

# Cardiovascular Risk in Adults Born Preterm

## Time to Act

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**Prematurity** currently accounts for around 10% of births with improved survival rates observed over the past 40 years thanks to substantial advances in perinatal care. However, long-term cohort studies have shown that being born preterm is associated with increased risks of hypertension and glucose intolerance<sup>1-3</sup> that may be associated with the observed higher incidence of cerebrovascular disease<sup>4</sup> and death caused by cardiovascular disease in young adulthood in this vulnerable population.<sup>5</sup> Whether this also translates into higher incidence of ischemic heart disease (IHD) has to date remained unclear because of the relatively young age of individuals born in the modern era of neonatology that started around the end of the 1980s and survival bias in those born before.

In this issue of *JAMA Pediatrics*, Crump et al<sup>6</sup> attempted to bridge this gap by examining the incidence of IHD in a large population-based cohort of more than 2 million people in Sweden who were born between 1973 and 1994. The authors were able to identify an increased risk of IHD in individuals born preterm age 18 to 43 years with an adjusted hazard ratio of 1.44 (95% CI, 1.19-1.73) compared with adults born full term. Therefore, this study shows that the adverse effects of preterm birth still persist more than 40 years later. Incidence rates were low in all studied groups (<10 per 100 000 person-years), which is to be expected given the young age of the cohort. Future studies will determine if the observed association between preterm birth and IHD holds as the population grows older and IHD incidence in the general population increases.

Similarly to previously published data,<sup>7</sup> in this study, mothers who gave birth prematurely were more likely to develop preeclampsia, hypertension, or diabetes and have a lower education level and a higher smoking rate. Therefore, whether the increased risk of IHD observed in the preterm population was because of preterm birth itself or other environmental and genetic factors was an issue. Crump et al<sup>6</sup> first adjusted for child and maternal characteristics and showed that the observed associations were still present. However, the adjustment could not account for unmeasured environmental and genetic factors. To do so, the authors performed a cosibling analysis that was made possible by the large cohort size and the level of information available on siblings. Interestingly, despite an expected loss of power in this analysis, the risk estimates remained similar, suggesting an independent role of preterm birth in the increased risk of IHD.

To date, to our knowledge, the pathophysiological mechanisms underlying cardiovascular disease in adults

born preterm are still undetermined. Preterm birth occurs during a critical period of organ system development. As a result, prematurity-associated complications, such as sepsis, impaired postnatal growth, and respiratory problems, and treatments, such as oxygen, parenteral nutrition, and corticosteroids, may permanently disrupt the normal ontogenesis and developmental programming of health. These may involve changes at the level of the heart, vessels, kidneys, and autonomic nervous system as well as increased glucose intolerance. Lewandowski et al<sup>8</sup> have shown cardiac remodeling in this population, with increased ventricular mass and a smaller ventricular diameter. They further found in young adults born preterm increased levels of serum endoglin and soluble fms-like tyrosine kinase 1, 2 antiangiogenic factors, suggesting the contribution of vascular structural dysfunction to elevated blood pressure.<sup>9</sup> In another study of young adults born younger than 29 weeks, we identified an association between blood pressure and kidney volume, which was smaller in the preterm-born population.<sup>10</sup> Emerging evidence also points toward possible dysfunction in cardiac autonomic regulation, including heart rate recovery after maximal exercise, an independent risk factor for cardiovascular disease, which was found to be slower in a small group of young adults born preterm.<sup>11</sup> Finally, a body of literature indicates increased glucose intolerance in adults born preterm<sup>2,10,12</sup>; interestingly, dyslipidemia is noted in some<sup>8</sup> but not all studies.<sup>2,12</sup> Understanding through what mechanisms preterm birth leads to cardiovascular disease is crucial to enhance preventative measures, screening strategies, and treatments that will improve the health and well-being of this growing at-risk population.

Crump et al<sup>6</sup> highlight the need to consider adults born preterm as an at-risk population for cardiovascular diseases. Despite the increased risk for hypertension and diabetes following preterm birth, being born prematurely is not listed as an indication for screening for these conditions by the most recent American Heart Association and American Diabetes Association guidelines, nor is it mentioned by their European counterparts. In addition, lifestyle modifications and pharmacological interventions that have been shown to be efficient in treating hypertension and glucose intolerance in the general population have not been specifically evaluated in the preterm-born population. Given that the pathophysiological pathways may differ in individuals born preterm, interventional clinical trials targeting this population are needed to determine optimal preventive and therapeutic strategies. Moreover, whether screening policies will translate into



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cardiovascular risk reduction over the long term in individuals born preterm should also be formally assessed.

In the meantime, physicians caring for adults should routinely inquire about birth history to identify this at-risk popu-

lation. Raising awareness among individuals born preterm and their families is equally important to promote healthy lifestyle habits and encourage protective behavioral changes (smoking cessation and reducing sedentary behaviors).

#### ARTICLE INFORMATION

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## Mitigating the Health Consequences for Youth in Families Affected by Immigration Policy Changes Opportunities for Health Care Professionals and Health Systems

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There are an estimated 18 million children in the United States with at least 1 immigrant parent, and 4.5 million children are citizens in families with mixed immigration status in which at least 1 family member is undocumented.<sup>1</sup> Immigration status is a social determinant of health.<sup>2</sup> The immigration status of parents poses an additional risk for child health, because children with a parent who is undocumented are at increased risk for developmental delay,<sup>3</sup> housing instability,<sup>3</sup> and limited access to social and health services<sup>4</sup> compared with children in low-income families with parents who are documented. Sociopolitical stress associated with immigration policy changes at the local, state, and national level can heighten the stress of undocumented immigration status on families<sup>4</sup> because of concerns about the elevated risk for deportation. One notable stressor was the recent presidential election, in which immigration policy was discussed in ways that heightened fears of deportation for immigrant communities; to our knowledge, the study by Eskenazi et al<sup>5</sup> is the first to

describe the health status of children born in the United States in immigrant families before and after the 2016 presidential election. A combination of increased enforcement, attempts to scale back temporary protections for noncitizens, and barriers to legal migration that have characterized the first years of the Trump Administration contribute to the climate of heightened fear of deportation.<sup>6</sup>

In this issue of *JAMA Pediatrics*, Eskenazi et al<sup>5</sup> evaluated the cross-sectional association between the perceived immigration policy vulnerability of Latinx adolescents who were born in the United States, using 2 subscales of the Perceived Immigration Policy Effects Scale,<sup>7</sup> and their mental and physical health after the 2016 presidential election. Authors also applied a difference-in-differences analytic approach to evaluate adolescents' perceived immigration policy vulnerability and the change in their mental and physical health before and after the 2016 presidential election. Eskenazi et al<sup>5</sup> conducted this study with a well-characterized cohort of 397 immigrant children aged 14 to 16 years from the Center for the Health Assessment of Mothers and Children of Salinas study,