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Infants admitted to the neonatal intensive care unit (NICU) are often those born between 32 and 38 weeks gestations. However, these older preterm and early term infants have not been well studied, possibly due to less risk of mortality than among infants born at earlier gestations. In the U.S., 10% of annual births are preterm and 26.5% are born early term at 37 and 38 weeks gestation (Martin, Hamilton, & Osterman, 2019). Of those born preterm, 71% were born late preterm between 34 to 36 weeks gestation and only 2.8% were born at less than 34 weeks gestation in the latest available U.S. data (Martin, Hamilton, Osterman, Driscoll, Drake, & Division of Vital Statistics, 2018).

This observational cohort study using secondary data examined 159,529 infants born at 32 to 38 weeks gestation. The dataset used for this study was provided by Mednax© using their Clinical Data Warehouse from provider chart data for years 2015 through 2017. A total of 303 NICUs (level II and above) across the U.S. were represented in the dataset. Infants with major congenital anomalies were included in the study. This sample represented approximately 1.5% of annual U.S. births (Martin et al., 2018).

The statistical methods for this study included basic analyses of sample characteristics with reporting of descriptive statistics. Additionally, statistical analyses focused on evaluation of infant development, health/illness and maternal relationships

using the Transitions Theory (Chick & Meleis, 2010; Chick & Meleis, 1986; Meleis, 2010; Meleis, Sawyer, Im, Hilfinger, & Shumacher, 2000) as a framework for the study.

The mean gestational age of infants in the dataset was 35.4 weeks and the largest group (19%) was infants born at 34 weeks gestation. Infants born at 32 weeks gestation totaled 8% of the sample and were the smallest group identified. Male infants comprised 56% of the sample, 87% were born in a hospital with a NICU, and 11% had major congenital anomalies. The mean length of stay was 13.1 days (*SD* +/- 13.3) and 91% of infants were singleton births. The mortality rate for this sample was only 1% (959 infants). Of the relationships examined, health/illness factors including chronic lung disease and major congenital anomalies had the largest effects on outcomes followed by situational or maternal factors including antenatal steroid administration and Black race. Gestational age and birthweight also had modest effects on outcomes but to a lesser degree than maternal factors.

Major findings include that in this sample of infants born at 32 through 38 weeks gestation, those diagnosed with chronic lung disease and those born with major congenital anomalies were at highest risk for needing more days of respiratory support and greater lengths of stay, and had higher odds of negative outcomes including death and needing equipment at discharge such as oxygen or a monitor. Since the definition of chronic lung disease includes infants requiring oxygen at a month of life or at 36 weeks corrected age, these infants were likely the most preterm infants in the sample. Infants with major anomalies primarily included those with cardiac, neurological, and renal anomalies since only 10% of the sample included infants with trisomies.

Keywords: Mid-preterm infants, late preterm infants, early term infants, older preterm infants

SHORT TERM OUTCOMES IN
HOSPITALIZED INFANTS

by

Kristi Coe

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Approved by

Robin Bartlett
Committee Chair

Dedicated to my husband Larry and son Kyle Hagan for their understanding and support and to my father Wayne Coe for believing in education and in pursuing your passion.

APPROVAL PAGE

This dissertation written by KRISTI COE has been approved by the following committee of the Faculty of The Graduate School at The University of North Carolina at Greensboro.

Committee Chair ______________________________
Robin Bartlett

Committee Members ______________________________
Debra C. Wallace

____
Heidi Krowchuk

____
Diane Hudson-Barr

____
Date of Acceptance by Committee

____
Date of Final Oral Examination

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CHAPTER I

INTRODUCTION

The first year of life or infancy is the period of greatest risk for childhood death (Centers for Disease Control and Prevention [CDC], 2019; CDCa, 2017; CDCb, 2017). In 2016, the number of children spanning ages 1-14 years who died was slightly below 10,000 compared to more than 23,000 infant deaths (CDCa, 2017; CDCb, 2017). The factors resulting in deaths over a lifetime are very different than those causing infant deaths dictating the need for studies examining contributors to infant deaths including morbidities. Reducing fetal and infant death rates is a leading health indicator and a high priority health issue according to Healthy People 2020 (Office of Disease Prevention and Health Promotion [ODPHP], 2019). Rate of infant mortality is an important metric to consider not only on a national level, but also in states and communities since measures of mortality may help predict past, current, and future health in multiple generations (CDC, 2019). This study examined factors associated with morbidity, mortality and other outcomes in a large group of U.S. infants admitted to neonatal intensive care units (NICU) from 2015 to 2017.

Improvements in neonatal intensive care in the past 50 years have led to better survival rates for infants in the U.S. despite the nation's persistent, higher-than-expected rate of infant mortality (Organisation for Economic Co-operation and Development [OECD], 2018). The first month of life or neonatal period is when two-thirds (68%) of infant deaths occur (Ely, Driscoll, & Mathews, 2018; Mathews, MacDorman, Thoma, & Division of Vital Statistics, 2015). Understanding factors contributing to morbidities and mortality in the neonatal period allows for the identification of areas for intervention to decrease these poor outcomes. When the U.S. infant mortality rate was compared with other industrialized countries, a higher rate of preterm birth was found to be the biggest contributor to the high mortality rate (Lorenz, Ananth, Polin, & D'Alton, 2016). Infants born at the earliest gestational ages and the smallest weights have a much greater risk of death and disability compared to those born at term, and thus have a large impact on infant mortality in the U.S. (Mathews et al., 2015). However, when comparing infant outcomes in the U.S. with similar countries, Lorenz et al. found that the U.S. had the fifth lowest number of deaths for infants 24 to 31 weeks gestation (2016). This study also found the U.S. had the highest number of infant deaths for gestations 37 weeks and greater and the second highest number of deaths for infants 32 through 36 weeks gestation (Lorenz et al., 2016). For the current study, infants 32 through 38 weeks gestation were the target population. Outcomes were examined in relation to factors shown in prior studies found to influence infant morbidity as well as mortality. This chapter focuses on the state of the science in care of newborns in the U.S. including a historical perspective of neonatal medicine, current recommendations for care following birth, and prevention of infant mortality, primarily during the first month of life.

Definitions of Population, Periods Surrounding Birth, and Resuscitation Interventions

Multiple terms will be used in these chapters to describe infants and significant periods surrounding birth. Describing infants by gestational age is the preferred method of reporting preterm infant data by professionals, societies and countries (Rysavy et al., 2016). Since preterm and infants born at later gestations will be discussed, this gestational age method is used in this and other chapters.

Table 1. Population Definitions.

Term	Definition	Reference(s)
Neonate	Newly-born infant through a month of age	Neonate, n.d.
Neonatal Period	Birth through 28 days of life	Neonatal Period, n.d.
Fetus	Unborn child from 8 weeks conception to birth	Fetus, n.d
Preterm and Premature	Birth before 37 weeks gestation	American Academy of Pediatrics (AAP) & American College of Obstetricians & Gynecologists (ACOG), 2017; ACOG, 2016a; ACOG, 2016b; Prematurity, n.d
Extremely premature	Birth below 28 weeks	AAP & ACOG, 2017; Patel et al., 2015; Stoll et al., 2015
Moderately preterm	Birth at 32 to 33 weeks	Raju, 2013
Late preterm	Birth at 34 to 36 weeks	AAP & ACOG, 2017; Raju, 2013; Raju, Higgins, Stark, & Leveno, 2006
Early term	Birth at 37 to 38 weeks	AAP & ACOG, 2017; ACOG & the Society for Maternal-Fetal Medicine [SMFM], 2013
Full term	Birth at 39-40 weeks	AAP & ACOG, 2017; ACOG & SMFM, 2013
Late term	Birth at 41 weeks	AAP & ACOG, 2017; ACOG & SMFM, 2013
Post-term	Birth at 42 weeks and beyond	AAP & ACOG, 2017; ACOG & SMFM, 2013
Birth number	Number and order of infants born including single versus twin(s) (and includes triplets and quadruplets)	Atashi, Abdolmohannadi, Dadpasand, & Asaadi, 2012

Other definitions that describe later gestations were used. A “Full Term” pregnancy is broadly considered 37 through 41 weeks gestation (Full Term, n.d.). Describing infants by gestational age and using subcategories based on this age are helpful to anticipate when important developmental stages, such as maturity of the lungs, occur.

While use of gestational age to discuss preterm infant data is suggested (Rysavy et al., 2016), it is also essential that accuracy of weeks of pregnancy be considered. When gestational age determination by last menstrual period (LMP) is used, problems in accuracy arise. Use of LMP assumes regular menstrual cycle lengths of 28 days with mid-cycle ovulation; however, this method does not account for imprecise recall of LMP date, irregular menstrual cycles, or variable ovulation timing (ACOG, Association for Medical Ultrasound [AIUM], & Society for Maternal-Fetal Medicine [SMFM], 2017) leading to uncertainty of actual conception date. While use of LMP was popular for many years, in 2014 the National Center for Health Statistics converted to using the best obstetric estimate of gestation (OE) at delivery after evidence of greater validity was observed when comparing OE to the LMP method and classification of births as preterm was less likely to occur (Martin, Osterman, Kirmeyer, Gregory, & Division of Vital Statistics, 2015). The OE method consists of obtaining early ultrasound measurements (gold standard) of the fetus or embryo (up to 14 weeks gestation), LMP data when available, or if assisted reproductive technology (ART) was used, embryo age and transfer date are used to determine estimated due date or gestational age at birth (ACOG, AIUM, & SMFM, 2017). For OE precision, it is imperative that mothers initiate prenatal care before 22 weeks since accuracy of ultrasound dating decreases after this period (ACOG, AIUM, & SMFM, 2017).

To identify infants at risk of developing complications, periods of time before, during, and immediately after birth are defined as well as whether resuscitative assistance was needed at birth (AAP & ACOG, 2017). Clarifying terms that describe the neonatal period is crucial since two thirds of infant deaths occur in this period according to the Centers for Disease Control and Prevention (CDC) (Ely et al., 2018; Mathews, MacDorman, Thoma, & the Division of Vital Statistics, 2015). These terms aid in describing significant time periods that affect neonates from birth to discharge. Of the categories defined in Table 2, "perinatal" is a broad term with multiple meanings which will be used in this study to describe events which occur during birth.

Table 2. Definitions of Time Periods Surrounding Birth.

Term	**Definition**	**Reference**
Prenatal	Preceding or before birth	Prenatal, n.d.
Perinatal	Before, during or after birth including the first 7 days following delivery	Perinatal, n.d.
Postnatal	Following birth; usually up to one year of birth	Postnatal, n.d

Resuscitation measures are needed in 10% of US births according to the AAP and American Heart Association (AHA) as well as the Cochrane Database of Systematic Reviews (AAP & American Heart Association [AHA], 2016; Dempsey, Pammi, Ryan, & Barrington, 2015). While interventions such as resuscitation measures are not the focus of this study, when neonates require (resuscitative) assistance at birth, they are often affected later in life (AAP & ACOG, 2017; Shepherd, Salam, Middleton, Han, Makrides, McIntyre et al., 2018), and many resuscitation measures used at birth involve breathing assistance which may continue after admission to the neonatal intensive care unit (NICU). Since this study focused on the neonatal period and a few weeks past this interval (primarily to obtain length of stay information), these interventions will be defined. Resuscitation at birth can include basic interventions such as giving supplemental oxygen to a full neonatal resuscitation. According to the AAP, the ACOG, and the AHA, less than 1% of infants need extensive resuscitation at birth (AAP & ACOG, 2017; AAP & AHA, 2016), such as use of epinephrine, therefore, resuscitation using medications was not addressed in this study.

Table 3. Resuscitation Measures for Neonates following Birth.

Term	**Definition**	**References**
Positive pressure ventilation (PPV) or **mechanical ventilation**	Helping a patient to breathe using an artificial device	Mechanical Ventilation, n.d.
Chest compressions	Forcible depressions of the chest wall during cardiopulmonary resuscitation to circulate blood	Chest Compression, n.d.
Intubation	Insertion of a tubular device into a cavity such as passage of a tracheal tube for control of pulmonary ventilation or for anesthesia	Intubation, n.d.
Continuous positive airway pressure (CPAP)	A method of ventilation used to keep alveoli open after exhalation in patients who are breathing	CPAP, n,d.

Historical Influences on Infant Health

Background

Historically, landmark events advocating U.S. infant health and survival started in 1912 with establishment of the Children's Bureau, an agency created to protect children, whose first initiative was public recording of births (U.S. Department of Health and Human Services [DHHS], n.d.). Following was approval of the Sheppard-Towner Maternity and Infancy Act of 1921 which established the first federal aid for state programs for prenatal and infant health to combat mortality (History, Art & Archives, U.S. House of Representatives, n.d.). This Act, initially approved for five years, later expired, but was resurrected in 1935 with approval of the Social Security Act (Social Security Administration [SSA], n.d.). Title V of the Social Security Act entitled "Grants to States for Maternal and Child Welfare" is also referred to as the Maternal-Child Block Grant which continues to support prenatal and newborn care primarily in rural areas through health departments (SSA, n.d.). In 1962, initiation of the National Institute of Child Health and Human Development (NICHD) created a funding source to study birth defects and intellectual and developmental disabilities in early childhood and infancy (Eunice Kennedy Shriver National Institute of Child Health and Human Development [NICHD], 2017). These early laws and funding sources shaped much of the care for infants remaining in place today.

A pivotal event affecting infant and specifically newborn care occurred in 1963 when President John F. Kennedy and wife Jacqueline's son, Patrick Bouvier Kennedy, was born prematurely at 34 weeks gestation in a small hospital, transferred to Boston

Children's Hospital, and then died within three days from respiratory failure (Altman, 2013). Although baby Kennedy was nearly the size of a term infant, his lungs were underdeveloped and his life could not be saved with the existing system of care for newborns in 1963. The death of the President's baby received an outpouring of public attention prompting pediatricians as well as obstetricians to examine how to reshape perinatal care in the US, especially the care of infants pre- and postnatally. Soon after this event, the neonatal period became recognized as a time of great risk for infants largely through collection of birth data (DHHS, n.d.) and later death certificates.

Influences on Infant Health Before and Soon After Birth

Advances in care of infants and recognition of risks for negative outcomes can be assessed by examining (medical) treatment during the prenatal, perinatal, and postnatal periods. Improvements during the pre- and perinatal periods include initiation of prenatal care in the first weeks of pregnancy (AAP & ACOG, 2017), delivery within a hospital (ACOG, 2017a), improved recognition and management of preterm labor (ACOG, 2016a), and delivery of high-risk infants in a setting with resources capable of caring for the infant (AAP & ACOG, 2017). Postnatal care of infants has been improved by increased availability of advanced (Level III and greater) NICUs, progressive technology including multiple modes and methods of ventilation as well as monitors and other equipment facilitating care of critically ill neonates (AAP & ACOG, 2017). These improvements have resulted in better outcomes for U.S. neonates, however, much work remains.

The prenatal period is a critical time not only for fetal growth and development, but also for establishing accurate dating of pregnancy (AAP, AIUM, & SMFM, 2017). Optimally, prenatal care should be initiated as early as possible in the first trimester of pregnancy (AAP & ACOG, 2017; ACOG, AIUM, & SMFM, 2017), and early dating (determination of gestational age) is essential to improve outcomes as well as for public health initiatives (ACOG, AIUM, & SMFM, 2017). According to ACOG, each of the three trimesters of pregnancy are 12-13 weeks in length or about 3 months (ACOG, 2018). Frequency of prenatal visits are individualized based on risks including outcomes in earlier pregnancies, chronic medical conditions, bleeding, use of assisted reproductive technologies, and if the mother is carrying multiple fetuses (AAP & ACOG, 2017). For an uncomplicated pregnancy, prenatal visits are scheduled monthly until 28 weeks gestation, every 2 weeks until 36 weeks gestation, then weekly until delivery (AAP & ACOG, 2017). Counseling and identification of complications such as inadequate growth or absent fetal heart rate occur during prenatal visits and are important for assessing health of the fetus as well as the mother.

The perinatal period is an opportune time to assess risks during labor and delivery when fetal monitoring can identify problems and prompt interventions to prevent undesirable outcomes (AAP & ACOG, 2017). The physical location of where birth will occur can significantly affect outcomes, especially for the infant (AAP & ACOG, 2017). While most births occurred at home in the first half of the 1900s, a shift to the hospital occurred in the second half of the 1900s so that by 1967, based on a sample of 20 to 50% of reported births, 98.3% of infants were delivered in a hospital setting (National Center for Health Statistics [NCHS], 1967). Currently about 0.9% of births occur in the home setting in the US (AAP & ACOG, 2017). While this setting may be beneficial for the mother (Snowden, Tildel, Snyder, Quigley, Caughey, & Cheng, 2015; ACOG, 2017b), there is more than a twofold risk of perinatal death (1 to 2 per 1,000) and a threefold risk of serious neurologic outcomes (0.4 to 0.6 per 1,000) with home births compared with births in the hospital setting (AAP & ACOG, 2017). The ACOG recommends delivery in hospitals (and accredited birth centers) as the safest location for birth (AAP & ACOG, 2017). In the 1970s, perinatal services began to be organized as a model of delivering care and regionalization of services began to be recognized as a necessity to match mother and infant need with available services (AAP & ACOG, 2017). Mothers who are at high risk of delivering an infant needing advanced care are encouraged to deliver at hospitals offering a Level III NICU to provide the best outcomes for the infant (AAP & ACOG, 2017).

In the postnatal period, care for infants has been influenced by not only birth in an appropriate level hospital, but by management of neonates needing resuscitation at birth and by opening of neonatal intensive care units (NICUs) to care for high-risk neonates in most urban areas and in a few rural areas. The American Academy of Pediatrics (AAP) created guidelines (as early as 2004) and established levels of NICU care (I-IV) based on infant need including risk of needing specialized care when born prematurely (AAP & ACOG, 2017). Hospitals with Level I services can provide resuscitation at birth and care for infants 35 weeks and greater. Level IV NICUs are able to provide a full range of pediatric subspecialists, surgical repair of congenital conditions, and facilitate transport of infants needing critical care.

Defining the Study Population

Despite medical advances and national guidelines to delivery infants closer to term, the number of infants born preterm continues to increase in the U.S. (CDC, 2018; Martin, Hamilton, & Osterman, 2019; Martin, Hamilton, & Osterman, 2018a), as does the rate of infants born early term at 37 and 38 weeks (Martin et al., 2019; Martin, Hamilton, Osterman, Driscoll, & Drake, 2018b). Although infants born 39 to 40 weeks gestation are much healthier than those born earlier, those born between 32 and 38 weeks are an important group to study since infants in this group are more likely to need care in a NICU than full term infants and since the U.S. rates of mortality are high among this group when compared to other nations (Lorenz et al., 2016). Preterm births rose to 10% in the latest 2018 birth data (Martin et al., 2019); an increase of 1% from 2016 (Martin et al., 2018a), and 3% from 2015 (Martin et al., 2018b). Interestingly, 72% of preterm births (Martin et al., 2018a) and 7.1% of total US births are considered late preterm (LPT) (34 through 36 completed weeks gestation) (CDC, 2018). This is more desirable than being born earlier since LPT infants tend to be healthier and likely require less time in the hospital than earlier-born infants. While this LPT birth rate was less than the rate in 2012 (8.1% of births) (Martin, Hamilton, Osterman, Curtin, & Mathews, 2014), this rate increased from 2015 when the rate was 6.9% (Martin et al., 2018b), indicating a decline in early 2012 followed by a steady increase over subsequent years as reflected in the latest data. The rate of early term births (37 and 38 weeks) increased slightly from

24% to 26.5% of total births in the same period (Martin et al., 2019). Birth rates for infants born mid-preterm or at 32 and 33 weeks gestation are not as clear and have not been widely studied. In 2016, there were 3,945,875 total registered births in the US (Martin et al., 2018b). Of these, ordered by numbers, 1,004,224 (25%) were born early term, 279,382 (7%) were born late preterm, and another 45,979 (1%) were born mid-preterm. Collectively, this group of infants 32 to 38 weeks gestation or older preterm and early term (OPET) were 34% of total annual births or 1,329,585 infants in 2016 (Martin et al., 2018b).

Consisting of more than a third of U.S. annual births and contributing to some extent to infant mortality and morbidity, OPET infants are an important group to study. This is a group and a group that has not been sufficiently studied and the group targeted for this study since many require admission to the NICU and experience a longer-than-expected hospital stay. Studying infants born before 28 weeks would be ideal if the research aim was purely to examine infant mortality since their risk of death is highest. However, large, longitudinal studies with these smallest infants have recently been published (Patel et al., 2015; Stoll et al., 2015), limiting the effectiveness of additional single studies examining the same gestational ages.

Although mortality rates of infants born later are considerably less than those born 22 to 28 weeks gestation (Patel et al., 2015), OPET infants are at risk for unfavorable outcomes including prolonged length of hospital stay compared to infants born at 39 to 40 weeks. This prolonged hospitalization contributes to parental lost work time as well as time away from home and family for parents. Many of these infants are admitted to a

NICU where parents may have limited bonding and feeding time with their infant based on the infant’s acuity and the NICU environment which may be unsuitable to continuous parent lodging.

Births of earlier-than-term but not extremely low gestational age (ELGA) are likely a result of several factors including professional-driven guidelines for close fetal surveillance in women at high risk for stillbirth. For those who have experienced stillbirth, it is a devastating event with life-long consequences, and for obstetricians, a feared outcome of pregnancy (Prosser-Snelling, 2016). An international study of 28 developed countries found those countries with high rates of middle to late preterm births had fewer stillbirths as well as fewer neonatal deaths among those born 32 weeks and later (Lisonkova, Sabr, Butler, & Joseph, 2012). The authors of this study suspect that delivery of compromised fetuses which otherwise would have died in utero or the neonatal period has resulted in an upward trend in preterm births (Lisonkova et al., 2012). Another study found the number of prenatal visits above normal increased the incidence of induced preterm birth likely by increasing detection of obstetric problems (VanderWeele, Lauderdale, & Lantos, 2013). The ACOG recommends increased antenatal fetal surveillance beginning at around 32 weeks for women at risk for stillbirth (ACOG, 2014; Preboth, 2000). Given that the stillbirth rate is shifting to live births that are slightly early, this is optimal for child-bearing families as well as for obstetrical providers, but of concern to neonatal staff. Neonatal intensive care units are challenged with creating better methods of caring for OPET infants to promote positive outcomes. Understanding how to better care for these infants could be informed by studying the population including those factors contributing to their morbidity and mortality during hospitalization.

