The environment of the neonatal intensive care unit (NICU) is commonly one of noise, light, and bustling activity as healthcare professionals conduct the caregiving tasks necessary to maintain the health of ill or premature infants. Paradoxically, this is also the environment in which these vulnerable infants must grow, develop, and even sometimes struggle to survive. Although NICU environments are changing with the implementation of neuroprotective, developmentally supportive care strategies (eg, dim lighting, comforting positioning, and single patient rooms), they cannot begin to mirror the intrauterine environment in which the premature infant was evolutionarily expected to develop before birth. Rather than the natural maternal environment meant to nurture an infant, the environment becomes one that may present multiple physical, psychosocial, and emotional challenges as an iatrogenic effect of the life-saving care these infants desperately need.

This concept article draws from the existing literature on pediatric medical trauma to develop a conceptual framework for understanding what we term Infant Medical Trauma in the Neonatal Intensive Care Unit (IMTN). It is our belief that use of this concept will facilitate an interdisciplinary (eg, nursing, medicine, psychology, social work) approach for studying the infant experience in the NICU, developmental consequences, and strategies for improved care. This article is organized into 5 sections: First, use of the term “trauma” to describe this experience. Second, a descriptive overview of the NICU with a focus on potential stressors. Third, the conceptual model of IMTN is examined, which comprises several factors identified in the literature as influential to infant health trajectories. Fourth, is a review of neurodevelopmental risks of preterm infants. Finally, implications for practice and health policy are considered.

ABSTRACT
Background: Trauma is an innately subjective experience ensuing from a deeply distressing event. Research has demonstrated that while the environment of the neonatal intensive care unit (NICU) is capable of providing extraordinary lifesaving measures following birth, the experience may be disruptive to several key aspects of early development, placing infants at risk for adverse behavioral, cognitive, and emotional outcomes.

Purpose: This article provides rationale for the concept of Infant Medical Trauma in the NICU (IMTN) as a means of describing this unique stress experience. A triad of cumulative early life NICU experiences (stress, parental separation, and pain) is proposed to influence an infant’s swinging neurodevelopmental pendulum amid the potential outcomes of risk and resilience.

Implications for Practice and Research: Creating language that describes the infant experience brings meaning and calls caregivers and parents to action to consider strategies that may improve long-term health. Actively seeking opportunities to decrease the allostatic load of at-risk infants may support an infant’s pendulum to swing toward a path of resilience, thereby moderating his or her early life adverse experience.

Key Words: brain, infants, medical trauma, neonatal intensive care, neurodevelopment, NICU, pain, parent-infant separation, preterm infants, resilience, stress

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Traditionally, the term “trauma” has been related to a physical wound. An understanding of
psychological trauma evolved in the 19th century and presently trauma symptoms refer to intrusive reexperiencing, avoidance behavior, alterations in cognition and mood, and hyperarousal. For years, researchers have described the traumatic experiences and the symptoms of prematurity and infant separation incurred during a NICU admission, however, primarily from the parents’ experience. Research has largely overlooked understanding these experiences from the infants’ perspective. Infants cannot present with commonly recognized symptoms because they do not yet possess the behavioral or verbal repertoire to describe their experience. Infants are, however, able to experience hyperarousal noted as cortisol surges, tachycardia, and agitation. These bodily “score-keeping phenomena” are reflected in studies reporting that male infants who were circumcised without analgesia have more crying compared with 4-month immunizations and heel hyperesthesia noted by parents of former preterm infants. Despite the obvious barrier to studying the infants’ perspective, their preverbal stage of development, this should not restrict attempts to understand the experience through alternative methodologies.

To date, there is no single term to adequately describe the infant’s combined physical, environmental, and relational stresses associated with a NICU hospitalization. Terminology for the infant experience, such as extreme stress, early life stress, toxic stress, developmental stress, or developmental adversity, may be less provocative; however, each of these terms does not seem to fully capture the intensity of the infant experience. The authors of this article acknowledge the potential for controversy in labeling an infant experience in the NICU as a trauma.

