Impact Of Single-Family-Room Nicu Design On Infant Neurodevelopment And Breast Milk Provision

Lucille Kohlenberg
Impact of Single-Family Room NICU Design on Infant Neurodevelopment and Breast Milk Provision

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by

Lucille Kohlenberg

MD Candidate Class of 2022
NEONATAL INTENSIVE CARE UNIT DESIGN IMPACTING INFANT OUTCOMES AND BREAST MILK PROVISION.

Lucille Kohlenberg and Angela Montgomery, MD, MSEd.
Section of Neonatal-Perinatal Medicine, Department of Pediatrics, Yale School of Medicine.
New Haven, CT.

Single-family room (SFR) NICUs have gradually replaced open-bay (OB) units over the last three decades. Compared to OB units, SFR units provide increased opportunities for parental rooming and maternal breast milk (MBM) provision; however, they may also present fewer sensory exposures and parental learning opportunities. Due to the presence of potentially beneficial and detrimental effects, it remains uncertain whether the SFR design offers aggregate advantages over the OB model. As such, this study compares the neurodevelopmental outcomes and MBM provision rates in infants cared for in OB and SFR NICUs.

This study is a retrospective chart review that compares outcomes between infants born at ≤ 34 weeks and hospitalized in an OB (n=121) or an SFR (n=105) NICU. Outcome measures were analyzed via the Student’s t-test, linear regression, and logistic regression for binary data.

This analysis found no differences between the OB and SFR cohorts in Bayley-III cognitive, language, or motor composite scores. However, infants in the SFR group scored lower on the fine motor subscale (9.6 vs 8.6; p = <.05) than OB infants and more often scored at least one standard deviation below the mean in two or three composite areas (4.3 vs. 17.9%; p < .05). MBM provision was similar between the OB and SFR groups on day of life 28 but decreased by NICU discharge, markedly so in the SFR group (55.3 vs. 40.0%; p < .05). No differences were noted in growth outcomes during or post-hospitalization. Independent of NICU design, infants with longer NICU lengths of stay had significantly lower developmental cognitive and language scores.

Infants in the SFR NICU had a greater number of neurodevelopmental scores at 12 months of age in concerning ranges and received less MBM by discharge compared to OB infants. Independent of NICU design, MBM provision is associated with higher language scores, and increased NICU length of stay is associated with lower cognitive and language scores, thus suggesting that mediators beyond the NICU environment itself modulate neurodevelopment.
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This research has previously been shared at the Yale School of Medicine Pediatric Research Forum and Pediatric Academic Societies:


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INTRODUCTION

Neonatal Intensive Care Unit History

Hospitals across the globe have implemented neonatal intensive care units (NICUs) to support infant growth and development ex-utero and to enhance long-term neurological outcomes of infants born prematurely or at low birth weight. Since the widespread institutionalization of the NICU during the late 1900s, survival rates of preterm infants have improved; today, 94% of infants born at 28 weeks survive to one year of age.¹⁻³ This marked improvement in survival is indicative of medical advances within the NICU and reflects innovation both in the use of NICUs themselves and in the development of neonatology as an independent subspecialty.

The rise of formal birth documentation heralded the inception of modern neonatology in the late 19th century when cities created public health commissions that documented infant birth and death rates.⁴⁻⁵ For example, recorded infant mortality in New York City peaked in 1870. Historians have attributed this statistic in part to widespread infection rates within the city, poor sanitation measures and unsanitary living conditions, and reduced rates of breastfeeding as women joined the workforce during the industrial period.⁴⁻⁵ At the turn of the 19th century, public knowledge of the rise in infant mortality grew and motivated interest in neonatal health. Simultaneously, the development of the Bureau of the Census via the 1902 Act of Congress facilitated formal record-keeping of infant births and deaths.⁶ By 1919, all states reported birth records. Quickly becoming an important source of perinatal epidemiology, these records increased medical and public awareness of neonatal health and mortality rates.⁴⁻⁶
The mid-20th century saw numerous developments in neonatology. By the 1920s, hospital births comprised over half of total births in the U.S. In response, hospitals incorporated nurseries for infants and pediatricians began practicing neonatal care on a routine basis. In 1948, Lewis Koch published the definition of prematurity as “any infant born alive who weighs 2,500 grams (5 pounds, 8 ounces) or less” in *The Journal of the American Medical Association* (JAMA). The American Academy of Pediatrics and the World Health Organization accepted this classification for use in neonatal care and clinical research. This historic definition spurred the advent of research into the causal role of birth weight in neonatal health outcomes. Further, physicians and researchers began studying the relationship between birth weight and gestational age, which ultimately led to distinctions between infants born prematurely and those small for gestational age. During this time, pediatric hospitals across the nation began incorporating the incubator into routine preterm infant care. This technology enabled thermoregulation and facilitated close observation of infants during their hospital stay, two advancements later integrated into the modern NICU that transformed neonatal medical practice.

The first NICU in the U.S. opened at Yale-New Haven Hospital in 1960, in direct response to increased awareness of high infant mortality rates and the need for specialized care for premature and low birth weight infants and infants with neonatal and congenital medical conditions. The American Board of Pediatrics then established the subspecialty of neonatology in 1975, which preceded the centralization of premature care in regional neonatal units throughout the country. In the decades that followed, community hospitals have also incorporated NICUs into their pediatric hospitals to care for infants with lower acuity prognoses closer to home.
NICU Hospitalization Rates

Since the inception of the NICU, infant mortality rates have declined and medical advances such as artificial surfactant and maternal steroids have contributed to an increased percentage of preterm infants surviving post-birth and to the time of hospital discharge.\textsuperscript{3,4} During the 2000s, survival rates for preterm infants at one year of life has remained stable, at approximately 6\% for those born at 22 weeks and rising with increasing gestational age to 94\% for those born at 28 weeks.\textsuperscript{1,2} Simultaneously, the rate of preterm births has remained constant: currently, preterm infants represent approximately 10\% of all live births in the U.S. Of these births, about 27\% are early preterm births (or less than 34.0 weeks) and 74\% are late preterm births (ranging from 34.0-36.6 weeks).\textsuperscript{9-12} Despite this stability in the preterm birth rate, NICU admission rates for newborns in the U.S. increased by 22.9\% between 2007 and 2012, from 64.0 per 1,000 to 77.9 per 1,000.\textsuperscript{9} This rise is attributed to increased admission of term infants or infants with medical conditions, with newborns less than 2,500 grams continuing to account for a majority of NICU admissions.\textsuperscript{9}

NICU Hospitalization Impacting Neurodevelopment

Together, increased survival rates of preterm infants at earlier gestational ages, rising NICU hospitalization rates, and extended NICU lengths of stay among infants with severe and previously terminal medical conditions have contributed to the surge in NICU utilization for infants across the U.S.\textsuperscript{3} With this rise in NICU hospitalization rates, researchers have emphasized the importance of the physical environment during the developmental process: neurodevelopment is dependent on sensory input, particularly during the third trimester of gestation.\textsuperscript{13} This cumulative increase in time spent hospitalized requires investigation into the environment of the NICU and how this setting alters infant
development. Evaluating the impact of the NICU physical environment on neurodevelopment is the purpose of this thesis.

Neonates, and even more so preterm neonates, are at a critical period in neurological development. Exposed to numerous early life stressors ex-utero, preterm infants are uniquely vulnerable to the sensory aspects of their environments. The long-term outcomes of children previously hospitalized in the NICU demonstrate the importance of the NICU environment on neurodevelopment and how preterm infants are predisposed to poor neurological outcomes. Meta-analysis shows that 60% of NICU graduates born premature have at least one neurodevelopmental deficit, such as cognitive impairment, general developmental delay, or learning disabilities, diagnosed in outpatient follow-up appointments at least six months post-hospital discharge. These neurological deficits in infancy and childhood are in part associated with long-term medical challenges due to prematurity and NICU hospitalization, such as intraventricular hemorrhage, retinopathy of prematurity, chronic lung disease, and hospital-acquired infections. The hospital physical environment must also be considered as a factor that contributes to longitudinal neurodevelopmental outcomes.

