HHS Public Access

Author manuscript

Curr Opin Pediatr. Author manuscript; available in PMC 2019 April 01.

Published in final edited form as:

Curr Opin Pediatr. 2018 April ; 30(2): 260–262. doi:10.1097/MOP.0000000000000600.

Environmental influences on Child Health Outcomes, a Research Program of the NIH

Matthew W. Gillman, MD, SM and **Carol J. Blaisdell, MD, MEd**

Environmental Influences on Child Health Outcomes (ECHO) Program, Office of the Director, National Institutes of Health, Bethesda, MD

Decades of animal, clinical, and population-based research suggest that events that occur at the earliest stages of human development may lead to long-term, sometimes irreversible, adverse health consequences. [1] Subtle cues during critical windows of development may be adaptive for the fetus or infant but maladaptive as the child grows and develops. The consequences may not reveal themselves until later in the life course. Modifying these factors during early periods of developmental plasticity likely entrains better trajectories of health, whereas later in life, attempts to improve health can be grounded on the shoals of entrenched metabolic, behavioral, and cultural systems.[2]

Yet the evidence base for action is still wanting. While individual cohort studies have identified a variety of potential early developmental risk and resilience factors for later health outcomes, the impact of this research has been limited by the numbers and diversity of participants, relatively short follow-up times, few investigations of mediating biological pathways, inconsistent application of methodologies to address causal inference, relatively little focus on complex systems, and lack of translation into effective and sustainable interventions. Thus how to prevent common chronic childhood conditions like asthma and obesity remains elusive.

To fill these gaps, in September 2016, NIH launched the Environmental influences on Child Health Outcomes (ECHO) program. This new 7-year nationwide research program supports observational and intervention studies to address crucial questions about effects of a broad range of early environmental exposures on child health and development (https://www.nih.gov/echo).

ECHO prioritizes five pediatric health outcome areas. The first four represent common disorders: pre, peri, and early postnatal outcomes, upper and lower airway conditions, obesity and its cardiometabolic consequences, and the several domains of neurodevelopment. Recognizing the importance of understanding early determinants of well-being in childhood, ECHO also incorporates an innovative fifth outcome, positive health.

6011 Executive Blvd, Suite 325, Rockville, MD 20852, matthew.gillman@nih.gov, Phone 1 301 435 5236, Fax 1 301 594 5669.

Conflicts of interest

Other than employment at the NIH, the authors have no conflicts of interest.

ECHO is a multi-dimensional program. It comprises 62 grant awards; 110 principal investigators and over 1200 investigators in total; academic and related institutions in 44 states, DC and Puerto Rico; different structures across its components; and multiple stakeholders including diverse sets of children and families across the United States. ECHO's wonderful complexity, while sometimes daunting, offers unparalleled opportunities for innovation in how to conduct—and evaluate—trans-disciplinary team science in the 21st century.[3]

Together, the 84 ECHO observational cohorts, with an anticipated combined sample size exceeding 50,000 children from diverse populations across the United States, will leverage rich existing and new data from primary and secondary sources and biosamples. Using these data, ECHO investigators will examine how myriad aspects of one's environment—including societal, medical, psychosocial, behavioral, and biological—from conception to age 5 years may affect health outcomes throughout childhood and adolescence. Amalgamating data from all of these studies into an ECHO-wide Cohort of that size allows investigation not only of less common early determinants and outcomes, but also how associations differ across sociodemographic, geographic, or other subgroups, a prerequisite for precision prevention.[4] This data platform will initially be accessible to ECHO investigators and soon thereafter a national research resource available to the broader scientific community.

Most of the ECHO cohorts started recruitment prenatally, and few even in the preconception period. Some date from as early as the 1980s and others from the past year or two. All are actively following up the children, and some continue to recruit new participants. During the first year of ECHO, through the leadership of several working groups, cohort investigators have designed the ECHO-wide Cohort protocol and have ratified publication, data sharing, biospecimen, and human subjects protection policies that underpin their research. They are aided by the NIH ECHO Program Office, project scientists from across NIH, a Coordinating Center, Data Analysis Center, Children's Health Exposure Analysis Resource, Patient-Reported Outcomes Core, and (to come later) Genetics Core.

As these activities mature, the cohorts are achieving early successes by conducting collective distributed data analyses that involve central meta-analysis of aggregated data.[5] Whether through collective aggregate analyses in the initial phases or later individual-level analyses, ECHO's methodologists are preparing to face the challenges of data harmonization through standardizing ontologies and innovative data reduction and missing data approaches.