This controversy may be particularly apparent for experts within the psychology and psychiatry disciplines, as their use of the term “trauma” is bound to specific diagnostic criteria that may lead to traumatic stress or posttraumatic stress disorder (PTSD). Accordingly, in this article, the term “trauma” is not intended to serve a diagnostic role; rather, it is meant to convey the perceived gestalt of the infant experience. For caregivers in the NICU, professionals who intend to help infants, the term may feel uncomfortable. However, maintaining a lens focused solely on the vulnerable newborn infant (a perspective that is imperative in this discussion), there are 2 focal points to consider: (1) the experiences that occur in the NICU to an infant are not “normal” or nurturing experiences; and (2) the potential for this trauma would not exist without the need for NICU care. As deleterious health outcomes persist and science develops, allowing for new and dynamic understandings of health and illness risks, there are important factors to consider when ensuring optimal care is provided to this vulnerable population.

EFFECTS OF EARLY LIFE EXPERIENCE IN THE NICU

Early life experiences are considered the developmental underpinning of physical, psychological, and emotional health across the life span. Nearly 500,000 infants are born prematurely each year in the United States, and approximately 10% of all newborns require neonatal intensive care. The evidence linking extended hospitalization and adverse behavioral, cognitive, and emotional health outcomes later in life is extensive. Although not all infants who require care in the NICU subsequently develop lifelong impairments, numerous associations have been identified between preterm birth and poorer long-term outcomes.

The typical infant admitted to the NICU is prematurely born, compromised with a congenital anomaly, incurred a birth-related complication, or has developed an illness shortly after birth. Children born prematurely face an increased risk of developing problematic social interactions, attentional deficiencies, learning impairments, and mental health issues. Historically, these adverse outcomes were attributed to the early developmental stage at birth or other factors related directly to gestational age. However, recent studies suggest that the “NICU experience,” with its chronic interwoven experiences of stress, parental separation, and pain influences, may serve as a separate factor impacting the neurodevelopmental trajectories of highly vulnerable infants.

Evidence of early childhood adversity and stress exposure has been correlated with a variety of illnesses later in life. On the basis of this evidence, some of the strongest adverse early life events in the NICU include stress, parental separation, and pain. By examining the impact of each variable individually, the full scope of collective impact experienced by many infants may be better understood. The model (Figure 1) provides a framework for conceptualizing the potential developmental burden imposed by routine care in the NICU. Providing a framework and label to adverse neonatal intensive care experiences creates a common language for healthcare staff and families and an opportunity to identify interventions to minimize the negative impact of NICU practices. This context also provides researchers with a common point of reference for future studies of this phenomenon.

THE CONCEPTUAL MODEL OF INFANT MEDICAL TRAUMA IN THE NICU (IMTN)

Infants of all gestational ages who require NICU care are potentially vulnerable to a traumatic experience; however, the greatest vulnerability has been
correlated to the degree of prematurity or illness at birth because of the duration of medical care and frequency of interventions.\textsuperscript{18,19} Bearing in mind that the meaning and pervasiveness of an experience are individually and contextually driven, some infants may be more susceptible to perceiving these experiences as traumatic than others. Simply stated, not all infants who are admitted to the NICU have the same experiences or responses to those experiences and, even when circumstances are similar, individuals may have different outcomes.

While there are a number of factors critically important to infant development, some are beyond the control of NICU clinicians. Such factors include infant maturity or immaturity at birth, state of health or illness that necessitates NICU care, as well as various prenatal factors. The foci of the IMTN conceptual model are those factors where NICU clinicians exert some control, such as the modification of pain and stress experiences and minimizing parental separation, which may lead to enhanced neuroprotective practices. See Box 1 for underlying assumptions for IMTN.

The proposed operational definition for IMTN is as follows:

**Infant Medical Trauma in the NICU** describes the intertwined and cumulative early life experiences of stress, parental separation, and pain. This term encompasses the potential for alterations in short- and long-term neurodevelopmental and physiological responses.

Figure 1 represents the conceptual model, Infant Medical Trauma in the NICU. The model illustrates the relationships and context for the internal and external factors that may lead to an infant’s suboptimal neurodevelopment during NICU care. Considering an infant’s burden of stress manifests itself within an allostatic load (body’s ability to adapt to stress), exposure to early life stressors in the NICU may place an infant on a risk or resilience trajectory. Although prenatal factors may be an influential stressor, that discussion is beyond the scope of this article.

