


## COMMENT



# Advocacy for research starting early in the life course

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This issue of *Pediatric Research* highlights the importance of pediatric research in optimizing health in childhood and setting the foundation for health into adulthood. Three articles demonstrate life course and intergenerational influences starting early. Two of these focus on preterm infants and later outcomes. Globally, preterm birth rates have increased in the past two decades and make up one in ten births in the US.<sup>1,2</sup> Woodward et al.<sup>3</sup> explore the visuospatial working memory of children who were born very preterm and/or very low birth weight in two prospective cohort studies. They found that both children and adults had difficulties that appear to persist into adulthood, continuing to impact everyday functioning, educational and occupational/socioeconomic achievement. Camerota et al.<sup>4</sup> identified four discrete neurodevelopmental profiles of infants born <30 weeks of gestation at 2 years of age that could facilitate the development of targeted intervention strategies for high-risk children.

Finally, in a multi-center cohort of infants born extremely preterm, Jackson et al.<sup>5</sup> found differential placental methylation within genes involved in fetal lung development that likely reflects signaling between the placenta and fetus mediating later health outcomes. Growing research demonstrates that there are developmental origins of health and disease and intergenerational transmission of disadvantage.<sup>6–8</sup> In summary, these and other studies confirm that maternal and child health research is critical to life course health. While it is often stated that children are not simply “little adults,” these studies strongly suggest that to prevent disease in childhood and adulthood, research on mechanisms and early antecedents requires prioritizing pediatric research.

Structurally, pediatric research is often at a disadvantage. Because of the proportion of children to adults, pediatric departments within universities are usually smaller than internal medicine departments serving adults. Requests for proposals that allow one applicant per institution often result in little attention to pediatric issues. Free-standing children’s hospitals may be excluded from federal requests for proposals that allow eligibility only for institutions of higher education. In addition, funding of pediatric care increasingly relies on Medicaid and the Children’s Health Insurance Program that are siloed by state and have low payment rates that strain health care system investment in pediatric research. From a biopharma standpoint, the size of pediatric markets, most of which entail rare disease diagnoses and are perceived to entail increased liability risks, makes research and development investments less appealing.

In addition, the pipeline of pediatric researchers is endangered by inadequate recruitment, funding limitations and attrition.<sup>9</sup> While these are challenges for all physician researchers, pediatrician investigators have been disproportionately affected.<sup>10</sup> Diversity in the research pipeline, including women and those underrepresented in medicine, is also sorely lacking.<sup>11–13</sup>

What are some legislative policy solutions to support pediatric research? We focus on three federal legislative initiatives, the PACT Act, Pediatric subspecialty loan repayment, and National Institutes of Health (NIH) Inclusion of Children in Research.

## PEDIATRICIANS ACCELERATE CHILDHOOD THERAPIES: THE PACT ACT OF 2019

The PACT Act of 2021 (H. R. 3773/S. 1357) prioritizes support for early-career pediatric physician scientists, who frequently struggle to balance clinical and research efforts. Increased support for laboratory activities, guidance on how to navigate funding pathways, and mentoring to develop an independent research career are key elements of the PACT Act. These factors are, of course, essential for all early-career scientists regardless of their field, but the PACT act is intended to reverse the historical trend of decreased support for pediatric research.<sup>14</sup> Furthermore, the PACT act recognizes the importance of increasing diversity in the pediatric research community by paying special attention to women and underrepresented minorities.

The PACT Act is intended to supplement rather than supplant existing NIH research and training funding while making use of existing NIH mechanisms. Specifically, the PACT act would be implemented through Trans-NIH individual awards and be led by the Director of the NIH in consultation with the Director of the National Institute for Child Health and Human Development (NICHD). This mechanism recognizes that the NICHD should be a tremendously important but not exclusive source for pediatric research. Moreover, the PACT Act codifies the Trans-NIH Pediatric Research Consortium initiated in 2018 to strengthen how the NIH coordinates and establishes priorities for pediatric research across all the Institutes and Centers of the NIH. In particular, research priorities should be informed by external stakeholders including research institutions, research societies, and industry.

