



**COMPILED RESPONSES¹ TO REQUEST FOR INFORMATION ON
ENHANCING THE SCIENCE OF THE ENVIRONMENTAL INFLUENCES ON C**

Innovative tools and approaches for remote data and biospecimen collection in large epidemiologic studies

Use of non-invasive devices for collecting e.g., environmental data, behavioral data, and physiologic--

Balance of essential and recommended protocol elements These measures can be performed on site or shipped to a central site at room temperature within a week or two of delivery, which makes them amenable to collection at any hospital in the US or the developed world.

II. Preconceptional Origins of Child Health Outcomes:

Identifying solution-

working groups; annual GOITs, meetings to plan meetings, etc). Simpler and more agile structures, ad hoc working groups, seamless additions or removal of protocol elements, smaller

question is whether preconception interventions can be more effective when they target the family unit/couple, rather focusing strictly on the mother.

Psychosocial and societal influences: Important scientific questions include: comprehensive assessment of the effects of adverse childhood experiences, stress and traumatic experiences, mood disorders (particularly maternal depression) on RPP health outcomes; long-term and transgenerational effects of racism and discrimination; whether these factors have direct biological effects (e.g., via stress hormones), or have effects primarily mediated through differential access to societal resources (e.g., access to healthy foods, health care, education, occupation, income, wealth), correlated behaviors (smoking) or postpartum mental health; how all these factors contribute to health disparities.

Strategies for recruiting participants preconceptionally, and retaining through pregnancy into childhood

- Feasibility of different strategies, including ensuring adequate sample sizes of births and participant diversity, from
 - Young women and men, already participating in ECHO cohort studies, entering reproductive age
 - Women with a recent pregnancy in ECHO, and their partners, who may have a subsequent pregnancy
 - Women and men of reproductive age irrespective of previous participation in ECHO

Broadly considered, preconception studies have three options: 1) recruit pregnant women and retrospectively collect data on the preconception time frame, either from records or interview; 2) recruit couples actively attempting pregnancy; 3) follow reproductive-aged individuals and assess pregnancies when they occur.

Advantages to Young women and men, already participating in ECHO cohort studies, entering reproductive age: efficient, captures both planned and unplanned pregnancies.

Disadvantages to #1: does not include sterile couples, may produce recall bias or bias in biomarkers whose levels are affected by time or pregnancy itself

Advantages to Women with a recent pregnancy in ECHO, and their partners, who may have a subsequent pregnancy: efficient, allows for detailed examination of the period prior to pregnancy, includes couples along the full spectrum of fertility (including those who conceive quickly, who never conceive, and who take longer than 12 months), allows full ascertainment of pregnancy outcomes other than live birth, allows for longitudinal data collection on changes in risk factors, particularly behavior

Disadvantages to Women with a recent pregnancy in ECHO, and their partners, who may have a subsequent pregnancy: couples planning pregnancy are not representative of all pregnancies and offspring; they may have better health behaviors but may also be more likely to be subfertile, especially if they are older or wait to enroll in the study, even for a month or two after trying to conceive

Advantages to Women and men of reproductive age irrespective of previous participation in ECHO: more generally representative, captures both planned and unplanned pregnancies,

all pregnancy outcomes. Collects preconception information during the preconception period, including on natural history of behavior and behavioral changes, and does not suffer the limitations of retrospective assessments.

Society for Research on Adolescence commissioned me as the lead author to write a consensus statement detailing the impact of racism on Black youth. Last summer, I organized and co-hosted an antiracism webinar for the Society for Research in Child Development on June 30, 2020. Last summer, I also participated in a Town Hall discussion on racism organized by my local PBS station. I am recognized as an international expert on racism, especially as it pertains to understanding the impact of racism on Black youth's development and health.

Promotion of diversity of the scientific workforce related to child health

I have perused the ECHO-wide Cohort Data Collection Protocol, and noticed something striking. The leadership team includes all White individuals despite the fact that the majority of youth under the age of 15 are non-

Furthermore, the physical environment measures don't include assessments of institutional racism, which does the most harm to ethnic-racial minority children and adolescents (see Seaton, 2020). Where are assessments related to whether families reside in a food desert, near a toxic waste site, and/or near a hospital? Where are assessments related to police indicators since ethnic-racial minority neighborhoods tend to be overpoliced, which is a risk factor for being swept into the penal system? All of these are indicators of institutional racism that are lacking in the current ECHO protocol. This needs to be rectified immediately.

I truly hope that the ECHO leadership team responds to this feedback and incorporates non-White scholars into the leadership team, and racism related measures into the protocol. I am happy to talk further if desired.