Factors Affecting Length of Stay in the Study Population

Late preterm (and likely early term) infants are at risk for respiratory illnesses, hypothermia, hypoglycemia, hyperbilirubinemia, and difficulties with feeding (AAP & ACOG, 2017) which can lead to NICU admission. Moderately preterm infants are also at risk for these morbidities (Boyle et al., 2015). These conditions, especially those involving the respiratory system, have causes that are infant-related such as immature organ systems and delayed transition to extrauterine life and they will be referred to as health/illness factors throughout this report. Other health and illness factors experienced by infants include major congenital anomalies, diagnosis of chronic lung disease, inborn versus outborn admission, and Apgar score at 5 minutes of life. These conditions can lead to NICU admissions, however, additional causes of NICU admission occur prenatally including maternal health factors during pregnancy. These factors including maternal age, race, and presence of illnesses such as pre-eclampsia and diabetes will be referred to as “prenatal” and then later as situational factors in subsequent chapters.

The number of NICU admissions by a percent of all births in the US varies annually as well as by time of year. In a recent study of 358,453 live births in California, 10% of infants were admitted to a NICU (Schulman, Braun, & Lee, 2018). According to a 2011 March of Dimes and National Perinatal Information Center report of 183,030 newborn births during the length of the study period, 14.4% required admission to a NICU (March of Dimes [MOD] & National Perinatal Information Center [NPIC], 2011).

A Centers for Disease Control and Prevention (CDC) study found that nearly 7% of births in the U.S. required NICU admission (Osterman, Martin, Mathews, & Hamilton, 2011). The next section will discuss factors involving infant health and illness such as chronic lung disease and major anomalies as well as maternal factors including mother's age and illnesses associated with NICU admission by two main categories- infant health/illness and prenatal factors.

Causes of NICU Admission Attributable to Infant Status

Prematurity. Infants born prematurely are born between 22 weeks gestational age (GA) based on accurate dating to 36 weeks and 6 days gestational age (AAP & ACOG, 2017). Although some centers resuscitate infants as early as 22 weeks gestational age (GA), others consider viability at 23 weeks and do not resuscitate at earlier GA due to a high incidence of mortality. In the US, 67% to nearly 70% of all infant deaths occur among those born preterm (Ely and Driscoll, 2019; MacDorman, 2011), making this the greatest cause of infant mortality, by far, in the first 12 months of life. While the earliest-born die more often, infants 32 to 33 weeks have a mortality rate nine times that of full-term infants (Mathews et al., 2015). Although infants born at less than 32 weeks GA comprise about 72% of NICU deaths, mid- to late preterm and early term infants have about a 5% risk of mortality while in the NICU (Jacob, Kamitsuka, Clark, Kelleher, & Spitzer, 2015). Since the number of older preterm infant births are increasing, this is likely a group that can impact overall mortality rates. Most infant deaths (67%) occur during the neonatal period (Ely, Driscoll, & Mathews, 2018; Mathews et al., 2015) and the majority die while still hospitalized, making deaths among hospitalized neonates a large contributor to infant mortality (Jacob et al., 2014). Since the older preterm and early term (OPET) group is at least one third of all births, their deaths are likely significant contributors to overall mortality and studying their outcomes could identify issues that, if addressed, could reduce their mortality.

Factors increasing risk for unfavorable outcomes in preterm infants are complex. Immature body systems, especially the respiratory system, significantly contribute to NICU admissions. In mid- to late preterm infants, lung hypoplasia was the top cause of NICU deaths in one study (Jacob et al., 2014). Another cause of NICU deaths in mid- to late preterm infants was presence of a lethal anomaly including those involving the brain, kidneys, and known or suspected genetic anomalies (Jacob et al., 2014).

Respiratory Illnesses. Although newly-born infants require support beyond the delivery room and newborn nursery for many causes, respiratory distress is the most common reason for admission to the NICU (Edwards, Kotecha, & Kotecha, 2013). The term "respiratory distress" in neonates is often confusing. While some authors use the term generally to describe most, if not all, respiratory diseases present in the newborn period (Reuter, Moser, & Baack, 2014), others only use the term to refer to respiratory distress syndrome (RDS), a condition of inadequate production of surfactant (Polin, Carlos, & Committee on Fetus & Newborn, 2014; Sun et al., 2013). Other terms used include respiratory insufficiency, respiratory failure, and more recently respiratory morbidity. Since the population used in this study was infants born at 32 to 38 weeks GA with differing degrees and causes of respiratory illness, respiratory diseases will be subsequently referred to as respiratory illnesses.

Prenatal Causes of NICU Admission

Maternal Demographics. Several factors related to mothers of premature infants influence the risk of NICU admission for their infants. Maternal age is steadily increasing in the U.S. and the average age of mothers at first birth was 26.6 years in 2016 (Martin et al., 2018b). In 2008, the rate of NICU admission per 1,000 births for women under 20 years was 63% compared to a rate of 54% in women 20 to 29 years (Osterman et al., 2011). For women 40 to 54 years, the rate of NICU admission was 78% for singleton births and 100% for multiple births in the same time period (Osterman et al., 2011). Maternal education level also has an impact on birth outcomes. Those with higher education levels more often give birth to fewer children and are less likely to engage in behaviors not conducive to health and pregnancy such as smoking and use of illicit drugs (Osterman et al., 2011). The month of pregnancy when women initiate prenatal care is another factor affecting birth outcomes. In 2017, 77% of women initiated prenatal care in the first trimester of pregnancy (Martin et al., 2018b), an increase of 71% from 2008 (Osterman et al., 2011). A recent study in China found that when timing of and number of prenatal visits were inadequate, deliveries were associated with an increased risk of preterm birth (Huang, Wu, Zhao, Hu, Yang, & Chen, 2018). Maternal demographic factors are important to consider when examining contributors to NICU admission.

Maternal Illnesses. As the nation's births to mothers aged 30 to 40 years has steadily increased (Martin et al., 2018b), the incidence of many maternal illnesses, both chronic and acute has increased (Osterman et al., 2011). A recent systematic review and meta-synthesis found that the incidence of hypertension (in pregnancy) was higher in women aged 35-40, and NICU admission and neonatal death were positively correlated with increasing maternal age (Lean, Derricott, Jones, Heazell, 2017). Researchers in France identified vascular placental disease as the number one cause of preterm delivery in a sample of 3915 infants (Chevalier et al., 2017). This group of researchers listed conditions comprising vascular placental disease as: maternal hypertension, preeclampsia (pregnancy-induced), eclampsia (hypertension causing seizures), and hemolysis, elevated liver enzymes, low platelet syndrome (HELLP) (Chevallier et al., 2017). Another study examined 8,947 births in Thailand and found that in infants requiring NICU admission, 33.7% had mothers with hypertensive disorders and/or diabetes (Phaloprakarn, Manusirivithaya, & Boonyarittipong, 2015). Obesity, in addition to advanced maternal age, is another factor that contributes to chronic illnesses such as diabetes and hypertension, as well as to adverse infant outcomes such as preterm birth, stillbirth, and NICU admission (Scott-Pillai, Spence, Cardwell, Hunter, & Holmes, 2013).

Diabetes is prevalent and increasing in the general population of women in the U.S. that includes those of childbearing age. Many sources now distinguish pre-pregnancy diabetes mellitus (DM) from gestational diabetes mellitus (GDM) to separate the onset of disease as chronic or acute. In 2008, the prevalence of DM increased steadily with maternal age from a rate of 2.3 per 1,000 mothers for those under 20 years of age to a rate of 14.0 per 1,000 for women 40 years and over (Osterman et al., 2011). For GDM, the rate was 4% of all mothers and the incidence increased strikingly with advancing maternal age (Osterman et al., 2011). Additionally, maternal diabetes is a known risk factor for respiratory illness in neonates (National Heart, Lung, and Blood Institute, n.d.). In a large study of 18,095 singleton births in France, the incidence of respiratory illness in infants born at 34 weeks GA or later was 5.7% in mothers with insulin-treated diabetes mellitus, and 2.1% in non-insulin treated diabetes (Becquet et al., 2015), likely reflecting a higher incidence of illness in infants whose mothers had advanced diabetes. Another recent study in Sweden examined maternal and pregnancy-related conditions and morbidity in late preterm (LPT) infants (Bonnevier, Brodszki, Björklung, & Källén, 2018). In this study, hypertensive diseases and preterm, pre-labor rupture of membranes (PPROM) occurred in 33.6% of late preterm births and were the most frequently occurring conditions affecting infant outcome in the study population. For respiratory-specific morbidity in LPT infants, antepartum hemorrhage or bleeding doubled the risk for any respiratory disease and need for respiratory support, and PPROM significantly increased the risk for respiratory disease in their sample (Bonnevier et al., 2018).

Summary

Neonates born at 32 to 38 weeks gestation are an important group to study since the incidence of adverse outcomes, although smaller in number than those born at less than 28 weeks gestation, have not been well established. Outcomes associated with this OPET group needing study include outcomes such as total length of hospital stay before and after birth, incidence of morbidity including respiratory illnesses, and mortality. Other covariates that should be examined as maternal contributors to NICU admission include maternal age at delivery, education status, initial onset of prenatal care, presence of chronic or acute illnesses such as hypertension and/or diabetes, obesity identified by mother's body mass index (BMI), antepartum hemorrhage, and PPROM. With numbers of OPET births increasing, the study of this group is imperative to understand not only causes, but consequences of these births. This study and others could help guide the development of interventions that may decrease the number of preterm births in this period and guide the development of appropriate interventions for mothers, fetuses, infants, and their families that could contribute to a decrease in morbidities in this population and when morbidities and NICU admissions arise, how to successfully navigate these events.

Theoretical Framework

Transitions Theory

The Theory of Transitions was first mentioned as a concept applicable to nursing in 1986 (Chick & Meleis, 1986). This Theory was generated by examining earlier developmental theories and models of stress and adaptation and was created to capture the idea that change and development experienced by individuals during various life events have a key impact on well-being (Chick & Meleis, 1986). Transition Theory evaluates movement of individuals from one state or condition to another (Chick & Meleis, 2010). Authors of the Theory recommend examining a transition as both a process (most popular for testing the theory) and outcome allowing one to alter the focus between final result and process (Chick & Meleis, 2010).

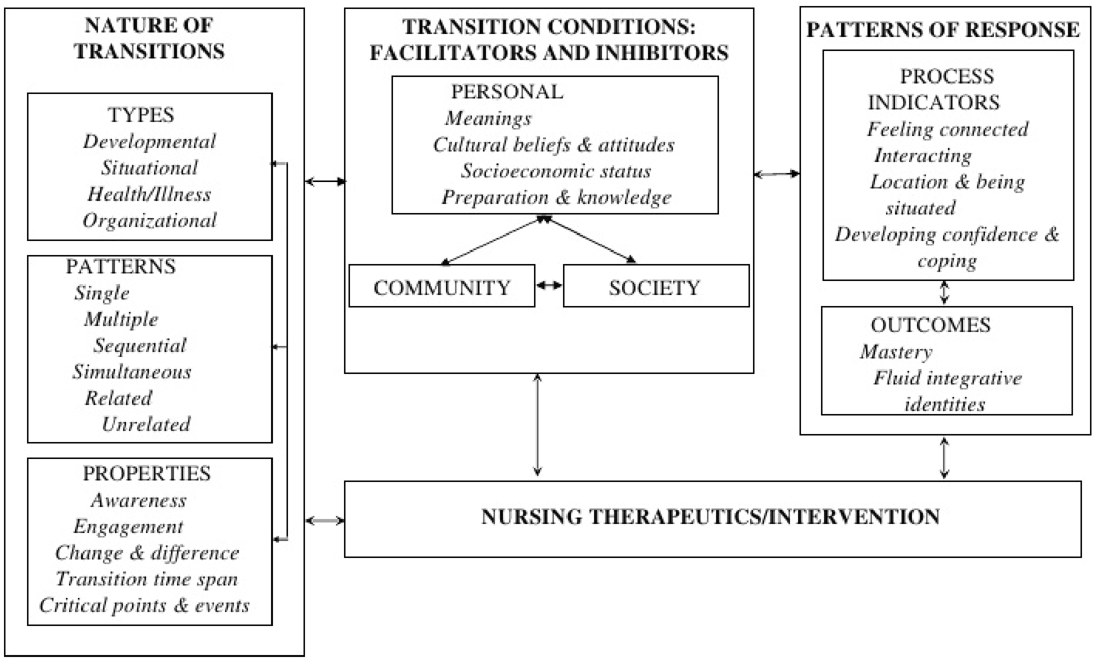
Important Concepts

The concepts in Transitions Theory can assist researchers, educators and potentially neonatal staff in understanding why some neonates with immature physiologic systems or other morbidities fail to adapt immediately after birth and in the first few weeks afterwards leading to a prolonged NICU stay and for some, mortality. First, the nature of the concept of transitions refers to factors before and after a life event such as birth, that influence one's progression and affect patterns of response, a second key concept in Transitions Theory. Nature of transition types include situational, health/illness, developmental, and organizational. Situational and health-illness events are often those which require the greatest adaptation and have a lasting impact on patients' health, family, and future (Chick & Meleis, 1986). Situational events pertinent to this study included prenatal factors- primarily maternal- that influenced neonates' NICU transition and hospitalization. Health-illness issues in this study included infants' five-minute Apgar scores (describing postnatal transition status at 5 minutes of life) and number of days and types of respiratory support needed. Developmental factors were included and consisted of gestational age and birthweight since these factors significantly affect mortality (AAP & ACOG, 2017) and likely influence other outcomes. Organizational factors examined in this study were limited since the sites were blinded in the dataset, however, basic information such as the number of infants contributed per site, average gestational age and number of respiratory support days were included and these organizational factors were a secondary study aim.

Another applicable concept of Transitions Theory used in this study was response patterns after a transition, primarily outcome indicators. For this study these outcomes were days of respiratory support needed, length of stay, disposition at discharge (transferred versus alive and died versus alive), and if equipment such as oxygen or a monitor were needed at discharge.

An important additional concept (not yet considered a main concept in Transitions Theory) is that during a transition period or event, patients are described as being “at risk” (Chick & Meleis, 1986). See Figure 1. Since the neonatal period is when 68% of infant mortality occurs (Ely et al., 2018; Mathews et al., 2015), this is a critical time when both mortality and morbidity are more likely to occur. While birth itself is a crucial period of abrupt physiological change for the neonate, the period following birth is a time when neonates often develop health problems such as respiratory illnesses, especially if they are born prematurely or have congenital anomalies. Transition after birth then extends beyond the first few minutes of life into days, weeks, and for some, months depending on developmental, situational, and health/illness factors. While the incidence of death declines after the first week of life, the remaining hospitalization period of OPET infants continues to be a period of transition where the preterm or early term infant recovers from illness and begins to achieve key developmental tasks such as initiation of enteral feedings. Hospitalized neonates are likely “at risk” throughout hospitalization since they are susceptible not only because of their immature physiology, but because of prenatal and environmental factors. This transition period is one where important steps occur in recovery of the process of maturing organs including the respiratory, neurological, and other systems.

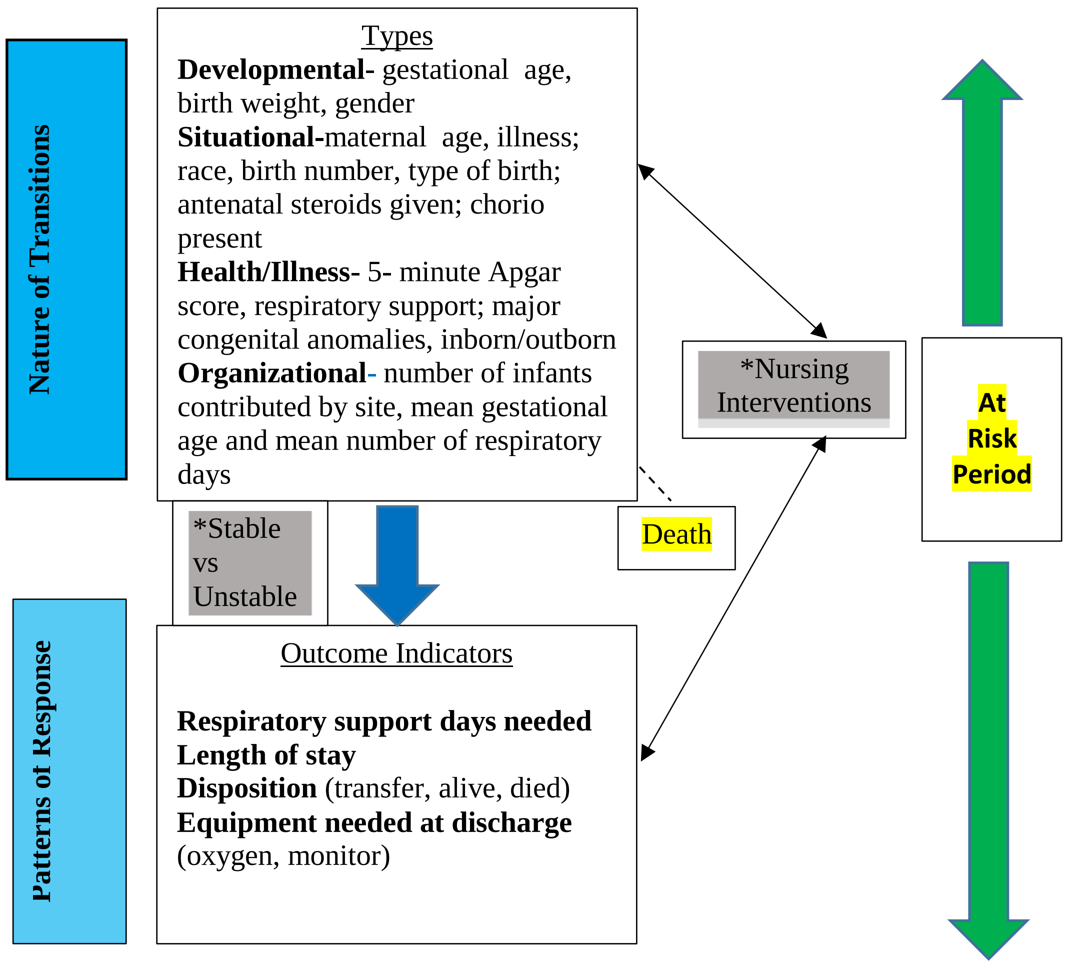
Figure 1. Experiencing Transitions: A Middle-Range Theory in Process.



From Meleis, A.I., Sawyer, L.M., Im, E-O., Hilfinger Messias, D.K., & Schumacher, K. (2000). Experiencing transitions: An emerging middle-range theory. *Advances in Nursing Science, 23,* 12-28. (Figure 1)

The overall study aim was to explore which factors influence successful transitions in infants admitted to the NICU. A proposed transition model for the postnatal course of the target group is listed in Figure 2. This model depicts an algorithm where infants progress as their condition/transition period improves to a level of stability, indicating a path toward discharge when successful transition ultimately occurs.

Figure 2. Proposed Conceptual Framework for Postnatal Course of Infants 32-38 Weeks Gestation.



*Not tested in this study
Abbreviations used: OB= obstetric; chorio = chorioamnionitis (infection of fluid surrounding baby)

Since this study involved use of observed, quantitative data from patient records and did not involve family or staff interviews, a conceptual framework based on Transitions Theory was proposed including relevant concepts and available variables. Most concepts in the proposed conceptual framework were adapted from a 2000 publication which proposed Transitions Theory as a middle-range theory (Figure 1) (Meleis, Sawyer, Im, Hilfinger Messias, & Shumacher, 2000). The concepts used from the 2000 version of the model were the types of transitions section from nature of transitions and process indicators from the patterns of response section. Patterns and properties as well as process indicators were removed because these sections appear to have been refined using subjective patient responses (University of Pennsylvania, n.d.) with survey methods not possible with an infant population. The middle section of the earlier model- transition conditions: Facilitators and inhibitors was removed for multiple reasons. First, these conditions include personal meanings requiring subjective data as well as community and society facilitators/inhibitors which need study beyond the hospital environment, such as with the geographic location of one's home, where transitions might be might directly affected. Second, these transition conditions as a between step for two concepts imply a potential mediating or moderating effect on the relationship between nature of transition and patterns of response which was beyond the scope of this study.

Mediating effects are the transmission of the effect between a predictor or independent variable on an outcome or dependent variable through a third intervening variable, known as the mediator (Fritz & MacKinnon, 2007). Mediators supply information regarding how or why two variables are strongly associated (Bennett, 2000). For a mediator to be considered, several steps to test the mediated effect are recommended including the effect of the predictor/independent variable on the mediator must be significant (Baron & Kenny, 1986; Fritz & MacKinnon, 2007). In the proposed study, there is little known about whether potential mediators such as infant race and gender are significantly affected by predictors such as situational factors like maternal hypertension.

The Influence of Nursing on the Transition Concepts

Another pertinent tenet of Transitions Theory is that not only do individual and environmental factors influence health outcomes, but nursing care has the potential to influence outcomes during a transition period. In the NICU, nurses are frontline staff with consistent patient contact. They are responsible for total care including support of breathing and circulation, providing and ensuring warmth, and delivering life-saving therapies such as medications and intravenous nutrition. Additionally, nurses impact neonatal outcomes by delivering evidence-based care and by recognizing abnormal vital signs or signs of worsening status and alerting NICU medical staff promptly. Nurse practitioners affect neonatal outcomes, but in a role often less visible but equally as important as nurses. Nurse practitioners examine groups of patients, present findings during medical rounds with a neonatologist and frequently additional specialists, write orders including nutrition and initiation of medications, and conduct procedures such as intubation of the trachea to provide surfactant and mechanical ventilation. Nurse practitioners attend high-risk births and help resuscitate as needed. While nurse practitioners do not typically obtain bedside data, they compile other data routinely such as that needed to assess hydration of infants and test results that may determine acuity or the need to wean support. Nurse practitioners manage abrupt changes in patient status such as respiratory arrest and intervene to mitigate these changes.