The PACT act would support a broad swath of pediatric research including childhood and adolescent mental and behavioral health, childhood cancer, genetics, genomics, precision medicine, fetal and postnatal development, and rare diseases. It currently has

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been endorsed by multiple organizations including the Coalition for Pediatric Medical Research, Academic Pediatric Association, American Academy of Pediatrics, American Pediatric Society, Association of Medical School Pediatric Department Chairs, Pediatric Policy Council, Society for Pediatric Research, Burroughs Wellcome Fund, Alex's Lemonade Stand, Kids v. Cancer, and St. Baldrick's Foundation.

### PEDIATRIC LOAN REPAYMENT PROGRAMS AND THE CARES ACT

The CARES Act reauthorized the Pediatric Subspecialty Loan Repayment Program (PSLRP) for 5 years. Once funded, the program will help address shortages of pediatric subspecialists in underserved areas. It is similar in structure to the successful NIH Loan Repayment Program (LRP).<sup>15</sup> In the most recent estimate by the NIH, the debt of graduating medical students for medical school loans averaged \$145,000, ranging as high as near \$250,000. This debt burden presents a major obstacle for individuals to remain in academic research careers and in subspecialty careers. The NIH LRP is a successful program, which has been shown to increase retention of physician doctorates in the NIH extramural workforce. The success rate for funded applications in the extramural LRP program has remained steady at 50% with the mean award of ~\$50,000 and an average age of awardee of 37 years. Total funding now exceeds \$715 million since the inception of the program. There have been specific programs for pediatric research, clinical research, health disparities research and clinical research for individuals from disadvantaged backgrounds. The NICHD funds over \$6 million/year in LRP awards. For pediatric subspecialists who care for children with complex medical conditions, the CARES Act would provide up to \$35,000 per year for up to 3 years in loan forgiveness for those pediatric subspecialists who agree to practice in underserved areas. PSLRP has not made any initial awards because it has yet to be funded by Congress. The American Academy of Pediatrics is urging Congress to provide \$50 million in funding for the program for the fiscal year 2021.

### NIH INCLUSION OF CHILDREN IN RESEARCH

In the US, there are over ten times the number of clinical trials involving adult participants than children.<sup>16</sup> The precise number of children participating in research studies is difficult to ascertain.<sup>17</sup> Legislation led by the American Academy of Pediatrics was passed in 2016 that, for the first time, required NIH to collect data and report on the ages of subjects included in NIH-funded studies.<sup>18</sup> Previously, studies simply reported whether they included children or not, with many studies recruiting small numbers of older adolescents. This change in the law led to two conferences held by the NIH and revision of their policy, "NIH Policy and Guidelines on Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects" NOT-OD-18-116. This policy outlines the acceptable criteria for excluding children from research. Children can be excluded only if:

- diseases do not occur in their age group,
- research already is available,
- a separate study for their age group is preferable,
- the study includes pre-enrolled participants,
- regulations prohibit their inclusion, or
- they would be subjected to unacceptable risk.

In addition, the NIH policy changes will improve accountability by requiring investigator progress reports to include data on participant ages for research grant applications beginning January 25, 2019. These changes will offer greater visibility to NIH research involving children.

These are three areas of legislative advocacy in different stages of progress. Persistent advocacy to move these initiatives forward and to monitor progress is critical. Support is needed through your networks and with your congressional representatives. Consistent messaging is essential emphasizing the importance of pediatric research for early intervention to improve child health and health in adulthood. Understanding mechanisms and prevention early in the life course are key to the translation of research to improved health outcomes.

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### AUTHOR CONTRIBUTIONS

T.L.C.: conceptualized and wrote the manuscript, revised each draft, and approved the final manuscript. C.R., C.C., and D.A.V.: wrote portions of the manuscript, revised each draft, and approved the final manuscript.

### COMPETING INTERESTS

The authors declare no competing interests.

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