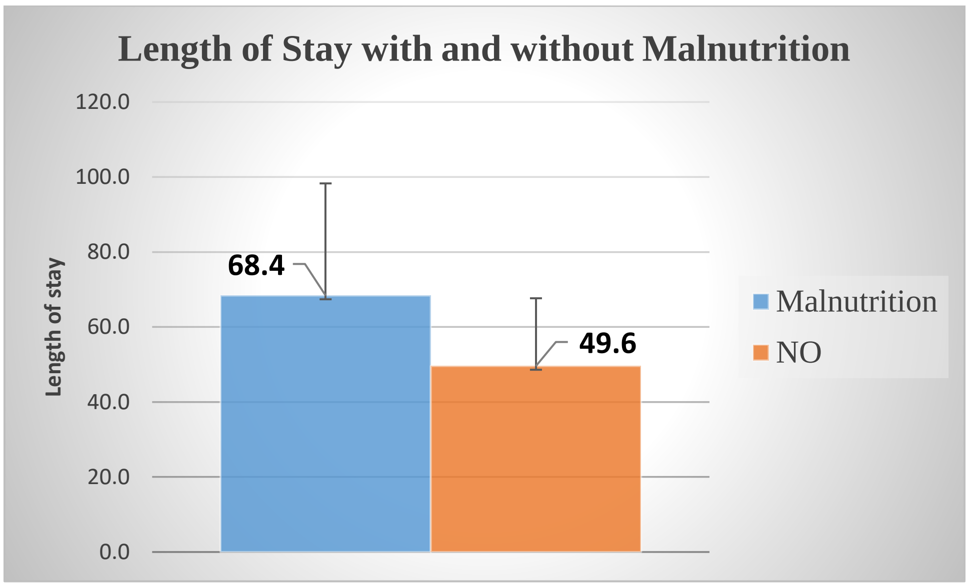
Variable	Result %, SD ±	Average LOS days	NO malnutrition, average LOS	Malnutrition, average LOS
Size class GA				
SGA	6 (11%)	51.5	4, 41.75±4.4	2, 71±48.1
AGA	42 (79%)	60.8	16, 48.7±29.6	26, 68±29.6
LGA	5 (10%)	58.8	5, 58.8±21.1	0,0
Birth weight age				
Extremely preterm < 28 weeks	13 (25%)	96	4, 83±12.4	9, 102±19
Very preterm 28-32 weeks	30 (57%)	52.2	13, 48.2±9.7	17, 55.2±17.3
Moderate/late preterm 32-36 weeks	10 (19%)	33.8	8, 35.3±3.69	2, 28
Prenatal Risks				
Substance abuse	5 (9%)	47.8	3, 40.7	2, 58.5
CHTN	9 (17%)	57.6	3, 50.7±23.7	6, 61±23.4
Unhealthy weight	2 (4%)	42	0, 0	2, 42
DM	2 (4%)	57.5	1, 70	1, 45
Previous PTD	5 (9%)	69.2	1, 46	4, 75
Multiples	8 (15%)	63.4	4, 49.3±19	4, 77.5±52.2
Advanced maternal age	9 (17%)	57.8	2, 53.5±23.3	7, 59±19.9
Teen	1 (2%)	106	0, 0	1, 106
Pregnancy Complications				
Infections of the Amniotic fluid or the lower genital tract	19 (36%)	67.6	8,49.9±23.9	11, 80.5±31.5
HTN	22 (42%)	57.3	9, 56.8±19.7	13, 57.6±26.3
DM	3 (6%)	50.7	2, 53.5	1, 45
Problems with uterus, cervix or placenta	16 (30%)	64.9	10, 50.2±28.9	6, 89.3±38.6
Preterm Complications				
Hypoglycemia	10 (19%)	55.1	6, 48	4, 65.8
BPD	10 (19%)	88.3	2, 79±14.1	8, 90.6±19.6
CHD	21 (40%)	73.3	9, 56.6±16.4	12, 85.8±33.4
IVH: stage 3-4	2 (4%)	97	0,0	2,97
Immature retina	33 (62%)	71.6	12, 61.4	21, 77.5
ROP: stage 3-4	1 (2%)	91	0, 0	1, 91
NEC	1 (2%)	88	0,0	1, 88
Length of Stay				
Count	53		25	28
Average LOS	59.5 +/-		49.6 +/-	68.4 +/-
SD	26.6		18.1	29.9
Min-max	28-145		28-97	28-145

Abbreviations: LOS, length of stay; Black/AA, Black African American; LBW, low body weight; VLBW, very low body weight; ELBW extremely low body weight; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age; CHTN, chronic hypertension; DM, diabetes mellitus; PTD, preterm delivery; HTN, hypertension; BPD, bronchopulmonary dysplasia; CHD, congenital heart disease; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity; SD, standard deviation

Malnutrition

Of the 53 subjects, 25 did not meet the criteria for malnutrition with a LOS of 49.6 ±18.1 days and 28 patients met the criteria for either mild or moderate malnutrition with a LOS of 68.4 ± 29.9, **Figure 4.1.** The longest LOS in the study was 145 days.

Figure 4.1 Average Length of Stay with and without Malnutrition



During the initial data collection process, the infants were classified based on degree of malnutrition, mild, moderate, or severe. Only one infant was considered in the severe category and was not included in the study related to severe medical complications requiring transfer to a higher-level facility for continuing care. Of the total number of subjects N=53, 25 were found to have no malnutrition with a LOS of 49.6±18.1 days, 19 were found to have mild malnutrition with a LOS of 57.05±24.02 days and 9 were found to have moderate malnutrition with a LOS of 92.33±27.4 days. The count, mean and SD are described between the groups and subjects as a whole in **Table 4.2**. The upward trend of LOS with the increase of malnutrition severity is shown in **Figure 4.2**.

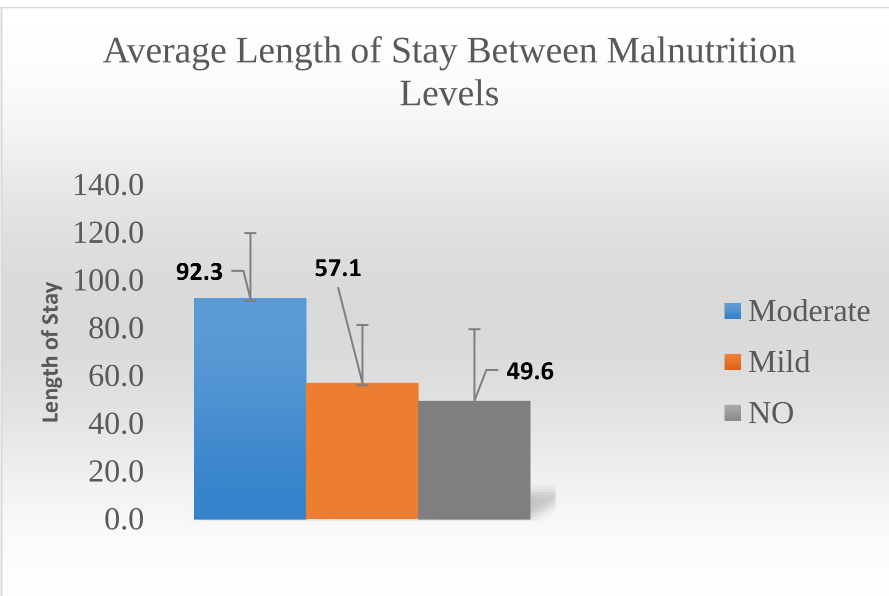
For the remainder of the study and statistical purposes, the study focused on malnutrition or no malnutrition, combining all mild and moderate malnutrition in one category.