Conclusion

Birth at 32 through 38 weeks gestation often results in several physiologic as well as environmental changes for the neonate. For example, as neonates adapt from intra- to extrauterine life, water-filled lungs are filled with air as the infant initiates postnatal respirations independent of the placenta (AAP & ACOG, 2017). Respiratory illnesses can develop in the first few hours after delivery and these illnesses as well as other factors might affect length and level of care during hospitalization overall as well as result in mortality. A study of how older preterm and early term infants transition to life outside the uterus is important to conduct and disseminate so that NICU staff can counsel parents as well as anticipate disease processes and additional needs of transitioning infants and their families.

Research Questions and Study Aims

Research Question #1

Which developmental transitions influence patterns of response among the outcome indicators in infants born at 32 to 38 weeks gestation?

Research Question #2

What situational transitions influence patterns of response among the outcome indicators in the intended population of infants?

Research Question #3

What health/illness transitions influence patterns of response among the outcome indicators in the intended population of infants?

Research Question #4

What combination of developmental, situational, and health/illness transitions most influence patterns of response in infants born 32 to 38 weeks?

Secondary Research Question

Are there differences in transitions related to organizational transition?

Aim

The aim of this study is to assess the impact of situational, health/illness, and developmental factors in older preterm and early term (OPET) infants on outcome indicators during the initial hospitalization following birth.

In the next chapter a review of the literature on short term outcomes in infants 32 to 38 weeks gestation is provided.

CHAPTER II

REVIEW OF THE LITERATURE

This study's focus was to assess the impact of situational, health/illness, and developmental factors in older preterm and early term (OPET) infants on outcome indicators during the initial hospitalization following birth. This focus is expected to enhance comprehension of factors contributing to both positive and negative transitions in infants admitted to the neonatal intensive care unit (NICU). This chapter will examine the literature surrounding the nature and type of transitions in the neonatal population, particularly respiratory conditions associated with NICU admissions, and response patterns or outcomes of this population. Most of the existing literature about morbidity and mortality in neonates has used the extremely low gestational age (ELGA) infant as the focus (Stoll et al., 2015). Less is known about neonates born at later gestational ages including those between 32 and 38 weeks and how they transition from birth to discharge. This review will examine existing studies of hospitalized neonates 32 to 38 weeks, especially information related to respiratory illnesses and outcomes. The main objectives for this chapter are to evaluate current literature surrounding morbidity and transitional outcomes in a select group of neonates, identify the unknown or gaps in the literature, and propose future studies for this group.

Neonates with gestational ages (GA) between 32 to 38 weeks were the source population examined in this review. Neonates are often listed separately in the literature according to gestational age groups including middle preterm (32 to 33 weeks gestation), late preterm (LPT; 34 to 36 weeks) and early term (37-38 weeks) infants. In this chapter, neonates 32 to 38 weeks will collectively be referred to as the older preterm and early term (OPET) group.

To link the intended population from nature of transitions to response patterns, several comparisons were used in this review, primarily the types of transitions surrounding neonates in the OPET group (Figures 1 and 2). These types were grouped by situational, health/illness, developmental, and organizational causes. In cases where the OPET group was not well-studied in the literature, comparisons of gestational age groups within or outside of 32 to 38 weeks were included such as studies of LPT infants or those with earlier and later gestations.

Outcomes are essential to review since they assist health care providers daily in making care decisions. In the proposed conceptual framework used for this study (Figure 2), a patterns of response category is listed along with an outcome indicator subcategory of variables that suggested areas for assessing and measuring a group's response to a transition event. Outcome indicators important for neonates overall include the average length of stay (LOS) in the hospital after birth which help NICU staff counsel parents and aids in planning care when a new OPET neonate is admitted. Other outcomes assessed in this chapter were the length of time respiratory support is needed which assesses respiratory stability, and disposition including mortality. These outcomes help obstetric and NICU staff prepare families for the types of support required for an OPET infant when an imminent delivery is suspected. Time to full or all enteral feedings and transitions to state changes are also important outcomes to assess infant progress with transition after birth, but data to assess these outcomes were not available at the time of this study.

Interventions in OPET infants were not a focus of this chapter but are mentioned in relation to support of the respiratory system to assist in identification of severity of illness in the population. Interventions that support the respiratory system in the NICU include administration of gas flow with a blended air and oxygen mixture (nasal cannula or high-flow nasal cannula), continuous positive airway pressure (CPAP) which delivers gas flow and provides pressure, and mechanical ventilation with conventional or high frequency ventilation. Another intervention seen in the OPET group that is mentioned in the literature is medication administration for respiratory conditions including surfactant administration via an endotracheal tube to help those neonates with a surfactant deficiency.

The last area assessed in this review was the methodology utilized for the articles chosen for the review. Although a scoring system could be used to assess the strength of evidence, since the literature pertaining to OPET infants was limited, this strategy was not feasible due to little to no earlier studies examining this gestational age group. Also, many studies pertaining to this topic were observational, more common in epidemiologic-type research than experimental designs, so studies with robust observational research designs were examined including cohort studies with large sample sizes. Priority was given to articles with the strongest evidence such as systematic reviews and meta-analyses or multi-site studies which may control for differences in unit and provider group practices.

Information Sources and Eligibility Criteria

Sources of information used for this review included systematic reviews, meta-analyses and additional reputable sources for nursing, medicine and allied health as well as publicly-reported US data. The Neonatal Cochrane and the Cochrane Pregnancy and Childbirth Libraries were accessed. PubMed, the primary medical database used in the US, and the Cumulative Index for Nursing and Allied Health Literature (CINAHL) database, specific to nursing literature and allied health were also used. The ProQuest database was then used to locate studies not captured in the prior sources.

Studies included in this review examined a specified neonatal population and occasionally those born earlier than 32 weeks or later than 38 weeks to encompass existing and current literature on the topic. Studies examining situational or prenatal factors associated with neonatal outcomes were also included. Sources for the review were published in the last 5 years covering 2014 through 2019. However, when little evidence was found, this time frame was extended to the last 10 years to include 2008 to 2019. Sources in English (or those sources translated to English) were used. The publications used included full text electronic sources as well as those available through the school's library resources. Only articles published in peer-reviewed journals were used for the review. Overall, 15 studies were included in this review and two were excluded due to weight of 500 grams or less and GA 22-30 weeks gestation.

Findings of the Literature Search

Systematic Reviews

Although the target population for this review was infants 32 to 38 weeks, no reviews were found that discussed this group as a whole. In the Neonatal Cochrane site, reviews mentioning middle (or "mid") preterm or early term infants were not found, but two reviews mentioned late preterm infants in the title and grouped them with term infants (El Shahed, Dargaville, Ohlsson, & Soll, 2014; Tan, Lai, & Sharma, 2012). The Cochrane Pregnancy and Childbirth site contained only one review pertinent to neonatal outcomes that mentioned births 24 -34 weeks gestation in the title (Churchill, Duley, Thornton, Moussa, Hind, & Walker, 2018), but most only mentioned preterm birth generically and did not specify specific gestations. The Pregnancy and Childbirth Library contained more updated reviews than the Neonatal Library and had more that were beneficial for this chapter. The pregnancy reviews included four that discussed maternal illnesses including diabetes and hypertension (Abalos, Duley, Steyn, & Gialdini, 2018; Brown, Grzeskowiak, Williamson, Downie, & Crowther, 2017; Churchill et al., 2018; Martis, Crowther, Shepherd, Alsweiler, Downie, & Brown, 2018). Other reviews included two that examined use of corticosteroids for prevention of neonatal respiratory morbidity and mortality in preterm infants (Roberts, Brown, Medley, & Dalziel, 2017) and to prevent respiratory morbidity in term infants (Sotiriadis, Makrydimas, Papatheodorou, Ioannidis, & McGoldrick, 2018). The last review included the delivery method for preterm birth in singleton pregnancies (Alfirevic, Milan, & Livio, 2013).

Tertiary Source. During the search for recent literature pertaining to OPET infants, a book was found discussing care of preterm and late preterm infants and was used as a tertiary literature source. The *Guidelines for Perinatal Care, 8th edition* is updated periodically by U.S. medical and nursing neonatal and obstetrics professionals (American Academy of Pediatrics [AAP] & American College of Obstetricians and Gynecologists [ACOG], 2017). Of importance to this study, this source contained a small section on assessment of late-preterm status that discussed risks of physiologic immaturity, inadequate compensatory responses to the extrauterine environment, and a greater risk of morbidity and mortality in this group compared to term infants. This source mentioned that mortality is higher in early term infants than in those at 39 weeks. The source also contained a section on newborn transitional care and defined this period as 2-24 hours after the initial newborn evaluation of condition at birth which was more pertinent to infants without medical problems and thus was not used as a definition for this study. This section listed potential signs of neonatal illness such as abnormal respiratory rate and included the screening tests needed during this period.

This guideline contained additional information relative to prenatal factors affecting neonatal outcomes. The triggers of preterm birth are largely unknown but may include hemorrhage, mechanical factors such as cervical incompetence, hormonal changes, infection and inflammation (AAP & ACOG, 2017). One of the strongest risk factors for preterm birth is a prior preterm birth which increases risk by 1.5 to 2 fold. Another strong risk factor is short cervical length less than 25 millimeters as also being associated with preterm birth. Also noted is that identification of women in preterm labor is difficult and that preterm labor is associated with urinary tract infection. Preterm, pre-labor rupture of membranes (PPROM) is a complication in a third of preterm births and is associated with perinatal infection, cord compression and significant perinatal morbidity and mortality. This source supports administration of antenatal corticosteroids to lessen the prevalence and severity of neonatal respiratory problems-especially surfactant deficiency, in mothers in active labor at 24 weeks and up to 36 weeks of pregnancy and states the treatment may be considered in mothers at 23 weeks gestation who are in labor. For maternal illnesses, this source noted that preexisting diabetes is associated with a risk of congenital anomalies and when this type of diabetes is poorly controlled, it is associated with increased risk of respiratory illnesses (especially surfactant deficiency), and fetal death (AAP & ACOG, 2017). This guide was more helpful for identifying prenatal factors affecting neonatal outcome than infant health/illness factors but was not specific in most cases at what gestational ages these prenatal factors were significant.

Individual Studies

The majority of studies reviewed were research studies and the largest two focused on infants born 22 to 28 weeks (Patel et al., 2015; Stoll et al., 2015). Another study examined outcomes in infants born less than 30 weeks gestation (Hornik, Sherwood, Cotton, Laughon, Clark, & Smith, 2016). Although the current recommendation in the U.S. is to use gestational age for reporting outcomes of extremely preterm births (Rysavy et al., 2016), published from other nations examined infants by birthweight when reporting data on the smallest infant population. For studies pertaining to older preterm infants, one group examined infants 28 to 31 weeks, referring to the group as very preterm and very low birth weight (Pascal, Govaert, Oostra, Naulaers, Ortibus, & Van den Broeck, 2018). Groups of researchers from the United Kingdom (UK) and Finland examined infants born 32 to 36 weeks and referred to the group as late preterm or moderately preterm (Boyle et al., 2015; Haataji et al., 2018). Another study examined all preterm births and costs based on gestational age (Johnston et al., 2014) and one study examined respiratory problems in infants of different gestational ages (Sun et al., 2013). Yet another study examined early and late preterm along with term infants and rehospitalization (Ray & Lorch, 2013). There was only one study that examined late preterm along with early term infants (Vohr, 2013) and another which grouped late preterm along with early and full term infants (Lucchini, Burtchen, Fifer, & Signorini, 2019). Two studies examined early term birth on infant outcomes (Craighead & Elswick, 2014; do Carmo Leal et al., 2017). One recent study was found which discussed only term infants 37 weeks and greater born in England (Battersby, Michaelides, Upton, & Rennie, 2017). So, pertaining to the OPET group, there were no studies if infants 32 to 38 weeks gestation, but there were two studies of infants 32-36 weeks (Boyle et al., 2015; Haataji et al., 2018) and another study of infants 34 to 37 weeks gestation (Vohr, 2013). Overall, 15 studies were included in this review and 2 studies were excluded. The excluded studies examined only infants less than 500 grams and gestational ages 22 to 30 weeks (Inoue et al., 2017; Wang, Liou, Chen, Chou, Hsieh, & Tsao, 2017) and not infants 32 through 38 weeks gestation.

Neonatal Mortality. Lorenz and colleagues (2016) compared the U.S. with 12 other developed nations and found the country's high preterm birth rate was a major contributor to the high infant mortality rate (Lorenz et al., 2016). This study also found that the US had the highest rates of death for infants 37 weeks and greater and was the second highest for infants 32 to 36 weeks among the 12 developed countries examined (Lorenz et al., 2016). For US-specific data, the Department of Health and Human Services (DHHS), Centers for Disease Control and Prevention (CDC), National Center for Health Statistics and the National Vital Statistics System periodically publishes a document with infant deaths that are linked to corresponding birth certificates (Ely & Driscoll, 2019; Mathews, MacDorman, Thoma, & Division of Vital Statistics, 2015). The purpose of this linkage is to conduct more detailed analyses of patterns of infant mortality since death certificates may lack sufficient detail, such as infant gestational age, to analyze factors surrounding infant death. In this linked birth/infant death data, the latest infant U.S. mortality rate was 5.8 deaths per 1,000 live births which was 22,341 deaths, 67% due to preterm-related causes (Ely & Driscoll, 2019). At least two thirds (3.85 per 1,000) of these deaths occurred in the neonatal period (Ely & Driscoll, 2019). According to Mathews and colleagues, "the gestational age of an infant is perhaps the most important predictor of his or her survival and subsequent health" (Mathews et al., 2015, p. 5) and preterm infants have a large impact on the U.S. infant mortality rate since they have a much higher risk of death. The rate of death is highest for those born under 32 weeks (188 per 1000), and for those born 32-33 weeks, the rate was 21 per 1000 or 10 times that of term infants. For late preterm infants, the rate was 8.5 or 4 times the rate of term infants (Ely & Driscoll, 2019). For infants born early term (37 and 38 weeks), the mortality rate was 3.01 or 63% higher than the rate for those born 39 to 40 weeks (1.85).

Deaths for early term infants accounted for 12.5% of all infant deaths (Mathews et al., 2015). Although the early term group are expected to have similar outcomes to infants 39 weeks and above, they are at higher risk of death for reasons discussed later.

One of the largest U.S. studies examining mortality included 46 NICUs and examined etiologies of 641 NICU deaths over two years (2010-2012) (Jacob et al., 2015). These researchers found that as gestational age increased, the etiology of deaths shifted from complications of preterm birth including respiratory distress syndrome (RDS) to hypoxic-ischemic encephalopathy and anomalies associated with genetics or altered structure including cardiac, respiratory (lung, diaphragm, and airway), and gastrointestinal anomalies. Deaths at earlier gestational ages were mostly contributed to extreme prematurity and its complications including RDS advancing to respiratory failure, intraventricular hemorrhage, necrotizing enterocolitis, and sepsis. The median age for death in this study was 5 days with a range of 0 to 40 days. The researchers noted that deaths occurring in NICUs (in the hospital) have a major impact on the infant mortality rate and that determining causes and changeable factors linked with death can potentially reduce mortality (Jacob et al., 2015).

Another epidemiological study done with a single U.S. state's (New Jersey) data examined annual births and found those born 32 to 36 weeks gestation had a neonatal mortality rate of 8.4 deaths per 1000 births which was much lower than that of infants born 31 weeks and less (205 deaths per 1000) (Roche, Abdul-Hakeem, Davidow, Thomas, & Kruse, 2016). These researchers also examined additional factors associated with mortality and found that the highest rates were associated with no prenatal care

(36.5 deaths per 1000 births), maternal age of 40 years or greater (18.3 deaths per 1000), non-Hispanic Black race (12.4 deaths per 1000), and not married marital status for the mother (11.4 per 1000) (Roche et al., 2017).

Other countries similar to the U.S. in available resources have also disseminated work related to factors affecting neonatal and infant mortality. A Brazilian study examined early term (37 and 38 weeks) infant risks and outcomes following birth compared to later term (39 to 40 weeks) infants (Do Carmo Leal et al., 2017). This study found early term infants comprised 35% of all births and when compared to infants 39 to 40 weeks gestation, early term infants were more likely to be admitted to NICU, have respiratory complications, and a higher risk of neonatal death (Do Carmo Leal et al., 2017). One Swedish study assessed Apgar or resuscitation scores at five minutes of life and risk of death by gestational age and found that a low heart rate was associated with the highest rate of neonatal mortality regardless of gestational age (Cnattingius, Norman, Granath, Petersson, Stephansson, & Frisell, 2017). Also, these researchers found that in infants 32 to 36 weeks, if the five-minute score was 0 to 3 (the lowest possible score), the rate of death was 182 per 1000 births or double that of infants 37 weeks gestation and greater (93.1) with identical Apgar scores of 0 to 3 (Cnattingius et al., 2017). The five-minute Apgar score is often used as an indicator of transition from intra- to extrauterine life in the immediate period after birth and is one of only a few tools utilized clinically to assess neonatal transition.

Respiratory Illnesses. Respiratory illnesses are relatively common in neonates, affecting as many as 7% of term newborns (Edwards, Kotecha, & Kotecha, 2013) and up to 40% of LPT infants (Altman, Vanpee, Cnattingius, & Norman, 2013; Natile, Ventura, Colombo, Bernasconi, Locatelli et al., 2014). Respiratory distress, the term commonly used to denote difficulty in breathing from an undetermined cause, is one of if not the most common reason for admission to the NICU (Battersby et al., 2017; Edwards et al., 2013; Reuter et al., 2014). For infants admitted to the NICU, up to 15% of term infants and as many as 29% of LPT infants developed major respiratory morbidity, and these numbers were even higher for those born before 34 weeks gestation (Hibbard et al., 2010). In two single-center studies (one in Sweden, one in Italy), the incidence of respiratory illness in LPT infants was 40% in those admitted to the NICU (Altman et al., 2013; Natile et al., 2014). For moderately preterm infants, the incidence of respiratory illness ranged from 59% in those born at 30 weeks to 17% in those born at 34 weeks (Altman et al., 2013).

Since the majority (72%) of preterm births occur between 34 and 36 weeks (Martin, Hamilton, Osterman, Driscoll, Drake, & Division of Vital Statistics, 2018), those respiratory illnesses common in infants born at later gestations are seen more often (Reuter et al., 2014). The most commonly-seen respiratory illness in neonates is transient tachypnea of the newborn (TTN) (Altman et al., 2013; Natile et al., 2014). The incidence of TTN is highest among moderately preterm infants 30 to 32 weeks (18%) and decreases with advancing gestational age to a low rate of 0.4% in those 37 to 41 weeks (Altman et al., 2013). Also known as retained fetal lung fluid, TTN is much more common in late preterm and term infants and while the condition typically self-resolves in 24 to 72 hours, it can result in infants needing respiratory support beyond oxygen (Reuter et al., 2014).

The next most common respiratory illness in neonates is respiratory distress syndrome (RDS) (Altman et al., 2013; Natile et al., 2014). This illness is associated with surfactant deficiency and usually occurs in preterm neonates, but can also be seen in term infants, especially in those exposed to maternal diabetes (AAP & ACOG, 2017). In an Italian, single-center study examining respiratory morbidity in late preterm through term infants, the incidence of RDS ranged from 11.3% in 34 week infants, 6.6% in 35 week infants down to 0.1% in 38 week infants (Natile et al., 2014). In the large mortality study by Jacob and colleagues, the majority of infants who died of respiratory failure were less than 25 weeks gestation (40%) and 12% were infants 34 weeks and greater (Jacob et al., 2015). In studies of respiratory illnesses in neonates, especially in infants 30 weeks and greater, some authors separate the illnesses by specific diagnoses such as TTN and RDS (Altman et al., 2013; Natile et al., 2014), while others only mention RDS (Sun et al., 2013). Studies which separated respiratory illnesses by diagnoses were preferentially included since it is suspected that some researchers combined respiratory illnesses such as RDS and TTN into a generalized RDS or respiratory distress category causing some confusion when attempting to distinguish these for infants born 32 through 38 weeks gestation.

Other respiratory illnesses seen in NICU infants included those resulting from developmental abnormalities or from abnormal transition from prenatal to postnatal life (Jacob et al., 2015; Reuter et al., 2014). For developmental or structural anomalies, lung hypoplasia (underdevelopment) was seen as a significant cause of mortality in infants 34-36 weeks (23%), a moderate cause in those at 29-33 weeks (16%) and to a lesser degree

(8%) in infants 36 weeks and greater (Jacob et al., 2015). In the Jacob study, for the 61 infants with lung hypoplasia, the most common cause for underdeveloped lungs was renal anomalies (38%), followed by prolonged rupture of membranes (33%), and hydrops (11%) (Jacob et al., 2015). In another source, developmental malformations occurring later in gestation include congenital cystic malformation, or pulmonary hypoplasia from congenital diaphragmatic hernia or severe oligohydramnios (low amniotic fluid volume) (Reuter et al., 2014).

Prenatal contributors to neonatal respiratory illness are limited, but have been studied more in recent times, especially in developed countries similar to the U.S. Researchers in Sweden found that PPROM significantly increased risk of respiratory illness, and maternal diabetes also increased the chance of neonatal respiratory disease (Bonnevier et al., 2018). These authors also found that antepartum hemorrhage doubled the risk for respiratory disease and support in neonates. A large French study found that the incidence of NICU admission for respiratory distress was 5.7% for mothers with diabetes mellitus who were treated with insulin and 2.1% for those not treated with insulin (Becquet et al., 2015), likely identifying that in mothers with more severe illness, NICU admissions increased. Another study in the UK found that in diabetic mothers who delivered between 29 to 37 weeks of pregnancy, 29% of their infants developed RDS and 8% required surfactant (Cope et al., 2017).