On equal footing to the ECHO Cohorts is the IDeA States Pediatric Clinical Trials Network, a component of ECHO that aims to enhance access to clinical trials among rural and medically underserved children. The network comprises clinical sites in 17 states with historically low rates of NIH funding, along with its own Data Coordinating and Operations Center. During its first year, the Network has realized two complementary goals: 1.) building capacity across the sites through professional development and infrastructure support, and 2.) developing protocols for intervention trials that address prevention or treatment of ECHO priority pediatric health outcome areas.

Scientific challenges attend to both observation and intervention. In these twin components of ECHO, an essential objective is to maintain focus on “solution-oriented” research questions, that is, questions that drive programs, policies, and practices.[6, 7] In the ECHO Cohorts, an example is research questions that help to disentangle competing concepts of intergenerational transmission through characterization of underlying pathways of social inheritance versus biological programming. Separating these pathways would guide design and timing of preventive interventions. A second example is refinement of methods to assess the influence of mixtures of chemicals, rather than a single chemical, as mothers, fathers, and children are typically exposed to more than one at a time. A third, more specific, example could be the use of metabolomics to distinguish the seemingly intractably interrelated effects of maternal obesity, gestational weight gain, and gestational diabetes on offspring obesity. The results could likewise steer the design of intervention studies. A fourth possibility is employing state-of-the-science approaches to time-varying mediation and confounding, or invoking computational systems science modeling, to address complex webs of etiology.

In the IDeA States Network, some of the challenges relate to identifying clinical trials that marry feasibility of implementation in rural or other hard to reach regions with overall impact. In the short term, tightly controlled trials within medical settings might be attractive to a group of pediatric researchers with varying specialty expertise and who hail from different settings. The Network’s research, however, will likely have most impact when its purview includes engagement of communities of our most needy children.

ECHO’s guiding principles are teamwork, impact, responsibility, and value. We operate under the premise that building mutual trust over time through continuous engagement of investigators and other stakeholders will yield a whole that is greater than the sum of its parts. Under ECHO’s cooperative agreement mechanism, investigators lead the scientific activities, while NIH participates as a partner to promote an overall vision for the program and ensure that its pursuits are consonant. We also envision that lessons learned in creating ECHO will facilitate the success of other large-scale research consortia.

We subscribe to the view that a good start to life can last a lifetime. What do children and adolescents, their families and other caretakers, their communities, and society as a whole need to know to ensure a good start for the largest number of children? ECHO research is meant to create that knowledge. Thus the long-term success of ECHO depends on addressing crucial observational and intervention research questions that smaller-scale cohorts or clinical trials cannot, and whose answers inform strategies to improve health outcomes of our nation’s youth. In so doing, ECHO is poised to enhance the health of children for generations to come.

Acknowledgments

We would like to thank Drs. Christina Park, Tania Lombo, and Manjit Hanspal for assistance with this program and review of this article.

Financial support and sponsorship

The authors are employees of the National Institutes of Health (NIH), Office of the Director, Bethesda, Maryland, USA. The views expressed in this article do not necessarily represent the views of the U.S. Government, the Department of Health and Human Services or the National Institutes of Health.

References

1. Gillman MW. Developmental origins of health and disease. The New England Journal of Medicine. 2005; 353(17):1848–1850. [PubMed: 16251542]
2. Baird J, Jacob C, Barker M, et al. Developmental Origins of Health and Disease: A Lifecourse Approach to the Prevention of Non-Communicable Diseases. Healthcare (Basel, Switzerland). 2017; 5(1)
3. Vogel AL, Stipelman BA, Hall KL, Nebeling L, Stokols D, Spruijt-Metz D. Pioneering the Transdisciplinary Team Science Approach: Lessons Learned from National Cancer Institute Grantees. Journal of Translational Medicine & Epidemiology. 2014; 2(2)
4. Gillman MW, Hammond RA. Precision Treatment and Precision Prevention: Integrating "Below and Above the Skin". JAMA Pediatrics. 2016; 170(1):9–10. [PubMed: 26595371]
5. Popovic JR. Distributed data networks: a blueprint for Big Data sharing and healthcare analytics. Annals of the New York Academy of Sciences. 2017; 1387(1):105–111. [PubMed: 27862002]
6. Kumanyika, SK.Parker, L., Sim, LJ., editors. Institute of Medicine Committee on an Evidence Framework for Obesity Prevention Decision M. Bridging the Evidence Gap in Obesity Prevention: A Framework to Inform Decision Making. Washington (DC): National Academies Press (US) Copyright 2010 by the National Academy of Sciences. All rights reserved; 2010.
7. Wallack L, Thornburg K. Developmental Origins, Epigenetics, and Equity: Moving Upstream. Maternal and Child Health Journal. 2016; 20(5):935–940. [PubMed: 27029539]