One critical component of the hospital’s physical environment that can affect neurodevelopmental outcomes is exposure to light and sound. Literature suggests that exposure to excess light and sound – beyond that typically experienced in the womb – exacerbates neonatal physiologic stress responses, thus influencing neurodevelopment. Specifically, Peng et al. demonstrated that when infants have increased exposure to light in their incubators, they experience parallel increases in heart rate and respiratory rate as well as decreases in blood oxygen saturation. As evidenced by altered vital signs, this
sensory overload leads to physiological stress signals, which may impact infant neurological development over time.\textsuperscript{16}

Interestingly, these stress responses to environmental stimuli occur more commonly in preterm rather than term infants.\textsuperscript{14} Mechanistically, experiences of pain and reductions in maternal care (as occurs when infants are isolated in their incubators) have been shown to promote activation of the hypothalamic-pituitary-adrenal (HPA) axis in neonates. Activation of the HPA axis is associated with pain-induced overstimulation of the brain, leading to neuronal damage by glutamate excitotoxicity.\textsuperscript{18} Preterm infants are particularly vulnerable to over-activation of the HPA axis due to their neuronal immaturity.\textsuperscript{14} High degrees of stressors in the NICU, such as care-handling, bedside procedures, and separation from parental figures, are also associated with infant stress responses, which are indicative of abnormal central nervous system function.\textsuperscript{14} Together, neural immaturity, environmental stressors, and parent-infant separation contribute to a unique neurobehavioral vulnerability for preterm infants in the NICU.\textsuperscript{14}

Infant neurological responses to NICU environmental stressors raise questions into how the NICU environment impacts infant development, and how NICUs can adapt this environment to lessen infant stress responses and to promote optimal neurodevelopment. NICUs have incorporated numerous interventions to lessen the long-term impact of NICU environmental stressors on infant neurodevelopment. Studies show that instituting quiet periods in NICUs by reducing noise, light, infant handling, and in-unit staff activity can decrease infant diastolic blood pressures and mean arterial pressures, as well as the number of infant movements per hour.\textsuperscript{19} These alterations in vitals suggest decreased activation of the HPA axis, with improvements in neuroregulation. Skin-to-skin contact (SSC),
frequently referred to in the literature as Kangaroo care (Edgar Rey Sanabria, 1979), can also counteract consequences from overstimulation of the physiologic stress response by inhibiting reception of stress signals, although this biological response is not well studied.18

Aiming to enhance neurodevelopment, hospitals have also altered the physical design of the NICU to reduce environmental stressors and modulate infant-parent interactions, as described in the following sections.

*NICU Physical Design*

The traditional NICU design is an open-bay (OB) ward. OB units have one or multiple large rooms that house neonates, medical personnel, and equipment. Physicians implemented this unit design – initially referred to as the “large-room concept” – in the first NICUs that opened in the 1960s-70s, including the original Yale New Haven Hospital NICU.3 During this time, physicians also began to assimilate infants of different gestational ages and with varying congenital and medical conditions within the same physical space, something they had previously avoided doing due to concerns about infection, particularly *staphylococcus.*3

Parents became increasingly involved in caring for their hospitalized infants during the 1970s-80s, thus prompting a gradual change in NICU design from large rooms that housed more than one dozen infants to pods containing four to six infants that could better accommodate parental presence. This change ultimately led to the incorporation of single-family room (SFR) units into hospitals beginning in the 1990s. SFR units house single infants, or multiple births, and often include accommodations for parental overnight stay. The emergence of the SFR NICU was also supported by physicians who were eager to
enhance infection prevention within the NICU, as well as by calls for increasing patient and family privacy under HIPAA.  

SFR NICUs have increasingly replaced OB NICUs over the last two decades as concerns regarding stressful environmental stimuli, developmental morbidity, and more limited opportunities for family-centered care in OB units have emerged in the literature.  

However, the NICU environment continues to pose a unique design dilemma as the needs of infants and their families tend to differ from the preferences of medical personnel. Specifically, while families tend to prioritize privacy, physicians and nurses favor accessibility and visibility of infants and staff on the unit. The following sections detail the respective strengths and weaknesses of the OB and SFR environments and how these different environments uniquely impact the experiences of parents, medical staff, and infants themselves, which in turn has lasting impacts on infant neurodevelopment.

Open-Bay Units

The conventional OB unit design promotes close monitoring of neonates, collaboration between physicians and nurses, and interaction between parents. The multi-patient, open-bay wards commonly have between ten to fifty beds or, alternatively, several smaller pods with four to six beds each. Due to the close physical proximity of medical personnel within these units and the ability to monitor multiple infants from one location on the ward, this structure encourages communication between nurses and physicians and enables prompt responses to bedside alarms and emergencies. Furthermore, the physical proximity of neonates in OB units may encourage parents to observe one another and to engage in forms of informal parent-parent learning, particularly from “veteran parents,” or

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* In this text, “parent” refers to any individual who is the primary caretaker or guardian for the infant.
parents who are already familiar with the NICU environment due to prolonged NICU stays or past experiences in the NICU.\(^{23}\) Whether direct or indirect (observational), these learning experiences may influence parents’ future interactions with their infants, such as amount of time they spend at their infants’ bedsides, degree of hands-on interactions they engage in, and amount of breast milk provided or number of attempts at breastfeeding. These interactions also provide much-needed social support for parents, which may in turn impact how they interact with their infants.\(^{23}\) Moreover, for infants whose parents are unable to visit regularly or who are unable to visit for long periods, the OB NICU offers consistent environmental stimuli in the form of ongoing activity from the nursing and medical teams and presence of other infants and parents on the unit that may serve to enrich the overall NICU environment.

Despite these reported benefits of the OB unit, research on short- and long-term infant outcomes following NICU hospitalization has raised concerns about this hospital environment. Potential limitations of the OB unit including sensory stimuli overload, lack of privacy for parents, increased NICU length of stay, and longer interval to enteric feeds compared to the SFR unit.\(^{24}\) Despite sound and light-controlling measures including sound-deadening construction materials, window and incubator coverings, and adjustable lighting, infants are exposed to numerous sensory stimuli at all hours.\(^{22}\) As aforementioned, infants respond to sensory overload with physiological stress signals, which impact current and enduring neurodevelopmental processes.\(^{16}\) These stress responses are associated with increased time spent on ventilation and length of stay in the NICU compared to infants hospitalized in the SFR NICU.\(^{20,13}\)
Further, OB units do not usually accommodate unlimited parent visiting hours and parent rooming or overnight stay, thus limiting daily hours of direct infant-parent interaction.\textsuperscript{25} Parents may not be permitted to remain in the unit when emergency procedures are performed on a neighboring infant. These limitations in parental presence can lessen the degree of social interactions and SSC shared between neonates and their parents, which may impact maternal breast milk production and neurodevelopment by altering sensory, tactile, and emotional experiences.\textsuperscript{26}

\textit{Single-Family Room Units}

Compared to the OB design, SFR units are more controlled, isolate neonates from the daily activity of the NICU, and tailor noise and light levels to each infant.\textsuperscript{27} These environmental changes contribute to several well-documented advantages of the SFR unit: shorter hospitalization stays, parental privacy, increased hands-on time for parents, and reduced rates of infections.\textsuperscript{28} An additional study comparing OB and SFR units has demonstrated that infants in SFR units have fewer apneic events, reduced incidence of sepsis, and earlier time to enteral nutrition.\textsuperscript{29} SFR infants have also shown improved attention, decreased physiological stress levels, reductions in hypertonicity and lethargy, and lower scores on the premature infant pain score compared to their OB counterparts.\textsuperscript{24} Lester et al. additionally demonstrated a reduction in sepsis rates in the SFR unit compared to the OB unit.\textsuperscript{24} Further, SFR NICUs have been associated with increased weight at NICU discharge and greater rate of weight gain during NICU stay.\textsuperscript{24} Researchers have attributed these benefits of the SFR unit to the environment of the unit itself, which is more conducive to parental presence than the OB unit. Indeed, the central advantage of SFR units is their ability to accommodate parental rooming and privacy, which increases opportunities for
infant-parent interaction and SSC. Based on prior report, parents in SFR units are present for a greater amount of time and initiate SSC earlier than parents in OB units. Parent-infant interaction and SSC are well known to enhance infant feeding and maternal breast milk production, which will be expanded on below.