In the IMTN model, the infant brain represents the fixed midpoint of the pendulum. This is not to suggest the infant brain is “fixed” at birth. Rather, the brain represents the dynamic and central locus of susceptibility to influencing factors while undergoing rapid changes and development. As the accumulation and intensity of the NICU experience increases so too does the force, or inertia, of the pendulum swing. As with any object in motion, during the course of the early life experience in the NICU, the pendulum will continue to swing unless there is intentional force exerted to slow or stop the pendulum. Allowing for uncontrolled swing may force the pendulum into the high-stress risk zone, potentially leading to lifelong negative consequences of cognitive, emotional, and mental health. Purposeful actions by caregivers and parents may support the

**BOX 1. Assumptions of IMTN Concept**

The context for the term “IMTN,” underlying assumptions:

1. Following birth, the infant’s health status is compromised and requires an enhanced level of medical care, including transfer to an NICU.
2. With admission to the NICU, the primary care of the infant is, for the most part, removed from his or her parents and transferred to NICU caregivers.
3. The NICU experience differs from a routine hospital stay for a healthy, full-term birth where the infant would often be cared for at his or her parent’s side.
4. In contrast to the care of a healthy newborn and as a result of NICU care, the infant experiences increased stress, parental separation, and pain.
5. The collective NICU experiences of stress, parental separation, and pain may contribute negatively to the infant’s allostatic load, increasing vulnerability and risks for poorer outcomes.

Abbreviations: IMTN, Infant Medical Trauma in the NICU; NICU, neonatal intensive care unit.
pendulum to swing into the zone of resilience and away from the risk zone. Thus, when care is deliberate and provided within the infant’s individual developmental trajectory, risk is redirected to support normative development. The variables included in the model are discussed in the following text: stress and allostatics; parental separation; pain; and genetic variation.

Stress and Allostasis
Stress is considered an overarching and bidirectional factor, implicated in both pain and separation. A stressor is conceptually defined here as any actual or potential encounter recognized by the brain as a threat to an individual’s environment, including physiological, psychological, or emotional demands. The developing brain is strongly influenced by stress. Acute stress response encourages behavioral adaptation to a challenge and mobilizes metabolic resources to make adaptation possible, whereas chronic stress even at low to moderate levels has been shown to negatively affect brain structure. While some degree of acute stress can have beneficial effects for growth and development, the intensity and chronicity of stress can overburden an individual, leading to detrimental effects. The deleterious effects of chronic stress have been preferentially attributed to prolonged exposure to glucocorticoids and/or cortisol.

Allostasis is a physiological compensatory mechanism that specifically targets the management of stress, allowing for great variability when promoting adaptability. Allostatic load negatively affects subsequent adaptations to environmental demands (ie, allostasis) and compromises the body’s ability to maintain homeostasis. While survival is allowed, there is the potential for decreased life expectancy and quality of life. The balancing point for an individual to adapt to stress, or not, largely depends upon a number of factors including stress chronicity, intensity, and the nature of the stressor stimulus. Smith et al determined that infants exposed to NICU stress had a decrease in brain size and altered microstructure and functional connectivity at term gestational age. These outcomes demonstrate an important relationship between early birth and institutional medical care, but further work is needed to identify whether the relationship is the result of NICU experience per se or is more related to the developmental immaturity and disease state associated with preterm birth. In summary, infants’ stress experiences and the augmented responses of their body to subsequent environmental challenges may affect the direction their neurodevelopmental pendulum swings toward either risk or resilience.

Parental Separation
A significant component of early life experience is the connectedness to attachment figures, foundationally important for healthy future relationships. Immediately following birth, an infant’s physical and emotional connection with his or her parent continues to facilitate the attachment process, which often begins to develop before birth. The physical and emotional availability, proximity, of the parent and the infant, is necessary for this process to continue to develop appropriately. Unfortunately, premature birth interrupts the normal early life experience of infants and parents, potentially leading to maladaptive attachment. During this formative time, infants admitted to the NICU are almost continuously cared for by virtual strangers, individuals who initially have no personal bond or connection with either the baby or the family, with parents providing only intermittent direct care.

