Preterm birth has increased in prevalence over the past 50 years and now affects nearly 11% of all births worldwide. During the same period, major advances in treatment have led to dramatically improved early survival. More than 95% of infants born preterm who receive modern neonatal and pediatric care now survive into adulthood. Consequently, unprecedented numbers of survivors of preterm birth are now transitioning from adolescence into adulthood each year (>10 million/year worldwide). Their long-term outcomes across the life course will have growing clinical and public health importance. Clinicians who care for adult patients will increasingly encounter survivors of preterm birth and will need to understand their long-term health risks to guide their follow-up care.

In the current issue of *JAMA Network Open*, Risnes and colleagues report an analysis of adult mortality associated with preterm and early-term birth in more than 6 million people born in 4 Nordic countries (ie, Sweden, Norway, Denmark, and Finland) from 1967 to 2002. Their findings showed that individuals born early preterm (<34 weeks), late preterm (34-36 weeks), and early term (37-38 weeks) had approximately 1.4-fold, 1.2-fold, and 1.1-fold mortality, respectively, at ages 15 to 50 years compared with those born full term (39-41 weeks). Importantly, these associations appeared to be consistent across the 4 countries. Furthermore, analyses that compared siblings born at different gestational ages suggested that the findings were not explained by confounding from shared determinants of preterm birth and early mortality within families.

This study corroborates findings from several large cohort studies that were included in a recent systematic review. All 6 previously published studies of cohorts born in the last 50 years (in Sweden, Norway, and Australia) found that preterm birth was associated with increased all-cause mortality in early adulthood after adjusting for other perinatal and sociodemographic factors. The present study's risk estimates were consistent with those previously reported, which ranged from 1.2 to 1.6 for any preterm birth (<37 weeks), 1.1 to 1.2 for early-term birth (37-38 weeks), and 1.9 to 4.0 for extremely preterm birth (22-27 weeks) compared with full-term birth (variably defined but including 39-41 weeks). In addition, these associations have previously been shown to be independent of unmeasured shared familial (genetic or environmental) factors in cosibling analyses, suggesting that preterm and early birth have direct effects that are associated with increased mortality risks in early adulthood.

A new contribution of the present study was the ability to assess for heterogeneity of findings across 4 Nordic countries by using a similar modeling approach in the respective data sets. The risk estimates for both all-cause and noncommunicable disease mortality were notably similar across these countries. This consistency further strengthens the evidence linking preterm birth with higher mortality risks in adulthood. Furthermore, analyses of cause-specific mortality suggested several major causes involving different organ systems, particularly cardiovascular disease, diabetes, and chronic lung disease. These findings further corroborate prior evidence from large cohorts.

In addition, Risnes et al reported a 10% to 15% increase in mortality risk in adulthood associated with early-term birth, consistent with previous findings from Sweden. This elevated risk, although modest, could nonetheless have substantial population impacts because early-term birth is 2 to 3 times more common than preterm birth. A recent analysis of all Swedish adults aged 18 to 45 years suggested that early-term birth was associated with 3.0% of all deaths that occurred at these adult ages and 13.0% of deaths at these ages among persons born at early term, compared with 2.6% and 29.7%, respectively, for preterm birth. The population health impacts are likely to be
even higher in countries, such as the United States, that have a much higher prevalence of both early-term and preterm birth. Future studies should examine early-term birth as a separate group whenever feasible to better understand its long-term health trajectory in adulthood.

Based on previous large population-based studies and new corroborating findings from Risnes et al, the evidence is now clear that preterm and early-term birth are important risk factors for premature mortality in adulthood. The mechanisms are not fully established but may involve persistent epigenetic changes and impaired organ development that affect cardiometabolic function and most organ systems, consistent with the developmental origins of health and disease hypothesis. However, the absolute mortality risks in early adulthood associated with preterm or early-term birth are modest. Most people who were born preterm or early term survive into adulthood without major comorbidities and frequently report a high level of function and quality of life.

What are the remaining knowledge gaps? First, the new study by Risnes et al showed that mortality risks in adulthood associated with preterm and early-term birth were overall consistent across 4 Nordic countries. However, these are high-income countries with universal health care systems and other sociodemographic differences compared with many other countries. Globally, only 8% of all preterm births occur in Europe and North America, compared with more than 80% in Asia and sub-Saharan Africa, which have much lower early survival rates. Studies of long-term outcomes are critically needed in other diverse socioeconomic contexts and in racial/ethnic groups that have higher rates of preterm birth. Longer follow-up of existing cohorts will also be needed to assess outcomes in older adulthood. In addition, follow-up will be needed for later birth cohorts, which may have a different long-term health trajectory due to ongoing changes in neonatal care. Compared with recently studied cohorts born in the 1970s through the 1990s, certain outcomes in later cohorts could potentially be worse owing to the survival of frailer infants born at earlier gestational ages, whereas others could be better owing to improved follow-up care. A better understanding of health outcomes into adulthood after different types of preterm birth (e.g., spontaneous or medically indicated) is also needed to improve long-term risk stratification. Early evidence suggests that even spontaneous preterm birth is associated with significant long-term health risks, albeit with lower risks than medically indicated preterm birth.

Preterm and early-term birth should now be recognized as chronic conditions that require long-term clinical follow-up for preventive actions, monitoring, and treatment of health sequelae across the life course. Most knowledge about preterm birth outcomes has been relegated to the specialties of neonatology and pediatrics, with little integration so far into internal medicine or family medicine, the primary disciplines that will provide care for these patients in adulthood. Consequently, the growing evidence on long-term health sequelae has yet to be incorporated into clinical practice. Currently, clinicians seldom seek birth history in adult patients. History-taking and electronic health records (EHRs) for patients of all ages should routinely include birth history, including gestational age at birth, to provide important early-life context for understanding patients’ health. Policy action is needed to make birth history a required element of EHRs and to improve access to this history for clinicians and continuity of care systems across patients’ life course. Specific preventive and therapeutic interventions and whether they will translate into long-term risk reduction will need to be formally assessed in survivors of preterm and early-term birth. Better awareness of their long-term sequelae is needed to inform risk assessment, preventive actions (including healthy lifestyle counseling), and anticipatory screening. Integration of new knowledge into clinical practice is a crucial next step to improve long-term health in this growing population with increased health risks.

ARTICLE INFORMATION
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