However, the SFR design also has disadvantages compared to OB units: the isolation of families and infants within the single room, reduction in informal parent-parent interactions, increased operational and construction costs for running and building these units, physical impediments to staff supervision of infants, and more limited social support for both parents and staff. Therefore, it remains unclear whether the advantages of the SFR unit outweigh these limitations when considering longitudinal infant outcomes.

Factors Mediating Neurodevelopmental Outcomes

Research has demonstrated that NICU design – particularly exposure to environmental stimuli – is associated with longitudinal neurodevelopmental outcomes. These outcomes are assessed months to years after infants are discharged from the NICU to ascertain long-term impacts of prematurity and time in the hospital environment. Psychologists commonly evaluate infants and toddlers for neurodevelopmental outcomes using the Bayley-III Scales of Infant and Toddler Development, which measure cognitive, language, and motor functioning and enable identification of developmental delays as well as comparison of development across cohorts.

In investigating the impact of NICU design on neurodevelopmental outcomes, numerous factors must be considered that may alter the relationship between environmental elements and neurodevelopment. Displayed in Fig. 1, these mediators include parental presence, maternal breast milk (“MBM”) provision rates, skin-to-skin contact between
infants and their caregivers, staff interaction with infants, family socioeconomic status, and infant neurological and medical conditions. The following sections will describe these mediators in depth.

**Figure 1.** Proposed relationship between the NICU environment and infant neurodevelopmental outcomes measured by Bayley-III Scales cognitive, language, and motor testing at 12 months of age. Potential mediators of neurodevelopmental outcomes within the NICU that may vary by NICU design include MBM provision rates, daily parental and staff presence and interaction with infants, family socioeconomic status, skin-to-skin contact between infants and their caregivers, and infant neurological and medical conditions.

*Maternal Breast Milk Provision and Neurodevelopmental Outcomes*

MBM provision is an important contributor to neurodevelopment and may in part mediate the relationship between NICU design and neurodevelopmental outcomes (Fig. 1). MBM provision can also serve as a proxy for the amount of time mothers spend in the NICU or engage in direct contact with their infants. Further, breast milk is independently associated with reduced rates of infection and with heightened neurodevelopmental outcomes in premature infants, which is attributed to the presence of certain long-chain fatty acids specific to breast milk. Vohr et al. demonstrated that increased consumption of breast
milk is associated with higher developmental scores at 30 months corrected age in former extremely low birth weight infants who were hospitalized in the NICU.\textsuperscript{26} Evaluating the impact of NICU environment on MBM, Grundt et al. demonstrated that the SFR NICU is associated with earlier first expression of breast milk by mothers, earlier first attempt at breastfeeding, and increased amount of direct breastfeeding received over the NICU stay compared to the OB NICU.\textsuperscript{32} However, mothers in both units displayed similar levels of breastfeeding self-efficacy and produced similar volumes of breast milk.\textsuperscript{32} This difference is attributed to the increased presence of mothers in the SFR unit, enabling more frequent SSC and breastfeeding.\textsuperscript{32}

This positive association between maternal involvement in neonatal care and breast milk provision on later infant neurodevelopment also holds when accounting for NICU design. Investigating neurodevelopmental outcomes of OB and SFR NICU graduates at 18-24 months of age, Vohr et al. demonstrated increased cognitive and language development ability in SFR infants compared to OB infants.\textsuperscript{33} Further, in their study, SFR infants were provided with more human milk than their OB counterparts, with human milk provision at 28 days in the NICU predictive of language composite scores.\textsuperscript{33} This suggests that MBM may in part mediate this relationship between NICU environment and composite language scores.

\textit{Parental Involvement and Neurodevelopmental Outcomes}

Influenced by numerous factors, parental presence in the hospital is important to neonatal neurodevelopment because infant stimulation, tactile experiences, and emotional regulation remain dependent on parent interaction, even in the NICU (Fig. 1). While nurses and support staff provide routine medical care, they do not have the resources to soothe
and interact with infants throughout the day as routinely as parents do in home environments. Therefore, parental presence is key for enriching the environment that infants experience.

Head-Zauche et al. established the five factors that account for 65.8% of the variance in parental presence in the unit. First, when parents have two or more other children at home, they are, on average, present in the NICU 60% less than parents with no other children or only one other child at home. Parental presence is also dependent on the presence or absence of neurologic comorbidities in infants: parents visit the NICU more often when their infant has no neurological comorbidity. Additionally, parents are present more often when their infants have not had surgery during their hospitalizations and when their perceived stressfulness of the NICU environment is lower. Lastly, parents in SFR units visit their infants more often than in OB units.

It is important to note when considering the impact of parental presence on infant neurodevelopment that socioeconomic status, family dynamics, and factors related to infant prognosis influence the total number of hours in which caregivers visit (Fig. 1). Families experiencing poverty and families with lower educational attainment more frequently experience barriers to visiting. Further, infants may not be in the care of their biological parents and may have state-assigned guardians, who experience variable visiting regulations. Suggesting that parental presence modulates neurodevelopmental outcomes, Medicaid, as an incomplete proxy for lower socioeconomic status (SES), is associated with decreased cognitive and language scores at 18-months follow-up: infants likely experience decreased sensory input crucial for infant development when caretakers are unable to visit routinely. This data suggests that infants whose families experience lower SES may be at
a developmental disadvantage when housed in SFR units as opposed to OB units, as these infants receive both reduced sensory input from the SFR NICU environment and potentially decreased parental presence.

In reviewing the literature, SFR units are frequently associated with increased daily parental presence, increased parental involvement in infant care, and increased total number of hours engaged in SSC with their offspring.\textsuperscript{35} Increases in parental presence are seen with both mothers and fathers, with fathers spending more time providing on hands-on care for their infants overall compared to OB units.\textsuperscript{36,37} Encouraging fathers to engage in SSC early on results in net gains in SSC for the infant during hospitalization and enhances paternal-infant attachment and family bonding.\textsuperscript{38,39} Tandberg et al. noted that, on average, mothers in the SFR unit initiated SSC four hours after the birth of their infants and engaged in 180 minutes of SSC daily, compared to mothers in the OB unit, who initiated SSC approximately 12 hours after delivering and averaged 120 minutes of SSC daily.\textsuperscript{25} This difference in onset and quantity of SSC is significant in that parental contact is associated with improved neurological outcomes, attributed to modulation of stress-response hormones and formation of secure parent-infant attachments.\textsuperscript{40}

Maternal presence not only impacts the amount of breast milk provided but also influences infants’ lengths of stay in the NICU and contributes to developmental outcomes. Higher levels of maternal involvement are associated with decreased lengths of hospitalization in the SFR NICU.\textsuperscript{35} Further, parents in SFR units report increased participation in medical rounds and higher levels of emotional support from hospital staff than parents in OB units, which may positively enhance their interactions with their infants.\textsuperscript{25} Independent of NICU design, high maternal involvement has been associated
with improved infant neurodevelopmental outcomes, particularly in language and cognition. This suggests that enhancing parental involvement, regardless of preexisting environmental stimuli, can positively alter early infant neural networking.

Despite, or perhaps related to, the increased parental presence and infant-parent interaction in the SFR unit, our understanding of how NICU design impacts parental stress levels remains inconsistent in the literature. Parental stress levels are significant because parents may be more hesitant to engage in caregiving for their infants when they experience high levels of stress, and parents who perceive higher levels of stress visit their infants less often than parents experiencing lower stress. SFR parents have more privacy with their infants compared to OB parents; however, they may experience more stress regarding NICU hospitalization than OB parents because they are more socially isolated on the unit and have fewer opportunities to engage with and learn from other parents. Indeed, Domanico et al. reported increased parental stress in the SFR unit compared to the OB unit. Accounting for levels of social support outside of the hospital, Pineda et al. observed that mothers in the SFR unit again reported more NICU-related stress than mothers in the OB unit despite receiving similar degrees of social support. Conversely, Tandberg et al. noted that both mothers and fathers in SFR units reported lower stress levels than parents in OB NICUs, and Lester et al. found that SFRs were associated with reduced NICU-related parental stress, without differences between the NICU types in parent-infant bonding.