In animal models, maternal separation is defined as brief (15 minutes), prolonged (3 hours), or, in some cases, as deprivation (≥24 hours). To parallel this language, the duration of time that extremely premature infants spend in the primary care of the NICU healthcare team must at least be considered prolonged but arguably is more in line with a parent deprivation model. Many scientists have studied maternal–infant separation and reported detrimental effects of prolonged separation on cognitive and emotional development. In humans, research on the long-term effects of early deprivation from infant–caregiver attachment for children in orphanages demonstrated that early interventions aimed at facilitating high-quality caregiving lessened the psychopathology and functional impairments in children. While some may dispute the comparison of NICU care with institutionalized care, many parallels exist between the quality of caregiving environments (eg, multiple caregivers, rotating shifts of caregivers, ratio of child-to-caregiver, and limited individualized care).

Pain
Pain is conceptually defined here as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. A hypersensitivity to pain develops for immature infants repeatedly exposed to painful episodes due to their hyperinnervation pattern for nociceptive neurons in the skin and the heightened excitability of the central nervous system. Increased numbers of painful episodes experienced within early life have been identified as a potential contributor to physical and mental dysfunction later in life. While the full scope of neurodevelopmental risks resulting from neonatal pain remains to be fully elucidated, researchers have reported both short- and long-term consequences to neonatal pain experience. Notably in 2005,
Grunau et al. described an inverse relationship between an increased number of painful procedures and a decreased cortisol stress response in an NICU infant sample. This process potentially leads to mal-adaptive developmental stress regulation, with researchers raising concerns about long-term learning and behavioral implications. This finding has also been demonstrated in animal models as researchers discovered long-term blunted stress responses of adult mice injured in the neonatal period.

Moreover, a greater number of invasive procedures have been associated with an alteration in the white matter microstructure of the brain in former premature infants. During NICU hospitalizations, infants are often repeatedly exposed to painful procedures, with a reported average of 16 daily painful and stressful procedures, and many without appropriate analgesia. In a recent systematic review focused on neonatal pain and developmental outcomes, researchers concluded that neonatal pain negatively affects development from the neonatal period through middle childhood. In summary, pain experienced in the NICU may have long-lasting effects.

Despite the patient-focused manner in which caregivers attempt to provide care, the NICU remains medically focused. Because of wide variations in developmental care practices and care driven by protocols and caregiver schedules, these high-risk infants are under a great deal of stress. In consideration of how care is delivered in the NICU, caregivers focus must not only be prioritized around short-term survival but also on the long-term quality of life for each infant.

**INDIVIDUAL DIFFERENCES IN NICU OUTCOMES**

Genetic variation describes individual differences within the genetic makeup (eg, genotype) within and among members of a given population. One’s phenotype encompasses the description of one’s personal characteristics, both physical and behavioral, many of which are presumably related to an individual’s unique genotype. For the purposes of the current discussion, it is important to remember that the most salient phenotype within the NICU is related to prematurity, which is not necessarily a reflection of the genetic makeup of the infant. Specific genetic variations within the infant could present as a phenotype of stress resilience or stress sensitivity, which could then interact with the IMNT experienced in the NICU and shape the long-term neurodevelopmental trajectory of infants.

Resilience is a complex phenomenon operationally defined as an individual’s outcome following a highly stressful event. This term is particularly important when considering the degree of resilience variability among individuals of common circumstances.

Factors including the type, severity, and duration of a stress event, as well as the personality and psychological status of the individual, play a role in shaping the stress response. Yet, within the adult resilience research, rarely does personality account for greater than 10% of variance in behavior across situations.

As previously noted, many infants exposed to the stressful early life experiences of the NICU show normal neurodevelopmental status and reach milestones as expected. Consequently, it is unlikely that the environmental impact of being cared for in the NICU is entirely responsible for the negative outcomes reported. Moreover, genetic susceptibility to stress and trauma may explain the variability in resilience seen in preterm infants. In adult populations, researchers have demonstrated associations between genotype and stress responses. However, more human gene studies are needed to determine whether genetic variation correlates with phenotypic variation.

