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Review

Long-term growth and general health for the tiniest or most immature infants

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SUMMARY

Given the improving survival rates of extremely preterm (EP, gestational age <28 weeks) infants, there is a need to understand their general growth and health outcomes not only in childhood, but also into adulthood. EP children are shorter and lighter compared with term children at term-equivalent age; with time, the weight disadvantage diminishes but the height disadvantage remains relatively unchanged. EP children and young adults also have higher rates of reported health concerns, medical conditions and visual impairment. Hospital readmissions are higher in early childhood, mostly attributed to respiratory illness. Individuals born EP have reduced bone health and are at increased risk for metabolic disorders. Increased rates of conditions such as diabetes or pathological fractures are not reported in the literature, although follow-up studies so far have only tracked EP individuals into young adulthood. Consequently, health care utilization and costs are increased in EP children and young adults. A thorough knowledge of the health risks related to EP birth is essential in planning surveillance and intervention strategies to optimize their health and wellbeing. Despite the increased risk of health problems, EP young adults generally report their quality of life to be similar to that reported in their term counterparts.

1. Introduction

The survival of infants born extremely preterm (EP, gestational age <28 weeks) has been steadily increasing over the last several decades [1,2]. More of these children are reaching adulthood than ever before [3]. Research into better understanding the outcomes for these individuals has progressed from crude estimates of mortality and major morbidity to a more nuanced understanding of their increased risk for many chronic conditions [3].

This review focuses on growth and the general health outcomes of individuals who were born EP and survived to discharge from the nursery. Gestational age and birthweight are continuous variables, and the gradient of outcomes across these variables provides important context to understanding the outcomes of EP individuals. Therefore, we will also review research that describes outcomes for cohorts defined according to birthweight. As cardiovascular and respiratory outcomes and cerebral palsy are covered elsewhere in this issue, they are not the focus of this review, and are only discussed briefly in the context of other health outcomes. It is important to note that most EP individuals will not have serious, life-limiting health conditions, and tend to self-report robust quality-of-life and health status [4]. Quality-of-life outcomes are discussed more fully in this issue by Saigal (Chapter 9).

The Millennium Cohort Study, a nationally representative, prospective UK cohort study, has clearly shown a gradient effect of gestation on adverse health outcomes, with children who are born at the lowest gestational ages at the greatest risk for poorer health outcomes, even after controlling for potential confounders such as sex, ethnicity, social risk, breast feeding and in-utero exposure to potentially harmful insults [5]. Therefore, the EP population is clearly a high-risk group for a variety of adverse health outcomes, with implications for counselling families in the nursery, screening and surveillance throughout childhood and early intervention, where possible, to prevent adult morbidity. Well-established population-level prevention theory suggests that the EP population is likely to benefit not only from the universal screening provided to the whole population, but also from selective prevention strategies, targeted to specific health issues that occur at a greater prevalence in this population [6].

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2. Growth

Children who are born preterm begin life both shorter and lighter than their term-born peers at term equivalent age [7]. However, this weight disadvantage tends to diminish during the adolescent years, although height disadvantages persist, compared with term controls [8]. A limitation of several studies in this field is the use of birthweight as the selection criterion: this can introduce bias, as more mature growth-restricted infants (who may be at higher risk of future growth disorders) are included with infants who are more premature, but appropriate weight for gestation [9]. Most studies in this field have reported data from the pre-surfactant era [8], when the survival rates from EP individuals were much lower than those seen in the modern era of neonatal intensive care [10]. Surfactant for treatment of respiratory distress syndrome in preterm infants was introduced in the late 1980s and early 1990s, and resulted in decreased mortality worldwide [10].

Roberts et al. [9] recently published data from a large, population-based cohort of EP adolescents and matched term controls, born in the early 1990s, when surfactant use was considered standard care for these tiny infants. These young people were recruited at birth, and assessed at 2, 5, 8 and 18 years of age. As seen in Fig. 1, the EP adolescents had lower weight *Z*-scores than controls at birth, but the greatest difference was seen at hospital discharge [EP weight *Z*-score: 1.16 SD (95% confidence interval (CI): 0.99–1.33) lower than term controls]. This difference decreased progressively until age 18 years [EP weight *Z*-score: 0.38 SD (95% CI: 0.09–0.67) lower than controls]. The EP children were shorter than controls at all ages, and this difference of ~0.7 SD did not alter greatly over time. The results previously reported in historical