These differing reports suggest that parental stress may be related to time spent exposed to the NICU environment and varying degrees of social support experienced both in and outside of the NICU setting. For example, Kainiemi et al. found that while parental
presence increased in the SFR unit, time spent engaged in SSC did not. In this study, parents rated quality of family-centered care equally high in both units. Further, in a qualitative study of one NICU undergoing transformation from an OB to an SFR unit, parents in the OB unit benefited from observational learning of other parents and the informal forms of social support that parents provided one another. This observational learning, and the informal role modeling parents provided one another, did not occur to the same degree in the new SFR unit. Conversely, parents in the SFR unit mainly spent time in their own infants’ rooms and did not interact frequently with other parents. On the whole, it remains unclear whether the SFR unit design reduces parental stress, and in turn, how this influences parental presence and involvement in infant care.

Staff Involvement and Neurodevelopmental Outcomes

In addition to the impact of NICU environment on parent experience and parent involvement, unit design has also altered the ways in which medical personnel provide care and interact with infants, parents, and one another, which may have resultant impacts on neurodevelopment (Fig. 1). In switching from OB to SFR units, staff have raised concerns about the relative isolation of neonates and the physical distances between them. Additionally, researchers have documented that nurses spend significantly more time during their shifts walking between patient and supply rooms on the unit, which decreases the amount of time they are able to spend at infants’ bedsides. These changes have the potential to impact delivery of care and lessen time that infants spend interacting with staff, increasing their isolation in individual rooms.

Following the conversion of one NICU from an OB to a SFR design, VanHeuvelen observed that nurses incorporated new practices while providing care during this transition
time, though it remains unclear how these adaptations influence infant outcomes. While many of these nursing practices upheld the culture of collaboration that had underscored the OB NICU, some new practices increased reliance on individual, rather than collective, skill. This change in culture resulted from the more-limited ability of nurses to develop close working relationships in SFR units as compared to OB units due to the physical distance between them on the SFR units. With restricted lines of sight between infants’ rooms in SFR units, nurses experienced more difficulty assisting colleagues because they could not easily see when coworkers could benefit from support. Further, nurses in SFR units tended to rely more heavily on their individual skills because they do not have team members physically present at all times, as they would in the OB unit. However, collaboration between SFR unit nurses still occurred at computer stations and in the hallways between infant rooms. Interestingly, Shepley et al. discovered that nurses in the SFR report higher job satisfaction and lower stress levels than nurses in OB units, perhaps due to their abilities to limit negative interactions between themselves and other staff members when needed via physical distancing and to give parents personal space with their infants. In sum, SFR units pose both advantages and disadvantages to infant care from a nursing perspective, and research suggests that the impact of these factors on infant neurodevelopment remains uncertain.

Less studied is the impact of NICU design changes on neonatologists in SFR units, and how the SFR environment influences physician behavior. Physicians may glance into a single-family room to speak with a colleague but not enter the room themselves. Comparatively, in the OB unit, physicians more often observed infants who were not their own patients, thus allowing them to offer suggestions on care that the infants’ primary
teams might not have otherwise considered. Neonatologists in SFR units also frequently conduct team rounds from outside the room, again resulting in potential missed opportunities to observe the infant. This observational data suggests that physicians in the SFR environment may experience fewer opportunities to exam infants and detect changes in clinical course; however, additional research is needed into how this translates into short-term and longitudinal clinical outcomes.

Additional Factors Impacting Neurodevelopment

Apart from prolonged hospitalization, NICU environment, and parental involvement, infant neurodevelopment is influenced by neurologic conditions and medical comorbidities (Fig. 1). Conditions common in premature infants including intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL) injure brain tissue, which predisposes these infants to adverse neurological outcomes. Sensory impairments, such as congenital deafness or blindness, or visual impairment resulting from retinopathy of prematurity (ROP), are also associated with longitudinal neurological impairments. Infants with these conditions have differences in integrating sensory information into developing neural networks. Additionally, infants with cerebral palsy (CP) have a range of impairments in motor functioning seen on developmental evaluation. Prior studies have not shown differences in percentages of IVH, PVL, and ROP, or blindness, deafness, or CP, in comparing infants hospitalized in OB and SFR units. These conditions are more so attributed to events occurring prior to birth or medical interventions such as prolonged ventilation occurring in both units. However, these conditions impact long-term developmental outcomes for these infants, and researchers must account for them when assessing neurodevelopment.
Research Question

Due to these heterogeneous factors impacting the NICU experience, does the SFR design offer more optimal long-term benefits to infant neurodevelopment than the OB NICU?
STATEMENT OF PURPOSE

The Yale New Haven Children’s Hospital (YNHCH) opened its single-family room NICU (“SFR NICU”) in January 2018 and retired the open-bay unit (“OB NICU”) that had housed infants through 2017. We are interested in how this change in physical design impacts the cognitive, language, and motor outcomes of infants at 12 months who were born at \( \leq 34 \) weeks and admitted to the YNHCH NICU.

Hypothesis

We hypothesize that infants hospitalized in the SFR NICU will have superior neurodevelopmental outcomes at 12 months corrected age compared to infants hospitalized in the OB NICU.

Specific Aims

We aim to determine whether there are differences in neurodevelopmental outcomes at 12 months corrected age in infants hospitalized in the OB ward compared to infants hospitalized in the SFR unit. Primary outcome measures include neurodevelopmental testing scores assessed via the Bayley-III Scales of Infant and Toddler Development, 4th Edition: cognitive, language, and motor composite scores and cognition, receptive and expressive communication, and fine and gross motor subscale scores.30

Secondary aims include identifying the impact of NICU environmental design on the following outcomes:

1. Neonatal morbidities including bronchopulmonary dysplasia, sepsis, necrotizing enterocolitis, intraventricular hemorrhage (grades III and IV), retinopathy of prematurity (severe), and periventricular leukomalacia;
2. Total NICU length of stay (days);
3. The cumulative number of days and percentage of total feeds of maternal breast milk (breastfed, expressed, or donor) measured at day 28 in the NICU and at NICU discharge;

4. Growth (assessed by weight, length, and head circumference) at four time points: birth, DOL 28, NICU discharge, and 12 months corrected age;

5. Whether infants at 12 months corrected age received diagnoses of blindness, deafness, or cerebral palsy during the first year of life; and

6. Whether infants at 12 months corrected age received birth-to-three services, physical therapy, or occupational therapy.

Any differences between the two groups in terms of MBM provision rates and growth (length, weight, or head circumference) during birth, NICU hospitalization, and 12-month follow-up will be evaluated for associations with neurodevelopmental scores.

*Proposed Interventions*

Outcomes of this study may result in adapting the physical and social environments of the YNHCH NICU to better support infant neurodevelopment in the current hospital environment. Examples of environmental alteration include incorporating additional sensory elements such as sound, light, or tactile experiences into the neonates’ surroundings and introducing new staff or parent education measures for hands-on care or breast milk provision into the pre-existing NICU framework.
METHODS

Student Contribution

This author coordinated all steps in the research process and in thesis preparation. This author completed the literature review and IRB and performed chart review and data analysis. Research mentor Angela Montgomery supervised the study, performed data analysis, and critically reviewed both this thesis and prior presentations by this author.

Statement on Ethics

The Yale Institutional Review Board approved the study protocol prior to the start of the project, and the IRB protocol was updated as needed with approval granted by the University. This study was retrospective and posed minimal risks to subjects as the intervention occurred prior to the onset of the study, and both OB and SFR NICUs followed all standards of care. Data collection occurred after infants were discharged from the OB or SFR NICUs and followed-up in the Great Results After Discharge (GRAD) Program. Data was collected following all HIPAA protocols. Patient information was stored electronically and secured at all times during this study.