Table 4.2 Average Length of Stay, No Malnutrition, Mild Malnutrition, and Moderate Malnutrition

	Total Subject	NO Malnutrition	Mild Malnutrition	Moderate Malnutrition
Count Mean LOS, SD	53 59.5 ± 26.6	25 49.6 ±18.1	19 57.05±24.2	9 92.33 ±27.4

Abbreviations: LOS, length of stay; SD= standard deviation

Figure 4.2 Average Length of Stay, Moderate Malnutrition Mild Malnutrition, and No Malnutrition



The expected goals for infants are to lose < 10% of birth weight related to the post-natal diuresis and to regain the birth weight by the 14th DOL.(Koletzko et al., 2021) In this study, the subjects had an average weight loss of 7.75%±5.07 and an average DOL that the birth weight regained of 8.85 ± 4.2 days. **Table 4.3** shows the mean, SD, and range of %weight loss from birth weight, the DOL the infant regained to their birth weight, the average birth weight grams and the average gestational age of the population.

Table 4.3 Mean and Standard Deviation of Selected Values

Population Variables	Mean, Standard Deviation, and Range
Percent loss from birth weight	7.75±5.07 (0-23)
Birth weight was regained on day of life	8.85 ± 4.2 (0-17)
Birth weight grams	1321 ± 472.61 (675-2401)
Gestational age	29.76 ± 2.8 grams (24-34.14)

Gender

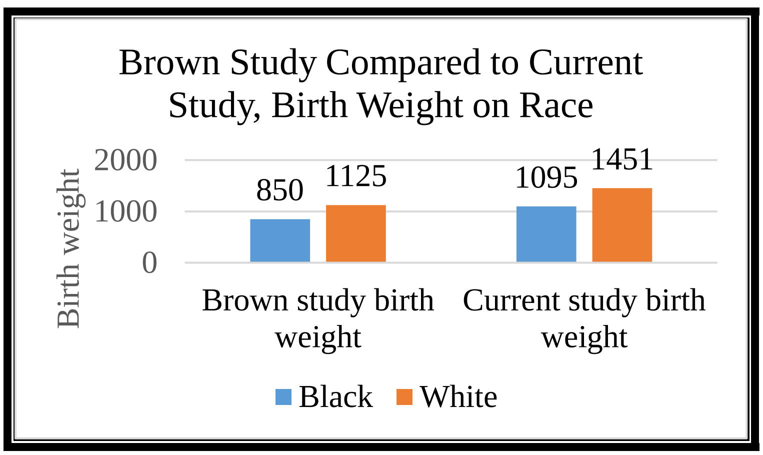
This study had minimal differences between male and female rates, diagnosed malnutrition, and LOS days. There were 26 (49%) male infants with an average LOS of 56.7±25.3 days and 27 (51%) female infants with an average LOS of 62.3 ±27.8 days. Malnutrition occurred 13 times with males with an average LOS of 69.8±28.9 days and 15 times with females with an average LOS of 67.±31.7 days. Based on this limited study, there were no significant differences in malnutrition and LOS based on gender.

There are conflicting results related to premature birth outcomes of males versus females. Peacock, et al concluded that in preterm infants' male sex was a significant risk factor in neonatal outcomes not explained by neonatal factors and support the concept of male vulnerability following preterm birth.(Peacock et al., 2012) Another study by Barzilay, concluded that there are no significant differences in neonatal mortality or morbidity in a study on twins, solely based on gender.(Barzilay et al., 2019)

Racial Disparities

Black African American women have an increased risk of preterm birth and their infants' have an increased LOS compared to non-Hispanic White women. (Brown et al., 2023; Lewis et al., 2022) In the study by Brown, et al, "Health disparities in preterm births", the Black/AA mothers gave birth to preterm infants earlier than non-Hispanic White women, and the NICU stay was extended >2 weeks for the significantly smaller Black/AA preterm infants. (Brown et al., 2023) In the multicenter cohort study by Lewis, et al, Black/AA race was significantly associated with increased LOS > 10 days for the preterm infants with BPD in the study.(Lewis et al., 2022) In the current study, the infants born to Black AA mothers were born at a 24% smaller mean birth weight (1095 grams comparable to 1451 grams) similar to the Brown study of 24% smaller mean birth weight (850 grams comparable to 1125 grams), **Figure 4.3**.(Brown et al., 2023)

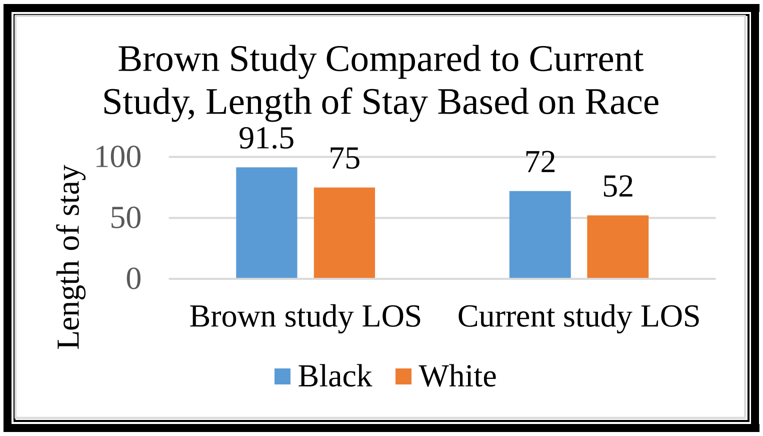
Figure 4.3 Brown Study Compared to Current Study on Birth Weight



(Brown et al., 2023)

In the study by Brown et al, the mean length of stays was also longer for the average Black AA, 91.5 days, compared to Whites, 75 days, an 18% increase in mean LOS between the two groups.(Brown et al., 2023) In the current study, the Black AA preterm infants had a mean LOS of 72 days vs the White preterm infants' LOS of 52 days, a 28% increase in LOS comparatively, **Figure 4.4**.

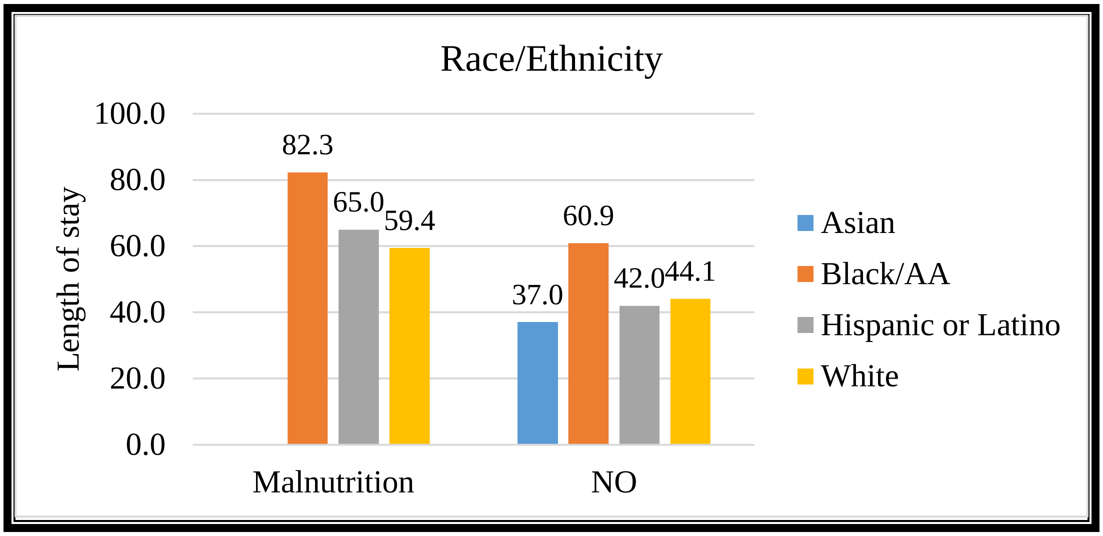
Figure 4.4 Brown Study Compared to Current Study, Length of Stay



Abbreviations: LOS, length of stay
(Brown et al., 2023)

In respect to risk of malnutrition and LOS, there were 10 Black/AA infants (N= 19, 53%) with an average LOS of 82.3±38.8 with malnutrition compared to 14 White infants (N=26, 54%) with a mean LOS of 59.4±24.2 days in the NICU. Indicating that the risk of malnutrition is similar between Black AA preterm infants and White preterm infants, but the Black AA preterm infants continue to have a longer LOS. **Figure 4.5** shows the larger LOS of the Black/AA for both infants with and without malnutrition compared to other races and ethnicities.