**IMTN Differs From Pediatric Medical Trauma**

While “medical trauma” is a term used in the literature to describe a broad scope of psychological sequelae for both children and adults related to medical care, this term has not been previously applied to infants who require intensive care following birth. The uniqueness of IMTN hinges upon the abnormal and cumulative early life NICU experiences of pain, stress, and parental separation colliding with neurodevelopmental immaturity and possible genetic vulnerabilities. The deleterious neurodevelopmental effects of this combination of innate and environmental factors may not be revealed for months to years after the NICU experience. In contrast, pediatric medical trauma is often described in relationship to childhood cancer, chronic illness, and accidents with the medical event typically triggering posttraumatic stress sequelae. In a study of infants and preschoolers with cancer, researchers reported an 18.8% incidence of patients with PTSD. The initiation of dialysis has been reported as traumatic in 12% of pediatric patients and 22% of their caregivers. Significant psychological and physiological reactivity has been described in burn victims aged 12 to 48 months. These children demonstrated symptoms of PTSD shortly after their injury; in some cases, within 1 week. While traumas do not always result in disordered outcomes, the prevalence of posttraumatic stress in children, resulting from a variety of events, has necessitated a heightened awareness for primary care providers.

Pediatric providers, in acute and community settings, have been encouraged to practice trauma-informed care as a means of early identification of traumatic stress symptoms, thus providing avenues for developing more targeted intervention.
Trauma-informed care is defined as an approach to patient care that incorporates both understanding and praxis of the effects trauma has on illness or injury, with the goal to improve physical and mental health outcomes. If NICU caregivers were to embrace trauma-informed care, there may be greater attunement to the infant burden of stress with a focus on health outcomes beyond the immediate health crisis. The purpose of highlighting the pediatric studies that measure the experience of healthcare-related traumatic stress in young children is to emphasize how profound medical experiences may be for some individuals. While we have yet to determine a standardized and well-tested mechanism by which to measure the existence of medical trauma in NICU infants, the highly adverse experiences often encountered in this environment suggests the need for critical examination and consideration of trauma exposure for this vulnerable population.

NEURODEVELOPMENTAL OUTCOMES: EVIDENCE THAT IMTN MAY AFFECT SUBSEQUENT BEHAVIOR

Social Interactions
Among the estimated 1 in 68 children with a diagnosis of autism spectrum disorder (ASD), the risk for autism may be as much as 3 times higher for former preterm infants, particularly those who were born small for gestational age, those with low birth weight, and infants with all grades of intracranial hemorrhage. This increased risk is similar to findings in other recent studies that have reported a prevalence of ASD for preterm infants of 2% to 8%, a risk that is inversely related to gestational age.

Attentional Deficiencies
An increased prevalence of attention-deficit/hyperactivity disorder (ADHD) has been described among former preterm infants; in some cases, twice as many when compared with control groups. Researchers have found that 20% to 30% of premature, very low birth-weight, or moderately low birth-weight infants are estimated to have at least 1 mental health issue. In comparison, in the general US population, 15.5% of children have mental health problems. In this same study, the mental health issues were largely explained by ASD, ADHD, and developmental delays, but statistically significant findings among depression, anxiety, behavioral conduct problems, and prematurity were also reported.

Psychological/Psychiatric Issues
Several studies have demonstrated premature birth to be a risk factor for future psychiatric disorders, with a higher prevalence of depression and anxiety found in young adults born extremely premature. Furthermore, when compared with term peers, children born extremely preterm have 4 times greater risk for anxiety disorders.

Learning Impairments
For many former preterm infants, learning does not come easily. Relative to term peers, former preterm cohorts have been shown to perform significantly worse on all cognitive and academic domains and display more severe responses on many behavior problem scales. A linear relationship between gestational age and cognitive ability has been described, indicating that as gestational age decreases so does long-term cognitive ability. However, not all adverse preterm birth outcomes are experienced only by infants of the lowest gestational ages. Children born at 37 to 38 weeks, as compared with 39- to 40-week peers, also have demonstrated increased cognitive risks.

While many of these behavioral, mental health, and cognitive correlates of preterm birth are highly complex and may be due to the disruption of normal physical development, they may also be the result of complex stress and/or trauma experienced in the NICU. The brain has been shown to be highly sensitive to experiences early in life; thus, infants exposed to early adverse experiences in the NICU may suffer consequences not yet fully appreciated.

