

Bending the arc for the extremely low gestational age newborn

DeWayne M Pursley^{1,2} and Marie C McCormick^{2,3} On behalf of the Pediatric Policy Council

Infants born to socioeconomically disadvantaged women, including women of color, are at increased risk for preterm birth and infant mortality in the United States (1,2). The mechanisms by which these social factors—which include wealth, income, and education—interact with preterm birth are complex; however, they may relate to pathways associated with low socioeconomic status (SES) including nutrition, preconceptional health, environmental exposures, stress, and adverse health behaviors. Less appreciated is the fact that this risk extends beyond birth to influence later outcomes. Preterm infants who are born to low-SES mothers at extremely low gestational age or very low birth weight, when compared with their more advantaged counterparts, are at a greater risk of long-term neurodevelopmental deficits (3).

In this issue, Joseph *et al.* report on 873 children born between 23 and 27 weeks of gestation who were assessed for cognitive and academic ability at the age of 10 years from the large cohort of the Extremely Low Gestational Age Newborn (ELGAN) Research Study (4). After adjustment for gestational age and other potential confounders, the results reinforce the relationship between child outcomes, as measured by validated and standardized neurocognitive testing and academic performance, and poorly educated mothers at the time of birth. What is new is the finding that the outcomes of children whose mothers advanced in education between birth and 10 years of age improved. Although the association did not reach statistical significance for several outcomes, the paper suggests that improvements in maternal SES after birth are associated with improved child outcomes.

There are extensive reviews documenting the effects of disadvantaged environments on cognitive functioning and health problems (5). The finding that SES affects the outcomes of preterm infants, even at the extremes of gestational age, is not really new but deserves reinforcement (3,6). The accumulating evidence indicates that measuring SES is critical when assessing the outcomes of very premature infants, especially when attributing the outcomes solely to prematurity. Thus, outcome studies must incorporate robust

measures of SES, and control groups and site comparisons must be carefully considered in these approaches.

One hypothesis suggested by the study of Joseph *et al.* is that improving the outcomes of premature infants might involve interventions to support low SES parents. An example of a successful approach is “Moving to Opportunity”, a randomized social experiment sponsored by the US Department of Housing and Urban Development in the 1990s (ref. 7)). In this study, groups of parents in public housing were randomized to different levels of housing support, including a move out of poor neighborhoods. Although short-term results showed little difference, it was only later, when children reached college age, that the advantages became evident. The age of the child at the time of the move was also important; benefits were less likely to be seen when the move occurred during adolescence (8). These findings are also consistent with school lottery and voucher programs and the effects of better schools on academic performance and eventual income, especially for children from poor families. However, it would appear that short-term results are elusive.

An alternative to the broad approach of parental intervention is to design targeted interventions for the early-childhood years (generally under 5 years of age) to improve developmental and behavioral outcomes important to school readiness and success. Targeting the preschool period reflects the importance of this period in physical, emotional, social, and cognitive development. There is a growing body of evidence from the psychology, neuroscience, and economics literature documenting the effectiveness of these interventions, especially for those at the greatest risk. Effective programs utilize different models including parent education, health and home visits, and government-transfer programs (9,10).

What about premature infants? A recent meta-analysis favors pre- and post-discharge interventions in improving motor and cognitive outcomes for premature infants as well (11). The most significant contribution to this report is from comprehensive programs such as the Infant Health and Development Program (12), which found that intensive early educational intervention can improve the outcomes for high-risk preterm infants of varying neurologic vulnerabilities and levels of SES (13). Community-based early-intervention programs may also be

¹Department of Neonatology, Beth Israel Deaconess Medical Center, Boston, Massachusetts; ²Department of Pediatrics, Harvard Medical School, Boston, Massachusetts; ³Department of Social and Behavioral Sciences, The Harvard T.H. Chan School of Public Health, Boston, Massachusetts. Correspondence: DeWayne M. Pursley (dpursley@bidmc.harvard.edu)

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effective in improving the outcomes if the services are sufficiently intense (14). What remains to be established is how to sustain the positive impact of early intervention.