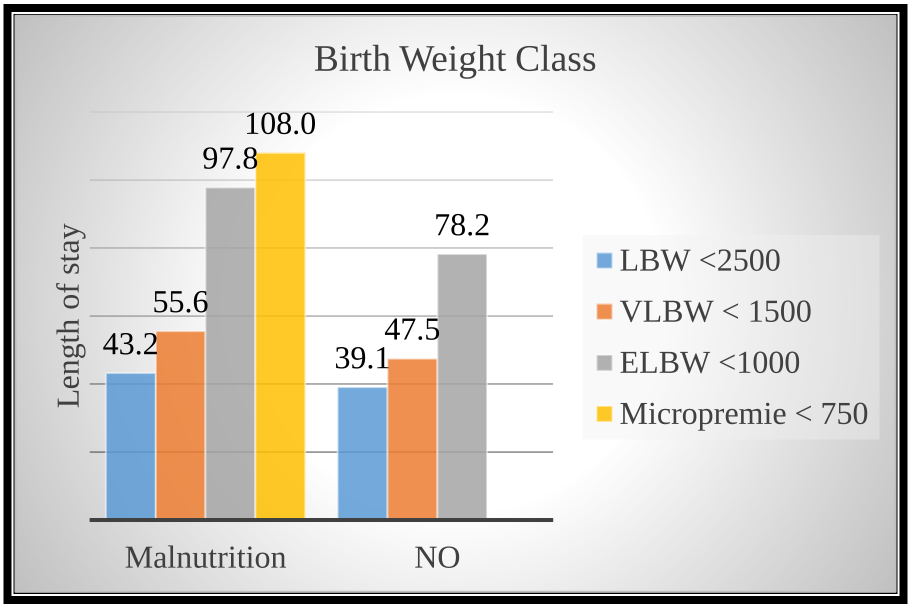
Figure 4.5 Race/Ethnicity, Malnutrition and Length of Stay



Birth Weight Class and Gestational Age

In the systematic review by Fu, et al, it was concluded that several of the most critical factors affecting LOS-NICU were identified to include birth weight, gestational age, necrotizing enterocolitis, bronchopulmonary dysplasia (BPD), congenital heart disease (CHD), and retinopathy of prematurity (ROP).(Fu et al., 2023) The trends in my study concluded that the higher LOS were evidenced by the decrease in birth weight class and lower gestational age. **Figure 4.6** shows the trend of increased LOS when comparing the birth weight class; larger babies had a shorter LOS than the micropremies with the longer LOS.

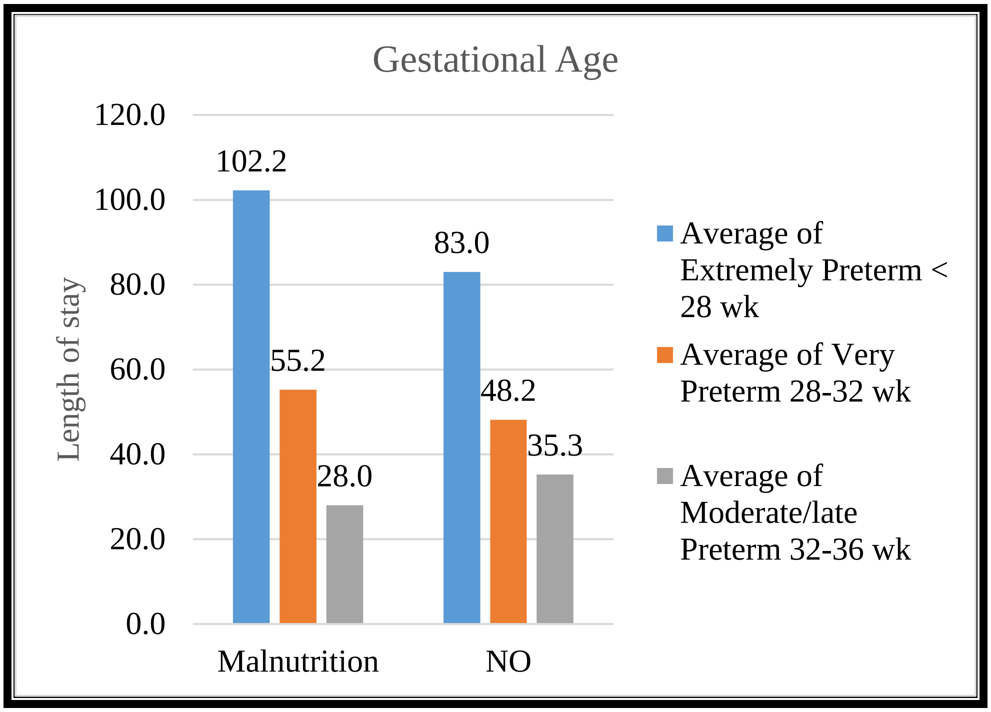
Figure 4.6 Birth Weight Class with Malnutrition and Length of Stay



Abbreviations: LBW, low birth weight; VLBW, very low birth weight; ELBW, extremely low birth weight

Figure 4.7 shows the increased LOS days for the earlier born infants of < 28 weeks gestational age and a shorter LOS for the moderate/late preterm infants of 32-36 weeks gestational age.

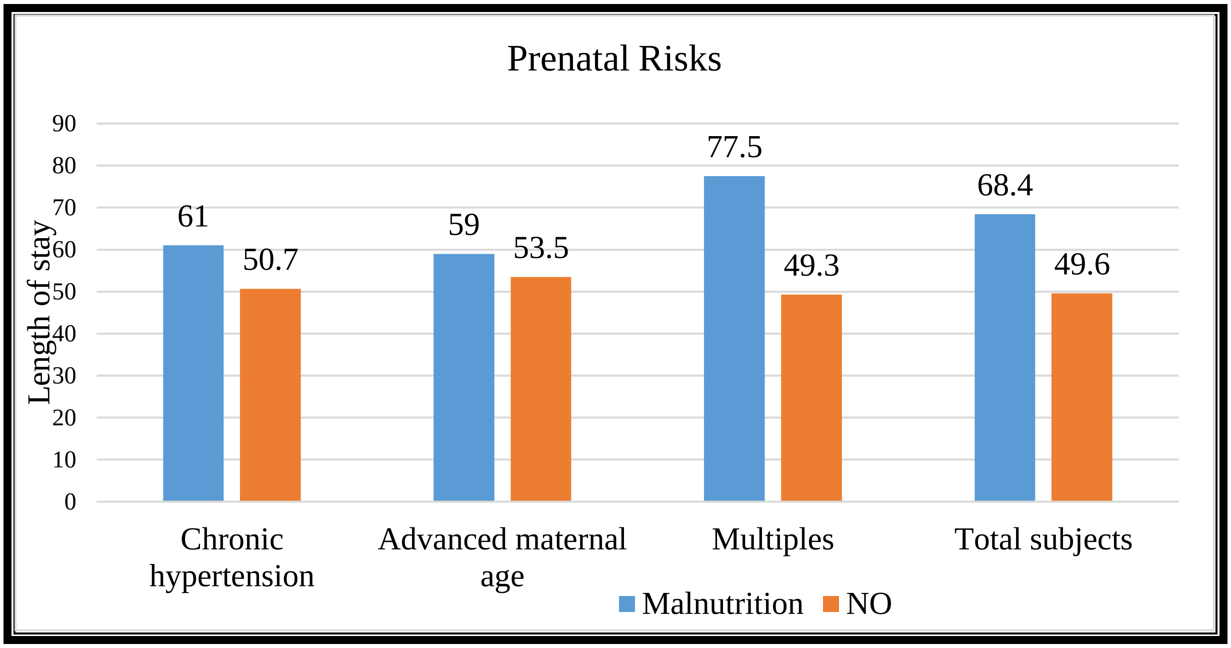
Figure 4.7 Gestational Age with Malnutrition and Length of Stay