Transitions Theory and the Neonatal Period. Support for using Transitions Theory for this study's conceptual framework was found from prior studies and from neonatal clinicians using transition as a process. First, in an earlier description of the

Theory, the authors discussed that during a transition in one's health, patients are vulnerable and their health is at risk (Meleis et al., 2000). Patients' experiences during the transition process and how nurses intervene are two of the Theory's major concepts. Events occurring during a transition are likely very important for the group of infants examined in this study. Time span and expectations of time were also discussed by the Theory's authors and were helpful for this study. The authors explained that over time all transitions have flow and movement but research in different populations including parents of infants with congenital heart defects showed not all patients or families transition chronologically over the same trajectory (Meleis et al., 2000). The authors suggested, instead of placing boundaries on time, to identify critical points and events such as periods of increased vulnerability or "at risk" periods (Meleis et al., 2000). This concept was also used in the neonatal literature with discussion of transitions referring to newborns and their adaptation to extrauterine life (AAP & ACOG, 2017; De Carolis et al., 2016; Hillman, Kallapur, & Jobe, 2012). Other authors discussed transition of extremely preterm infants (Armentrout, 2014; Evans, 2016) and others expanded on how transition may take weeks to occur in some infants (Armentrout, 2014; Hoffman, 2017).

Although chronologically, time is not as imperative as critical points according to Transitions Theory (Meleis et al., 2000), one neonatal study examined infants less than 32 weeks during a 3-day transition period and use of inotropes for hypotension (Rabe, Rojas-Anaya, 2016). This study considered the transition period as the first month of life and for those born earlier than 32 weeks gestation, the entire NICU stay. This and other neonatal literature are important since the transition period for infants in the study are likely different based on several factors.

Antenatal Steroid Use. The most effective methods for reducing the incidence of RDS in neonates are administration of antenatal corticosteroids and postnatal surfactant (AAP & ACOG, 2017). For mothers at risk of preterm delivery who are between 24 and up to 36 weeks of pregnancy, antenatal steroid administration is recommended to stimulate maturation of the fetal lung both structurally and functionally (AAP & ACOG, 2017). Use of this medication increased from 24% in 1993 to more widespread use in 87% in 2012 (Stoll et al., 2015). While a course of antenatal steroids is typically two doses 24 hours apart, any exposure prenatally has been shown to result in a lower rate of death in extremely preterm infants (Travers et al, 2018). While antenatal steroids are most commonly given to women at risk of preterm birth, there also may be benefits to giving them in other situations (Nada, Shafeek, Maraghy, Nageeb, Din, & Awad, 2016). In a recent randomized trial in Egypt, researchers gave half of the participants antenatal steroids before elective cesarean section at 38 weeks and found a 2.5 fold reduction in risk of admission to the NICU for respiratory illnesses (Nada et al., 2016).

Synthesis of Results

There is much more information available regarding outcomes in ELGA infants less than 28 weeks (Jacob et al., 2015; Patel et al., 2015; Stoll, et al., 2015) and infants below 30 weeks gestation (AAP & ACOG, 2017) than in middle or moderately preterm infants (Altman et al, 2013; Boyle, 2015). Although infant mortality rates were highest for infants born before 32 weeks (Ely & Driscoll, 2019; Mathews et al., 2015), trends in current birth rates indicate that 72% of preterm births are among infants 34 to 36 weeks (Martin et al., 2018). Although studies involving late preterm infants, particularly related to respiratory morbidity, seem to be increasing (El Shahed et al., 2014; Natile et al., 2014; Sun et al., 2013; Tan et al., 2012), multi-center studies, systematic reviews, and national guidelines are lacking. A newer area of study is to examine outcomes in neonates born early term (37 to 38 weeks gestation). While most expect these more mature infants to have similar outcomes to those born 39 weeks gestation and later, some studies have found higher incidences of NICU admission (Craighead & Elswick, 2014) and death (Lorenz et al., 2016; Mathews et al., 2015) in early term infants than in those born later. Gaining a better understanding of the issues associated with birth at 32 through 38 weeks allows for the planning of appropriate interventions to decrease morbidities and decrease mortality among this population.

For studies examining respiratory morbidity, prevention of RDS in any preterm gestation by giving antenatal steroids is likely the most important intervention for avoiding respiratory illnesses in neonates (AAP & ACOG, 2017; Stoll et al., 2015) and preventing death in infants born extremely preterm (Travers et al, 2018). Administration of steroids antenatally in other situations such as in 38 week infants before C-section was also found to be helpful in decreasing RDS and NICU admission (Nada et al., 2016). Researchers outside the U.S. have published studies examining the incidence of respiratory illnesses in infants (Altman et al, 2013; Battersby et al., 2017; Edwards et al, 2013; Natile et al, 2014; Reuter et al., 2014; Sun et al, 2013). Others have studied risk factors for extubation or mechanical ventilation failure in low birth weight infants (Wang et al., 2017). Other outcomes studied in neonates included length of stay (Craighead & Elswick, 2014), NICU admission (Battersby et al., 2017; Craighead & Elswick, 2014), and mortality (Jacob et al., 2015; Lorenz et al., 2016; Travers et al., 2017). For maternal conditions affecting neonatal outcomes, one group studied prenatal predictors of NICU admission for respiratory distress (Kitano, Takagi, Arai, Yasuhara, Ebisu, et al., 2018) and another group studied underlying maternal and pregnancy-related conditions on neonatal morbidity (Bonnevier et al., 2018).

Discussion

Summary of Evidence

There is limited study of infants born at 32 to 38 weeks gestation. Much of what is known about infant deaths in the neonatal period is from studies pertaining to infants 28 weeks gestation and less. Assessment of hospital outcomes for this group of infants is important to identify areas for improvement to maximize resource utilization and prevent morbidity and mortality. To obtain concise information about outcomes in OPET infants, the literature was searched by gestational age group. Studies related to infant outcomes often focus on those born at the earliest gestations less than 28 weeks since morbidity and LOS are substantially higher in this group. While late preterm infants and LOS are studied occasionally, less is known about mid-preterm and early term infants. Searching the literature by gestational age group and LOS resulted in more thorough results.

Limitations

The limitations to this review are multifactorial. First, since little is published about infants born at later preterm gestations and early term, overall outcomes are difficult to assess. Although the late preterm group is the largest group of preterm infants born annually (Martin et al., 2018), they are not well studied. Second, although the U.S. infant mortality rate is high compared to other nations, deaths by gestational age are not well studied. While the US linked birth to infant death publication is encouraging for assessing causes in many infant deaths, the document may not fully assess the impact of preterm birth in infants whose mothers move from state to state or come into the country from another nation, limiting its full application in current research.

Conclusion

While infant mortality in the U.S. is gradually decreasing, it continues to be high compared to other countries. The nation's preterm birth rate contributes greatly to the infant mortality rate. Infants are admitted to the NICU with respiratory illnesses more than for other causes and these illnesses are a significant cause of deaths in infants born at the earliest gestational ages. Some infants born 32 through 38 weeks may require an extended transition period before they are ready for hospital discharge and chronological age may not be the best method of predicting readiness for discharge.

With the U.S. preterm birth rate increasing primarily with increased numbers of late preterm births, admissions to the NICU will continue but with a population of mid- to late preterm and early term infants. Studies examining this group of infants is important to determine outcomes such as length of stay and survival to identify areas for improvement and for interventions that nurses and other providers can use to promote health and decrease mortality.

CHAPTER III

RESEARCH DESIGN AND METHODS

This retrospective cohort study using existing data examined the effects of transition type on multiple outcomes in a heterogenous population of infants born between 32 and 38 weeks gestation and admitted to multiple neonatal intensive care units (NICUs) across the U.S., including Puerto Rico. The Theory of Transitions (Chick & Meleis, 1986) guided the study's design, research questions, choice of variables, and analysis of the study's results.

Research Questions

1. Which developmental transitions influence patterns of response among the outcome indicators in infants born 32 to 38 weeks gestation?
2. What situational transitions influence patterns of response among the outcome indicators in the intended population of infants?
3. What health/illness transitions influence patterns of response among the outcome indicators in the intended population of infants?
4. What combination of developmental, situational, and health/illness transitions most influence patterns of response in infants born 32 to 38 weeks?

Secondary Research Question

Are there differences in transitions for infants born 32 to 38 weeks gestation related to organizational site?

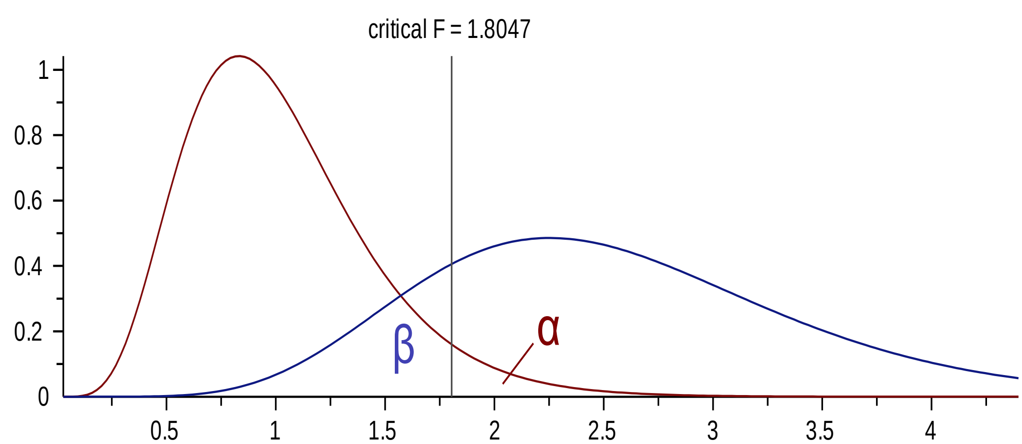
Aim

The aim of this study was to assess the impact of situational, health/illness, and developmental factors in older preterm and early term (OPET) infants (born at 32 to 38 weeks gestation) on outcome indicators during the initial hospitalization following birth.

Power and Sample Size Consideration

To estimate the number of infants needed to conduct this study, a power analysis was performed before the study began. A sample of 131 participants was needed to detect an effect size of 0.15 with an alpha of 0.05 with 0.8 power with 13 tested predictors and 13 total predictors in multiple linear regression using G*Power (Figure 3). For logistic regression, a larger sample was needed, but the study dataset contained more than 150,000 cases which was sufficient for all study analyses.

Figure 3. Sample Size Estimation from G*Power.



*Note. For an effect size (f^2) of 0.15 with and alpha of 0.05 and power of 0.8 with 13 tested predictors and 13 total predictors would need a sample size of 131.

Setting and Participants

Participants and Sample Characteristics

Infants with gestational ages of 32 to 38 weeks admitted to any of the 303 US NICUs included in the dataset within the defined study period were the source population in this study. The sample size was 159,529 infants and the mean gestational age was 35.4 weeks. Over half were male infants and 87% were born in a hospital with a NICU (Table 4).

Eligibility

Inclusion criteria for study participants included newborn infants admitted to one of the 303 NICUs in the U.S. staffed by the Pediatrix medical group with: (1) gestational age of 32 through 38 weeks at birth; (2) admitted to a NICU after birth/delivery; (3) born during the study period of January 1, 2015 through December 31, 2017; and (4) those infants with known or unknown congenital anomalies.

There were no exclusion criteria for this study. All infants in the dataset were included in the analyses.

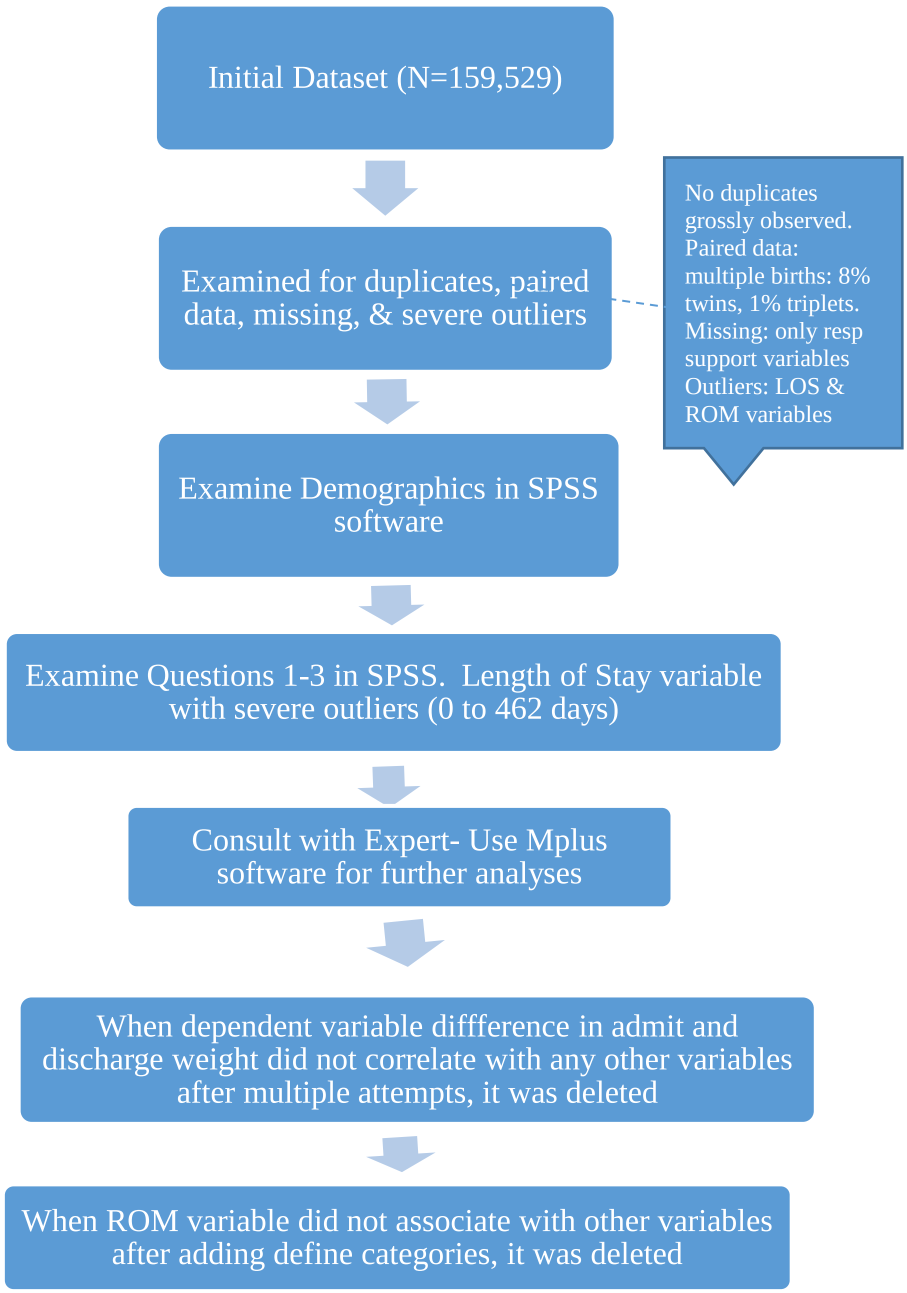
Methods

Data for this study were obtained from deidentified medical records of infants in the targeted gestational age group. Source records were retrieved from Mednax® (parent company of Pediatrix). This company has maintained a Clinical Data Warehouse (CDW) of prospectively collected clinical data on NICU inpatients and their mothers' associated obstetric and delivery records since 1996 (Pediatrix University b, n.d.). A health information technology system called BabySteps® is used as the electronic medical record for Mednax® medical providers and this system sends weekly, deidentified updates to the CDW. The CDW includes 970,000 infants and 17.7 million patient days from 303 NICUs across 35 U.S. states and in Puerto Rico (Pediatrix University b, n.d.). Regions of the U.S. represented include the Northwest, Northeast, Midwest, the deep South, and the Southeast (Mednax, n.d.). Infants in the CDW range from gestational ages of 22 to 43 weeks (Pediatrix University b, n.d.). Although many infants in the CDW are inborn (born in a hospital with a NICU), some are outborn (born in hospitals with levels I or II neonatal units), then transferred to the closest NICU. Infants whose medical records are submitted to the CDW are medically managed by Mednax® neonatology staff. Some records contain history information obtained from outborn or referral hospital staff by verbal or written report during or after transfer of the infant. The CDW is often used by many universities for research and quality reports to improve neonatal care.

Data Analysis Plan

A total of 159,529 infants were included in the dataset. The dataset was examined for duplicates, paired data, missingness, and severe outliers. No duplicates were grossly observed. For paired data, the incidence of multiples was found to be 8% which is acceptable considering the large sample size. Missing data were found only to be excessive in the types of respiratory support needed. Severe outliers were seen in the rupture of membranes (ROM) and length of stay (LOS) variables and ROM was ultimately deleted. The LOS variable needed more complex analyses as reported in Chapter IV. (See Figure 5 for additional details of the Data Analysis Plan).

Figure 4. Data Analysis Plan.



Variables. The variables examined in this study were consistent with the Transitions Theory model (Figure 2) and the proposed conceptual framework (Figures 1 and 3). The following were included in the data analyses as independent variables:

Nature of Transition: Types:

a) Developmental- gestational age in weeks, birth weight in kilograms, female gender

b) Situational- maternal age, maternal race, administration of antenatal steroids, maternal illnesses (diabetes, pre-eclampsia, abruption), birth number, type/method of birth (vaginal or Cesarean section), and chorioamnionitis if present. Length of membrane rupture (ROM) was initially included then eliminated from final analyses due to no association with any other variables in the model as a continuous level variable and after adjusting as a categorical variable to less than and more than 24 hours based on literature and expert opinion.

c) Health/Illness- Apgar score at 5 minutes (values 1-10), admit group (inborn or outborn), major congenital anomalies if present, weight percentile by growth chart, chronic lung disease, ventilator days, high frequency ventilator days (to assess the sickest infants), and room air days

d) Combination of developmental, situational, and health illness transition types- gestational age, birthweight, female gender, maternal age, maternal race, antenatal steroids, diabetes, pre-eclampsia, abruption, birth number, type of birth, chorioamnionitis, Apgar score at 5 minutes, outborn admit group, major congenital anomalies, weight percentile, chronic lung disease, respiratory support days, ventilator days, high frequency ventilator days, and room air days.

e) Organizational- multilevel facility differences in number of infants admitted with average gestational ages and average number of respiratory days in the top 255 facilities by number of infants contributed to dataset.

Outcomes. The outcomes examined for this study were consistent with the Transitions Theory Model (Figure 1), the proposed conceptual framework (Figure 2), and the source population of neonates. These outcomes contained the following objective items in the analyses:

Patterns of Response: Outcome Indicators

a) Days of respiratory support needed (to indicate stability)
b) Length of stay (represented as days since birth)
c) Initially used difference between birth and discharge weights but after this variable did not correlate with others in the model, it was deleted
d) Disposition of infant (i.e., transferred from unit/hospital versus alive, died versus alive at discharge)
e) Oxygen needed at discharge in survivors
f) Monitor needed at discharge in survivors

Data Management

Protection of Human Subjects

This study was submitted to the University of North Carolina-Greensboro (UNCG) Institutional Review Board (IRB) for review. The IRB determined it did not represent human subjects research as defined in federal guidelines (45 CFR 46.102[d or f]) and did not require IRB approval. A Data Use Agreement was finalized between the researcher and the third party company providing data. The researcher was trained in Human Subjects protection and is a former member of two IRBs for roles in nursing research and advanced practice nursing. The intended data source, the Clinical Data Warehouse has been approved annually by the Western IRB for research using its data since 2003 without the typical informed consent requirements (Pediatrix University b, n.d.). Information is de-identified before reaching the CDW and typically meets the exempt regulatory category for conducting research, but this requirement is institution-specific.

Data Safety and Monitoring

After both the Data Use Agreement was established and the IRB reviewed the protocol, a research dataset was securely obtained from the Mednax® research team and was downloaded onto a secured University drive by the researcher. Access by the researcher and statistician were on a secured UNCG platform with a low level of security as determined by the university's IRB and federal guidelines for de-identified data. Data were password-protected and stored with analysis datasets on a secure UNCG drive. Per Data Use Agreement recommendations, data will be stored for a period of 24 months to allow for additional analyses for dissemination products. Data analyses for this study were conducted at the UNCG campus with consultation from the nursing school's statistician and other faculty.

Original CDW data are stored on a secured research server at Mednax® and an additional copy of CDW records is stored on a secured research server at Duke University in Durham, North Carolina. The data stored are deidentified and in order to access the CDW, an individual needs permission from either the Mednax® data management/research team or the Duke Neonatology team. This researcher consulted with a member of the Mednax® research team. Data received and analyzed were for years 2015, 2016 and 2017 for infants who were born between 32 and 38 weeks' gestation.

Data Management and Analysis

The primary statistical software utilized for this study was Mplus© version 8.3 (Muthén and Muthén,, Los Angeles, CA) software. Initial analyses were performed in SPSS® version 25.0 (IBM Inc, Armonk, NY) in order to prepare and manage data for the study. The sample was described using descriptive statistics. For nominal level and other categorical data, frequencies were used to describe data. For continuous and interval data, means and standard deviations were calculated.

Demographics. Demographic variables were initially analyzed using SPSS® and Mplus© software with descriptive statistics as described above.

Analysis by Research Question. Research question #1 asked which developmental transitions influenced patterns of response among the outcome indicators in infants born 32 to 38 weeks gestation? The predictor variables utilized for assessing developmental transitions were: gestational age in weeks at birth, birthweight in kilograms, and gender. These were evaluated in relation to the outcome variables: days of respiratory support needed (to indicate stability), length of stay (by days since birth), difference in admission and discharge weight (to assess growth), disposition of infant (to assess if infant was alive, dead, or needed transfer), oxygen needed at discharge and monitor needed at discharge. Since the outcome variables contained count, interval, nominal and dichotomous level data, a combination of regression techniques was utilized. For count data, negative binomial count regression was performed. Interval data were analyzed with linear regression, then this method was no longer needed once the difference between birth and discharge weight variable was eliminated after initial analysis due to spurious results such as negative values. Nominal and dichotomous data were analyzed with logistic regression. Logistic regression uses odds ratios to estimate the effect on the odds of each nominal or dichotomous dependent variable occurring.