Study Populations

Data from two groups were compared. The open-bay NICU (OB) group includes infants born at YNHH at ≤ 34 weeks between 01/01/17 and 12/31/17, admitted to and discharged from the OB NICU, and evaluated at 12 months corrected age in Yale New Haven Hospital’s GRAD program. The single-family room NICU (SFR) group includes infants born at ≤ 34 weeks between 01/01/18 and 1/31/19, admitted to and discharged from the SFR NICU, and evaluated at 12 months corrected age in the GRAD Program. Of note,
follow-up in the GRAD Program post NICU discharge is standard of care for infants born at ≤ 32 weeks.

*Exclusion Criteria*

Infants excluded from the study included those born at YNHH who received treatment in both the OB and SFR NICUs during the time of transition between units and infants admitted to the YNHCH NICU who were born at an outside hospital. Not included in the neurodevelopmental analysis were infants who did not receive follow-up care in the GRAD program as well as those who did follow-up in the GRAD program but were not assessed at 12 months corrected age using the Bayley-III Scales of Infant and Toddler Development, 4th Ed.

*Retrospective Chart Review*

This was a retrospective study: all infants included in the study received the intervention prior to data collection. Data gathered via chart review in the electronic medical record include:

1. Demographic information: sex, race, gestational age at birth, and insurance type.
2. Growth information: weight (g), length (cm), and head circumference (cm) measured at birth, day of life 28 (DOL28), NICU discharge, and each follow-up appointment during the first year of life.
3. Comorbidities: infants who received diagnoses of bronchopulmonary dysplasia, sepsis, necrotizing enterocolitis, intraventricular hemorrhage (grades III and IV), retinopathy of prematurity (severe), and periventricular leukomalacia based on chart diagnoses.
4. Total NICU length of stay, in days.
5. Cumulative number of days and percentage of feeds of MBM (breastfed, expressed, or donor) measured at day 28 in the NICU and at NICU discharge.

6. Diagnoses of blindness, deafness, or cerebral palsy by 12 months corrected age, gathered from outpatient follow-up documentation.

7. Infants at 12 months corrected age currently receiving any outpatient support services (birth-to-three, physical therapy, or occupational therapy), gathered from outpatient follow-up documentation.

8. Neurodevelopmental testing composite and subscale scores measured during Bayley III Scales of Infant and Toddler Development, 4th Ed. developmental evaluations, performed at 12 months corrected age in the GRAD program, with scores gathered from outpatient follow-up documentation.

Statistical Analyses

Data was processed using Statistical Product and Service Solutions (IBM, Armonk, New York, USA) and Stata SE 15 (StataCorp). Comparisons across the SFR and OB groups were made using the Student’s t-test for continuous variables. Linear and logistic regressions were performed to assess for differences in Bayley composite and subscale scores and to evaluate whether differences in Bayley scores correlate with maternal breast milk provision trends during hospitalization and NICU length of stay, independent of NICU environment. All statistical analyses were conducted with α set at .05, and 2-tailed.
RESULTS

OB and SFR Cohorts

Presented in Figure 2, during the time range in which data was gathered, 121 infants in the OB NICU met study criteria, while 105 infants in the SFR unit met criteria. In the OB group, 23.1% (28/121) of these infants died, and 6.6% (8/121) were transferred out of the NICU. In the SFR group, 14.3% (15/105) of infants died during this time period, and 9.5% (10/105) of infants were transferred. These groups did not differ significantly in deaths occurring in the NICU or in the number of transfers. Omitting infants who died during NICU hospitalization or who were transferred, 85 infants were admitted to and discharged from the OB NICU and 80 infants from the SFR NICU (Fig. 2).

Figure 2. Open-Bay and Single-Family Room Cohorts. Total number of infants born at ≤34 weeks and admitted to and discharged from the OB and SFR units, excluding infants who died during NICU hospitalization or were transferred.
Demographics

There were no differences between the OB and SFR groups in sex, gestational age at birth, and percentage covered by public insurance (Table 1). The SFR NICU had a significantly lower percentage of infants identified as Asian (18.8% vs. 0.0%; p = <.05). The cohorts did not differ in percentages of infants identified as Black, white, and other. The two groups did not differ in total average length of NICU stay, but of note, the SFR group averaged four fewer days in the NICU than the OB group (75.62 days vs. 71.34 days) (Table 1).

Table 1. Infant Demographics in the OB and SFR NICUs.

<table>
<thead>
<tr>
<th></th>
<th>OB NICU n = 85</th>
<th>SFR NICU n = 80</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, Male</td>
<td>52.9%</td>
<td>50.0%</td>
<td>.71</td>
</tr>
<tr>
<td>Race, White</td>
<td>44.7</td>
<td>45.0</td>
<td>.97</td>
</tr>
<tr>
<td>Race, Black</td>
<td>25.9</td>
<td>32.5</td>
<td>.35</td>
</tr>
<tr>
<td>Race, Asian</td>
<td>18.8</td>
<td>0.0</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Race, Other</td>
<td>22.0</td>
<td>22.5</td>
<td>.98</td>
</tr>
<tr>
<td>Public Insurance</td>
<td>47.1</td>
<td>52.5</td>
<td>.70</td>
</tr>
<tr>
<td>Gestational Age at Birth (wks)</td>
<td>28.7</td>
<td>28.6</td>
<td>.76</td>
</tr>
</tbody>
</table>
Neonatal Comorbidities

The OB and SFR infants were assessed for the presence of neonatal comorbidities, including intraventricular hemorrhage (grades III and IV), periventricular leukomalacia, retinopathy of prematurity (severe), bronchopulmonary dysplasia, necrotizing enterocolitis, and sepsis. No differences in the presence of these six comorbidities exist between the two groups (Table 2).

Table 2. Neonatal Comorbidities in the NICU.

<table>
<thead>
<tr>
<th></th>
<th>OB NICU n = 85</th>
<th>SFR NICU n = 80</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraventricular HemorrhageA</td>
<td>2.4%</td>
<td>2.5%</td>
<td>.60</td>
</tr>
<tr>
<td>Periventricular Leukomalacia</td>
<td>0.0</td>
<td>3.8</td>
<td>.07</td>
</tr>
<tr>
<td>Retinopathy of PrematurityB</td>
<td>4.7</td>
<td>8.8</td>
<td>.29</td>
</tr>
<tr>
<td>Bronchopulmonary Dysplasia</td>
<td>35.3</td>
<td>32.5</td>
<td>.71</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1.2</td>
<td>2.5</td>
<td>.53</td>
</tr>
<tr>
<td>Necrotizing Enterocolitis</td>
<td>3.5</td>
<td>10.0</td>
<td>.10</td>
</tr>
</tbody>
</table>

A Intraventricular hemorrhage grades III-IV.
B Retinopathy of prematurity classified as severe.

Follow-Up Rates in the Great Results After Discharge Program

Of the infants admitted to and discharged from the NICU, 82.4% of OB infants and 78.5% of SFR infants followed-up in the NICU GRAD Program (Table 3). There were no differences in the percentages of discharged infants who attended initial (approximately 0-
3 months of age), second (3-6 months of age), and 12-month appointments in the GRAD program. Rates of follow-up declined during the first year of life in both groups prior to the 12-month appointment, with fewer infants in the SFR group attending their third (6-9 months of age) follow-up appointment (43.5% vs 25.3%; p < .05).

**Table 3.** Great Results After Discharge (GRAD) Program Follow-Up Rates.

<table>
<thead>
<tr>
<th></th>
<th>OB NICU</th>
<th>SFR NICU</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n = 85</strong></td>
<td></td>
<td>n = 79B</td>
<td></td>
</tr>
<tr>
<td><strong>Initial</strong></td>
<td>82.4%</td>
<td>78.5%</td>
<td>.54</td>
</tr>
<tr>
<td><strong>Follow-Up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Second</strong></td>
<td>67.1</td>
<td>54.4</td>
<td>.10</td>
</tr>
<tr>
<td><strong>Follow-Up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Third</strong></td>
<td>43.5</td>
<td>25.3</td>
<td>&lt;.05</td>
</tr>
<tr>
<td><strong>Follow-Up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>12-Month</strong></td>
<td>58.8</td>
<td>60.8</td>
<td>.93</td>
</tr>
</tbody>
</table>

A Initial, second, and third refer to follow-up appointments that occurred sequentially. B One death occurred in the SFR group after NICU discharge.

