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Is preterm birth overlooked in child and adolescent psychiatry?

Running head: Preterm birth overlooked in psychiatry

Eilis Kennedy^{a,b}, MB, BCh, BAO, MRCPsych ekennedy@tavi-port.nhs.uk

Elizabeth O’Nions^{a,b}, PhD, eo'nions@tavi-port.nhs.uk

Dieter Wolke^{c,d}, PhD, Dr rer. nat. h.c, d.wolke@warwick.ac.uk

Samantha Johnson^e, PhD, sjj19@leicester.ac.uk

^a Research and Development Unit, The Tavistock & Portman NHS Foundation Trust, London, UK

^b Research Department of Clinical, Educational, and Health Psychology, Division of Psychology and Language Sciences, University College London, London, UK

^c Department of Psychology, University of Warwick, Coventry, UK

^d Division of Mental Health and Wellbeing, Warwick Medical School, Coventry, UK

^e Department of Health Sciences, University of Leicester, Leicester, UK

Corresponding author: Eilis Kennedy, Research and Development Unit, The Tavistock & Portman NHS Foundation Trust, 120 Belsize Lane, London, UK, ekennedy@tavi-port.nhs.uk, + 44 (0)207 435 7111

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Is preterm birth overlooked in child and adolescent psychiatry?

Obstetric factors have long been recognised as risk factors for the later development of poor mental health. One of the most consistently reported of these associations is for preterm birth (birth before 37 weeks' gestation), a form of early adversity that impacts health and development across the life course. Preterm birth is not uncommon: in 2014, 10.6% of live births globally (nearly 15 million babies) were preterm¹. Advances in neonatal care since the early 1990s have dramatically increased the numbers of babies who survive extreme preterm birth (birth at < 28 weeks' gestation) in high-income countries. This has led to growing interest in how extreme preterm birth impacts longer term outcomes including psychosocial development across the life-span.

Findings consistently suggest that being born extremely preterm is linked to an increased risk of neurodevelopmental disorders, intellectual impairments, and psychiatric sequelae that persist throughout childhood and adolescence². As many as 40% of individuals born at < 26 weeks have an intellectual impairment³, though rates reduce rapidly with increasing gestational age at birth. Difficulties with executive functioning are common, as are problems with inattention, social-communication difficulties, anxiety, and poor social skills².

In this issue, Upadhyaya and colleagues⁴ investigate the relationship between gestational age at birth, poor fetal growth, and the odds of receiving a depression diagnosis during childhood and adolescence/ young adulthood. The study used Finnish nation-wide registry data for all singleton births between 1987 and 2007. A sample of 37,682 children and young people were identified who had been diagnosed with depression by specialised services between ages 5 and 25 (around 3% of the source population), including those with mild, moderate, and severe depressive episodes, as well as depression with psychotic features. Mean age at diagnosis was 16.2 ± 3.5 years, and age at diagnosis ranged from 5 – 25 years.

Each child or young person with depression was matched to four non-depressed comparison individuals ($n = 148,795$) based on date of birth, sex, birthplace, and place of residence at the time their matched case was diagnosed. Adjusting for possible confounders including parent psychopathology, maternal substance misuse, maternal smoking during pregnancy, and socio-economic status, the study found links between depression and extreme preterm birth in girls, and post-term birth in both sexes.

Analyses stratified by age when diagnosed and sex found that the odds of being diagnosed with depression between ages 5 and 18 were nearly three times as high in girls born extremely preterm at < 28 weeks compared to girls born at term (40 weeks). However, there was no significantly increased odds of diagnosis in extremely preterm boys, or in either sex for very preterm births (28 - 31 weeks) or moderate to late preterm births (32 – 36 weeks). In boys, post-term birth (≥ 42 weeks' gestation) was linked to a 28% increase in the odds of being diagnosed with depression from ages 19 - 25. In children born at term, poor fetal growth was linked to a 6% increase in the odds of depression, and in children born post-term, to a 24% increase.

Upadhyaya and colleagues' study is important because births took place predominantly during the era of contemporary neonatal care, making findings relevant to present-day outcomes. The authors controlled for numerous potential confounders that may increase the likelihood of both preterm birth and depression, which could otherwise lead to an overestimation of the risk conferred by preterm birth specifically. However, as the authors note, there are variations in the reliability of diagnoses, which may be assigned more often to those who potentially have greater contact with health services such as children born extremely preterm². It is therefore important to replicate findings from register studies using cohort studies that assess all participants using the same diagnostic instruments.

Upadhyaya and colleagues' findings are consistent with data from the EPICure cohort study of all babies born < 26 weeks' gestation in the UK and Ireland from March to December 1995. Assessment at age 11, which included 71% of eligible preterm children, found a 4.5-fold increase in the likelihood of emotional disorders (9% vs. 2.1% in term-born controls)⁵–Follow-up in a subsample (42% of eligible preterm children) at age 19 showed increased symptoms of depression compared to controls, but no differences in rates of diagnoses⁶.

Whilst register studies can control for demographic variables to isolate the independent impact of gestational age at birth, they cannot investigate exposures to social experiences such as parenting, friendships, and negative peer relationships. These factors can be assessed in cohort studies to identify mechanisms underpinning risk and resilience in preterm populations. Work in cohort studies suggests that perinatal adversity amplifies the impact of traditional risk factors for depression and anxiety. Compared to normal birthweight peers, extremely low birthweight children (< 1,000g) are more

susceptible to poor mental health when they have experienced psychosocial adversity, such as family dysfunction, peer victimization, or child abuse⁷.

Preterm-born children may also be more exposed to certain forms of adversity. A three-fold increase in the risk of chronic bullying has been reported in children born at < 32 weeks⁸. Bullying victimisation has been shown to mediate internalising symptoms in children born preterm and psychotic symptoms in young adults born preterm^{9,10}. Therefore, interventions targeting psychosocial factors that extremely preterm children may be more exposed to, such as bullying, fewer friendships, or overprotective parenting could help to improve their longer term mental health.

At present, there is a lack of widespread recognition of the impact of preterm birth across the lifespan, despite its lasting impact on brain development. A four-fold increase in cortical volume typically occurs between 28 and 40 weeks' gestation¹¹. Disturbance of the developmental cascades that trigger brain maturation due to preterm birth leads to reorganization of cortical and subcortical structures¹¹, resulting in the “building of a different brain” compared to babies born at term^{2, p. 82}.

Babies born very or extremely preterm in high income settings usually spend their first few months in a neonatal intensive care unit (NICU). Lifesaving medical procedures in the NICU involve repeated exposure to pain and physiological stress. Hospitalised preterm infants undergo extended periods of separation from caregivers; a situation exacerbated by the current Covid-19 pandemic, which has led to restrictions on parents' access to their babies. Besides the distress caused to parents, this is especially concerning given evidence that, for preterm babies, augmenting parental contact during the perinatal period, including periods of skin-to-skin “Kangaroo” care, is linked to better long-term outcomes¹².

In recent years, there has been an emerging awareness of the need to consider the impact of preterm birth in physical healthcare settings. The implications of preterm birth for psychosocial development suggest that it warrants greater consideration in mental health and education too, although it is frequently overlooked as an important risk factor for later difficulties. This lack of awareness is starting to shift due to parent-led advocacy for greater recognition of the educational and mental health challenges their preterm children face. Those with lived experience of preterm birth, notably absent from research to date, are also starting to find a voice¹³. Affecting a growing population of children

worldwide, child and adolescent psychiatry has an important contribution to make in considering the biopsychosocial impact of preterm birth and how to improve outcomes for preterm-born children and their families.

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