IMPLICATIONS AND CONCLUSIONS
Not all individuals respond to stressful experiences in the same manner. On the basis of multiple factors, intense stress experiences can place some individuals more at risk for adverse outcomes whereas others exhibit resilience to extreme stress. In this IMTN model, the concepts of risk and resilience represent an infant’s ability to adapt to the imposed stress experiences in the NICU. Infancy is considered a highly sensitive period of life when the brain is acutely influenced by genetic factors and the environment, intensified by premature birth. When trauma occurs early in life, there is potentially significant risk for the experience to affect the child’s developmental trajectory. Research has demonstrated an association between the timing and chronicity of a highly stressful event during development with the risk for an adverse outcome, resulting in a dose-dependent effect. Furthermore, when children lack the presence of a stable and loving caregiver during times of stress exposure, the impact of the experience may be greater than it otherwise would be. This is a common occurrence for infants in the NICU due to the intermittent presence of many parents during extended infant hospitalizations, as parents juggle the needs of their home lives and their NICU infant.
In the NICU, there are many infants of similar gestational ages who develop similar illnesses. With these similarities, then why do some infants have better neurodevelopmental outcomes than others? While some of the answers may lie within genetic variation, in many situations, there is not a clear explanation. Significant individual variability in the response to preterm birth and the NICU stay has been noted in both research and clinical settings.\(^7\)\(^2\)\(^,\)\(^9\)\(^6\)\(^,\)\(^7\) It is unlikely that the environmental impact of being cared for in the NICU is solely responsible for the negative outcomes reported. As with many outcomes of complex etiology, the interaction of genetic and environmental factors shapes our developmental course.\(^9\)\(^6\)\(^-\)\(^10\)\(^0\)

### Practice and Health Policy Implication of IMTN

During prolonged periods of parent–infant separation in the NICU, parents may develop a perception that they are somehow less important to their infant than the healthcare team. Nurses and physicians may be viewed as the most important and knowledgeable individuals to care for an infant, and parents may see themselves as far less important to the survival of their infant. However, research findings suggest that this perception could have a negative impact on the long-term development of the child because optimal survival of an infant is highly related to parental attachment.\(^1\)\(^9\)\(^,\)\(^1\)\(^0\) Early teaching and encouraging parent-owned activities, such as breastfeeding and skin-to-skin holding, convey a sense of purpose and meaningfulness for parents and support attachment with their infants.\(^1\)\(^0\)\(^2\)\(^,\)\(^1\)\(^0\)\(^3\) In addition, facilitating early and active parent physical contact and care with a vulnerable infant may decrease neurodevelopmental risks and strengthen infant resilience. The adoption of trauma-informed, age-appropriate care into clinical practice may be the initial step needed to begin to modify care toward a more infant-focused model.\(^8\)\(^7\)

Within primary care settings, infants are commonly evaluated for neurodevelopmental milestones as they mature, namely, cognitive, behavioral, and motor functions. Given the numerous factors that may interfere with early or ill-born infant development, this ongoing evaluation is critically important for infants who have received care in an NICU. While referral to early intervention programs is common for high-risk children in the United States, strengthening and broadening the scope of potential at-risk children are critical.

Based on the synthesis of research presented in this article, all infants born before term should be considered at-risk, given the accumulating literature highlighting the developmental risks not just for preterm but also for late preterm infants. Implementing preventative programs and practices to ameliorate these risks would result in a cost burden shift that would require society to increase financial costs in early life to lessen costs later in life.\(^1\)\(^0\)\(^4\)\(^-\)\(^1\)\(^0\)\(^6\)

Despite the lifesaving work accomplished in NICUs across the globe, the time has come to acknowledge that infants who begin life in this medicalized care delivery system bear a tremendous burden of stress. Therefore, it is critical that our clinical practices reflect this understanding to best protect long-term neurodevelopmental outcomes. With the knowledge that NICU care providers seek to deliver the highest-quality care possible, it is our hope that the conceptualization of IMTN may initiate dialogues with the theme of “How can we do this better?”

### Summary of Recommendations

| What we know: | • Infants compromised at birth will continue to need NICU care. |
| What needs to be studied: | • Alternative NICU caregiving practices that are protective of neurodevelopment. |
| What we can do today: | • Increase awareness of the prevalence of pain, stress, and parent–infant separation in practice. |