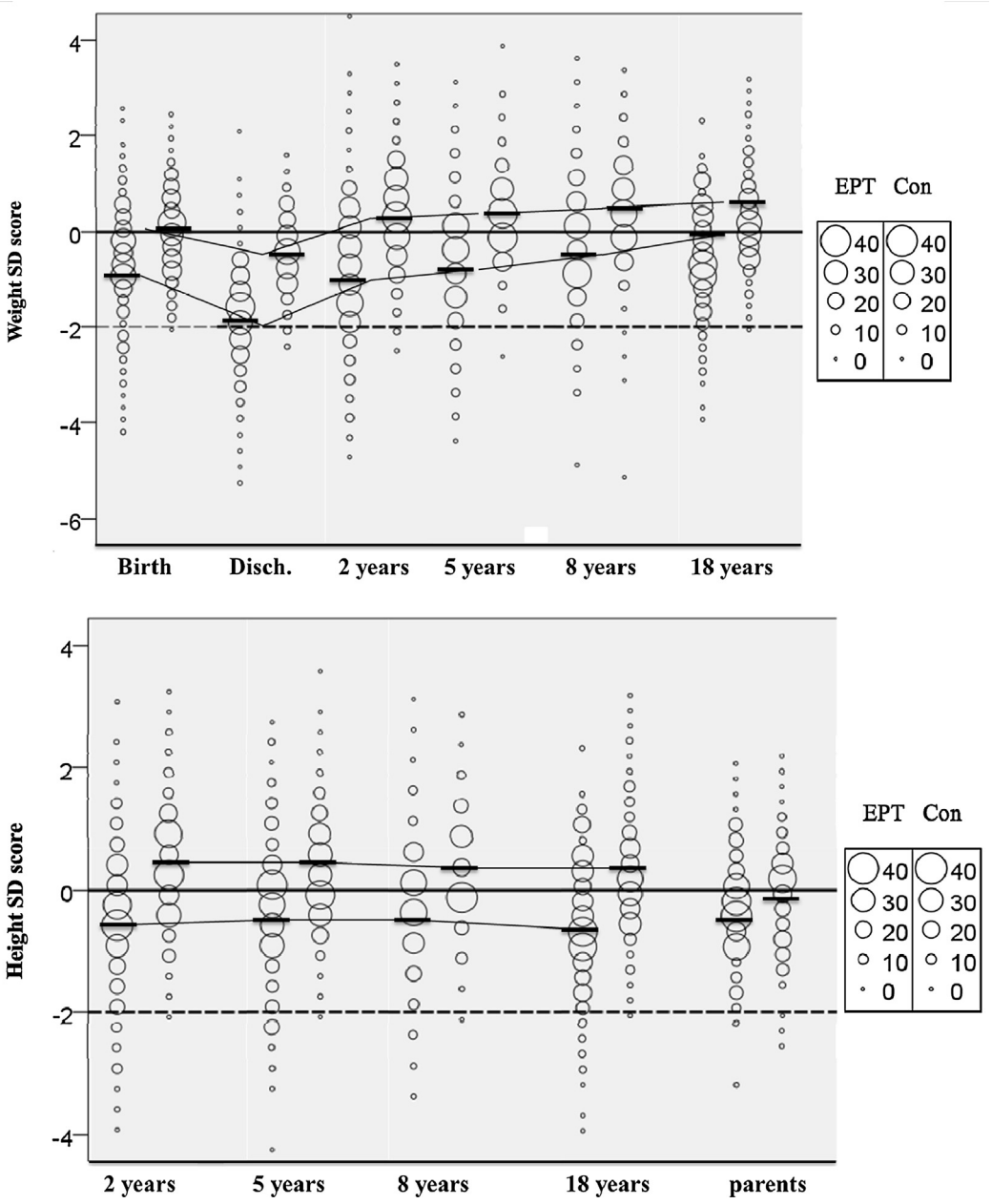

Fig. 1. Changes in weight and height standard deviation (SD) scores between birth and age 18 years in extremely preterm (EPT) and term control (Con) individuals born in Victoria, Australia, in 1991–1992. The size of the circles in the figure is proportional to the number of individuals. Mid-parental height SD score is shown in the height panel. Disch., discharge.