Prenatal Risks Category

Prenatal risk for preterm delivery includes substance abuse, tobacco use, chronic hypertension, unhealthy weight, existing diabetes, previous preterm delivery, multiples, short time < 18 months between deliveries, advanced maternal age, and teen pregnancy. In my retrospective electronic chart reviews, there was very little documentation on the mother's smoking status and no documentation of births < 18 months apart. The most prominent subject groups in these categories were chronic hypertension (N=9, 17%) with 67% falling in the malnutrition category, advanced maternal age (N=9, 17%) with 78% falling in the malnutrition category, and pregnancy of multiples (twins +) (N=8, 15%) with 50% falling in the malnutrition category as shown in **Figure 4.8**. The pregnancies of multiples had a more significant average LOS of 77.5 days than the total of the malnutrition population of 68.4 days. In terms of prevention of preterm births, these areas are well documented as high risk groups by the March of Dimes. (*World Health Organization Fact Sheet on Preterm Birth*, 2023)

Figure 4.8 Prenatal Risks, Malnutrition and Length of Stay

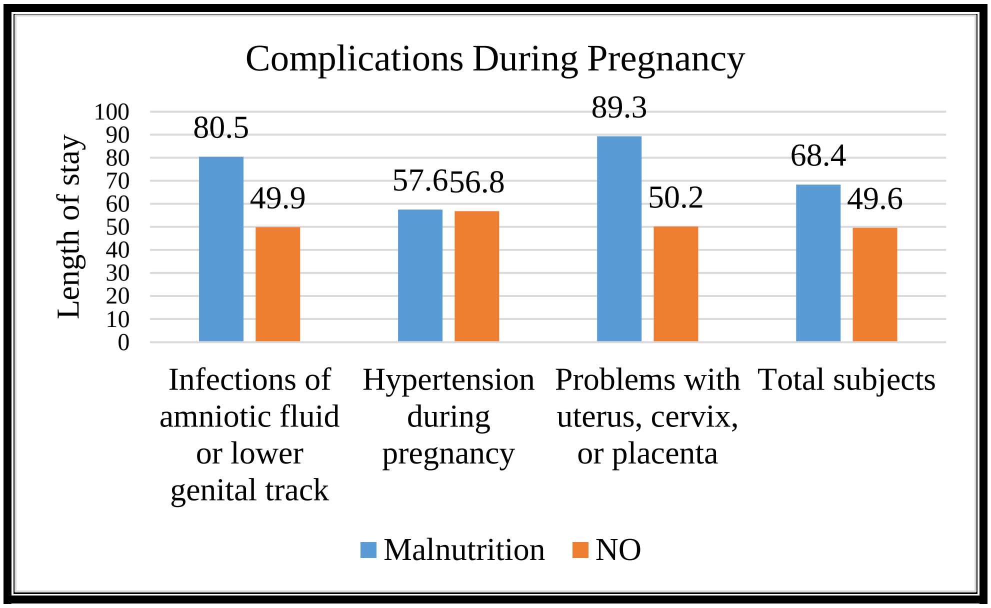


Complications of Pregnancy

Preterm births related to complications during pregnancy are affected by infections of amniotic fluid or lower genital tract, hypertension of pregnancy/preeclampsia, gestational diabetes, and problems with the uterus, cervix, or placenta. Inflammation in pregnancy induces an exaggerated immune response that increases the production of cytokines, elastases and MMPs (matrix metalloproteinases) and causes the functional withdrawal of progesterone, a vital hormone for maintaining the pregnancy.(Daskalakis et al., 2023)

The patient population with the largest preterm delivery in this study related to complications during the pregnancy included infections (N=19, 36%), with 58% meeting criteria for malnutrition and with a LOS of 80.5 days, 15% above the average LOS for all patients with malnutrition during the study. Hypertension during pregnancy and/or preeclampsia contributed to (N=22, 42%) of the total study group, 59% of which met the malnutrition criteria and had an average LOS of 57.6 days. Problems with the uterus, cervix or placenta contributed to (N=16, 30%) of the total study population, 38% met the criteria for malnutrition with a LOS of 89.3 days. As shown in Figure 4.9, the complication of having problems with the uterus, cervix or placenta had the most significant impact on LOS when malnutrition was indicated and hypertension had the most significant impact on LOS without a malnutrition diagnosis.

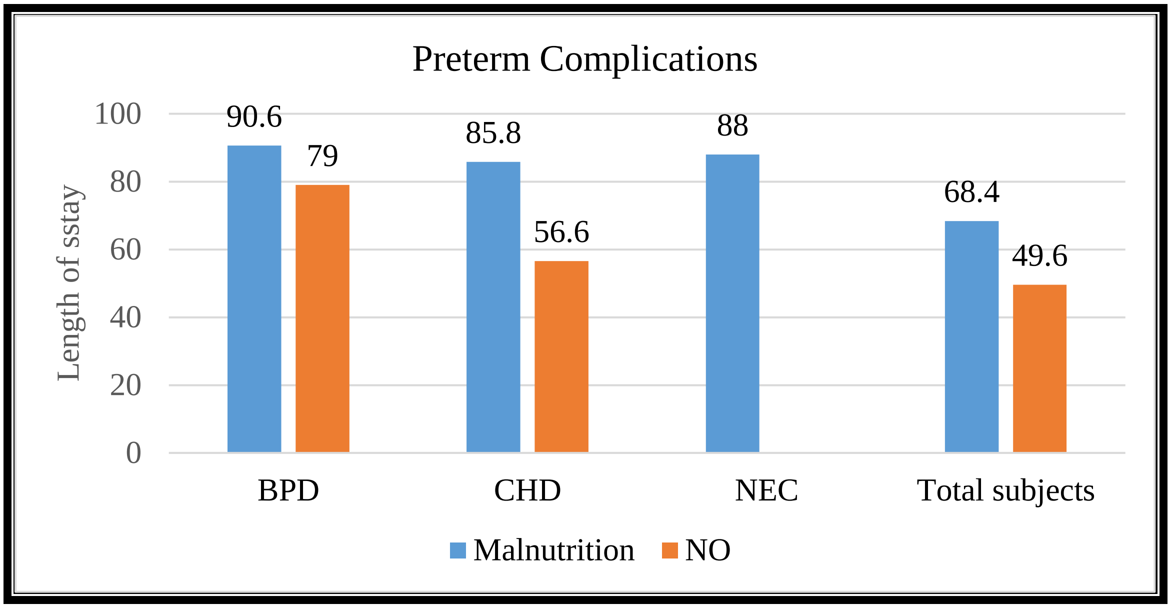
Figure 4.9 Complications of Pregnancy, Malnutrition and Length of Stay