The findings of this body of work are illustrative of both the opportunities and shortcomings of our current approach to assessing the outcomes of our nation's most vulnerable children (15). Similar to most follow-up reports, the Joseph study focuses on neurodevelopmental test scores and neurological examinations. Although an important marker of development, test scores provide only limited evidence of how well or poorly children function. The narrow focus on neurodevelopment fails to consider the contribution of various comorbidities (e.g., asthma, obesity, and sensory deficits), movement disorders, and behavioral factors (e.g., attention and autism spectrum disorders). Moreover, the test scores do not indicate, except at the extremes, how well these children are functioning in their homes and schools. Other factors that might influence functioning at a given test score include exercise tolerance, resiliency, and peer relationships. In addition, the study focuses on maternal education as a proxy for SES with little consideration of parenting skills, other social determinants, and physical factors (e.g., toxin exposure and pollution). A research agenda that addresses these broader concerns could provide many benefits. For one, it might identify environmental influences that could be changed to improve the outcomes (e.g., exposure to pollution). Second, focusing on functional status (e.g., school performance and play) rather than diagnosis (e.g., hearing and visual disorders, and cerebral palsy) or test results (e.g., developmental and intelligence quotients) might suggest targets for interventions (e.g., improving muscle mass, stamina, attention, and coordination) that would improve a child's health-related quality of life for a given level of tested ability. Finally, it might more precisely answer what parents want to know: what will my child be able to do, will she walk, will he go to school, and will they be able to care for themselves?

The microcosm of extreme prematurity illustrates the concepts elucidated in the 2010 World Health Organization Commission on Social Determinants of Health. This conceptual framework provides guidance for science and policy for health equity, defined as the absence of unfair and avoidable or remediable differences in health among social groups (16). In their model, the commission described how material circumstances (e.g., housing, neighborhood quality, food security, and warm clothing), behavioral and biological factors (e.g., nutrition, physical activity, tobacco and alcohol consumption, and genetics), and psychosocial factors (e.g., stressful living conditions, relationships, social support, and coping style) have an impact on health equity and well-being. These intermediary social factors are influenced by SES, gender, ethnicity (and racism), education, occupation, and income. It is critically important that our society addresses the intermediary determinants of health that shape the outcomes and their disparities. Effectively addressing social determinants of health requires the support of cultural and societal values, and the focus and commitment of governance and economic, social, and public policies. Addressing inequities

may serve to both improve the outcomes and reduce prematurity, and there is certainly an opportunity in the United States where public social spending ranks 24th among 35 member countries of the Organization for Economic Cooperation and Development (17). Public social spending is critical in reducing the effects of low income (18).

We should note that improving the outcomes of premature infants is not just a US problem or even a problem of developed countries. With the rapid reduction of deaths in children under the age of 5 due to infectious and nutritional causes, prematurity now is a major cause of death in this age group globally (19). Absent a major breakthrough in reducing premature births, further reductions in child mortality will involve the gradual increase in the survival of premature infants (as has been observed in developed countries in the last century). These survivors will face all the threats to development as their full-term peers and will need to receive the same types of interventions to improve their outcomes (20).

The American Academy of Pediatrics (AAP) has already begun to lay out strategies to address the social determinants agenda. The AAP Committee on Child Health Financing has recently promulgated policy recommendations related to health insurance, essential benefits, and provider payments to strengthen family- and patient-centered medical homes (21). Similarly, the AAP Council on Community Pediatrics has identified opportunities for public policy advocacy, including support for measures to improve early childhood education, nutrition support, and home visiting (22). Likewise, there is a critical need to support comprehensive services that target the poor including two-generation strategies focusing on adults and children simultaneously, strategies that promote employment and income, and programs that support community infrastructure. An ongoing agenda is the need to establish an evidence base for the most effective ways to implement these strategies.

As recently noted by Berwick (23), physicians can no longer remain silent in the face of social injustice. As pediatricians, we must continue to provide strong advocacy for policies and programs that support the health of our nation's children, particularly the sickest, smallest, and most vulnerable among them. Relying on this approach alone, however, potentially puts at risk generations of low SES children who may continue to suffer similar fates while awaiting changes in our social and economic structures. We remain hopeful that the long arc of the moral universe will continue to bend toward justice. However, now as much as ever, it is critical that we fully utilize established, effective, and targeted interventions while we remain steadfast in the exploration of novel approaches to improve the outcomes of the extremely preterm newborn.

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