

EDITORIAL

‘Does _____ predict neurodevelopmental impairment in former preterm infants?’ Is this the right question to be asked?

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In an article in this journal, Logan *et al.*¹ help to inform a piece of the outcomes prediction puzzle as they report on the potential link between a composite of physiologic markers in the neonate in the first 12 h of life (score for neonatal acute physiology II (SNAP-II)) and multifaceted neuropsychosocial outcomes at 10 years of age in the Extremely Low Gestational Age Newborn (ELGAN) study.¹ The ELGAN study represents a prospective multicenter group of infants born at < 28 weeks between the years 2002 to 2004, with prospectively planned neurodevelopmental assessments at multiple time points.² With the original sample size of 1506, the investigators were able to assess nearly 900 children at 10 years of age.¹ This remarkable cohort has helped to inform some of our understanding of the pathophysiology associated with brain injury in ELGANs, as well as provide insight into the long-term outcomes, which are often lacking in clinical trials. Not surprisingly, the authors found that a high SNAP-II score in the first 12 h of life is associated with an increased risk of neurodevelopmental and social issues at 10 years of age.¹ The authors offer one of the four possible explanations for their findings. The first two describe that physiologic derangements early in life are on the causal pathway to brain injury, as well as other preterm morbidities (for example, sepsis, chronic lung disease (CLD), and so on), and are thus predictors of neurodevelopment. The third explanation builds on the idea behind SNAP’s development, which involves additional factors besides gestational age and birth weight, and perhaps the SNAP score depicts a more accurate picture of the infant. The fourth involves the role inflammation on the early neonatal physiology and path to brain injury.

One of the biggest challenges for Neonatal Intensive Care Unit (NICU) providers is to help inform families regarding the outcomes of their infants. A big part of that conversation is devoted to the periviable antenatal counseling, where prior to birth, a decision is often asked to be made regarding intensive care versus comfort measures. Once past that decision point (or in situations where palliative care is not an option), parents and NICU staff both find themselves yearning for information that will help predict the outcomes of their baby for the days, months, years and decades to come.

Among the different prediction tools for neonates,^{3–6} one of the earliest that expanded beyond gestational age and birth weight was the SNAP score.⁶ It was developed by Richardson *et al.*⁶ as a potential risk adjustor for outcomes across centers, where it was noted that markers such as birth weight and gestational age alone were inadequate to describing the full story. While the SNAP score correlates well with mortality, nursing workload and length of stay, the complexity due to the large number of data elements led the investigator group to develop more user friendly versions, such as SNAP-II and SNAP-perinatal extension.⁷

These observations by Logan *et al.*¹ are informative and help build on the ELGAN study investigators’ previous work looking at the association between versions of the SNAP score and mortality,⁸ and brain injury in the NICU/neurodevelopment at 2 years of age.⁹ While all three SNAP studies in the ELGAN cohort perform a multivariate analysis adjusting for multiple confounders, the further one gets from the event (that is, the first 12 to 24 h of

birth), the more challenging it is to make the link along the causal pathway between the predictor (SNAP-II) and outcomes, which the authors acknowledge as a limitation.

The authors add to the literature the importance of using a powerful risk adjustor such as SNAP or one of its derivatives as the impact is felt well beyond NICU mortality. In addition, it further emphasizes the importance of the critical time period after birth, including the first hour, or so called ‘golden hour’.¹⁰ Furthermore, it provides the NICU providers with data on a modern cohort of very small and very premature babies, which can be used to help with shared decision-making and information provided to families. The need for this predictive information is used to help inform families and identify potential modifiable targets that can then be used to develop therapies to mitigate some of the harm.

There is likely an additional component from information we seek as providers (consciously or subconsciously): we need reassurance that we are doing the right thing for a critically ill neonate (that is, avoiding futile care, pain and suffering for both the child and their family). Starting with the delivery room, the ‘wait and see’ approach to what a periviable neonate looks like before deciding on resuscitation has been shown to be misleading,¹¹ and is frankly a moving target as resuscitation has shifted toward a younger gestational age over time. The attempt to inform the antenatal counseling using the National Institute of Child Health and Development calculator and four simple predictors (sex, antenatal steroids, gestational age and singleton birth)¹² is appealing in its simplicity and desire to provide some tangible numeracy to the family. Yet, we know that the probability of an adverse neurodevelopmental outcome in a neonate is affected by morbidities during their NICU course (for example, CLD, brain injury or severe retinopathy of prematurity).¹³ In addition, that trajectory is quite dynamic and can shift vastly (in either positive or negative direction) from the antenatal predictors through events occurring during the NICU stay.¹⁴ Finally, we also know that a number of infants will improve in their neurodevelopment with time. The cohort from the Caffeine for Apnea of Prematurity trial¹⁵ had the prevalence of combined mortality or morbidity reduced from 40% at 18 months corrected age to 23% at 5 years of age, when combining the caffeine and placebo group together, with similar improvement noted in both groups.

The aforementioned attempts to predict outcome, along with multiple other articles, try to account statistically for potential confounders such as clinical course and socioeconomic milieu. Yet, there are other intangibles, including potential interventions that the infants are exposed to post discharge (for example, early intervention), environmental toxins, and the underlying genetics and epigenetics that further modify outcomes and have yet to be fully incorporated into either risk adjustment or prediction models. Thus, while continuing to link predictors to outcomes for informative, risk adjustment and innovative purposes are critical, we must continue to recognize the dynamic trajectory of a neonate through to adulthood. Both NICU providers and families should use caution when asking and answering the question ‘what does _____ mean for my child’, and acknowledge the unknown in either positive or negative direction.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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