Preterm Complications

Complications after birth that may affect the development of malnutrition and increase the LOS include hypoglycemia soon after birth, BPD, CHD, IVH stage 3-4, and ROP stages 3-4. In this study, only one patient was diagnosed with NEC, and the infant also met the criteria for malnutrition with a LOS of 88 days. This supports the literature regarding the high risk of NEC diagnosis in the NICU and the contribution to a higher LOS. Two studies reviewed had a 15-day and 12-day longer LOS in each study, with infants diagnosed with NEC than those without NEC diagnoses.(Shulhan et al., 2017) There were two patients diagnosed with IVH stage 3-4, both met criteria for malnutrition with an average LOS of 97 days. The infant with ROP stage 3-4 also met the criteria for malnutrition with an average LOS of 91 days. These two groups, the IVH stage 3-4 and ROP stage 3-4, would likely represent more complex infants in the NICU even if the numbers in the study are low. About (N=33,62%) of the study group were diagnosed with immature retina, which is common in this population, but only (N=1, 2%) progressed to ROP stage 3-4. In this study group, the most significant complications were CHD at (N=21, 40%) of the study group, 50% that met malnutrition criteria, and a LOS of 85.8 days. Infants with BPD were (N=10, 19%) of the total study group, 89% met criteria for malnutrition with an average LOS of 90.6 days. Infants with hypoglycemia soon after birth made up (N=10,19%) of the study group with only 40% meeting the criteria for malnutrition and an average LOS of 65.8 days. It appears similar to the research published that infants who develop BPD have a longer LOS and higher costs during their hospitalization compared to those without BPD, and had higher in-hospital mortalities, hospital readmissions, and pulmonary morbidities during their first year of life.(Mowitz et al., 2019) **Figure 14** shows a similar higher LOS for all 3 of the preterm complications evaluated, BPD, CHD, and NEC compared to the overall total subjects reviewed.

Figure 4.10 Preterm Complications, Malnutrition and Length of Stay



Abbreviations: BPD, bronchopulmonary dysplasia; CHD= congenital heart disease;
NEC, necrotizing enterocolitis

Chapter 5 - Statistical Analyses

Statistical Analyses

Statistically, comparing the length of stay of the infants with bronchopulmonary dysplasia and malnutrition to infants without bronchopulmonary dysplasia and malnutrition, infants with BPD resulted in a higher length of stay (M=90.6, SD=19.6) than was found in the infants that had malnutrition but did not have BPD in this study, t(19)= 3.28, p= 0.002, **Tables 5.1-5.2**.

Table 5.1 t-Test for Malnutrition with BPD Compared to without BPD

t-Test: Two-Sample Assuming Unequal Variances		
	Malnutrition LOS with BPD	**Malnutrition LOS without BPD**
Mean	90.625	59.5
Variance	384.5535714	839.8421053
Observations	8	20
Hypothesized Mean Difference	0	
df	19	
t Stat	3.279746296	
P(T<=t) one-tail	0.001970521	
t Critical one-tail	1.729132812	
P(T<=t) two-tail	0.003941043	
t Critical two-tail	2.093024054	

Abbreviations: LOS, Length of Stay; BPD, Bronchopulmonary Dysplasia

Table 5.2 Descriptive Statistics for Malnutrition with BPD Compared to without BPD

Malnutrition LOS with BPD	Statistics	Malnutrition LOS without BPD	Statistics
Mean	90.625	Mean	59.5
Standard Error	6.933195254	Standard Error	6.480131578
Median	93.5	Median	50
Mode	#N/A	Mode	45
Standard Deviation	19.61003752	Standard Deviation	28.98002942
Sample Variance	384.5535714	Sample Variance	839.8421053
Kurtosis	-0.595070026	Kurtosis	2.858441369
Skewness	-0.781045026	Skewness	1.580966824
Range	53	Range	117
Minimum	58	Minimum	28
Maximum	111	Maximum	145
Sum	725	Sum	1190
Count	8	Count	20
Confidence Level (95.0%)	16.39440164	Confidence Level (95.0%)	13.56307127

Abbreviations: LOS, Length of Stay; BPD, Bronchopulmonary Dysplasia

The null hypothesis H_o expected is that malnutrition does not affect LOS. The alternative hypothesis H_a is that malnutrition affects LOS. The control group does not have malnutrition, and the independent variable has malnutrition. A t-test Two-Sample Assuming Unequal Variances was used to determine statistical significance with (P=<0.05). The mean for the infants without meeting the criteria for malnutrition was 49.6 +/- 18.1 SD days and the mean for the infants that met the criteria for malnutrition was 68.4 +/-29.9 SD days—comparing the LOS of infants meeting the criteria for malnutrition to infants not meeting the criteria for malnutrition (M= 68.4 ± 29.9) t(45)= -2.8, *p*= 0.003, **Tables 5.3-5.4**.

Table 5.3 t-Test for Malnutrition and No Malnutrition

t-Test: Two-Sample Assuming Unequal Variances		
	NO	**Malnutrition**
Mean	49.6	68.39285714
Variance	326.25	895.728836
Observations	25	28
Hypothesized Mean Difference	0	
df	45	
t Stat	-2.800219658	
P(T<=t) one-tail	0.003749186	
t Critical one-tail	1.679427393	
P(T<=t) two-tail	0.007498372	
t Critical two-tail	2.014103389	

Table 5.4 Descriptive Statistics for Malnutrition and No Malnutrition

NO	**Statistics**	**Malnutrition**	**Statistics**
Mean	49.6	Mean	68.39286
Standard Error	3.612478374	Standard Error	5.655998
Median	45	Median	62
Mode	37	Mode	45
Standard Deviation	18.06239187	Standard Deviation	29.92873
Sample Variance	326.25	Sample Variance	895.7288
Kurtosis	1.069685605	Kurtosis	-0.14673
Skewness	1.30664862	Skewness	0.676571
Range	69	Range	117
Minimum	28	Minimum	28
Maximum	97	Maximum	145
Sum	1240	Sum	1915
Count	25	Count	28
Confidence Level (95.0%)	7.455788919	Confidence Level (95.0%)	11.60515

Chapter 6 - Conclusions, Discussion and Future Research

This study has shown that infants who met the criteria for malnutrition on the 28th day of life have a higher risk of longer length of stays than infants that do not meet the malnutrition criteria. From this study, it can be concluded that an infant on the 28th day of life meeting the criteria for malnutrition, would be at higher risk of a longer length of stay than the infants not meeting the criteria for malnutrition. Many other factors drive the need for a more extended stay, such as feeding tolerances and other diagnoses as previously described in the study. There was a balanced number of male infants and female infants in this study, somewhat different than expected by the literature that generally indicates that male infants are at higher risk of preterm delivery. Prenatal care was received by 92% of the infant's mothers before the preterm delivery. Consistent with findings of others, the birth weight class and gestational age of the infant followed expected trends. In the research by Mehretie et al, the gestational age and presence of complications, had a significant association with the length of stay for the very low birth weight preterm neonates.(Mehretie et al., 2024)

The lower the birth weight, the higher percentage of infants met the malnutrition criteria and had longer lengths of stay. The earlier the gestational age at birth, the higher the percentage of infants who met the malnutrition criteria and had longer lengths of stay. The prenatal risks that had the most effect on malnutrition and length of stay were consistent with the literature, concluding that chronic hypertension, multiple pregnancies, and advanced maternal age carry a more significant risk of both malnutrition and longer lengths of stay. HTN in pregnancy increased the risk of preeclampsia in pregnancy and had a high risk of delivering SGA infants with associated neonatal risks.(Al Khalaf et al., 2021) Pregnancies of multiples are complicated by increased risk of preterm birth, potential health complications and longer LOS.(Kalikkot Thekkeveedu et al., 2021) The research is conflicting on the overall effect of advanced maternal age in preterm births and neonatal outcomes. Advanced maternal age is complicated by the risk of other age-related complications during pregnancy, such as HTN, placenta previa, and a more significant risk of c-sections.(*World Health Organization Fact Sheet on Preterm Birth*, 2023) As an independent risk, the research is conflicting on its impact on neonate risks, malnutrition, and LOS.