Research question #2 was what situational transitions influenced patterns of response among the outcome indicators in the intended population of infants? Variables used to assess situational transitions were maternal age, race, administration of antenatal steroids, type/method of birth (vaginal or Cesarean section), maternal illness (including hypertension, diabetes, and abruption), birth number if applicable (applies to multiple gestations primarily including twins and triplets), chorioamnionitis if present, and initially length of membrane rupture (ROM) in hours was used, but eliminated from final analyses. These variables were evaluated in relation to the outcome variables: days of respiratory support needed, length of stay, disposition of infant, oxygen needed at discharge and monitor needed at discharge. Because there were multiple levels of data including dichotomous, nominal, and count, a combination of regression techniques was used. Count outcomes were analyzed using negative binomial count regression and dichotomous and nominal outcomes were analyzed with logistic regression.

Research question #3 asked what health/illness transitions influenced patterns of response among the outcome indicators in the intended population of infants? Health and illness transition variables were infant Apgar score at 5 minutes (values 1-10), admit group (inborn or outborn), major congenital anomalies if present, birth weight percentile, presence of chronic lung disease, ventilator days, high frequency ventilator days, and room air days. These variables were evaluated in relation to the outcome variables: days of respiratory support needed, length of stay, disposition of infant, oxygen needed at discharge and monitor needed at discharge. As in questions one and two, because there were multiple measurement levels of outcomes, a combination of regression techniques was used. Dichotomous and nominal level data were analyzed with logistic regression and count data were analyzed using negative binomial count regression.

Research question #4 was what combination of developmental, situational, and health/illness transitions most influenced patterns of response in infants born 32 to 38 weeks? The significant and most influential effects found in research questions 1-3 were evaluated in relation to outcomes by multiple regression modeling techniques. The outcome variables included: days of respiratory support needed, length of stay, disposition of infant, oxygen needed at discharge, and monitor needed at discharge.

Modeling techniques included simultaneous multiple regression where all predictors were entered at the same time and variable constraints were listed (see Chapter IV).

Multiple regression analyses were used to determine if a relationship existed between nature/types of transition and patterns of response or outcomes indicating a trajectory toward successful transition. Categorical variables were compared using logistic analysis. Because the sample contained 91% singletons and older infants whose twin or triplet may not have been included in the dataset because they did not require NICU admission, and because the dataset was large at nearly 160,000 infants, the composition of paired data was suspected to be fairly low, so paired analysis methods were not utilized. As is common in prior research, the continuous variable "length of stay" was skewed, so analysis techniques robust to effects of outliers were used (T. McCoy, personal communication, February 22, 2019).

The secondary research question was are there differences in transitions related to organizational site. Analysis of the secondary question was conducted using descriptive statistics. The facility code variable was assigned randomly by the third party supplying the dataset and information about the facility such as location by state or whether this facility contains a level I-IV NICU was not known to the researcher to protect the site's identity. A graph representing sites with the largest numbers of infants was utilized for the intended purpose and contained some basic information such as the number of infants contributed by site, average gestational age, and average respiratory days.

Data Cleaning

Data were examined according to inclusion and exclusion criteria and no cases were identified that did not meet criteria. Four to five cases had extreme outliers such as rupture of membranes and methods were utilized in the modeling to account for these extremes to reduce their influence on results. The rupture of membranes variable was ultimately eliminated when it did not correlate with any other variable in the model.

A codebook was developed which included frequencies of all variables from the original CDW dataset and definitions of the variables. The codebook included four sections: *section 1. demographics*: gestational age, birthweight, gender, race, site code; *section II. developmental:* gestational age, birth weight, gender; *section III. situational:* maternal age, race, delivery type, antenatal steroids given, illnesses including presence of maternal hypertension, eclampsia, diabetes, abruption; birth number, length of membranes rupture, if chorioamnionitis was present; *section IV: illness:* 5- minute Apgar score, admit group/type, major congenital anomalies if present and incidence of trisomies, weight percentile, incidence of chronic lung disease, room air days, ventilator days, and high frequency ventilator days; and *section V. outcomes:* days of respiratory support, length of stay, discharge weight, disposition (home, transfer, death), equipment needed at discharge including oxygen and monitor.

Cases with missing data were examined closely and most were only missing data pertaining to the respiratory support needed. Since the cases with adequate respiratory support represented about 5,000 and the remaining were about 155,000, they were left in the dataset for question three and four analysis. The sample sizes for questions 1, 2, and

4 were over 133,000 and for question 3, was nearly 700 which exceeded the initial required sample size estimation.

A statistical expert was consulted after the initial analysis and modeling and offered several suggestions, most related to the outcome variables. First, because the variable total days of respiratory support included days on room air along with other methods of support, the room air days column was subtracted from this column and a new variable "respiratory days" was created. The variable discharge weight was examined and since it did not reflect that most infants lose weight in the first few days of life, the birthweight variable was subtracted from the discharge weight and a new one "difference between birthweight and discharge weight" was created. The respiratory days and LOS variables were discussed and since both were right skewed and consisted of numbers zero and above which met requirements of count regression, they were analyzed by negative binomial modeling. A variable discharge post-menstrual age (PMA) was examined and the gestational age variable was subtracted from this creating a new variable "difference in PMA" since it did not include infants being transferred in the first few days of life. On further inspection, this variable included decimal places that were not easily interpreted such as 35.9 weeks, so this new variable was rounded up or down to the nearest week and the variable "rounded difference in PMA" was created. This variable was deleted early in analysis when it did not correlate with other variables in the model.

CHAPTER IV

RESULTS

The purpose of this study was to assess short term outcomes in a group of infants admitted to neonatal intensive care units (NICU) using a dataset from the Pediatrix Medical Group. This medical group employees neonatal providers which staff over 300 NICUs in most areas of the United States (U.S.) except the Southwest. The sample included infants born between 32 and 38 weeks gestation, collectively known as older preterm and early term (OPET) infants. This chapter provides a description of the sample and a report of the results of the analyses to answer the research questions. Because of the conceptual framework used, there were four separate research questions examined and a secondary research question. This chapter will discuss analyses in the following order: a) sample characteristics; b) question 1: Which developmental transitions influence patterns of response among outcome indicators in infants born 32 to 28 weeks; c) question 2: What situational transitions influence patterns of response among the outcome indicators in the intended population of infants; d) question 3: What health/illness transitions influence patterns of response among the outcome indicators in the intended population of infants; e) question 4: What combination of developmental, situational, and health/illness transitions most influence patterns of response in infants born 32 to 38 weeks; and then f) the secondary question: Are there differences in transitions related to organizational site?

Sample Characteristics

This was a secondary data analysis using a dataset derived from clinical records of hospitalized infants born in the U.S. including hospitals in Puerto Rico, for the years 2015 through 2017. The total sample size was 159,529 infants with gestational ages of 32 through 38 weeks. Sample characteristics were divided into three separate tables and discussed separately due to the large amount of information in the dataset.

Infant Characteristics

Table 4 shows the demographic characteristics of infant cases evaluated in this study. The mean gestational age of study participants was 35.4 weeks (*SD* = 1.9 weeks), and the largest gestational age group represented was 34 weeks (18.8%); the smallest group of infants was 32 weeks (7.5%). The mean birthweight in kilograms (kg) was 2.69 kg (*SD* = 0.69), and the majority of cases (78%) were classified by weight percentile as appropriate for gestational age (AGA). The percentage of males was slightly higher than females (56% versus 44%). The largest proportion of mothers were in the race/ethnicity category non-Hispanic White (49%) and the next largest group was Hispanic (21%). The majority of infants (87%) were inborn (born in a hospital with a NICU) and 13% were outborn (no NICU in hospital), then transferred to a hospital with a NICU for further management.

Most of the participants were singletons (91%) and of the remaining, 8% were from twin gestations and less than 1% were from higher order multiples such as triplets and quadruplets. Apgar scores at five minutes of life in 96% of participants were in the range of 6 to 10 (meaning more stable after delivery) and 4% of scores were lower at 0 to

5. Most infants (89%) did not have a major congenital anomaly and of the participants with a major anomaly, 10% of these had a genetic trisomy (1% of the total sample). Only a small proportion of infants (0.6%) died during their NICU stay during the three year time period included in the dataset.

The average length of hospital stay for the infants in the sample was 13.1 days (*SD* = 13.3) with a median of 9 and a range of 0-462 days; there were 50 outliers present. The majority (75%) of infants were discharged before 17 days of life and 99% by 60 days of life. Most infants were discharged home (89%) followed by transfer of service (4.9%). About 5% required acute transfer to another facility and a small percentage (0.9%) were transferred to convalescent care. The mean discharge weight was 2.70 kg (*SD* = 0.63) and mean gestational age at discharge was 37.3 weeks (*SD* = 2.1). In infants surviving to discharge, 2.3% were sent home on oxygen and 1.5% were sent home with a monitor (including apnea, cardiac, or pulse oximeter). All infants in the dataset were included for analysis.

Table 4. Infant Demographic Characteristics.

Variable	*M* ± *SD* or *n* (%)	Number missing
Gestational age (weeks)	35.4 ± 1.9	0
32	11,897 (8)	
34	29,915 (19)	
36	23,866 (15)	
38	27,184 (17)	
Birthweight in kilograms (kg)	2.6 ± 0.7	0
Weight class percentile		0
AGA	123,902 (78)	
SGA	19,806 (12)	
LGA	15,821 (10)	
Gender		0

Male	88,776 (56)	
Female	70,753 (44)	
Race/ethnicity		0
White, non-Hispanic	78,101 (49)	
Hispanic	33,161 (21)	
Black, non-Hispanic	26,704 (17)	
Other	16,487 (10)	
Asian	5,076 (3)	
Admit type		0
Inborn	138,498 (87)	
Outborn	21,000 (13)	
Birth number		305 (*N*=159,224)
#1 (singletons)	145,327 (91)	
#2 (twins)	13,418 (8)	
#3 (triplets)	468 (0.3)	
#4 (quadruplets)	11 (0.0)	
Five-minute Apgar score		4,345 (*N*=155,184)
0 to 5	6,226 (4)	
6 to 10	148,958 (96)	
Major congenital anomalies	16,947 (11)	0
Trisomies	1,701 (1)	0
Trisomy 21	1,472 (1)	
Discharge information:		
Days since birth	13.1 ± 13.3; median 9; range 0-462 days	3
Weight in kg	2.7 ± 0.6	1809 (*N*=157,720)
Post menstrual age (weeks)	37.3 ± 2.1	3
Type:		0
-Home	142,196 (89)	
-Transferred service	7,854 (5)	
-Acute transfer	7,118 (5)	
-Convalescent transfer	1,402 (1)	
-Died	959 (1)	
Survivors home on monitor	2,380 (2)	0
Survivors home on gastrostomy tube	729 (1)	0

Note*:* Mean (*M*). Standard deviation (*SD*). Number (*n*). Weight class percentiles: appropriate for gestational age (AGA), small for gestational age (SGA), large for gestational age (LGA). Kilogram (kg).

Maternal Characteristics. Table 5 shows the maternal characteristics associated with the infant cases in the study. The mean age for infant mothers was 29 years (*SD* = 6.2) and by percent: 25% of mothers were 24 years old and younger and 25% were age 33 years and older. For obstetrics history, the greatest proportion of mothers (54%) included prima-gravidas and those with their second pregnancy, and the range of number of pregnancies for the entire sample was 1 to 20. More than half delivered by Cesarean section (57%). The administration rate of antenatal steroids was moderately low (34%), but those mothers giving birth at later gestations did not qualify unless they experienced or were at risk of preterm labor earlier in the pregnancy. The percent of mothers with chorioamnionitis was low (2.6%) and prevalence of fever was low (1.8%). For group B beta-hemolytic *Streptococcus* (GBS) culture status, 36% were negative followed by unknown status (31%).

For assessment of maternal illness, the percent of mothers with hypertension, diabetes, and abruption were examined. When maternal illness was present, diabetes occurred most commonly (17%) followed by pre-eclampsia (12%), and pregnancy-induced hypertension (11%). Pre-eclampsia included those mothers with chronic hypertension. The prevalence of abruption was low (3.1%) as was eclampsia (0.2%), which is a seizure induced by hypertension. The use of insulin was minimal (5.9%). For preventable maternal risk factors, smoking was reported in 6.5% of mothers.

Table 5. Maternal Characteristics.

Variable	*M* ± *SD* or *n* (%)	Number missing
Age during pregnancy (years)	29.0 ± 6.2	765 (*N*=158,764)
Gravida	range 1-20	1142 (*N*=158,387)
1:	45,799 (29)	
2:	39,797 (25)	
>5:	13,643 (9)	
Delivery method		0
Cesarean section	90,649 (57)	
Vaginal	66,196 (42)	
Antenatal steroids received	53,441 (34)	0
Chorioamnionitis	4,108 (3)	0
Pre-eclampsia	19,260 (12)	0
Pregnancy-induced hypertension	16,765 (11)	0
Diabetes	26,626 (17)	0
Abruption	4,914 (3)	0
Eclampsia	379 (0.2)	0

Note. Mean (*M*). Standard deviation (*SD*). Number (*n*). Gravida= number of pregnancies.

Infant Respiratory Characteristics. Table 6 lists infant respiratory characteristics of the sample evaluated for the study. The prevalence of chronic lung disease among participants was low (1%) totaling 1,523 cases. The mean total days of respiratory support needed was 2.9 days (*SD* = 5.6) with a range of 0 to 265 days. More than one-third of participants (43%) did not require any respiratory support (were spontaneously breathing room air) during days 0, 1, or 2 of their NICU stay when infants are typically the sickest following birth. The mean number of room air days (during NICU hospitalization) was 10.9 days (*SD* = 10). For those who needed respiratory support in the first three days, the most commonly used methods were continuous positive airway pressure (CPAP) (23%) followed by high flow nasal cannula (12%). On average, infants needed CPAP for 2.8 days (*SD* = 2.8) and high flow nasal cannula for 3.3 days (*SD* 3.3). For other types of support, the mean nasal cannula days (excludes high flow nasal cannula) was 4.7 (*SD* = 6.7) followed by noninvasive nasal prong ventilator days at 3.5 (*SD* = 4.1). The type of support needed by the smallest number of infants was oxygen by hood (0.9%) and this was needed a mean of 1.9 days (*SD* = 1.6). The maximum fraction of inspired oxygen (FiO2) needed during days 0 to 2 was 0.28 (*SD* = 0.15) with a range of 0.21 to 1.00.

For the sickest infants, the percent who required any mechanical ventilation at days 0, 1, or 2 was 8.7%. Slightly less than 1% needed high frequency ventilation (HFV) (0.9%), and 7.8% needed conventional ventilation (a type of mechanical ventilation for milder cases of respiratory distress). The average HFV days was 5.1 (*SD* = 6.2) with a median of 4.0 and range of 1-96. The conventional ventilation mean was 3.8 days (*SD* = 8.3) with a median of 2.0, range 1-245 days. Most infants had relatively low levels of respiratory morbidity or degree of respiratory illness. For support needed at discharge, 2.3% of infants surviving to discharge needed oxygen and only 0.1% of survivors required a tracheostomy.

Table 6. Infant Respiratory Characteristics (*N*= 159,529).

Variable	*M* ± *SD* or *n* (%)	Number missing
Chronic lung disease	1,523 (1)	0
Support days excluding room air/no support	2.8 ± 5.6; range 0-265	2,040 (*N*=157,489)
Maximum support on days 0-2 of life		8,332 (*N*=151,197)
Room air	68,088 (43)	
Hood oxygen	1,453 (1)	
Nasal cannula	7,682 (5)	
High flow nasal cannula	18,946 (12)	
Continuous positive airway pressure	36,723 (23)	
Nasal prong ventilation	4,442 (3)	
Conventional ventilation	12,384 (8)	
High frequency ventilation	1,479 (1)	
On ventilator days 0-2 of life	13,863 (9)	0
Ventilator days	3.8 ± 8.3; median 2; range 1-245	144,746 (*N*=14,783)
High frequency ventilator days	5.1 ± 6.2; median 4; range 1-96	157,787 (*N*=1,742)
Maximum FiO2 needed days 0-2	0.28 ± 0.15	9,552 (*N*=149,977)
Other support:		
Nasal cannula days	4.7 ± 6.7	129,165 (*N*=29,914)
Noninvasive vent days	3.5 ± 4.1	153,195 (*N*=6334)
High flow nasal cannula days	3.3 ± 3.6	121,618 (N=37,911)
CPAP days	2.8 ± 2.8	115,451 (*N*=115,451)
Hood oxygen	1.9 ± 1.6	157,229 (*N*=2,300)
Room air/ no support days	10.9 ± 10.3	9,226 (*N*=150,303)
Only room air days	67,035 (44.6)	
Survivors sent home on oxygen	3,636 (2)	0
Survivors sent home with tracheostomy	112 (0.1)	0

Note. Mean (*M*). Standard deviation (*SD*). Number (*n*) Fraction of inspired oxygen (FiO_2). Continuous positive airway pressure (CPAP).

Analyses for Research Questions

As guided by the conceptual framework Transitions Theory, four separate research questions were examined which assessed transition type and outcomes along with a secondary research question pertaining to differences found by facility. This section will discuss initial analyses of questions 1 to 3, final analyses of questions 1 to 3 sequentially, followed by findings for question 4 and the secondary research question. Findings from the earlier research questions informed data that could be used in the subsequent analysis.

Initial Analyses

First, data analyses consisted of checking variable performance and relationships for normality using the initial software program (SPSS®). Normality testing for the variables addressing questions 1through 3 was conducted by simultaneous variable entry per research question (individual variable details listed below). Two dependent variables (length of stay and support days) did not fulfill requirements for assumptions. Length of stay (LOS) likely did not meet required assumptions because of severe outliers (range of 0 to 462 days). Support days was inappropriately large when examined closely. This variable included infants whose only "support" was room air days which was counterintuitive- i.e. did not involve respiratory support. To conform this variable to one that examined only days of actual respiratory support, room air days was subtracted from support days and a new variable was created and named respiratory days. Problems such as negative numbers were also found in the variables discharge weight and discharge post menstrual age (PMA). Since infants typically lose weight for the first week of life and many were discharged around this time, the discharge weight variable was subtracted from birth weight to create a new variable named difference between birth and discharge weight. The post-menstrual age variable was rounded and renamed as appropriate.

Some independent variables in the dataset also did not meet required assumptions in the original analyses. Several of the independent variables associated with respiratory status such as days on oxygen had excessive missingness likely due to insufficient provider charting, but the variables were kept because they were important to the study's aims and because they met sample size calculations.

Since several of the variables including the outcomes respiratory days and length of stay were vital to the study's aims, robust methods of analysis were explored with alternative software (Mplus©). A second statistical program was needed because assumptions of normality are not necessary with the available robust methods and the ability to simultaneously examine continuous, categorical, and count variables is possible with current methods.

Question One. This question pertained to which developmental transitions influence response patterns in infants 32 to 38 weeks gestation. The independent variables (IVs) representing developmental transitions examined were gestational age, birthweight, and gender. The dependent variables (DVs) included respiratory days, length of stay, difference between birth and discharge weight, rounded post-menstrual discharge age, discharge type (transferred, alive, died), survivors discharged home on oxygen, and survivors discharged home on a monitor. Types of regression used in the analyses included negative binomial count, linear and logistic based on DV measurement level. Confidence intervals were calculated for reporting precision of estimated relationships. When, on two occasions, the DVs difference between birth and discharge weight and rounded post-menstrual age were uncorrelated with any of IVs in the model, these variables were deleted from further analyses.

The results for question one had several significant findings which are listed in Table 7. Significance was considered at a level of $p<0.05$ and many results were at $p<0.001$ most likely due to the large sample size (N=159,529). The length of stay and respiratory days DVs were modeled using count regression and the effect size, confidence intervals, and significance were considered for interpretation of associations between the IVs with each DV. Female gender and gestational age had an effect ($\exp(b) = 0.87$ and 0.81, respectively; both $p < .001$) on the number of days of respiratory support needed. The predicted mean number of respiratory days needed was 13% lower in females versus males, and for every additional 1 week increase in gestational age, the predicted mean number of respiratory days decreased by 19%, adjusting for birthweight and gender. This is likely due to increasingly mature lungs as gestational age increases along with less need for respiratory support.

When length of stay (LOS) was examined, gender, gestational age, and birthweight also had significant effects ($\exp(b) = 0.98$ for gender, 0.86 for age, 0.82 for weight) on LOS. The predicted average LOS was 2% lower for female infants relative to male infants, adjusting for the other variables in the model. Also, the predicted mean LOS days was 14% lower for every additional 1 week increase in gestational age, and the predicted mean LOS was 18% lower for every 1 kilogram increase in birthweight, adjusting for female gender.

For the categorical DVs using logistic regression, the adjusted odds ratios (AOR), *p*-values, and confidence intervals (CI) were considered for interpreting the effect size of IVs to DVs. The largest increase in odds was with the DV disposition transferred versus alive, where for every additional 1 week increase in gestational age, the odds of transfer versus alive increased by 23% (AOR=1.23). The odds of the DV decreased (AORs 0.57-0.92) for two independent variables. The largest decrease in odds was noted when the DV died versus alive was tested. For every 1 kilogram increase in birthweight, the odds of death decreased 43% (AOR 0.57; 95% CI=[0.47, 0.69]; $p<0.001$), adjusting for gestational age and gender.

For discharge home on a monitor, the odds of being discharged home on a monitor decreased by 24% for every additional 1 week increase in gestational age, adjusting for birthweight and gender (AOR 0.76; 95% CI=[0.74, 0.78]; $p<0.001$). The remaining odds ratios were between 0.88 and 0.92, indicating increases in the IVs were associated with decreased odds of DVs. Scaling of the IVs such as with birthweight listed in kilograms and gestational age in weeks could help explain the effect sizes.

Table 7. Multivariate Count and Logistic Regression for Developmental Predictors (N=159,529).