*Medical Conditions at 12 Months*

Of infants who followed-up in the GRAD program at 12 months, no infants in either group received the diagnosis of deafness (Table 4). No differences existed in prevalence of blindness (2.0% OB vs. 4.3% SFR) or cerebral palsy (0.0% OB vs. 2.1% SFR) at 12 months. The groups did not differ in percentage receiving outpatient services (birth-to-three, physical therapy, and/or occupational therapy) at 12 months of age (Table 4).
Table 4. Medical Conditions Diagnosed and Services Received at 12 Months.

<table>
<thead>
<tr>
<th></th>
<th>OB NICU n = 50</th>
<th>SFR NICU n = 47</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral Palsy</td>
<td>0.0%</td>
<td>2.1%</td>
<td>.30</td>
</tr>
<tr>
<td>Deafness</td>
<td>0.0</td>
<td>0.0</td>
<td>--</td>
</tr>
<tr>
<td>Blindness</td>
<td>2.0</td>
<td>4.3</td>
<td>.52</td>
</tr>
<tr>
<td>Outpatient Services</td>
<td>74</td>
<td>77</td>
<td>.77</td>
</tr>
</tbody>
</table>

-- No analysis performed.

Neurodevelopmental Outcomes

The groups did not differ in percentage completing Bayley-III Scales testing, with 55.3% of the OB group completing testing, compared to 47.5% in the SFR group (Table 5). Infants in the SFR group averaged one month older at Bayley-III testing than infants in the OB group (12.1 vs 13.0 months, p = <.05). There were no differences in Bayley-III composite cognitive, language, or motor scores. For the Bayley-III subscale scores, no differences existed between the SFR and OB cohorts in cognition, receptive language, expressive language, and gross motor subscales. However, the SFR group had a lower fine motor subscale score compared to the OB group (9.6 vs. 8.6; p = <.05) (Table 5).

Infants in the OB and SFR groups had similar percentages of infants scoring at least one standard deviation below the mean in cognitive, language, and motor composite scales (Table 6). More infants in the SFR group had scores at least one standard deviation below the mean in two or three developmental areas (4.3 vs. 17.9%; p = <.05). The cohorts did
not differ in the percentage of infants scoring at least one standard deviation below the mean in at least one composite scale (Table 6).

**Table 5.** Bayley-III Neurodevelopmental Scores at 12 Months.

<table>
<thead>
<tr>
<th></th>
<th>OB NICU</th>
<th>SFR NICU</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bayley Completed at 12 Months</td>
<td>47/85 (55.3%)</td>
<td>39/78 (50.0%)</td>
<td>.50</td>
</tr>
<tr>
<td>Age at Bayley (months)</td>
<td>12.1</td>
<td>13.0</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Bayley Composite Cognitive</td>
<td>101.3</td>
<td>101.9</td>
<td>.85</td>
</tr>
<tr>
<td>Bayley Composite Language</td>
<td>95.8</td>
<td>95.7</td>
<td>.97</td>
</tr>
<tr>
<td>Bayley Composite Motor</td>
<td>93.9</td>
<td>91.5</td>
<td>.37</td>
</tr>
<tr>
<td>Cognition Subscale</td>
<td>10.3</td>
<td>10.4</td>
<td>.85</td>
</tr>
<tr>
<td>Receptive Language Subscale</td>
<td>8.9</td>
<td>8.6</td>
<td>.52</td>
</tr>
<tr>
<td>Expressive Language Subscale</td>
<td>9.6</td>
<td>9.9</td>
<td>.68</td>
</tr>
<tr>
<td>Fine Motor Subscale</td>
<td>9.6</td>
<td>8.6</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Gross Motor Subscale</td>
<td>8.4</td>
<td>8.5</td>
<td>.86</td>
</tr>
</tbody>
</table>
Table 6. Bayley-III Neurodevelopmental Scores Concern Areas.

<table>
<thead>
<tr>
<th>Concern Area</th>
<th>OB NICU n = 47</th>
<th>SFR NICU n = 39</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive</td>
<td>4.3%</td>
<td>12.8%</td>
<td>.15</td>
</tr>
<tr>
<td>Language</td>
<td>14.9</td>
<td>17.9</td>
<td>.71</td>
</tr>
<tr>
<td>Motor</td>
<td>12.8</td>
<td>25.6</td>
<td>.13</td>
</tr>
<tr>
<td>Cognitive Composite</td>
<td>27.7</td>
<td>33.3</td>
<td>.57</td>
</tr>
<tr>
<td>≥ 2 Composites</td>
<td>4.3</td>
<td>17.9</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

*Concern indicates scores fall at least one standard deviation below the mean in a given composite.

Maternal Breast Milk Provision

There were no differences in MBM provision at day of life 28 (87.5% OB vs. 86.7% SFR) (Table 7). Infants in the OB NICU tended to receive a higher percentage of feeds of MBM during their stay, although this finding was not statistically significant (68.1% OB vs. 59.9% SFR) (Fig. 3). By discharge, rates of MBM provision had decreased significantly in the SFR group compared to the OB group (55.3% vs 40.0%; p <.05) (Fig. 4).
Table 7. Maternal Breast Milk Provision.

<table>
<thead>
<tr>
<th></th>
<th>OB NICU</th>
<th>SFR NICU</th>
<th><em>P</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MBM DOL 28</strong></td>
<td>70/80 (87.5%)</td>
<td>65/75 (86.7%)</td>
<td>.88</td>
</tr>
<tr>
<td><strong>MBM Discharge Date</strong></td>
<td>47/85 (55.3%)</td>
<td>32/80 (40.0%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td><strong>Percent of Days Receiving MBM</strong></td>
<td>68.1%</td>
<td>59.9%</td>
<td>.14</td>
</tr>
</tbody>
</table>

Figure 3. Percentage of Total Feeds as Maternal Breast Milk During the NICU Course. The x-axis represents NICU design and the y-axis represents the percentage of feeds during NICU hospitalization that included maternal breast milk (breastfed, expressed, or donor, with or without formula supplementation). OB is in dark gray, and SFR in light gray. Bars display 95% confidence intervals.
Figure 4. Maternal Breast Milk Provision at Day of Life 28 and at NICU Discharge. The x-axis represents time: day of life 28 and NICU discharge. The y-axis indicates the percentage of infants receiving maternal breast milk (breastfed, expressed, or donor, with or without formula supplementation). OB is depicted in dark gray, and SFR in light gray. Bars represent 95% confidence intervals.

Growth Trends

Both birth and discharge weights, lengths, and head circumferences did not differ between OB and SFR cohorts (Table 8). Changes in weight, length, and head circumference z-scores over the NICU stay did not differ between OB and SFR groups. At
12-month follow-up appointments, weights, lengths, and head circumferences did not differ significantly between OB and SFR groups (Table 8).

Table 8. Growth Outcomes.