References

Alhusen, J. L., Bower, K. M., Epstein, E., & Sharps, P. (2016). Racial discrimination and adverse birth outcomes: An integrative review. *Journal of Midwifery & Women's Health*, 61, 707–720. doi:10.1111/jmwh.12490

Coker, T. R., Elliott, M. N., Kanouse, D. E., Grunbaum, J. A., Schwebel, D. C., Gilliland, . . . Schuster, M. A. (2009). Perceived racial-g that are lacking in

Has sibling recruitment been considered?

There is a need to address approaches to reduce burden on participants and staff. Suggestions for doing so include: 1) lessen the administrative work on PIs; and 2) allow cohorts to carryover funds in a more seamless and less cumbersome manner to facilitate study staff retention, maintenance of cohort recruitment and retention, collection of high quality data, and

use of echo but are there analyses that echo can do that smaller more isolated populations just can't accomplish on their own? Are there regional effects to healthcare, are there fundamental differences in the populations, are their societal or economic differences that persist or don't persist regionally?

Respondent 9

Hello,

I attended the presentation last Thursday on the environmental influences on child health. My close friend Dr. Leslie Thompson, who works in your department, speaks very passionately about the work that he does.

Despite me not having any related experience or knowledge to this field of study, I feel like the team did an excellent job presenting what they're seeking to do. I may not have understood all the technical terms but what I did get out of it is that the team is doing very important work to better understand the different factors that may affect child health.

I appreciate how you made this open to the public and kudos to Dr. Thompson for making it known that I could attend!

As a lay person, I would be interested to learn more about what your department discovers regarding the various contributors to the health of children. I think it will provide valuable information so the public can have a better understanding on how to raise children and see to it they live healthier lives.

Thank you for the time you took for the presentation!

Respondent 10

Included below are some "cutting-edge" papers that should be of interest to the organizers of this meeting. It fits directly into the underlying mechanism that is the theme of the ECHO Preconception Workshop.

If there are any questions, please do not hesitate to contact me.

- 1) Trosko JE (2018) Modulation of Cell-Cell Communication and Epigenetic Mechanisms as a Shared Cellular Mechanism in Diverse Childhood Brain Diseases, Such as Cancer and Autism. *EC Neurology* 10.3: 134-156.
- 2) Trosko JE (2016) A Conceptual Integration of Extra-, Intra- and Gap Junctional Intercellular Communication in the Evolution of Multi-cellularity and Stem Cells: How Disrupted Cell-Cell Communication during Development can Affect Diseases later in Life. *Int J Stem Cell Res Ther* 3:021
- 3) Trosko JE (2011) Pre-Natal Epigenetic Influences on Acute and Chronic Diseases Later in Life, such as Cancer: Global Health Crises Resulting from a Collision of Biological and Cultural Evolution. *J Food Sci Nutr* 16:394-407. DOI: 10.3746/jfn.2011.16.4.394

and returned by mail -

25% of women get pregnant in the first cycle, and another 25% in the second cycle. The chances of identifying such women on any form of cross-

Respondent 16

Dear Dr. Arteaga,

As leaders of an ECHO cohort, it has been a privilege to participate in this team science enterprise and impressive effort to engage as a community of scientists aligned in common goals of improving child health through consideration of environmental influences. On behalf of our

5. Preconceptional Origins of Child Health Outcomes:

As ECHO children age, ECHO should not discount the value of examining exposures and outcomes throughout the life course, including later in childhood, adolescence, and through adulthood. Environmental epidemiology focusing on the adolescent period is scant, despite the unique and important changes in exposure and organ system growth and functional development in this period. The adolescent period is also when the incidence of some of the neurodevelopmental outcomes with very high public health burden (e.g., depression) increase rapidly.

Attention to exploration of intergenerational exposures and outcomes related to current ECHO participants might be more compelling and feasible than expanding ECHO's aims to preconception.

The National Children's Study attempted to collect pre

Respondent 17

Dear ECHO,

There is increasing discussion about data libraries and languages and harmonizing data elements to facilitate data sharing. We need to enhance our efforts to standardize our collection of data on the 'environmental' side of environmental health. The expertise to do so may lie outside the EH

requirement that cohorts do a certain percentage of the recommended elements based on the focus, interests and expertise of their individual research groups. We believe this will lead to a higher quality dataset.