Characteristic: **DV by IV**	**Effect**	**95% CI**	***p*-value**
Respiratory days by:	(exp[b] for count)		
-Gestational age (GA) (weeks)	0.81	(0.80, 0.81)	<0.001
-Birthweight (BW) (kilograms)	1.17	(1.14, 1.20)	<0.001
-Gender if female	0.87	(0.85, 0.88)	<0.001
Length of stay by:			
-GA	0.86	(0.86, 0.86)	<0.001
-BW	0.82	(0.81, 0.83)	<0.001
-Gender if female	0.98	(0.97, 0.99)	<0.001
Disposition:			
Transferred vs. Alive by:	(AOR)		
-GA	1.23	(1.22, 1.25)	<0.001
-BW	1.14	(1.10, 1.17)	<0.001
-Gender if female	1.01	(0.98, 1.05)	0.439
Died vs. Alive by:			
-GA	1.12	(0.85, 0.96)	<0.001
-BW	0.57	(0.47, 0.69)	<0.001
-Gender if female	1.01	(0.89, 1.14)	0.927
Discharge home on oxygen by:			
-GA	0.92	(0.83, 0.95)	<0.001
-BW	0.90	(0.84, 0.97)	0.005
-Gender if female	0.88	(0.83, 0.95)	<0.001
Discharge home on monitor by:			
-GA	0.76	(0.74, 0.78)	<0.001
-BW	0.94	(0.86, 1.02)	0.150
-Gender if female	0.99	(0.91, 1.07)	0.802

Note. Dependent variable (DV). Independent variable (IV). Confidence interval (CI). Negative binomial regression slope (exp[*b*]). Adjusted odds ratio (AOR). Birthweight (BW). Discharge (DC). Post menstrual age (PMA).

Question Two. This question was which situational transitions influence patterns of response among the outcome indicators in the sample of infants? Situational transitions examined were primarily those pertaining to infants' mothers and the pregnancy. The indicator variables were maternal age, whether mother received antenatal steroids, race of mother, delivery method, rupture of membranes length (removed from final analysis due to failure to correlate with other variables despite defining as a categorical variable), presence of chorioamnionitis, diabetes, pre-eclampsia, pregnancy-induced hypertension (removed from final analysis due to concern for multicollinearity with pre-eclampsia), abruption, and birth order (to assess for multiples). Maternal age initially was not associated with any of the outcome variables, so it was then defined into three categories as adolescence (19 and less), 20 to 39 years, and age 40 years and over. When this variable remained uncorrelated with others in the model, the variable was then defined as age 40 and over to assess the effect of advanced maternal age on the other variables. This had been shown in prior studies to increase NICU admission (Osterman, Martin, Mathews, & Hamilton, 2011) and has been correlated with greater neonatal death (Lean, Derricott, Jones, & Heazell, 2017). Race of mother was initially coded to assess for differences in all races, but there were no differences noted. In the final analysis, Black race was examined since negative outcomes have been reported for Black women with chronic illnesses such as hypertension and diabetes and for Black pregnant women, preterm birth (Ely & Driscoll, 2019).

The results for question two had several significant findings which are listed in Table 8. Significance was considered at a level of $p<0.05$ and several results were highly significant at $p<0.001$, likely due to sample size (N=155,948**)**. The length of stay and respiratory support days DVs were modeled and analyzed using count regression, and the effect size, confidence intervals, and significance were considered for interpretation of the effect size of IVs to DVs. For respiratory support, antenatal steroids, cesarean section delivery, and abruption increased the predicted mean number of support days by approximately 38% to 43% (exp(b) = 1.38 to 1.43) accounting for the other variables in the model. Diabetes, pre-eclampsia, maternal age, and birth number also had significant effects on the number of respiratory support days (exp(*b*)=0.97, 0.96, 0.95, 0.92, respectively). The predicted mean number of respiratory days for mothers 40 years and older was 5% lower compared to mothers 39 and younger, adjusting for the other variables (exp(*b*) = 0.95). Black race and chorioamnionitis had additional significant effects on respiratory support days (exp(*b*) = 0.72 and 0.53, respectively).

Length of stay modeling had similar findings. Antenatal steroids increased the predicted mean length of stay by 67%, adjusting for the other variables in the model (exp(*b*) = 1.67). Abruption increased predicted average length of stay by 23% (exp(*b*) = 1.23). Diabetes, race and chorioamnionitis had additional significant effects (exp(*b*) = 0.94, 0.93, 0.63) on length of stay. Black race was associated with decreased predicted average number of length of stay days by 7% (exp(*b*) = 0.93), while chorioamnionitis decreased length of stay days by 37% (exp(*b*) = 0.63), adjusting for the other variables in the model. Since chorioamnionitis is associated with inflammation and inducing a stress response, it is suspected that infant organs are more mature at birth when their mothers have chorioamnionitis.

For the categorical DVs using logistic regression, the adjusted odds ratios (AOR), confidence intervals (CI) and significance were considered for interpreting the effects. The largest effect noted overall was delivery by cesarean section which increased odds of death by 111% (AOR 2.11; 95% CI=[1.82, 2.44]; $p<0.001$). This could be due to intrapartum complications such as fetal bradycardia or a maternal complication leading to altered placental perfusion such as abruption. The next largest effect was with use of antenatal steroids which increased odds of monitor use by 102% (AOR 2.02; 95% CI=[1.86, 2.19]; $p<0.001$). Abruption also increased the odds of infant death by 84% (AOR 1.84; 95% CI [1.42, 2.38]; $p=0.001$). The remaining effects ranged from AORs of 1.08 to 1.71. There were several decreased odds noted when the DVs were examined by IVs in this model. The largest effect was Black race which was associated with 70% lower odds in infants who required oxygen at discharge (AOR 0.30; 95% CI [0.26, 0.34]; $p<0.001$). Chorioamnionitis also decreased the odds of needing oxygen at discharge (AOR 0.51; 95% CI [0.38, 0.69]; $p<0.001$) but to a lesser effect than race. Those with chorioamnionitis had 54% decreased odds of monitor use at discharge (AOR 0.46; 95% CI [0.31, 0.68], $p<0.001$). This is suspected to be due to accelerated maturation of lungs when mothers have chorioamnionitis due to inflammation and response to stress.

With the disposition variables, antenatal steroids, chorioamnionitis, pre-eclampsia, and birth number decreased the odds of death by 18-60% (AOR 0.82, 0.53, 0.46, 0.40, respectively) accounting for the other variables in the model. For transferred versus alive, pre-eclampsia, birth order, and antenatal steroids (AOR 0.81, 0.79, 0.54) decreased the odds of being transferred 19-46% accounting for the other variables in the model. The remaining AORs were 0.88 to 0.93.

Table 8. Multivariate Count and Logistic Regression for Situational Predictors (N=155,948).

Characteristic: DV by IV	Effect	95% CI	*p*-value
Respiratory Days by:	(exp[b] for count)		
-Advanced maternal age*	0.95	(0.90, 0.99)	0.034
-Black maternal race**	0.72	(0.70, 0.74)	<0.001
-Antenatal steroids given	1.43	(1.40, 1.46)	<0.001
-Cesarean delivery***	1.40	(1.37, 1.43)	<0.001
-Chorioamnionitis	0.53	(0.49, 0.57)	<0.001
-Preeclampsia	0.96	(0.93, 0.99)	0.007
-Diabetes	0.97	(0.95, 1.00)	0.045
-Abruption	1.38	(1.30, 1.45)	<0.001
-Infant birth number	0.92	(0.89, 0.95)	<0.001
Length of Stay by:			
-Advanced maternal age	0.99	(0.96, 1.01)	0.271
-Black maternal race	0.93	(0.92, 0.94)	<0.001
-Antenatal steroids given	1.67	(1.66, 1.69)	<0.001
-Cesarean delivery	1.10	(1.09, 1.11)	<0.001
-Chorioamnionitis	0.63	(0.61, 0.65)	<0.001
-Preeclampsia	1.00	(0.98, 1.01)	0.431
-Diabetes	0.94	(0.92, 0.95)	<0.001
-Abruption	1.23	(1.19, 1.26)	<0.001
-Infant birth number	1.09	(1.08, 1.10)	<0.001
Disposition:			
Transferred vs. Alive by:	(logistic)		
-Advanced maternal age	1.14	(1.06 1.23)	0.001
-Black maternal race	1.08	(1.04, 1.13)	<0.001
-Antenatal steroids given	0.54	(0.52, 0.57)	<0.001
-Cesarean delivery	1.61	(1.55, 1.67)	<0.001
-Chorioamnionitis	1.71	(1.56, 1.86)	<0.001
-Preeclampsia	0.81	(0.77, 0.86)	<0.001
-Diabetes	1.04	(0.99, 1.08)	0.107
-Abruption	0.97	(0.88, 1.06)	0.471
-Infant birth number	0.79	(0.74, 0.84)	<0.001
Died vs Alive by:			
-Advanced maternal age	1.06	(0.79, 1.43)	0.707
-Black maternal race	1.11	(0.94, 1.31)	0.222
-Antenatal steroids given	0.82	(0.71, 0.94)	0.005
-Cesarean delivery	2.11	(1.82, 2.44)	<0.001
-Chorioamnionitis	0.53	(0.30, 0.94)	0.030
-Preeclampsia	0.46	(0.35, 0.60)	<0.001
-Diabetes	0.82	(0.69, 0.98)	0.029

-Abruption	1.84	(1.42, 2.38)	<0.001
-Infant birth number	0.40	(0.29, 0.54)	<0.001
DC home on oxygen by:			
-Advanced maternal age	1.14	(0.98, 1.32)	0.097
-Black maternal race	0.30	(0.26, 0.34)	<0.001
-Antenatal steroids given	1.60	(1.49, 1.71)	<0.001
-Cesarean delivery	0.93	(0.87, 1.00)	0.042
-Chorioamnionitis	0.51	(0.38, 0.69)	<0.001
-Preeclampsia	1.31	(1.19, 1.44)	<0.001
-Diabetes	0.92	(0.84, 1.01)	0.082
-Abruption	1.17	(0.98, 1.41)	0.086
-Infant birth number	0.93	(0.83, 1.04)	0.205
DC home on monitor by:			
-Advanced maternal age	1.02	(0.84, 1.24)	0.852
-Black maternal race	0.54	(0.47, 0.62)	<0.001
-Antenatal steroids given	2.02	(1.86, 2.19)	<0.001
-Cesarean delivery	1.12	(1.02, 1.22)	0.014
-Chorioamnionitis	0.46	(0.31, 0.68)	<0.001
-Preeclampsia	1.08	(0.96, 1.21)	0.208
-Diabetes	0.88	(0.78, 0.98)	0.024
-Abruption	1.34	(1.09, 1.65)	0.006
-Infant birth number	1.27	(1.13, 1.43)	<0.001

Note. DV=dependent variable. IV=independent variable. AOR=adjusted odds ratio. CI= confidence interval. Negative binomial regression slope (exp[*b]*). *maternal age: 0= ages 39 and under; 1= ages 40 and above. ** race codes: 0 = other than Black, 1= Black. ***delivery codes: 0=vaginal, 1=Cesarean section.

Question Three. Question three asked what health/illness transitions influence patterns of response among the outcome indicators in the intended sample of infants. The IVs examined were major anomalies, weight percentile, Apgar score at 5 minutes of age, admit group (inborn or outborn), chronic lung disease, ventilator days, high frequency ventilator days, and room air days. The DVs are discussed individually. The data were unable to capture respiratory medications administered due to inconsistencies in provider charting, especially when these medications were discontinued.

When this model was run in Mplus© there was a large amount of missing data in the IVs which decreased the sample size substantially to only 673 cases (0.42% of all cases) (see Table 9). Although this size was lower than the size used for other questions, it still exceeded initial estimates for the number of subjects needed which was 131. This was suspected to primarily be due to inconsistent charting of the variables used for this question. Also, some infants were transferred or did not survive many days and likely did not have complete records allowing assessment of these IVs relating to health/illness.

The length of stay and respiratory days DVs were modeled and analyzed using count regression, and the effect size, confidence intervals, and significance were considered for interpretation of the association of each IV with each DV. For respiratory support days, having chronic lung disease increased the predicted mean number by 77% days ($\exp(b) = 1.77$), and for every additional 1 point increase in Apgar score at 5 minutes, the predicted mean number of respiratory days decreased by 2%, adjusting for the other variables in the model ($\exp(b) = 0.98$). Outborn admit group was associated ($\exp(b) = 0.96$, $p<0.001$) with length of stay. The predicted mean number of length of stay days was 4% lower in outborn infants than in inborn infants, adjusting for the other variables in the model. Typically outborn infants have worse outcomes (AAP & ACOG, 2017), however, infants at more mature gestational ages may be more resilient. The other effect sizes for the count variables ranged from $\exp(b) = 1.00$ to 1.13.

For the categorical DVs using logistic regression, the adjusted odds ratios (AOR), confidence intervals (CI) and *p*-values were considered for interpreting the effect size of the IV on the DV. There were very few statistically significant results noted among the

DVs examined. For the DV disposition transfer versus alive, infants with major anomalies had 321% higher odds of being transferred (AOR 4.21; $p<0.05$), and those with chronic lung disease had 257% higher odds of being transferred (AOR 3.57; $p<0.05$). Infants in the outborn admit group had 64% lower odds of being transferred (AOR 0.36; $p<0.001$). This may suggest that infants in this dataset who needed transfer could have had surgical conditions that were noted shortly after birth, so infants who were outborn were more likely not to be transferred because they had been transported from birth hospital to a tertiary NICU not represented in the dataset. Infants with major anomalies had 201% higher odds of death (AOR 3.01; $p<0.05$). For each 1 point increase in Apgar score at 5 minutes, the odds of needing a monitor decreased by 16% (AOR 0.84; $p<0.05$). The remaining significant AOR was respiratory days (AOR 1.06; $p<0.001$) for the discharge home on oxygen DV. For the disposition died vs. alive DV, there were no statistically significant findings in the model.

Table 9. Multivariate Count and Logistic Regression for Health/Illness Predictors (N=673).

Characteristic: DV by IV	**Effect**	**95% CI**	***p*-value**
Respiratory days by:	(exp[b]for count)		
-Major anomalies	1.13	(1.03, 1.23)	0.008
-Weight percentile	1.02	(0.97, 1.07)	0.349
-Apgar score at 5 minutes	0.98	(0.96, 1.00)	0.016
-Outborn admit group*	1.01	(0.92, 1.09)	0.891
-Chronic Lung Disease (CLD)	1.77	(1.55, 1.98)	<0.001
-Ventilator days	1.04	(1.03, 1.05)	<0.001
-HFV days	1.05	(1.03, 1.06)	<0.001
-Room air days	1.00	(1.00, 1.00)	0.712
Length of stay by:			
-Major anomalies	1.13	(1.08, 1.18)	<0.001
-Weight percentile	1.00	(0.98, 1.03)	0.766

-Apgar score at 5 minutes	0.99	(0.98, 0.99)	<0.001
-Outborn admit group	0.96	(0.93, 1.00)	0.028
-CLD	1.10	(1.05, 1.16)	<0.001
-Respiratory days	1.02	(0.99, 1.00)	<0.001
-Ventilator days	1.00	(0.99, 1.00)	0.214
-HFV days	1.01	(1.00, 1.01)	0.002
-Room air days	1.02	(1.02, 1.02)	<0.001
Disposition:			
Transferred vs Alive by:	(logistic)		
-Major anomalies	4.21	(1.69, 10.52)	0.002
-Weight percentile	1.43	(0.46, 1.05)	0.084
-Apgar score at 5 minutes	1.03	(0.83, 1.15)	0.772
-Outborn admit group	0.36	(1.04, 7.62)	0.042
-CLD	3.57	(0.08, 0.95)	0.040
-Respiratory days	0.98	(0.98, 1.05)	0.346
-Ventilator days	1.06	(0.90, 0.99)	0.023
-HFV days	0.99	(0.93, 1.09)	0.869
-Room air days	1.01	(0.98, 1.00)	0.094
Died vs Alive by:			
-Major anomalies	3.01	(0.18, 2.88)	0.045
-Weight percentile	0.93	(0.35, 1.23)	0.794
-Apgar score at 5 minutes	1.14	(0.77, 1.61)	0.439
-Outborn admit group	0.47	(0.23, 7.31)	0.292
-CLD	1.16	(0.04, 2.86)	0.879
-Respiratory days	1.02	(0.98, 1.09)	0.488
-Ventilator days	0.99	(0.83, 1.07)	0.913
-HFV days	0.95	(0.72, 1.26)	0.683
-Room air days	0.98	(0.93, 1.02)	0.423
DC home on oxygen by:			
-Major anomalies	0.41	(0.10, 1.67)	0.213
-Weight percentile	1.02	(0.43, 2.46)	0.960
-Apgar score at 5 minutes	0.98	(0.76, 1.25)	0.863
-Outborn admit group	1.47	(0.55, 3.93)	0.442
-CLD	0.79	(0.15, 4.26)	0.781
-Respiratory days	1.06	(1.03, 1.10)	<0.001
-Ventilator days	0.93	(0.86, 1.01)	0.079
-HFV days	1.06	(0.96, 1.17	0.243
-Room air days	0.96	(0.90, 1.02)	0.147
DC home on monitor by:			
-Major anomalies	1.28	(0.49, 3.37)	0.613
-Weight percentile	0.90	(0.49, 1.66)	0.745
-Apgar score at 5 minutes	0.84	(0.71, 0.99)	0.041
-Outborn admit group	0.79	(0.32, 1.97)	0.614
-CLD	3.55	(0.68, 18.51)	0.133

-Respiratory days	1.02	(0.99, 1.06)	0.150
-Ventilator days	0.96	(0.91, 1.02)	0.196
-HFV days	0.88	(0.77, 1.01)	0.072
-Room air days	1.00	(0.99, 1.02)	0.910

Note. DV=dependent variable. IV=independent variable. b=regression slope. CI= confidence interval. Negative binomial regression slope (exp[*b]*). *admit group coded as 0=inborn, 1=outborn.

Question Four. The fourth question was what combination of developmental, situational, and health/illness transitions most influence patterns of response in infants born 32 to 38 weeks gestation. For this question, the most associated count variables and the categorical variables with the most influential AORs from prior analyses of questions 1 through 3 and listed in Table 10. Significance at $p<0.05$ was considered as well as confidence intervals for the variables tested in this model were considered.

All of the IVs examined for the two count variables were statistically significant and several had large effects with the DV. For the outcome respiratory support days, all the IVs tested were significant except abruption and had effects of exp(b) = 0.61 and above. Infants with chronic lung disease (CLD) had 764% increase in predicted mean respiratory support days (exp(b) = 8.64; $p<0.001$) and infants with major anomalies had a 145% increase in the predicted average respiratory days (exp(b) = 2.45; $p<0.001$), adjusting for the other variables in the model. Other IVs with effects on respiratory support days were preeclampsia (exp(b) = 0.94), maternal age (exp(b) = 0.93), antenatal steroids (exp(b) = 0.91), and birth order (exp(b) = 0.91). Diabetes (exp(b) = 0.88), female gender (exp(b) = 0.85), increasing five-minute Apgar score (exp(b) = 0.79), and increasing gestational age in weeks (exp(b) = 0.78), were also associated with respiratory days.

Chronic lung disease, major anomalies, and outborn admit group increased the expected length of stay by 132%, 97%, and 30% respectively when examined with the other IVs in the model (exp(*b*) =2.32, 1.97, 1.30; $p<0.001$). For length of stay, birth number (exp(*b*)=0.99), female gender (0.98), advanced maternal age (0.97), increasing five-minute Apgar score (0.96), and pre-eclampsia (0.95), Black race (0.89), increasing gestational age (0.86), and chorioamnionitis (0.80) were all associated with the outcome.

The remaining categorical DVs required logistic regression analysis and reporting of AORs, confidence intervals, and significance levels. There were fewer statistically significant relationships seen among the IVs tested for the categorical variables. For the disposition transferred versus alive, increased odds were seen among the IVs tested with major anomalies (AOR 15.26), chronic lung disease (AOR 9.14), and outborn admit group (AOR 2.00) and all were significant at $p<0.05$. Decreased odds for this DV were seen with birthweight (AOR 0.67; $p<0.001$) and increasing five-minute Apgar score (AOR 0.78; $p<0.001$).

With the DV died versus alive was examined, increased odds were seen with major anomalies (20.28), chronic lung disease (1.67), cesarean delivery (1.42), and outborn admit group (1.33). For this DV, Black race, increasing birth weight, birth order, increasing five-minute Apgar score, and pre-eclampsia had lower odds from 21% seen for Black race to 48% noted with pre-eclampsia (AORs 0.79, 0.58, 0.57, 0.52, and 0.52; $p<0.05$).

When the survivors discharged home on oxygen DV was examined by the IVs (following the removal of the CLD variable from final analysis due to an inappropriately high odds ratio likely due to a low one percent incidence of CLD), there were increased odds with major anomalies (AOR 6.19; $p<0.001$) and outborn admit group (AOR 2.15; $p<0.001$), and smaller odds seen with antenatal steroids given (AOR 1.30; $p<0.05$). This could reflect an influence of the earliest gestation of infants in the sample. The odds of needing oxygen at discharge were decreased by Black race (AOR 0.33; $p<0.001$), increasing birthweight (AOR 0.52; $p<0.001$), and to a lesser degree by increasing gestational age (AOR 0.78; $p<0.001$) and by increasing five-minute Apgar score (AOR 0.81; $p<0.001$) when examined by the other variables in the model.

The DV survivors discharged home on a monitor was associated with increased odds with CLD (AOR 3.43; $p<0.001$), major anomalies (AOR 2.53; $p<0.001$), and smaller effects were noted from outborn admit group (AOR 1.25; $p<0.05$), birth number (AOR 1.23; $p<0.05$), and antenatal steroids (AOR 1.20; $p<0.05$). The IVs five-minute Apgar score, diabetes, gestational age, chorioamnionitis, and Black race decreased the odds of monitor use by approximately 6% to 44% (AORs 0.94, 0.88, 0.77, 0.64, and 0.56 respectively; $p<0.05$) when examined by the other variables in the model.

Table 10. Multivariate Count, Linear, and Logistic Regression for All Factors (N=134,451).