<table>
<thead>
<tr>
<th></th>
<th>OB NICU</th>
<th>SFR NICU</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Birth Weight (z-score)</strong></td>
<td>-0.28</td>
<td>-0.32</td>
<td>.57</td>
</tr>
<tr>
<td><strong>Birth Length (z-score)</strong></td>
<td>-0.35</td>
<td>-0.21</td>
<td>.73</td>
</tr>
<tr>
<td><strong>Birth Head Circumference (HC)</strong> (z-score)</td>
<td>-0.34</td>
<td>-0.36</td>
<td>.86</td>
</tr>
<tr>
<td><strong>Weight on DOL 28 (z-score)</strong></td>
<td>-1.10</td>
<td>-1.16</td>
<td>.61</td>
</tr>
<tr>
<td><strong>Weight at Discharge (z-score)</strong></td>
<td>-1.27</td>
<td>-1.30</td>
<td>.84</td>
</tr>
<tr>
<td><strong>Length at Discharge (z-score)</strong></td>
<td>-1.40</td>
<td>-1.26</td>
<td>.45</td>
</tr>
<tr>
<td><strong>HC at Discharge (z-score)</strong></td>
<td>-.97</td>
<td>-.73</td>
<td>.10</td>
</tr>
<tr>
<td><strong>Weight Gain (g/day)</strong></td>
<td>22.78</td>
<td>22.43</td>
<td>.54</td>
</tr>
<tr>
<td>Change* in Weight (z-score)</td>
<td>-1.00</td>
<td>-.99</td>
<td>.92</td>
</tr>
<tr>
<td>Change* in Length (z-score)</td>
<td>-1.06</td>
<td>-1.05</td>
<td>.97</td>
</tr>
<tr>
<td>Change* in HC (z-score)</td>
<td>-.63</td>
<td>-.36</td>
<td>.07</td>
</tr>
<tr>
<td><strong>Discharge Weight z-score &lt; 2 SDs below mean</strong></td>
<td>18/85 (21.2)</td>
<td>18/80 (22.5)</td>
<td>.84</td>
</tr>
<tr>
<td><strong>Discharge HC z-score &lt; 2 SDs below mean</strong></td>
<td>13/85 (15.9)</td>
<td>10/80 (12.5)</td>
<td>.61</td>
</tr>
</tbody>
</table>
Discharge Length z-score < 2 SDs below mean | 26/85 (30.6) | 16/80 (20.0) | .12
---|---|---|---
Weight at GRAD 12 Months (g) | 7723 | 7451 | .66
Length at GRAD 12 Months (cm) | 73.4 | 74.2 | .20
HC at GRAD 12 Months (cm) | 45.7 | 45.8 | .75

*Change represents the NICU discharge measurement minus the birth measurement.

**Neurodevelopmental Outcomes and NICU Length of Stay**

Independent of NICU design, infants with longer lengths of stay in the hospital had significantly lower developmental composite scores in cognition (p = <.05) and language (p <.05) (Table 9). This correlation was not present with infants who scored at least one standard deviation below the mean in either one, or in more than one, composite area. Infants with longer lengths of stay also had significantly correlated lower subscale scores in cognition (p <.05), expressive language (p <.05), and fine motor (p <.05) subscales (Table 9).

**Table 9. Neurodevelopmental Outcomes and NICU Length of Stay.**

<table>
<thead>
<tr>
<th></th>
<th>Coefficient</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive Composite</td>
<td>-.128</td>
<td>[-.206, -.049]</td>
</tr>
<tr>
<td>Language Composite</td>
<td>-.084</td>
<td>[-.147, -.021]</td>
</tr>
<tr>
<td>Motor Composite</td>
<td>-.045</td>
<td>[-.110, .021]</td>
</tr>
<tr>
<td>Cognitive Concern*</td>
<td>.000</td>
<td>[-.001, .002]</td>
</tr>
<tr>
<td>Concern</td>
<td>p-value</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>------------------------------</td>
<td>---------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Language Concern*</td>
<td>.000</td>
<td>[-.002, .002]</td>
</tr>
<tr>
<td>Motor Concern*</td>
<td>.001</td>
<td>[-.001, .003]</td>
</tr>
<tr>
<td>1 Concern*</td>
<td>.001</td>
<td>[-.001, .004]</td>
</tr>
<tr>
<td>≥ 2 Concerns*</td>
<td>.001</td>
<td>[-.001, .002]</td>
</tr>
<tr>
<td>Cognition Subscale</td>
<td>-.026</td>
<td>[-.041, -.010]</td>
</tr>
<tr>
<td>Receptive Language</td>
<td>-.008</td>
<td>[-.020, .003]</td>
</tr>
<tr>
<td>Expressive Language</td>
<td>-.021</td>
<td>[-.034, -.007]</td>
</tr>
<tr>
<td>Fine Motor</td>
<td>-.008</td>
<td>[-.016, -.0001]</td>
</tr>
<tr>
<td>Gross Motor</td>
<td>-.006</td>
<td>[-.024, .011]</td>
</tr>
</tbody>
</table>

*Concern indicates scores fall at least one standard deviation below the mean in a given composite.

**Neurodevelopmental Outcomes and Maternal Breast Milk Provision**

Percent total feeds of MBM were associated positively with Bayley-III composite language scores, independent of NICU design (p < .05) (Figure 5). Although neither the association between sex and Bayley-III composite language scores nor the interaction between MBM and infant sex was significant, there is a trend toward higher Bayley-III composite language scores in male infants receiving greater percentages of MBM. This trend is not seen with female infants, who tend to score more consistently on Bayley-III language testing across varying percentages of MBM received (Figure 5). For all other Bayley composite and subscale areas, neurodevelopmental outcomes were not associated
with percent total feeds of MBM, and percent total feeds of MBM did not differ with infant sex or NICU length of stay.

**Figure 5.** Language Composite Scores and Maternal Breast Milk Provision. The x-axis represents percentage of total days of maternal breast milk received, and the y-axis represents Bayley-III Scales composite language scores, with values differentiated by sex. Female infants are in light gray, and male infants are in dark gray. Lines of best fit are represented in corresponding colors.
DISCUSSION

Differing from our proposed hypothesis and prior reports in the literature, these results suggest that infants hospitalized in the SFR unit perform similarly to their OB counterparts on cognitive, language, and motor composite scales of neurodevelopmental testing. While SFR infants perform lower than their OB peers on the fine motor subscale during neurodevelopmental testing at 12 months, they do not differ on performance in the cognition, expressive language, receptive language, and gross motor subscales at the same timepoint. Further, SFR infants do not fall at least one standard deviation below the mean in any one composite area more frequently than OB infants. However, SFR infants more often score at least one standard deviation below the mean in two or three composite scales.

Medical practices did not differ between the OB and SFR NICUs, thus indicating that these reported neurodevelopmental scoring differences do not result from variations in medical care between the two units, but rather from factors within these two units and the environment of the units themselves. Recent reports in the literature attribute the stated SFR infants’ higher cognitive and language scores to elements unique to the SFR NICU environment, primarily the ability for parents to room in the NICU and engage in greater amounts of SSC and MBM provision than parents in the OB NICU. In this study, SFR infants’ lower scores in the fine motor subscale may reflect reduced provision of MBM in the SFR unit by discharge, as we observed that SFR infants are less likely than OB infants to receive MBM by NICU discharge. However, this difference in fine motor scoring likely has minimal clinical significance: despite scoring significantly lower than the OB infants, the SFR infants scored on average within one standard deviation below the mean, which on its own is not indicative of developmental delay. The increased frequency of SFR infants
scoring at least one standard deviation below the mean on two or three composite areas – cognitive, language, and motor – suggests that in this study SFR infants presented more often with aggregate concerns in development than OB infants. However, it is also possible that due to the small sample size of the SFR group, this data represents a subset of infants who were more neurodevelopmentally delayed than their OB counterparts, perhaps due to other comorbid medical conditions occurring during or post-NICU discharge that were not measured in this study.

Despite these scoring differences, infants in the OB and SFR units did not differ in NICU comorbidities during hospitalization, in neurological outcomes including cerebral palsy, deafness, and blindness diagnosed by 12 months of age, or in percentages receiving early intervention services. As these comorbidities and neurological outcomes occurred in similar frequencies in both units, this suggests that neither these comorbid health conditions during infancy nor the neurological impairments listed above impacted neurodevelopmental data when compared between the two groups. Additionally, many infants were identified as developmentally delayed and received intervention services prior to Bayley testing at 12 months, but infants in both groups received similar percentages of early invention services. Therefore, it is unlikely that these additional services influenced comparisons of Bayley scores between the OB and SFR cohorts.

Demonstrated here, MBM provision rates differed between the two units by NICU discharge. As previously reported in the literature, NICU environment and MBM provision across the NICU stay are interrelated, with MBM provision or rates of direct breastfeeding associated with the degree to which parents are present in the NICU and engage in SSC and hands-on care.\textsuperscript{26,31,33} In the analysis presented here, MBM provision rates were
comparable within the first month of NICU hospitalization and rates in both units declined between DOL 28 and NICU discharge, with this decline occurring more rapidly in the SFR unit. Differences in MBM provision rates after DOL28 may be attributed to variables not investigated here, such as variations in the quantity of lactational support provided to parents between the two units. Additionally, parents in the SFR unit may have experienced more limited informal parent-parent interaction due to structural barriers to gathering and conversation, including isolation within a single room and limited open areas for congregation on the unit. Previous research shows that this informal parent-parent interaction plays a role in exposing parents to breastfeeding and encouraging mothers to begin breastfeeding or to seek more information on providing MBM to their infants. While the literature has suggested that maternal involvement in the NICU, represented by the total number of days mothers engage in SSC or hands-on care, is higher in the SFR NICU than in the OB NICU, we were unable to gather this data in the YNHH NICU because it was not documented during NICU hospitalization.