Preterm diagnoses that increase the possibility of meeting the criteria for malnutrition and increasing average length of stay included BPD, CHD, Stages 3-4 IVH, stages 3-4 ROP and NEC, consistent with the literature findings.(Gidi et al., 2020) Feeding difficulties in the first 28 days of life place the infant at an increased risk of developing many of the preterm complications that contribute to increasing the need for length of time in the NICU, including BPD, CHD, Stages 3-4 IVH, stages 3-4 ROP and NEC.(Fu et al., 2023)

The strength of this study included a well-defined research question that addressed the problem or contribution of malnutrition to overall outcome and length of stay in the NICU. The methodology is appropriate for the research question, with retrospective data collection. The sample included all infants that met the inclusion criteria. The findings are consistent with other reliable results and could be replicated in other studies.

Limitations and Future Research Directions

There are several limitations to the current study, including study design, time limitations, measurement errors, small sample size, and differences in gestational birth age. The retrospective design increased the risk of missing patient data and unidentified confounders that could affect the results. The time limitation and retrospective nature of the study meant the study ended before all the potential subjects were available for inclusion in the study. The measurements of the subjects are affected by accuracy and possible human error, especially in relationship to the linear measurements. The small sample size and the single center location could reduce the validity of the results. In this study, bias prevention included clearly defining and consistently applied inclusion and exclusion criteria which is crucial for minimizing bias and following the established criteria for defining malnutrition in preterm infants.

There were expected differences in LOS and malnutrition percentage between the birth gestational ages with longer LOS for the extremely preterm infant < 28 weeks gestation, the very preterm infants 28-32 weeks gestation and the moderate/late preterm infants > 32 weeks gestation. It may be helpful to look at the different categories individually to better assess the risk of malnutrition and LOS for each birth gestational age. Each subject is an individual, and there are varying diagnoses, feeding difficulties, and other potential complications, each of which plays a role in developing malnutrition and the LOS needed for optimal health outcomes. There are additional factors that contribute to LOS beyond the diagnosis of malnutrition or not within the first 28 days of life.

The current study shows the relationship of a malnutrition diagnosis in the first 28 days of life for the preterm infant and the potential effect on length of hospital stay. Nutrition in the NICU is both a lifesaving and life sustaining intervention that is needed for the appropriate growth and development of premature infants. Malnutrition in the NICU is clinically significant due to potential severe acute and chronic negative impacts on growth, development, and overall health, including the increased risk of mortality, impaired neurodevelopment, compromised immune function, making proper nutrition a critical component of NICU care to optimize outcomes for vulnerable infants. Early identification and management of malnutrition is essential to diminishing these risks in the NICU. Optimum nutrition leads to improved long-term neurodevelopmental outcomes, lower length of stay, decreased financial burdens and potentially lower social/mental stress for the family. Future studies are needed on the importance of an interdisciplinary team within the NICU to identify the infants with malnutrition in the first 28 days of life and developing a care plan to address feeding difficulties to improve LOS, decrease costs associated with the hospital stay, and decrease stress and concerns for the family.

Validation studies are needed to formally assess the malnutrition criteria for the infants within the first 28 days of life. Future studies need to evaluate the feeding strategies within the first 28 days in the NICU and evaluate any potential impact on growth, development, feeding tolerance, and LOS. Additional research could compare the diagnosis of malnutrition during the first 28 days to the values at discharge to see if continued criteria were met or improved. The results of this study open up discussions for future studies of NICU malnutrition, the effect on health outcome, and the potential to reduce the length of stay in the NICU. This can impact the bottom line dollar costs for hospital and parents and impact the social and behavior well-being of the infants' caretakers. If ignored that decision will affect the child throughout their life.

References

Abdelhadi, R. A., Bouma, S., Bairdain, S., Wolff, J., Legro, A., Plogsted, S., Guenter, P., Resnick, H., Slaughter-Acey, J. C., Corkins, M. R., & ASPEN Malnutrition Committee. (2016). Characteristics of hospitalized children with a diagnosis of malnutrition: United states, 2010. *JPEN. Journal of Parenteral and Enteral Nutrition*, *40*(5), 623–635. https://doi.org/10.1177/0148607116633800

Al Khalaf, S. Y., O'Reilly, É. J., Barrett, P. M., B. Leite, D. F., Pawley, L. C., McCarthy, F. P., & Khashan, A. S. (2021). Impact of Chronic Hypertension and Antihypertensive Treatment on Adverse Perinatal Outcomes: Systematic Review and Meta-Analysis. *Journal of the American Heart Association*, *10*(9), e018494. https://doi.org/10.1161/JAHA.120.018494

Ambinder, E. P. (2005). Electronic Health Records. *Journal of Oncology Practice*, *1*(2), 57–63. https://doi.org/10.1200/jop.2005.1.2.57

Barzilay, B., Shirman, N., Bibi, H., & Abu-Kishk, I. (2019). Newborn gender as a predictor of neonatal outcome in mixed gender twins born with very low birth weight. *BMC Pediatrics*, *19*(1), 328. https://doi.org/10.1186/s12887-019-1713-2

Bauer, S. E., Vanderpool, C. P. B., Ren, C., & Cristea, A. I. (2021). Nutrition and growth in infants with established bronchopulmonary dysplasia. *Pediatric Pulmonology*, *56*(11), 3557–3562. https://doi.org/10.1002/ppul.25638

Beam, A. L., Fried, I., Palmer, N., Agniel, D., Brat, G., Fox, K., Kohane, I., Sinaiko, A., Zupancic, J. A. F., & Armstrong, J. (2020). Estimates of healthcare spending for preterm and low-birthweight infants in a commercially insured population: 2008-2016. *Journal of*

Perinatology: Official Journal of the California Perinatal Association, *40*(7), 1091–1099. https://doi.org/10.1038/s41372-020-0635-z

Behrman, R. E., Butler, A. S., & Institute of Medicine (U.S.) (Eds.). (2007). *Preterm birth: Causes, consequences, and prevention*. National Academies Press.

Bhatia, J., Griffin, I., Anderson, D., Kler, N., & Domellöf, M. (2013). Selected macro/micronutrient needs of the routine preterm infant. *The Journal of Pediatrics*, *162*(3 Suppl), S48-55. https://doi.org/10.1016/j.jpeds.2012.11.053

Braveman, P., Dominguez, T. P., Burke, W., Dolan, S. M., Stevenson, D. K., Jackson, F. M., Collins, J. W., Driscoll, D. A., Haley, T., Acker, J., Shaw, G. M., McCabe, E. R. B., Hay, W. W., Thornburg, K., Acevedo-Garcia, D., Cordero, J. F., Wise, P. H., Legaz, G., Rashied-Henry, K., … Waddell, L. (2021). Explaining the Black-White Disparity in Preterm Birth: A Consensus Statement From a Multi-Disciplinary Scientific Work Group Convened by the March of Dimes. *Frontiers in Reproductive Health*, *3*, 684207. https://doi.org/10.3389/frph.2021.684207

Brown, J., Chang, X., Matson, A., Lainwala, S., Chen, M.-H., Cong, X., & Casavant, S. G. (2023). Health disparities in preterm births. *Frontiers in Public Health*, *11*, 1275776. https://doi.org/10.3389/fpubh.2023.1275776

Casirati, A., Somaschini, A., Perrone, M., Vandoni, G., Sebastiani, F., Montagna, E., Somaschini, M., & Caccialanza, R. (2022). Preterm birth and metabolic implications on later life: A narrative review focused on body composition. *Frontiers in Nutrition*, *9*, 978271. https://doi.org/10.3389/fnut.2022.978271

