**Global perspectives of premature birth across the life course**

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Globally, an estimated 15 million children are born before 37 weeks gestation, accounting for more than one in every 10 live births.1 Whilst prevalence rates vary by region, globally rates continue to rise; by 0.8% per year over the last three decades.1 Survival amongst preterm infants in the highest of resource settings has also significantly increased over the same time period, largely through advances in obstetric management and the inception of neonatal intensive care in the 1970’s. Neonates born before 26 weeks gestation have seen the greatest improvement in survival; in the UK alone survival rates for this group improved from 39% to 52% between 1995 and 2006 respectively, and again to 66% by 2014.2,3 Most preterm infants however are not born at these extreme gestations; in low- and middle-income countries, the greatest burden of mortality and morbidity falls amongst the estimated 85% of preterm infants born ≥32 weeks gestation.1 As the prevalence of adults born prematurely around the world continues to rise, the far reaching implications for health and well-being across the life course become ever more important.

In this edition of *The Lancet Child & Adolescent Health*, Crump and colleagues crucially examine the longer-term effects of prematurity extending into adulthood in a national cohort of more than 4 million singleton live births in Sweden (1973-2015).4 For the first time, they report on the associations between mortality and prematurity to mid-adulthood (30-45 years) presenting significantly increased hazard ratios for mortality, relative to individuals born at term. Whilst mortality was significantly increased in all groups born prematurely, including even the least preterm, an inverse relationship between the risk of mortality and gestational age at birth was seen.4 As well as adjusting for the important potential confounders of birth year, sex, birth order, maternal age at delivery, maternal education level, and maternal smoking, this study had the added advantage of including a co-sibling analysis, controlling for possible unmeasured confounders including genetic and environmental effects. The results of the co-sibling analysis suggest that the increased mortality rates were unlikely to be due to unmeasured familial effects.4

To date, limited existing data suggests a u-shaped relationship between prematurity and risk of mortality, with increased rates of early childhood mortality disappearing in later childhood and adolescence and re-appearing in early adulthood.5-7 Crump and colleague’s largest and longest longitudinal follow-up study to date, suggests that the apparent increase in mortality into adulthood may be mediated by diabetes, cardiovascular and respiratory disease, and not by congenital anomalies or socio-economic disorders.5 Indeed studies by other groups have suggested a strong association between preterm birth (<32 weeks) and heart failure into early adulthood.8 There has been speculation that increased risks of these types of chronic illness amongst those born prematurely may be mediated by aberrant DNA methylation patterns through the developmental origin of health and disease hypothesis.9

The findings presented by Crump and colleagues undoubtably have important implications for health services caring for individuals born prematurely, however, it remains to be seen if these findings are replicable across more diverse geographical settings and populations. In high-income countries improvements in obstetric and neonatal care over more recent decades may continue to translate to improved adult mortality and morbidity outcomes going forward.10 In countries with high neonatal mortality rates, the focus must still remain on improving newborn survival amongst preterm infants, however, in mid-resource settings, evidence of falling mortality accompanied by increasing childhood morbidity amongst survivors 1 implies important longer-term consequences on adult health. More longitudinal studies, following affected children through adolescence into adulthood are certainly needed to determine the global impact of preterm birth across the life course.

Never the less, the results presented here are vital in highlighting the potential long-term consequences of prematurity. The findings advocate for improved long term follow-up and health surveillance for affected individuals, aiming to implement early disease prevention strategies and improve outcomes across the life course for survivors of preterm birth around the world.

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**References**

1.Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832):2162-72.

2. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). BMJ. 2012;345:e7976.

3. Moore T, Hennessy EM, Myles J, Johnson SJ, Draper ES, Costeloe KL, et al. Neurological and developmental outcome in extremely preterm children born in England in 1995 and 2006: the EPICure studies. BMJ. 2012;345:e7961.

4. Crump C, Sundquist J, Winkleby MA, Sundquist K. Gestational age at birth and mortality from infancy into mid-adulthood: A National cohort study.Lancet CAH

5. Crump C, Sundquist K, Sundquist J, Winkleby MA. Gestational age at birth and mortality in young adulthood. JAMA. 2011;306(11):1233-40.

6. Srinivasjois R, Nembhard W, Wong K, Bourke J, Pereira G, Leonard H. Risk of Mortality into Adulthood According to Gestational Age at Birth. J Pediatr. 2017;190:185-91 e1.

7. Swamy GK, Ostbye T, Skjaerven R. Association of preterm birth with long-term survival, reproduction, and next-generation preterm birth. JAMA. 2008;299(12):1429-36.

8. Carr H, Cnattingius S, Granath F, Ludvigsson JF, Edstedt Bonamy AK. Preterm Birth and Risk of Heart Failure Up to Early Adulthood. J Am Coll Cardiol. 2017;69(21):2634-42.

9. Parets SE, Bedient CE, Menon R, Smith AK. Preterm birth and its long-term effects: methylation to mechanisms. Biology (Basel). 2014;3(3):498-513.

10. [Early and long-term outcome of infants born extremely preterm.](https://www.ncbi.nlm.nih.gov/pubmed/27512082) Johnson S, Marlow N. Arch Dis Child. 2017 Jan;102(1):97-102