II. Preconceptional Origins of Child Health Outcomes:

Identifying solution-oriented (“so what”) scientific questions about preconceptional origins of child health outcomes, based on knowledge from pre-clinical, clinical work, and population research, including but not necessarily limited to the following preconception factors:

- Obesity and lifestyle factors such as diet, sleep, physical activity
- Physical and chemical exposures
- Fathers
- Psychosocial and societal influences

We recommend that ECHO NOT be expanded to include a preconception arm. While preconception factors are vitally important and understudied, preconception studies are challengin

Overall, we recommend that NIH put most of its resources going forward into maintaining and following the children already enrolled in the ECHO cohort. The investment in ECHO has been substantial with an enrollment goal of over 50,000 children and their families and over 50% representation of non-white participants. We recommend that any additional funds be devoted to increasing participation in ECHO among under-represented groups.

I. General Topics

Regarding reducing burden on participants and staff: we strongly recommend that there be a thorough evaluation conducted to identify lessons learned from implementation of the ECHO

II. Preconception Origins of Child Health Outcomes

We recommend that NIH put most of its resources going forward into maintaining and following the children already enrolled in the ECHO cohort. The investment in ECHO has been substantial with an enrollment goal of over 50,000 children and their families and over 50% representation of non-white participants. We recommend that any additional funds be devoted to increasing participation in ECHO among under-represented groups, for example expanding efforts to include different Asian groups such as Southeast Asians and South Asians.

Preconception studies are very challenging to conduct and very resource intensive and would be very difficult to successfully implement within the large and complex framework of ECHO without a large influx of new funds for research and infrastructure. If NIH is strongly committed to adding a preconception arm, then we recommend it would be through additional pregnancies of women already enrolled in ECHO or children already enrolled in ECHO that are reaching reproductive e

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health status than those not retained." From: Holt CL, Le D, Calvanelli J, Huang J, Clark EM, Roth DL, Williams B, Schulz E. Participant Retention in a Longitudinal National Telephone Survey of African American Men and Women. *Ethn Dis*. 2015 Spring;25(2):187-92. PMID: 26118147; PMCID: PMC4593062.

4. " Consistent with prior research, higher retention rates were found among Whites, females, and married individuals as well as those with better health and more education." From: Radler BT, Ryff CD. Who participates? Accounting for longitudinal retention in the MIDUS national study of health and well-being. *J Aging Health*. 2010 Apr;22(3):307-31. doi: 10.1177/0898264309358617. Epub 2010 Jan 26. PMID: 20103686; PMCID: PMC2837791.

One suggestion is to have a VERY STREAMLINED core protocol that includes biospecimens plus a minimum set of outcome assessment for all 5 ECHO outcomes and then have more detailed protocols for each of the 5 ECHO outcomes that cohorts could opt into. This would be analogous to how a single cohort study might attempt to collect their core protocol on all participants but then offer participants additional incentives to opt into ancillary studies.

Respondent 22

Dear Dr. Sonia Arteaga:

Thank you for extending the deadline for the ECHO RFI. Please find brief comments below for the two RFI sections, also noting that these suggestions are my own and are not intended to represent any affiliated institution or program.

I hope that some of the strategies or recommendations prove useful.

I. General Topics

Approaches to promote scientific value while reducing burden on participants and staff in large consortia of parent-child cohort studies that involve primary data collection:

The ECHO program might benefit from hosting an annual virtual forum that specifically highlights innovative tools and approaches for remote data and biospecimen collection in large epidemiologic studies. As an example, cohorts such as the Safe Passage Study (PASS) Cohort are implementing novel remote blood collection protocols that might be vetted for approval to use ECHO-wide.

Cohorts can be encouraged or provided tools and resources to collaborate with institutions and scholars who are engaged in community-based participatory research, primarily for continual engagement and feedback to enhance recruitment and retention of diverse study populations. Doing so might additionally impact your interest in understanding of optimal frequencies of data collection, balance of essential and recommended protocol elements, and nimbleness to address public health emergencies in large collaborative consortia of longitudinal studies.

ECHO can partner with the Office of Scientific Workforce Diversity and the NIH extramural research community for strategic and targeted efforts to recruit and retain a diverse scientific workforce related to child health, also working closely with the NIH UNITE Initiative.

II. Preconceptional Origins of Child Health Outcomes:

Identifying solution-oriented (“so what”) scientific questions about preconceptional origins of child health outcomes, based on knowledge from pre-clinical, clinical work, and population research, will benefit from a strong focus on the role of structural racism and the implications of persistent residential segregation. Structural racism may relate to or potentially undergird potential disparities in all the factors listed in the RFI including: Obesity and lifestyle factors such as diet, sleep, physical activity; Physical and chemical exposures; Fathers; and Psychosocial and societal influences.

ECHO might also consider coordinating data collection and research efforts with the All of Us Research Program and other diverse and established cohorts, e.g. the Black Women's Health

is pregnant or attempting to conceive, this could yield some excellent prospective data that could begin to be collected even before ECHO2 is launched (and then, these data could be incorporated into ECHO2 as extant data).