Chawla, D., Agarwal, R., Deorari, A. K., & Paul, V. K. (2008). Fluid and electrolyte management in term and preterm neonates. *Indian Journal of Pediatrics*, *75*(3), 255–259. https://doi.org/10.1007/s12098-008-0055-0

Chou, J. H., Roumiantsev, S., & Singh, R. (2020). PediTools electronic growth chart calculators: Applications in clinical care, research, and quality improvement. *Journal of Medical Internet Research*, *22*(1), e16204. https://doi.org/10.2196/16204

Corkins, M. R. (2017). Why is diagnosing pediatric malnutrition important? *Nutrition in Clinical Practice: Official Publication of the American Society for Parenteral and Enteral Nutrition*, *32*(1), 15–18. https://doi.org/10.1177/0884533616678767

Damhuis, S. E., Ganzevoort, W., & Gordijn, S. J. (2021). Abnormal fetal growth: Small for gestational age, fetal growth restriction, large for gestational age: definitions and epidemiology. *Obstetrics and Gynecology Clinics of North America*, *48*(2), 267–279. https://doi.org/10.1016/j.ogc.2021.02.002

Daskalakis, G., Psarris, A., Koutras, A., Fasoulakis, Z., Prokopakis, I., Varthaliti, A., Karasmani, C., Ntounis, T., Domali, E., Theodora, M., Antsaklis, P., Pappa, K. I., & Papapanagiotou, A. (2023). Maternal Infection and Preterm Birth: From Molecular Basis to Clinical Implications. *Children*, *10*(5), 907. https://doi.org/10.3390/children10050907

Fenton, T. R., & Kim, J. H. (2013). A systematic review and meta-analysis to revise the fenton growth chart for preterm infants. *BMC Pediatrics*, *13*, 59. https://doi.org/10.1186/1471-2431-13-59

Fenton, T. R., Senterre, T., & Griffin, I. J. (2019). Time interval for preterm infant weight gain velocity calculation precision. *Archives of Disease in Childhood. Fetal and Neonatal Edition*, *104*(2), F218–F219. https://doi.org/10.1136/archdischild-2018-314843

Fu, M., Song, W., Yu, G., Yu, Y., & Yang, Q. (2023). Risk factors for length of NICU stay of newborns: A systematic review. *Frontiers in Pediatrics*, *11*, 1121406. https://doi.org/10.3389/fped.2023.1121406

Gao, C., Ehsan, L., Jones, M., Khan, M., Middleton, J., Vergales, B., Perks, P., & Syed, S. (2020). Time to regain birth weight predicts neonatal growth velocity: A single-center experience. *Clinical Nutrition ESPEN*, *38*, 165–171. https://doi.org/10.1016/j.clnesp.2020.05.010

Gidi, N. W., Mekasha, A., Nigussie, A. K., Goldenberg, R. L., McClure, E. M., Worku, B., Amaru, G. M., Tazu Bonger, Z., Demtse, A. G., Kebede, Z. T., Siebeck, M., Genzel-Boroviczény, O., & Muhe, L. M. (2020). Preterm nutrition and clinical outcomes. *Global Pediatric Health*, *7*, 2333794X20937851. https://doi.org/10.1177/2333794X20937851

Goldberg, D. L., & Becker, P. J. (2022). Applying the recommended indicators for the diagnosis of preterm and neonatal malnutrition: Answers to frequently asked questions. *Nutrition in Clinical Practice: Official Publication of the American Society for Parenteral and Enteral Nutrition*, *37*(1), 50–58. https://doi.org/10.1002/ncp.10814

Goldberg, D. L., Becker, P. J., Brigham, K., Carlson, S., Fleck, L., Gollins, L., Sandrock, M., Fullmer, M., & Van Poots, H. A. (2018). Identifying malnutrition in preterm and neonatal populations: Recommended indicators. *Journal of the Academy of Nutrition and Dietetics*, *118*(9), 1571–1582. https://doi.org/10.1016/j.jand.2017.10.006

Gray, R. F., Indurkhya, A., & McCormick, M. C. (2004). Prevalence, stability, and predictors of clinically significant behavior problems in low birth weight children at 3, 5, and 8 years of age. *Pediatrics*, *114*(3), 736–743. https://doi.org/10.1542/peds.2003-1150-L

Grunberg, V. A., Geller, P. A., Bonacquisti, A., & Patterson, C. A. (2019). NICU infant health severity and family outcomes: A systematic review of assessments and findings in psychosocial research. *Journal of Perinatology: Official Journal of the California Perinatal Association*, *39*(2), 156–172. https://doi.org/10.1038/s41372-018-0282-9

Grunberg, V. A., Vranceanu, A.-M., & Lerou, P. H. (2022). Caring for our caretakers: Building resiliency in NICU parents and staff. *European Journal of Pediatrics*, *181*(9), 3545–3548. https://doi.org/10.1007/s00431-022-04553-1

Harvey, E. M., McNeer, E., McDonald, M. F., Shapiro-Mendoza, C. K., Dupont, W. D., Barfield, W., & Patrick, S. W. (2021). Association of preterm birth rate with COVID-19 statewide stay-at-home orders in tennessee. *JAMA Pediatrics*, *175*(6), 635–637. https://doi.org/10.1001/jamapediatrics.2020.6512

Hay, W. W. (2018). Nutritional support strategies for the preterm infant in the neonatal intensive care unit. *Pediatric Gastroenterology, Hepatology & Nutrition*, *21*(4), 234–247. https://doi.org/10.5223/pghn.2018.21.4.234

Hellström, A., Kermorvant-Duchemin, E., Johnson, M., Sáenz de Pipaón, M., Smith, L. E., Hård, A.-L., & ESPR Nutrition council members. (2024). Nutritional interventions to prevent retinopathy of prematurity. *Pediatric Research*, *96*(4), 905–911. https://doi.org/10.1038/s41390-024-03208-1

Ilahi, Z., Capolongo, T., DiMeglio, A., Demissie, S., & Rahman, A. (2023). Impact of an infant-driven feeding initiative on feeding outcomes in the preterm neonate. *Advances in Neonatal Care*, *23*(3), 205–211. https://doi.org/10.1097/ANC.0000000000001033

Kalikkot Thekkeveedu, R., Dankhara, N., Desai, J., Klar, A. L., & Patel, J. (2021). Outcomes of multiple gestation births compared to singleton: Analysis of multicenter KID database.

Maternal Health, Neonatology and Perinatology, *7*(1), 15. https://doi.org/10.1186/s40748-021-00135-5

Karatza, A. A., Gkentzi, D., & Varvarigou, A. (2022). Nutrition of infants with bronchopulmonary dysplasia before and after discharge from the neonatal intensive care unit. *Nutrients*, *14*(16), 3311. https://doi.org/10.3390/nu14163311

Kleinman, R. E., & Greer, F. R. (Eds.). (2020). Nutritional needs of the preterm infant. In *Pediatric Nutrition* (8th ed.). American Academy of PediatricsItasca, IL. https://doi.org/10.1542/9781610023610-5

Koletzko, B., Cheah, F.-C., Domellöf, M., Poindexter, B. B., Vain, N., & Van Goudoever, J. B. (Eds.). (2021). *Nutritional care of preterm infants: Scientific basis and practical guidelines* (Vol. 122). S. Karger AG. https://doi.org/10.1159/isbn.978-3-318-06647-0

Kowlessar, N. M., Jiang, H. J., & Steiner, C. (2011). Hospital stays for newborns, 2011. In *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Agency for Healthcare Research and Quality (US). http://www.ncbi.nlm.nih.gov/books/NBK173954/