Characteristic: DV by IV	**effect**	**95% CI**	***p*-value**
Respiratory days by:	(exp[b])		
-Gestational age in weeks	0.78	(0.78, 0.79)	<0.001
-Birthweight in kilograms	1.29	(1.26, 1.32)	<0.001
-Gender if female	0.85	(0.84, 0.87)	<0.001
-Advanced maternal age (years)*	0.93	(0.89, 0.97)	0.001
-Black maternal race**	0.69	(0.68, 0.71)	<0.001
-Antenatal steroids	0.91	(0.89, 0.93)	<0.001
-Cesarean vs. vaginal delivery	1.40	(1.36, 1.42)	<0.001

-Chorioamnionitis	0.61	(0.57, 0.65)	<0.001
-Preeclampsia	0.94	(0.91, 0.96)	<0.001
-Diabetes	0.88	(0.85, 0.90)	<0.001
-Abruption	0.99	(0.95, 1.04)	0.702
-Birth number	0.91	(0.88, 0.93)	<0.001
-Major anomalies	2.45	(2.36, 2.54)	<0.001
-Chronic lung disease (CLD)	8.64	(8.21, 9.07)	<0.001
-5 minute Apgar score	0.79	(0.78, 0.79)	<0.001
-Outborn admit group***	1.25	(1.22, 1.29)	<0.001
Length of stay by:			
-Gestational age	0.86	(0.86, 0.86)	<0.001
-Birthweight	0.81	(0.80, 0.82)	<0.001
-Gender if female	0.98	(0.97, 0.99)	<0.001
-Advanced maternal age	0.97	(0.95, 0.98)	<0.001
-Black maternal race	0.89	(0.89, 0.98)	<0.001
-Antenatal steroids	1.06	(1.05, 1.08)	<0.001
-Cesarean vs. vaginal delivery	1.07	(1.06, 1.08)	<0.001
-Chorioamnionitis	0.80	(0.78, 0.82)	<0.001
-Preeclampsia	0.95	(0.94, 0.96)	<0.001
-Diabetes	1.05	(1.05, 1.07)	<0.001
-Abruption	1.01	(0.99, 1.03)	0.333
-Birth number	0.99	(0.98, 1.00)	0.021
-Major anomalies	1.97	(1.93, 2.01)	<0.001
-CLD	2.32	(2.24, 2.41)	<0.001
-5 minute Apgar score	0.96	(0.96, 0.97)	<0.001
-Outborn admit group	1.30	(1.28, 1.32)	<0.001
Disposition:			
Transfer vs. Alive by:	(AOR)		
-Gestational age	0.92	(0.87, 0.98)	0.580
-Birthweight	0.67	(0.56, 0.81)	<0.001
-Gender if female	1.12	(0.96, 1.30)	0.147
-Advanced maternal age	1.15	(0.99, 1.02)	0.273
-Black maternal race	0.97	(0.87, 1.02)	0.021
-Antenatal steroids given	1.30	(1.08, 1.56)	0.305
-Cesarean vs. vaginal delivery	1.12	(0.74, 1.03)	<0.001
-Chorioamnionitis	1.14	(0.50, 1.63)	0.312
-Preeclampsia	0.85	(0.93, 1.51)	<0.001
-Diabetes	1.26	(1.04, 1.53)	0.989
-Abruption	1.04	(0.71, 1.52)	0.210
-Birth number	0.82	(0.62, 1.09)	0.002
-Major anomalies	15.26	(12.97, 17.95)	<0.001
-CLD	9.14	(7.42, 11.26)	0.004
-5 minute Apgar score	0.78	(0.74, 0.81)	<0.001
-Outborn admit group	2.00	(1.66, 2.41)	0.003

Died vs. alive by:			
-Gestational age	1.02	(0.96, 1.08)	0.580
-Birthweight	0.58	(0.56, 0.81)	<0.001
-Gender if female	1.12	(0.96, 1.30)	0.147
-Advanced maternal age	0.80	(0.53, 1.20)	0.273
-Black maternal race	0.79	(0.64, 0.96)	0.021
-Antenatal steroids given	0.90	(0.73, 1.10)	0.305
-Cesarean vs. vaginal delivery	1.42	(1.20, 1.69)	<0.001
-Chorioamnionitis	0.69	(0.34, 1.41)	0.312
-Preeclampsia	0.52	(0.38, 0.72)	<0.001
-Diabetes	1.00	(0.81, 1.24)	0.989
-Abruption	0.80	(0.57, 1.13)	0.210
-Birth number	0.57	(0.40, 0.81)	0.002
-Major anomalies	20.28	(17.34, 23.71)	<0.001
-CLD	1.67	(1.18, 2.35)	0.004
-5 minute Apgar score	0.52	(0.51, 0.54)	<0.001
-Outborn admit group	1.33	(1.11, 1.61)	0.003
Survivors discharged home on oxygen by:			
-Gestational age	0.78	(0.83, 0.97)	<0.001
-Birthweight	0.52	(0.59, 0.88)	<0.001
-Gender if female	0.89	(0.83, 1.19)	0.137
-Advanced maternal age	1.05	(0.61, 1.40)	0.773
-Black maternal race	0.33	(0.25, 0.43)	<0.001
-Antenatal steroids given	1.37	(1.02, 1.61)	<0.001
-Cesarean vs. vaginal delivery	1.09	(0.81, 1.19)	0.308
-Chorioamnionitis	0.76	(0.36, 1.46)	0.447
-Preeclampsia	1.18	(0.97, 1.57)	0.108
-Diabetes	1.05	(0.74, 1.21)	0.663
-Abruption	0.98	(0.70, 1.61)	0.902
-Birth number	0.88	(0.67, 1.19)	0.294
-Major anomalies	6.19	(1.48, 2.49)	<0.001
-5 minute Apgar score	0.81	(0.87, 0.99)	<0.001
-Outborn admit group	2.15	(1.39, 2.28)	<0.001
Survivors discharged home on monitor by:			
-Gestational age	0.77	(0.74, 0.80)	<0.001
-Birthweight	0.98	(0.89, 1.08)	0.688
-Gender if female	1.02	(0.93, 1.11)	0.739
-Advanced maternal age	0.93	(0.75, 1.14)	0.467
-Black maternal race	0.56	(0.48, 0.64)	<0.001
-Antenatal steroids given	1.20	(1.07, 1.33)	0.001
-Cesarean vs. vaginal delivery	1.06	(0.96, 1.16)	0.249
-Chorioamnionitis	0.64	(0.43, 0.98)	0.038

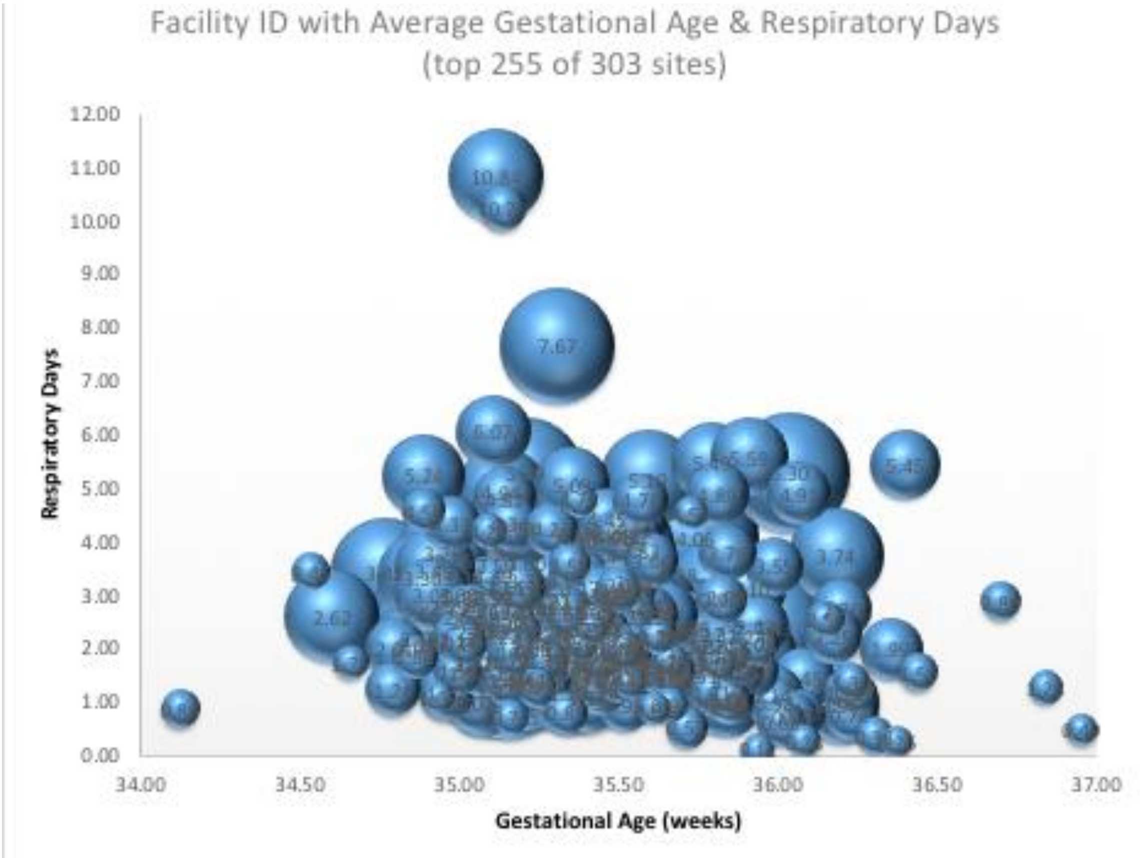
-Preeclampsia	1.07	(0.94, 1.21)	0.314
-Diabetes	0.88	(0.77, 1.00)	0.047
-Abruption	1.06	(0.85, 1.33)	0.584
-Birth number	1.23	(1.09, 1.39)	0.001
-Major anomalies	2.53	(2.26, 2.83)	<0.001
-CLD	3.43	(2.81, 4.17)	<0.001
-5 minute Apgar score	0.94	(0.91, 0.97)	<0.001
-Outborn admit group	1.25	(1.10, 1.42)	0.001

Note. DV=dependent variable. IV=independent variable. b=regression slope. CI= confidence interval. Negative binomial regression slope (exp[*b]*). * age codes: 0 = below 40 years, 1= 40 years and above. ** delivery codes: 0=vaginal, 1=Cesarean section. ***admit group coded as 0=inborn, 1=outborn.

Secondary Question. The secondary research question asked if there were differences between any of the variables and the different facilities represented? This question was analyzed using descriptive methods since the facilities were anonymous and numbered with random codes from 2 to over 7,000. There were a total of 303 facilities represented in the dataset. Of these, the number of infants per facility ranged from 1 to over 3300. A graphic representation known as a bubble plot was used to visualize the majority of facilities and some of their characteristics (see Figure 5). Due to software limitations, the top 255 facilities were included in the graph based on number of infants represented (99 and above). Also in the graph is the average gestational age represented on the X-axis and the average respiratory days plotted on the Y-axis. The size of the "bubbles" represents the number of infants in the database, those born at 32 to 38 weeks gestation from 2015 to 2017. The largest bubbles are facilities with more older preterm and early term admissions and the smallest bubbles represent those with the fewest number of infants. Information such as geographical location, state, or economic payor mix was not provided in the database, so little else could be examined with the facility variable.

As seen in Figure 8, the majority of facilities had a population of infants with an average gestational age of 35 to 35.5 weeks who needed an average of 0.5 to 5 days of respiratory support. There were three moderate-sized sites whose infants required respiratory support days averaging 7 to 11.5, and these sites seemed to have a larger number of slightly smaller infants born at around 35 weeks gestation. One smaller site had infants with an average gestational age of around 34.2 weeks who also required very low number of respiratory support days (average of one), indicating optimal outcomes for those infants and suggesting this site could have a high rate of antenatal steroid use in mothers at risk for preterm birth or their respiratory management is different than other sites. Another issue could be that this site did not have accurate charting of respiratory days explaining its minimal number of respiratory support days. Three other small sites had older babies (near 36.8 to 37 weeks gestation) who required a low average number of respiratory support days (0.5 to 3.0). This finding would be expected for infants with more mature lungs. Although this bubble plot only includes a small portion of data, it accurately represents some of the demographics for the entire sample including average gestational age (around 35 weeks) and the average number of respiratory support days required (around three).

Figure 5. Plot of Facility Identification with Gestational Age and Respiratory Days.



CHAPTER V

DISCUSSION

The purpose of this study was to examine hospital outcomes in infants born at 32 to 38 weeks gestation. Chapter V provides an interpretation of the findings for the four research questions and situates these findings in current literature. Transitions Theory was the framework used to identify relationships between different types of neonatal transitions including developmental, situational, and those related to health and illness and these were examined related to outcomes of infants during their hospitalization in the neonatal intensive care unit (NICU). In this chapter, these findings are compared with prior research that identified risks and outcomes for neonates requiring hospitalization. Implications for research, nursing, and the clinical setting will be presented and limitations are discussed. Future research recommendations are addressed.

There are few published studies of infants born at 32 to 38 weeks gestation, particularly pertaining to their outcomes while and after hospitalization in the NICU. Recent studies have focused on underdeveloped cardiorespiratory regulation in infants born at 35 to 36 weeks gestation (Lucchini, Burtchen, Fifer, & Signorini, 2018), the incidence of NICU admission and respiratory illnesses in infants born at early term (37-38 weeks) gestation (Do Carmo Leal et al., 2017), the need for resuscitation following birth and use of respiratory and nutritional support during neonatal unit stay in mid- to late preterm infants born at 32 to 36 weeks gestation (Boyle et al., 2015), and the incidence of NICU admission and etiology of these admissions including respiratory morbidity in late preterm infants (34 to 36 weeks gestation) (Natile et al., 2014). There are few published studies in the most commonly used U.S. databases examining outcomes of infants deemed "mid preterm" (born at 29 to 33 weeks gestation). There is also a paucity of research examining infants born mid- to late preterm and those born mid-preterm through early term gestations. The older preterm and early term (OPET) group was selected for this study to add to current literature and assist clinical staff in preparing and counseling families of older preterm, late preterm, and early term infants requiring NICU admission.

This study had a large sample size of 159,529 infants whose data were obtained from a clinical data warehouse of medical records from over 300 U.S. NICUs. Findings revealed OPET infants were at a relatively low risk for mortality (0.6%), but when they were born with congenital anomalies or developed a chronic respiratory illness their outcomes were greatly influenced during hospitalization and at time of discharge. Other infants negatively affected during hospitalization and at discharge, but to a lesser degree, were those who were outborn and transported to the NICUs represented in the dataset.

Based on this study, infants with chronic lung disease (CLD) and major congenital anomalies were at greatest risk for needing more days of respiratory support, longer lengths of stay, and were more likely to need equipment for continued monitoring or support at discharge, transfer to another facility, and death. Although the low 1% incidence of CLD for neonates in the dataset examined could explain some of the study's findings, there seems to be some relationship between illness acuity in infants with this condition and negative outcomes. First, infants who typically develop CLD (also called bronchopulmonary dysplasia [BPD]) are less than 28 weeks gestation and require mechanical ventilation, but a history of receiving positive pressure ventilation (PPV) as a preterm infant is present in all infants with CLD suggesting alveolar or lung overstretching as the etiology (Davidson & Berkelhamer, 2017). Although all uses of PPV such as the manual form in the delivery room were not assessed, alveolar overstretching could be the cause of negative outcomes for the 32-38 week group of infants in this study.

Of the other variables tested in this study, infants with CLD not only needed 764% more mean respiratory support days, but they also had increased lengths of stay by 132%. Also as expected, some infants with CLD continue to need oxygen at discharge. Chronic lung disease and need for oxygen at discharge were initially examined in the study, but omitted from final analysis due to an excessive odds ratio which was likely a result of the low prevalence of CLD among this population. Increased likelihood of needing a monitor at discharge was noted in infants with CLD as was a slightly increased odds of death, but odds of death was less for those with CLD than with major anomalies. This was the only outcome variable in the study with a greater effect from major anomalies than CLD. Infants identified from the study as needing a transition period beyond most other infants in the 32 to 38 week gestation group were those with CLD and major congenital anomalies. Since infants with these conditions in this gestational age group require a prolonged transition period, it will be important to further study this group to determine critical events and milestones in order to develop recommendations and interventions to optimize short- and long-term outcomes.

Sample Demographics

Infant Characteristics

Overall, infants in the 32 to 38 week gestation group examined in this study were born at the older gestations in this range (*M* 35.4 weeks; *SD* 1.86), and infants at the earliest gestations of 32-33 weeks comprised only 18% of the sample. This is likely reflective of the current trend in U.S. births where most preterm infants are born late preterm (34 to 36 weeks gestation) and infants 37 and 38 weeks gestation make up one quarter of all U.S. births annually (one million) (Martin, Hamilton, & Osterman, 2019; Martin, Hamilton, Osterman, Driscoll, & Drake, 2018b). In this study, nearly half of the sample was born late preterm. These infants also had robust birthweights corresponding to those with older gestational ages (*M* 2.569 kg; *SD* 1.864) and the majority (78%) were considered appropriate for gestational age when weight and head size were examined on standard growth curves.

There were slightly more males (56%) than females represented in the database and the database represented approximately 1.5% of annual U.S. births (Martin et al., 2019). The largest group of mothers was White (49%), followed by Hispanic (21%), then Black (17%). Studies of extremely low gestational age infants have shown that Black infants are more commonly born at the earliest gestations (Lorenz, Ananth, Polin, D'Alton, 2016), but this study did not examine race or other characteristics by gestational age group.

Other characteristics of infants were assessed in this study since these traits have been found to be associated with adverse outcomes in prior studies including major anomalies (Ely & Driscoll, 2019; Jacob, Kamitsuka, Clark, Kelleher, & Spitzer, 2015), five-minute Apgar score (Cnattingius, Norman, Granath, Petersson, Stephansson, & Frisell, 2017), and multiple births (Lorenz et al., 2016). These traits can be associated with altered transitions since they involve multiple organ systems, a delay in response to resuscitation in the delivery room following birth, and prohibited intrauterine growth from additional fetuses.

Since congenital malformations caused 21% of U.S. infant deaths in 2017 and are the second leading cause of infant mortality (Ely & Driscoll, 2019; Lorenz et al., 2016), assessment of these conditions was important in this study to identify infants at risk for morbidity and death in the OPET population of infants. In this dataset, congenital malformations were labeled "major anomalies" and 11% of infants had a major anomaly with 10% of those infants having a chromosomal disorder known as trisomy. The remaining anomalies consisted of heart defects, abnormalities of the lung and respiratory system, gastrointestinal defects, and neurological anomalies (Clark, 2019; Jacob et al., 2015). After CLD, infants with major anomalies required more respiratory days, longer lengths of stay and were at higher odds of being transferred to another NICU and needing equipment at discharge. Having a major anomaly increased the odds of death by over 100% in this study and this was an expected finding given the latest Centers for Disease Control and Prevention (CDC) and National Center for Health Statistics data on infant mortality (Ely & Driscoll, 2019) and a recent study comparing the United States' infant mortality rate to other nations (Lorenz et al., 2016).

Overall, infants in the study had favorable five-minute Apgar scores which are more correlated with short- and long-term outcomes than the 1-minute Apgar score (Cnattingius et al., 2017). In this study, 96% of infants had five-minute Apgar scores in the highest range of 6-10, indicating good overall responses to delivery and resuscitation and only occasional need for resuscitation after 5 minutes of life. This finding is somewhat expected since the average gestational age of infants in the dataset was 35 weeks indicating more mature infants at lower risk of needing resuscitation.

To determine which infants were from multiple births, birth number was examined and the majority (91%) of infants were singletons; only 8% were from twin births. This low incidence of multiples lessened concern about statistical analysis of paired data as with relatives. In this study, advancing birth number was associated with a lower percentage of respiratory support and an decreased length of stay. Increasing birth number was also associated with lower odds of death by 60% and increased odds of needing a monitor at discharge, neither of which were noted in prior literature.

Length of NICU stay was assessed in this study and was slightly less than two weeks (*M* 13.1 days; *SD* 13.3). This is probably because infants studied were of later gestations and they tend to have fewer complications including those associated with the respiratory system or immature lungs, or from problems with oral feeding, and are typically discharged home earlier. Boyle and colleagues (2015) found that infants born at 32 to 36 weeks gestation and admitted to the NICU had a median length of stay of five days with a range of 1 to 78 days; the earliest infants in their study (32 and 33 weeks) had a median length of stay of 16 days with a range of 4 to 78 days. Their study did not include early term infants with gestational ages 37 and 38 weeks admitted to the NICU. Infants of these older gestational ages likely have shorter lengths of stay due to their more mature lungs and neurologic systems and an ability to transition to extra-uterine life more quickly. They are also able to establish oral feedings faster.

Other demographics examined included the NICU admission type. This is important to examine since infants born preterm fare better when born in a facility with a NICU (American Academy of Pediatrics [AAP] & American College of Obstetricians and Gynecologists [ACOG], 2017). In this study, most infants were inborn, or born in a hospital with a NICU, and 13% were outborn, then transported to a hospital with a NICU. Outborn infants were noted to have required slightly more days of respiratory support and increased lengths of stay. They were also more likely to be transferred or discharged home on oxygen. These findings were expected given current literature recommending delivery in an appropriate level hospital so as to best meet mother and baby's needs (AAP & ACOG, 2017).

Maternal Characteristics

Maternal demographics including age and incidence of illness are important to examine since they often affect infant outcomes. In the U.S., teenage pregnancy is declining and more women are delaying childbearing until older ages (Martin et al., 2019; Martin, Hamilton, Osterman, Driscoll, & Drake, 2018c). While this likely contributes to financial stability, older maternal age is when chronic illnesses such as hypertension tend to occur which often worsens during pregnancy (AAP & ACOG, 2017). Hypertension during pregnancy occurs more often in women ages 35 to 40 years (Lean, Derricott, Jones, & Heazell, 2017) than it does in younger women. The mean maternal age for mothers in this study was 29 years (*SD* 6.15). Maternal age above 40 has been associated with adverse outcomes including preterm birth (Roche, Abdul-Hakeem, Davidow, Thomas, & Kruse, 2016) and increased neonatal death has been found to be correlated with increasing maternal age (Lean et al., 2017). Advanced maternal age (40 and above) was ultimately examined in this study after leaving the variable continuous, then examining by less than 20 years, 20 to 39, and 40 and over, when both methods failed to correlate with other variables in the model.

For prevention of infant respiratory disease or surfactant deficiency, 34% of mothers in this study received antenatal steroids. During the years of 2015-2017, administration of antenatal steroids to mothers likely to give birth to late preterm infants was on the horizon and for those likely to give birth to early term infants, steroids were not indicated perhaps due to a much lower incidence of immature lung disease or lower recognition of surfactant deficiency contributing to lung disease in these infants. The majority of mothers receiving antenatal steroids during 2015 to 2017 were those whose infants were born at 32 and 33 weeks gestation; 18% of the sample. Since this is lower than the actual 34% who received steroids, it is suspected that some obstetricians were starting to give mothers steroids at 34 weeks gestation (19% of sample) and maybe 35 weeks gestation during the 2015 to 2017 time period.