Independent of NICU design, we observed that MBM is associated positively with Bayley-III composite language scores, without a statistically significant interaction between MBM and infant sex on this composite language score. However, there is a trend toward higher Bayley-III composite language scores in male infants who received increased percentages of MBM across their NICU stays. This suggests that MBM may impact long-term neurodevelopmental outcomes, particularly for males. Reports in the literature investigating differential impacts of MBM on neurodevelopment by sex are limited. Mansson et al. reported that extreme prematurity impacts male infants more so than female infants, with females consistently scoring higher on Bayley-III measures.
However, receiving MBM during the NICU stay enhances neurodevelopment of both males and females. Comparing neurodevelopmental outcomes at 20 months corrected age in a cohort of former preterm infants who received MBM during their NICU stay, Macedo et al. demonstrated that male sex is an independent risk factor for lower neurodevelopmental outcomes. Physiologic mechanisms underlying this male vulnerability have not been fully explored, but are proposed to relate to differential stress responses in the prenatal and early infancy periods. This finding presents numerous opportunities for future investigation and intervention.

Consistent with prior literature, the growth data in this study imply that the NICU environment does not directly impact infant growth parameters during hospitalization or across the first year of life. While a few prior studies reported higher infant weight at DOL 28 and by NICU discharge in the SFR unit and attributed this to differences in the original size of the infants studied, other reports have demonstrated no differences in growth outcomes between OB and SFR NICUs. Lack of differences in weight, length, and head circumference have previously been reported as independent of MBM provision.

Interestingly, while NICU length of stay did not differ significantly between the OB and SFR cohorts, infants in the SFR group were discharged on average four days earlier than infants in the OB group. Similar data has been reported in the literature, with no statistically significant differences in lengths of stay between the unit types. However, this finding is clinically significant, as reductions in NICU lengths of stay are associated with reduced operational cost, lower rates of hospital-acquired infections, and higher admission rates for the unit overall, thus enabling care for additional infants. Further, independent of NICU environment, we found that increased NICU length of stay is
correlated with lower scores on cognitive and language composite testing and the cognition, expressive language, and fine motor subscales. It is likely that infants requiring extended NICU stays have additional medical needs or comorbidities that impact their long-term neurodevelopment independent of environment-dependent mediators within the NICU.

**Impacting NICU Care**

The outcomes demonstrated in this study have the potential to impact delivery of care in the current SFR NICU. For example, MBM provision may be enhanced by including greater support for breastfeeding in the NICU: units can incorporate routine lactation consultant visits for parents or additional support from nurses and providers. Additionally, providing opportunities for parents to engage with one another informally in the NICU may also enhance parental support, encourage breastfeeding or MBM provision, and reduce parental stress in the unit. In turn, these benefits may strengthen neurodevelopmental outcomes, particularly for male infants receiving MBM. Further, incorporating family-centered rounds in the NICU will provide parents the opportunity to engage in daily care and to share their concerns with the medical team. Lastly, documenting the amount of time that parents and staff spend in direct infant interaction and SSC would enable tracking of whether certain infants receive less hands-on interaction and sensory stimuli. Incorporating more social and sensory elements for infants, such as engagement with child life staff, occupational therapists, or NICU volunteers, may augment the levels of stimuli these infants need for optimal neurodevelopment.
Limitations

This data is limited in part by the small sample size of infants following-up in the GRAD Program, which reduced the number of infants ultimately completing the Bayley-III assessment. Although rates of follow-up did not differ between the OB and SFR groups during the initial, second, and 12-month GRAD Program appointments, infants who did follow-up and ultimately complete Bayley-III testing may have done so for numerous reasons. Parents may have been seeking additional support or reassurance for infants with developmental delays or with certain medical conditions, and thus their infants may represent a particular subset in the study. Conversely, parents of infants with more complex medical needs may be less likely to bring their infants to follow-up GRAD program appointments due to the time-consuming nature of coordinating and attending numerous medical appointments across different specialties.

With the small number of infants completing Bayley-III testing, it is likely our analysis is underpowered to detect small differences in developmental outcomes and how these outcomes associate with MBM provision. While only fine motor subscale outcomes differed between the OB and SFR groups, it is likely more differences may exist between the two cohorts in terms of long-term neurodevelopmental findings. Additionally, the trend toward higher composite language scores in male infants who receive additional MBM provision over their peers may represent a clinically relevant finding but may be underpowered in this study, as the literature has reported a particular male vulnerability toward decreased neurodevelopment outcomes during the early natal phase.

As additional limitations of this study, we were unable to quantify both the degree of lactation support offered to mothers and the social supports provided to parents in the
OB and SFR NICUS. Thus, we are unsure if mothers with infants in these cohorts utilized lactation support services similarly. Since we were unable to assess the degree of social interaction between parents on the unit and between parents and staff (nursing, physicians, respiratory therapists, etc.), we cannot determine how these interactions influence parental presence at the bedside, via SSC, hands-on care, or MBM provision.

Lastly, we did not gather data on environmental stimuli, such as exposure to sound or light, in the OB or SFR units. As such, it is difficult to assess whether infants in these units differed in exposure to these environmental elements and how these stimuli may have impacted their neurological development.

COVID Challenges

In addition to neurodevelopmental, growth, and MBM provision at 12 months, data was also collected on neurodevelopment and growth outcomes for both the OB and SFR infants at 24- and 36-months follow-up appointments in the GRAD Program during 2020-2021. Due to the COVID-19 pandemic, follow-up rates for toddlers at 24 and 36 months were lower than at 12 months because developmental and clinical appointments were canceled or rescheduled. Additionally, many of these follow-up visits were conducted via telemedicine. While some toddlers were evaluated virtually using the Ages and Stages Questionnaire, most were not able to be assessed in-person using the Bayley Scales. Aggregated data on toddlers with developmental concerns in either the in-person Bayley testing or the virtual Ages and Stages Questionnaire was too low-powered to assess the impact of NICU environment on neurodevelopment and growth outcomes at 24- and 36-months.
Future Directions

Our results call into question whether male infants in the NICU are particularly vulnerable to environmental stressors and how MBM provision and parent interaction modulate these stress responses to impact infant neurodevelopment over time. Future directions for research include further investigating the components of the NICU environment that impact MBM provision, assessing parent and staff interactions with infants in the NICU, and measuring exposure levels to environmental stimuli experienced by infants. Quantifying the degree of support (e.g. number of sessions) parents had with lactation consultants or nurses would provide more insight into breast milk provision.

Additional study into the amount of time infants spend with parents and staff in the NICU would enable a more thorough assessment into how interaction with caregivers impacts neurodevelopment, and whether this interaction changes when comparing OB and SFR units. Future studies focusing on developmental and family-centered care in the SFR NICU are warranted to lessen isolation of neonates within single rooms and to encourage parental participation in care. Lastly, quality-improvement initiatives focused on enhancing GRAD program follow-up rates would ideally improve the monitoring of infants over time, increase opportunities for early intervention, and increase the number of infants evaluated with the Bayley Scales.
CONCLUSION

Enhancing neurodevelopmental outcomes for early preterm infants graduated from the NICU remains challenging. Our results suggest that the SFR NICU, intended in part to reduce neurodevelopmental morbidities, may not enhance neurodevelopmental outcomes without broad consideration of the mediators within the NICU that impact neonatal outcomes: exposure to environmental stimuli, quantity and quality of parents’ interactions with neonates, and parental access to lactation assistance and social supports. Based on the data reported above, more investigation of these mediators is needed to assess how the SFR NICU environment interacts with mediators in the NICU to impact infant neurodevelopment. Ideally, the NICU environment can be optimized further to promote neurodevelopment and maximize neonatal outcomes.
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