Lewis, T. R., Kielt, M. J., Walker, V. P., Levin, J. C., Guaman, M. C., Panitch, H. B., Nelin, L. D., Abman, S. H., Bronchopulmonary Dysplasia Collaborative, Sindelar, R., Truog, W. E., Collaco, J. M., Keszler, M., Moore, P. E., Schulman, B., Sood, B. G., Hayden, L. P., Cristea, A. I., Lai, K., … Lagatta, J. M. (2022). Association of Racial Disparities With In-Hospital Outcomes in Severe Bronchopulmonary Dysplasia. *JAMA Pediatrics*, *176*(9), 852. https://doi.org/10.1001/jamapediatrics.2022.2663

Mandala, V. K., Urakurva, A. K., Gangadhari, S., & Kotha, R. (2023). The Effects of Early Enteral and Parental Nutrition on Retinopathy of Prematurity: A Systematic Review. *Cureus*, *15*(11), e49029. https://doi.org/10.7759/cureus.49029

Mehretie, Y., Amare, A. T., Getnet, G. B., & Mekonnen, B. A. (2024). Length of hospital stay and factors associated with very-low-birth-weight preterm neonates surviving to discharge a cross-sectional study, 2022. *BMC Pediatrics*, *24*(1), 80. https://doi.org/10.1186/s12887-024-04532-5

Mills, K. I., Kim, J. H., Fogg, K., Goldshtrom, N., Graham, E. M., Kataria-Hale, J., Osborne, S. W., & Figueroa, M. (2022). Nutritional considerations for the neonate with congenital heart disease. *Pediatrics*, *150*(Suppl 2), e2022056415G. https://doi.org/10.1542/peds.2022-056415G

Mowitz, M. E., Ayyagari, R., Gao, W., Zhao, J., Mangili, A., & Sarda, S. P. (2019). Health Care Burden of Bronchopulmonary Dysplasia Among Extremely Preterm Infants. *Frontiers in Pediatrics*, *7*, 510. https://doi.org/10.3389/fped.2019.00510

National Institutes of Health (NIH) Office of Dietary Supplements. (n.d.-a). *2024 march of dimes report card.* https://www.marchofdimes.org/sites/default/files/2024-11/2024_MOD_Report_Card_and_Policy_Actions_Booklet_V1.pdf

National Institutes of Health (NIH) Office of Dietary Supplements. (n.d.-b). *Calcium: Fact sheet for the health professionals.* https://ods.od.nih.gov/factsheets/Calcium-HealthProfessional/

National Institutes of Health (NIH) Office of Dietary Supplements. (n.d.-c). *Copper: Fact sheet for health professionals.* https://ods.od.nih.gov/factsheets/Copper-HealthProfessional/

National Institutes of Health (NIH) Office of Dietary Supplements. (n.d.-d). *Iron: Fact sheet for the health professionals*. https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/

National Institutes of Health (NIH) Office of Dietary Supplements. (n.d.-e). *Phosphorous: Fact sheet for health professionals.* https://ods.od.nih.gov/factsheets/Phosphorus-HealthProfessional/

National Institutes of Health (NIH) Office of Dietary Supplements. (n.d.-f). *Vitamin D: fact sheet for health professionals.* https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/

National Institutes of Health (NIH) Office of Dietary Supplements. (n.d.-g). *Zinc: Fact sheet for health professionals.* https://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/

National Institutes of Health (NIH) Office of Dietary Supplements. (2022). *Magnesium: Fact sheet for health professionals.* https://ods.od.nih.gov/factsheets/Magnesium-HealthProfessional/

Peacock, J. L., Marston, L., Marlow, N., Calvert, S. A., & Greenough, A. (2012). Neonatal and infant outcome in boys and girls born very prematurely. *Pediatric Research*, *71*(3), 305–310. https://doi.org/10.1038/pr.2011.50

Preda, A., Iliescu, D.-G., Comănescu, A., Zorilă, G.-L., Vladu, I. M., Forțofoiu, M.-C., Țenea-Cojan, T. S., Preda, S.-D., Diaconu, I.-D., Moța, E., Gheorghe, I.-O., & Moța, M. (2023). Gestational Diabetes and Preterm Birth: What Do We Know? Our Experience and Mini-Review of the Literature. *Journal of Clinical Medicine*, *12*(14), 4572. https://doi.org/10.3390/jcm12144572

Rocha, G., Guimarães, H., & Pereira-da-Silva, L. (2021). The Role of Nutrition in the Prevention and Management of Bronchopulmonary Dysplasia: A Literature Review and Clinical Approach. *International Journal of Environmental Research and Public Health*, *18*(12), 6245. https://doi.org/10.3390/ijerph18126245

Rolnitsky, A., Unger, S., Urbach, D., & Bell, C. M. (2023). The price of neonatal intensive care outcomes—In-hospital costs of morbidities related to preterm birth. *Frontiers in Pediatrics*, *11*, 1068367. https://doi.org/10.3389/fped.2023.1068367

Shulhan, J., Dicken, B., Hartling, L., & Larsen, B. M. (2017). Current Knowledge of Necrotizing Enterocolitis in Preterm Infants and the Impact of Different Types of Enteral Nutrition Products. *Advances in Nutrition (Bethesda, Md.)*, *8*(1), 80–91. https://doi.org/10.3945/an.116.013193

Silveira, R. C., Corso, A. L., & Procianoy, R. S. (2023). The influence of early nutrition on neurodevelopmental outcomes in preterm infants. *Nutrients*, *15*(21), 4644. https://doi.org/10.3390/nu15214644

Sinha, B., Dudeja, N., Chowdhury, R., Choudhary, T. S., Upadhyay, R. P., Rongsen-Chandola, T., Mazumder, S., Taneja, S., & Bhandari, N. (2022). Enteral zinc supplementation in preterm or low birth weight infants: A systematic review and meta-analysis. *Pediatrics, 150*(Suppl 1), e2022057092J. https://doi.org/10.1542/peds.2022-057092J

Skinner, A. M., & Narchi, H. (2021). Preterm nutrition and neurodevelopmental outcomes. *World Journal of Methodology*, *11*(6), 278–293. https://doi.org/10.5662/wjm.v11.i6.278

Texas Children's Hospital. (2022). *Pediatric nutrition reference guide* (13th ed.).

Treyvaud, K., & Brown, S. J. (2022). Mental health of children and parents after very preterm birth. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA), 21*(1), 148–149. https://doi.org/10.1002/wps.20936

Waitzman, N. J., Jalali, A., & Grosse, S. D. (2021). Preterm birth lifetime costs in the united states in 2016: An update. *Seminars in Perinatology, 45*(3), 151390. https://doi.org/10.1016/j.semperi.2021.151390

Wang, N., Zhang, J., Yu, Z., Tang, B., Zhang, L., Yin, Y., Wang, Z., Li, S., Jiang, S., Hou, W., Gao, Y., Wang, H., Chen, X., Deng, X., Lu, Y., Zhu, L., Bo, L., & Han, S. (2021). Evaluation of nutrition status of very preterm infants in neonatal intensive care units using different growth indicators. *Nutrition in Clinical Practice: Official Publication of the American Society for Parenteral and Enteral Nutrition*, *36*(6), 1312–1319. https://doi.org/10.1002/ncp.10741

World health organization fact sheet on preterm birth. (2023). https://www.who.int/news-room/fact-sheets/detail/preterm-birth

Zheng, Z., Shen, W., Tang, L.-X., Zhang, R., Cheng, R., Wang, S.-N., Chen, D.-M., Chen, C., & Lin, X.-Z. (2023). High-proportion breast milk feeding is associated with a reduction in the incidence of IVH in very preterm infants. *Frontiers in Neurology*, *13*, 993985. https://doi.org/10.3389/fneur.2022.993985