For assessment of maternal illness, several variables were available in the database. For maternal-specific morbidity among these mothers, diabetes was the most prevalent (17%), followed by pre-eclampsia (12%). Another variable, pregnancy-induced hypertension (PIH), was present in 11% of the maternal sample, but this variable did not include women with pre-existing or chronic hypertension and was not used in the final analysis when examining infant outcomes. It is possible that many neonatal and obstetric providers use the terms pre-eclampsia and PIH interchangeably when charting, and that the incidence of any maternal hypertension in this dataset could be a combination of the two variables. If this is true, then the incidence of hypertension was 23%. When the first 4000 cases were examined closely, terms related to any hypertension were not charted more than once per case. The pre-eclampsia variable was ultimately chosen for examining hypertension since this variable also included mothers with any hypertension before pregnancy and using pre-eclampsia is consistent with reporting in the literature (Churchill, Duley, Thornton, Moussa, Hind, & Walker. (2018).

Infant Respiratory Characteristics

Respiratory morbidity is a common cause for NICU admission and is typically the result of inadequate surfactant production common in preterm infants, especially in those whose mothers did not receive antenatal steroids. In an attempt to capture the extent of respiratory morbidity in this study, several variables were examined. Total respiratory support days was initially thought to be an average of 13.5 days (*SD* 12.7), but when further evaluated this variable included the total number of room air days for the infants, so once room air days was subtracted and a new variable created, the mean number of respiratory support days was much lower at 2.8 days (*SD* 5.6). Of interest, 45% of infants in the study did not require any respiratory support and remained on room air throughout their hospitalizations. Using the maximum support rank day which examined the day when the highest amount of respiratory support was needed from birth through day 7 of life, the highest number or 45% of infants required the most support on the day of birth, and the next highest, 24% required the most support on day four of life. This requirement of more respiratory support on the fourth day of life could be due to the time it takes for surfactant deficiency to manifest.

Other variables examined included the type of respiratory support needed during the most acute period, days 0 to 2 of life, and 8.7% of infants required mechanical ventilation for their illness during this period. The maximum amount of oxygen required was 0.28 fraction of inspired oxygen (possible range of 0.21 to 1.00), which is a relatively low volume.

Other variables were also used to examine respiratory morbidity including the number of days of respiratory support needed. The mean ventilator (conventional) days required was 3.8 (*SD* 8.3) and the mean high frequency ventilator days was 5.12 (*SD* 6.2). This means the sickest infants who required high frequency ventilation needed this ventilator for longer periods. This suggests that once infants progressed to high frequency ventilation, they were either too unstable to wean or providers were not as comfortable weaning them from support. For other types of respiratory support needed, the most frequently used method was nasal cannula oxygen at 4.7 (*SD* 6.7) mean days followed by noninvasive nasal prong vent at 3.5 days (*SD* 4.1). The types of support used for one of the fewest number of days was continuous positive airway pressure (CPAP) at 2.8 days (*SD* 2.8). These findings suggest that infants in this sample required nasal cannula oxygen for the longest of any non-ventilatory method of respiratory support. Finally the mean number of room air days for infants in the study was 10.9 days (*SD* 10.3). This likely indicates that most infants in this study required respiratory support for less than half of their time in the NICU, which would be expected for more mature infants without surfactant deficiency. Typically, after infants recover from their respiratory illness immediately following birth, NICU interventions are focused on achieving adequate nutrition and establishing oral feedings.

For equipment or support needed at discharge, four variables were included in the database pertaining to infants who survived to discharge. Only 2.3% of infants needed oxygen at discharge and 0.1% needed a tracheostomy. Overall, infants in this study required short intervals of respiratory support and likely had low respiratory morbidities, especially when compared to extremely low gestational age infants.

Discussion of Research Questions

The Theory of Transitions was the conceptual framework that guided this study. In this theory, experiences that occur during a transition event have an important and oftentimes lasting impact on patients, their families, and at times, the staff involved in care. As a conceptual framework, Transitions Theory helped explain the transition process involved with the older preterm and early term population of infants studied.

Developmental Transitions

The first research question assessed which developmental transitions influence outcomes in infants born at 32 to 38 weeks gestation. The predicted mean number of respiratory days decreased by 19% for every 1 week increase in gestational age, and respiratory days were 13% lower in female infants compared to males, adjusting for birthweight. Infants with older gestational ages have more mature lungs and are capable of producing surfactant, so this finding of decreasing respiratory support days as gestational age increases is expected. Infants of female gender requiring fewer respiratory support days is consistent with past research and a recent study evaluating outcomes in infants that suggests preterm males fare worse than preterm females (O'Driscoll, McGovern, Greene, & Molloy, 2018; Peacock, Marston, Marlow, Calvert, Greenough, 2012). Of note, the earlier studies examined infants born at less than 28 weeks gestation, so prior to the current study it was unclear if gender affected hospital outcomes in older preterm and early term infants.

Female infants also had 2% lower estimated lengths of stay than male infants in this study. Infants with higher birthweights and those born at older gestational ages had shorter length of stays than others as would be expected, largely due to their advanced lung and other organ maturity. Finally, there was a decrease in odds of death by 43% as birthweight increased, also reported in a prior study (Ray, Park, & Fell, 2017). In this large Canadian cohort study of all gestations of newborns, small-for-gestational age at birth was considered a high predictor of mortality especially in infants born preterm (Ray et al., 2017).

Situational Transitions

This question addressed which situational or maternal transitions influence outcome indicators in infants born at 32 to 38 weeks gestation. In late preterm infants, according to at least one study, maternal and pregnancy-related conditions account for a large proportion of neonatal morbidity (Bonnevier, Brodszki, Bjorklung, & Kallen, 2018). Determining the best choice of variables for this model from the dataset was challenging, but in the final analysis, there were several significant, but not surprising findings..

The mean number of respiratory days was affected by all variables modeled with the greatest effects seen from antenatal steroids, cesarean birth and abruption. Antenatal steroids were given to most mothers anticipated to have a preterm birth which means these babies would be expected to require the most respiratory support. Cesarean birth and increasing days of respiratory support could be associated with birth of smaller infants with immature lungs. One large cohort study found that the number of extremely low gestational age infants delivered by cesarean section increased over a 19 year study period (Stoll et al., 2015), and another large study discovered infants delivered by operative delivery at the earliest gestational ages were more likely to be live births than those born vaginally (Patel et al., 2015). Abruption and other antepartum hemorrhages have been found to double the risk for neonatal respiratory disease and need for respiratory support (Bonnevier et al, 2018) which would help to explain the finding of maternal abruption in this study increasing the number of required days of respiratory support.

Diabetes, pre-eclampsia, and maternal age were associated with fewer days of respiratory support needed for the infants in this study. There have been some studies examining the relationship of diabetes in mother and infant outcomes. Admissions to the NICU for respiratory distress were reportedly increased among infants born to mothers with diabetes (Becquet et al., 2015). Maternal age has been examined as a factor in neonatal morbidity in a recent study and as age increased, morbidity also increased (Lean et al., 2017). It is possible that these findings suggest spurious and paradoxical outcomes which need to be verified in additional studies of infants 32 through 38 weeks gestation.

In terms of length of stay, antenatal steroids were positively associated with length of stay among the infants in this sample. This was likely due to mothers whose babies were born at earlier gestations qualifying to receive steroids. Other factors that were negatively associated with length of stay were diabetes, race, and chorioamnionitis. Length of stay has not been well-studied for the NICU population, but NICU admission has been studied in women with diabetes delivering late preterm infants and severity of diabetes increased incidence of NICU admission and treatment of neonatal hypoglycemia (Becquet et al., 2015). Diabetes could have affected length of stay in this study because stress from early birth or growth from exposure to insulin could increase maturation of organ systems.

For the remaining outcomes, delivery by cesarean section increased the odds of death by 111% (AOR 2.11). The significance of this finding is unclear and has not been well studied in this population. In studies of smaller infants, odds of death were decreased when born by cesarean section (Patel et al., 2015). The group of infants born at 32 to 38 weeks gestation studied may not be delivered as often by cesarean section as smaller infants (57% of infants in this study compared to 64% of infants 22 to 28 weeks gestation in another study [Stoll et al., 2015]). Smaller and those born at earlier gestations may not be able to tolerate the stress of labor as well as infants who are more mature.

For other findings related to situational transitions, mothers receiving antenatal steroids had a 102% increased odds of their infant needing a monitor at discharge. As mentioned earlier, only mothers in this study expecting to deliver their infants at earlier gestational ages received steroids. Infants born at earlier gestational ages are more immature and may not have established coordinated respiratory patterns by discharge (Lucchini, Burtchen, Fifer, & Signorini, 2019), thus needing post-discharge monitoring. Race decreased the odds of needing oxygen at discharge by 70% and this was not found in prior literature as being protective. Antenatal steroids, chorioamnionitis, pre-eclampsia, and birth number decreased the odds of death by about 20% to 60%. This protective effect of steroids has been supported in another recent study of infants 23 to 34 weeks gestation (Travers et al., 2017) on discharge outcomes.

Health/Illness Transitions

This research question addressed what health/illness transitions influence outcomes in infants born at 32 to 38 weeks gestation. Although the sample size decreased to 673 when this model was run, there were still some significant findings and the sample size continued to meet initial calculations for study power estimation. Chronic lung disease (CLD) increased the mean number of respiratory days by 77% in the study. Chronic lung disease is typically diagnosed when an infant persistently requires oxygen at either 28 days of life or 36 weeks corrected gestational age and is more commonly seen in infants 30 weeks gestational age and below (Davidson & Berkelhamer, 2016). Increasing Apgar score was also associated with lower number of days of respiratory support needed and has been studied as a marker of illness severity (Cnattingius et al., 2017). For length of stay, increasing Apgar score and outborn admit group were negatively associated which suggests less severity of illness with high Apgar scores (Cnattingius et al., 2017) and perhaps the infants in this database who were transferred were stable (AAP & ACOG, 2017). There were no significant findings for the death dependent variable in this model.

Combined Demographic, Situational, and Health/Illness Transitions

The final research question addressed the combination of developmental, situational, and health/illness transitions that influenced outcomes in infants born at 32 to 38 weeks gestation. The model for this question was refined based on early findings in this study and certain variable responses that required the elimination of variables uncorrelated with others in the model and categorizing some continuous variables that were not correlated. Maternal age in years over age 40 years was ultimately defined in the model to examine the effect on infant outcomes. Pregnancy-induced hypertension was removed from modeling due to concerns of multicollinearity with pre-eclampsia. Rupture of membranes was removed earlier due to unreliable findings despite making it a categorical variable of more than 24 hours and less than 24 hours (Clark, 2019). After these changes, several significant findings were noted. The effects of older maternal age and Black race on negative infant outcomes in existing literature (Lorenz et al., 2016) were found in this study to be associated with positive outcomes. The meaning of these findings for this population of infants is unclear, and warrants further study.

For number of days of respiratory support, there were several effects seen, but only the most prominent are discussed in this chapter. Chronic lung disease and major anomalies increased the mean percentage of days of respiratory support (8.64, 2.45) and pre-eclampsia, maternal age, antenatal steroids, and birth number were associated with a lower percentage of respiratory support. These findings indicate that when several select health/illness factors are combined along with situational factors the result is an increase or decrease in the number of respiratory days infants need when they are born at 32 to 38 weeks gestation and in need of NICU care, adjusting for the other variables in the model. Cumulative factors increase the time needed for successful transition to life outside the womb.

There were similar findings with length of stay as with number of days of respiratory support. Chronic lung disease and major anomalies increased the length of stay by 132% and 97%, and birth number, female gender, advanced maternal age, 5-minute Apgar score, and pre-eclampsia decreased length of stay by 1-5%. This indicates that although not as many factors affect length of stay, there are still several infant and maternal factors that when combined can increase the expected length of hospital stay for OPET infants.

For the disposition variable, changes were made in the final model since some loadings were causing contradictory findings such as with the chorioamnionitis independent variable. This outcome variable was recoded to assess the effects of infants transferred versus alive and infants who died versus those who were alive at discharge. For infants transferred, major anomalies, CLD, and admit group outborn increased the odds of transfer. This likely was related to the severity of illness in the infants seen in these groups and could be related to the level of NICUs represented in the database. For odds of death, major anomalies increased the odds the most (AOR 20.28), followed by chronic lung disease, cesarean delivery and outborn. This finding is consistent with prior literature that found that infants with major anomalies, CLD, and those born by Cesarean delivery were most likely more acutely ill and at a higher risk of death (Jacob et al., 2015).

For discharge needs, infants with CLD and major anomalies also had oxygen and monitor needs. Although infants with CLD was ultimately not tested for oxygen need due to extraneous findings in prior models, those needing oxygen at discharge were more likely to have major anomalies, be outborn, or had antenatal steroids given. Similar findings were seen with the variable needing a monitor at discharge except having CLD increased the odds for this outcome. Variables that were protective for decreasing the odds of needing discharge equipment were Black race and gestational age and these results were not found in earlier studies. The findings of CLD, major anomalies, and admit group outborn on need for discharge equipment were not overall surprising as these infants are sick and often for longer periods. For protective effects, perhaps inflammation seen with chorioamnionitis increases physiologic maturation in infants or maybe these infants are hospitalized longer than others. For Black race, this warrants further examination since preterm infants who are Black tend to have worse outcomes (Lorenz et al., 2016).

Application of the Transitions Model

The concepts taken from the original Transitions Theory model included nature of transitions comprised of transition types and patterns of response which included outcomes. For transition type, developmental, situational, and health/illness factors were examined in this study. Health/illness factors had the greatest influence on outcomes followed by situational factors. For patterns of response, outcomes examined were number of respiratory days, length of stay, disposition on the last day of admission which included transferred versus alive and died versus alive, and equipment needed at discharge in survivors which included use of oxygen and any monitor use. In the combined model used to examine question 4, the largest effects were seen with CLD on the mean number of respiratory days (8.64) and the effect of major anomalies on died versus alive (AOR 20.28); both were significant at $p<0.001$.

Model Limitations

There were a few limitations to using the Transitions Model as a guide for a study of this type. The variable categories available in the dataset were not exact matches to the three transition types (developmental, situational, and health/illness) and required category adjustments after initial analyses and literature review. Apgar score is an example since originally this variable was to be examined as a situational transition but ultimately was used to assess health/illness of the infant since literature supported using Apgar to assess infant status (Cnattingius et al., 2017). Also, the organization type transition and corresponding variable were limited for a few reasons. This variable was a random code in the database in order for the organizations to remain de-identified. While a de-identified dataset provides protection to its participants (individuals and organizations), this means assessing outcomes by organization is limited. In this study since the organization type (e.g., level of NICU) could not be identified and the region of the country or state where the hospital is located so as to examine local practice norms was not known, this limited the opportunity to examine major differences by facility type. Another limitation to using the Model was that many of the listed concepts in previous applications were provided through qualitative studies with subjective responses, but the dataset and population studied here were observed. Using observed data required more reliance on prior literature to determine the most pertinent variables to study.

Implications

Implications for Research

This study is foundational for future studies of the older preterm and early term population of infants admitted to the NICU because few studies have previously examined these groups. Most research of preterm infants is focused on those of very early gestational ages and the poorest outcomes. Despite the fact that the number of annual births of infants born at 32 to 38 weeks is more than 1.3 million annually in the U.S., as with most new study populations, this project could open channels for future work. One place research could start is to investigate causes of mortality in the 1% of infants in this group who did not survive to hospital discharge. Understanding these causes could help in identification and treatment of these infants, ultimately decreasing the U.S. infant mortality rate. Infants with chronic lung disease and those born with major anomalies need additional study since they appear to be at higher risk for medical problems during hospitalization and require additional support at discharge. Infants whose mothers have certain situational factors such as cesarean section and diabetes are at risk for unfavorable outcomes in the NICU and warrant more study including how these factors in combination act to mediate outcomes. Finally, additional studies are needed to evaluate the degree of respiratory illness and types of support needed both in the hospital and after discharge for infants born at 32 to 38 weeks gestation.

Implications for Nursing Practice

This study has multiple implications for nursing practice. Since the sample size was large and the dataset represented most areas of the U.S., the study adds important information such as the percentage of babies admitted to the NICU that are in the 32 to 38 weeks gestational age group, what their typical length of stay in the NICU is, and how long and what types of respiratory support infants in this group require. Other insights this study provides related to the Transitions Theory framework include that infants are at risk for a decline in health while undergoing a health transition and that it is reasonable to view birth and the first month of life or longer as a major life transition.

Major transitions after birth include adaptation to extrauterine life, the use of lungs that for some infants are immature, and the immaturity of other major organ systems. Nurses as frontline staff are in a position to support parents, so the results of this study provides a better understanding of what is typical for this population of infants and information can be used to better educated families. Nurses also train families to care for infants before discharge and when infants have special needs such as CLD or major anomalies and need oxygen or a cardiac monitor for discharge home. Nurses are vital to ensuring a successful transition to home for those neonates and the findings of this study can inform the materials shared and the timing of when it is provided in order to facilitate a successful transition. Nurses not only assist infants in facilitating a successful transition, they also are vital to helping parents during this journey while in the NICU. These findings provide information that nurses could share with parents to help them anticipate the near term future for their child and plan for its impact on their family.

This study could also affect organizational measures such as NICU length of stay which affects staffing levels. These findings could be used to aide in the calculation of number of full time employees needed. Results of this study also affects quality measures including what gestations of infants are most commonly born and admitted to the NICU and their rates of morbidity and mortality.

Implications for Clinicians

For clinicians, this study provides several implications for practice. Transitions Theory suggests normalizing a longer time period for adjustment during critical periods of development and changes in life. Some infants may need extra time to navigate or reach milestones during those critical periods. Expectations of a time projection for these transitions are often counterintuitive. In neonatal medicine, clinicians may have expectations that infants reach milestones when the infant may not have fully developed and cannot yet fully function at this new phase. This might include not yet reaching neurological maturity and the inability to maintain respirations without apnea.

Another study practice implication is greater awareness of the typical time frames for infants born 32 to 38 weeks gestation in terms of their anticipated hospital stay, and for how often and how long respiratory support may be needed. This information gives clinicians more guidance in terms of typical parameters and could help clinicians make more informed observations and treatment decisions. The findings of this study can also help clinicians counsel parents who not only have infants born at 32 to 38 weeks in the NICU, but also those who have infants with major anomalies and with CLD including typical needs associated with these infants.

Limitations

Many researchers have started using large databases to conduct research because conducting randomized trials are expensive, labor-intensive, and may not be feasible. There are other reasons to use large databases. Large databases contain rich data that is often prospectively collected that can be used to answer important research questions. With the NICU population, using a large dataset of medical record data can address many of the issues related to large randomized studies such as cost and time. However, use of studies using big data should be approached with caution.

Studies using large datasets can have problems with validity especially internal validity. According to Polit and Beck (2018), internal validity is the degree or amount to which one can infer that an observed outcome was caused by an independent variable or treatment rather than by uncontrolled, nonessential causes. Validity as well as reliability should be regarded as occurring in varying degrees rather than viewed from an all-or-none perspective. Rarely are study designs or findings 100% reliable or valid. Issues with large datasets and validity include missing data which can result in larger standard errors from a diminished sample size (due to excess missingness) and an increased risk of Type II error or having a false negative finding. Another issue with using a large dataset is with biases that may emerge. In an existing dataset where participants are not randomized to a group, the groups being compared many not be equal (i.e., not only unequal in size, but in other characteristics as well) (Polit & Beck, 2018). Sampling bias is more likely a threat to internal validity when researchers have latitude in selecting cases from a bigger dataset for their study (Zedeck, 2014), not the case for this study.

Kaplan and colleagues (2014) caution that large sample sizes can amplify the bias accompanying error occurring from a study's sampling or study design. These authors identified additional types of biases in using big data including sampling error, measurement error, multiple comparisons errors, aggregation error, and the errors connected with systematic exclusion of information. They concluded that while observational studies can provide valuable information, this is dependent upon investigators selecting the correct analytic or theoretical model. When the sampling model is inappropriate, for example, a large sample size can magnify the bias (Kaplan, Chambers, & Glasgow, 2014). In this study, the large sample size obstructed the researcher from using gross observation to identify obvious errors such as missingness or extremely skewed variables. The sampling model was chosen for this study primarily based on prior literature using convenience sampling but also based on the theoretical framework for the study which provided the researcher with guidance when questions arose.

The paradoxical results seen in this study included decreased odds of negative outcomes with pre-eclampsia, chorioamnionitis, and Black race. These results were not found in prior studies of more immature infants for reasons that are not clear. The cause is suspected to be multifactorial. For pre-eclampsia, the other variable called pregnancy-induced hypertension may have affected the results seen in this study since the variables are very similar in that they assess hypertension. Chorioamnionitis likely affected results due to an inflammatory response inducing stress and organ, especially lung, maturity. Black race also had paradoxical results not captured in prior studies. Perhaps since Black race accounted for only 17% of the sample whereas 49% of the sample was Caucasian, the effect was spurious. The finding of pre-eclampsia, chorioamnionitis, and Black race associated with decreased odds of negative outcomes needs further study in infants 32 to 38 weeks gestation to investigate these findings due to the large sample size.

Conclusions

Infants born at 32 through 38 weeks gestation respond to their birth transitions differently than those born much earlier and later. They appear to be influenced by not only the transition from intra- to extrauterine life but also by other factors including health/illness and situational conditions. While these infants are similar in some ways to term infants, they are not mature enough to be discharged from the hospital as soon after birth as term infants typically are discharged. Conversely, these infants also do not have the same needs as much smaller infants born less than 32 weeks gestation who require much more support and a longer NICU course. The OPET group are in the middle. While many may think this group is unimportant, they make up 75% of the 400,000 preterm infants now being born in the U.S. Thus, they are indeed important and the burden is on clinicians to gain more insight into the unique needs of this group so neonatal staff can properly care for OPET infants and insure their best outcomes.

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