

Neurodevelopmental Outcomes of Preterm Children at School Age and Beyond



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KEYWORDS

- Preterm • Child development • Neuro development • Developmental disabilities
- Follow-up • Outcomes • Cognitive • Motor

KEY POINTS

- Prematurity is associated with motor, cognitive, behavioral, psychiatric, and other disabilities in adolescents and adults and the frequency and severity is inversely associated with gestational age at birth.
- Most teens and adults with prematurity-associated disabilities were born moderately or late preterm, but this group is less well studied compared with those born extremely preterm.
- Preterm adolescents and young adults have similar well-being and greater risk avoidance than controls.
- Disability-free preterm survivors attain a lower level of education and income than term-born peers but health-related quality of life is unaffected.

IMPORTANCE OF THE PROBLEM

Globally, approximately 15 million infants every year (11.1% of all births) are born preterm, at less than 37 completed weeks' gestation, with national rates varying from 5% to 18%.¹ As a result of the large number of preterm births and the increasing preterm birth survival rates, the long-term sequelae of prematurity will impact annually approximately 14 million children, their families, and societies. Unfortunately, the advances in survival have not been accompanied by an equal reduction in adverse outcomes.²

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Most children born preterm are doing very well with a very good quality of life. The goal of this review was to highlight the challenges that some preterm survivors face so that they will receive the necessary supports and that we can strive to continuously improve the antenatal, perinatal, postnatal, and childhood care of these children.

Although many trials and cohort studies of preterm populations evaluate outcomes at 18 to 24 months of age, they are limited in their ability to describe the full neurodevelopmental impact of prematurity. A review of prematurity-associated school-age and adult outcomes is therefore important. The focus in this review is on neurodevelopment because of its clinical significance and frequency. Other health outcomes have been reviewed by Luu and colleagues.³

Most preterm births are late preterm, defined as occurring between 34 0/7 weeks and 36 6/7 weeks' gestational age or moderate preterm, 32 0/7 to 33 6/7 weeks' gestational age. In the United States in 2015, only 1.59% were born very preterm at less than 32 weeks' gestation and 0.68% extremely preterm at less than 28 weeks' gestation.⁴ The frequency and severity of adverse outcomes vary inversely with gestational age. The research methods to describe outcomes in the larger late preterm cohorts often differ from those used in the smaller very preterm cohorts. Very preterm and moderate-late preterm outcomes are therefore described separately.

RESEARCH CHALLENGES

Research on school-age neurodevelopmental outcomes in the preterm population is derived mostly from observational cohort studies. The reader must therefore consider the potential biases and limitations of the research methods. Population-based samples are preferred over multicenter or single-center cohorts to minimize referral biases. Small sample size may be a problem in single-center cohorts, especially when studying the lowest gestational ages. With variability in preterm care between sites and over time, the region and year(s) of birth of the cohort need to be considered. Attention must be paid to the denominator. Especially for the most premature babies with the highest mortality, the incidence of adverse outcome(s) varies significantly for the denominators live births compared with all births (live and stillbirths). Less obvious but equally significant is when the denominator includes only children who could complete a test or when children with a sensory, behavioral, or very severe impairment are excluded. Much of the data related to neurodevelopmental outcomes for adults born preterm come from national birth registries and large birth cohorts with linkage to intelligence testing at time of conscription at 18 or 19 years of age.⁵ Adults with disabilities may be excluded from conscription and therefore observed associations likely underestimate the effect of prematurity on adult outcome. In addition, typically only male adults were registered in conscription databases and results therefore may not be relevant to female adults born preterm. When subjects of different gestational ages are lumped together, comparisons between studies with different gestational age cutoffs are difficult. Attrition bias is a major concern, as children lost to follow-up differ from those assessed.⁶ Whereas greater than 90% follow-up is ideal, in longitudinal cohort studies this gets increasingly difficult as children get older. Finally, many studies that examine adult outcome do not use a healthy, nonadmitted term control group as a comparison for late preterm infants, which limits the conclusions that can be drawn from any analysis.⁷

WHY LOOK AT SCHOOL-AGE AND LONGER-TERM OUTCOMES?

Parents, families, health care providers, and society are interested in knowing what the long-term future holds for the infant born preterm, either to support the child and the child's family, provide counseling, assist with decision making, providing

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