

Assessing Cognitive Outcomes in Studies of Extreme Prematurity

Louis A. Schmidt, PhD,^a Saroj Saigal, MD^b

In this issue of *Pediatrics*, O'Reilly et al¹ report on neuropsychological outcomes at 19 years of age after extremely preterm (EP) birth using the 1995 EPICure birth cohort of infants born EP (<26 weeks' gestation) in the United Kingdom and Ireland. Previously, the cohort had been found at 2.5, 6, and 11 years of age to score significantly lower on measures of general cognitive impairment compared with term controls. Now, at 19 years of age, the authors report that cognitive impairments have persisted, including deficits in general cognitive functioning and visuomotor abilities. The report also describes an increase in the proportion of the cohort with intellectual impairment (IQ <70) between 11 and 19 years of age.

Even with >50% loss to follow-up, O'Reilly et al¹ provide compelling evidence for persistent effects of general cognitive impairments in their impressive longitudinal studies of EP birth to emerging adulthood. These findings are generally consistent with older and longer prospectively followed birth cohorts of EP survivors in childhood,^{2,3} adolescence,^{4,5} and adulthood,⁶⁻⁹ although this is the first study focusing on neuropsychological outcomes to adulthood in the most immature infants. However, the study by O'Reilly et al¹ brings to our attention 3 lessons that we have learned over the years for reliably assessing psychological and cognitive measures in survivors of EP birth that we believe are worthy of comment.

The first lesson learned is that context is critical. In his seminal work in 1951,

Kurt Lewin,¹⁰ one of the founders of social psychology, argued that human behavior is a function of the person's disposition and the context or situation. The demand characteristics of the laboratory may evoke anxiety on performance-based measures such as the IQ and executive functioning measures used in the study by O'Reilly et al.¹ Moreover, individuals born premature are known to exhibit anxiety.¹¹⁻¹³ Although including additional state and trait anxiety measures increases the respondent burden, and are therefore seldom used, it is important to control for them in the future to eliminate potential confounding influences of anxiety when examining performance-based measures in the laboratory setting.

The second lesson is that it is important to consider group heterogeneity. All survivors of prematurity are not alike. Unreliable effects may result from treating a group as homogeneous when it is, in fact, not. O'Reilly et al¹ treated their EP group as homogeneous. Recent work by our group has shown that not all survivors of EP birth are alike across different domains of adaptive functioning. For example, extremely low birth weight survivors who were also small versus appropriate for gestational age and had poorer fluid intelligence (ie, ability to reason and solve problems in novel situations in real time)¹⁴ or those who were exposed versus nonexposed to prenatal steroids¹² were more likely to exhibit externalizing- and internalizing-related problems, respectively, in adulthood.

Departments of ^aPsychology, Neuroscience, and Behaviour and ^bPediatrics, McMaster University, Hamilton, Ontario, Canada

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Address correspondence to Louis A. Schmidt, PhD, Department of Psychology, Neuroscience, and Behaviour, McMaster University, Hamilton, ON L8S 4K1, Canada. E-mail: schmidt@mcmaster.ca

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The third lesson learned is that measurement equivalency should be established between groups. That is, does the measure have the same meaning across groups? Although many of the measures used by O'Reilly et al¹ have been normed, issues of measurement invariance have not been established between EP and control groups on some of the measures reported in their recent study. The O'Reilly et al¹ study is, unfortunately, not unique in this oversight because many other studies fail to consider this fundamental measurement property,¹⁵ although this is now beginning to be addressed in literature on EP birth.¹⁶ Considering issues of measurement equivalency is of critical importance to ensuring unbiased interpretations of findings.

As the percentage of preterm birth continues to rise worldwide, coupled with reduced morbidity and mortality, and with more EP infants reaching adulthood,¹⁷ there is a need for prospective, long-term outcome studies of extreme prematurity. The findings by O'Reilly et al¹ of persistent cognitive deficits among adults born EP are important contributions and also confirm many findings from previous studies of extreme prematurity. This convergence across birth cohorts and eras allows us to examine how robust and conserved these cognitive deficits are, which informs how we effectively manage these problems.

ABBREVIATION

EP: extremely premature

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