

Future of Environmental influences on Child Health Outcomes

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Office of the Director, NIH
Advisory Committee to the Director
December 14, 2023

Today

- ECHO's first 7 years
 - Contributions to enhancing child health
 - Cross-cutting themes
- Looking to the future
- ECHO as nationwide research resource
- Discussion



Bottom Lines

- ECHO is unique large NIH child health program
 - Has matured from standing start in 2016
 - ACD helped get it off the ground
- ECHO research enhances health of US children
 - Long-term implications of influences at earliest stages of human development
 - Combination observational and intervention research
- Poised to make even larger impact



Some (of Many) Scientific Questions

- Nationwide opioid crisis
 - Neonatal opioid withdrawal syndrome (NOWS) distressing, prevalent, recalcitrant, costly
 - What can we do to lower its burden?
- Asthma one of most common chronic conditions of childhood
 - Racial/ethnic disparities persist
 - When do they start? How can we prevent them?
- Childhood obesity resistant to individual interventions
 - How well do policy solutions work?
 - When might community-level interventions be most effective?



What's common to these questions? (1 of 4)

- Solution orientation
 - Answers inform policy, program, practice
- Important to end-user stakeholders
 - Actionable
- Driven by investigator passion
- Feasible



What's common to these questions? (2 of 4)

- Take advantage of innovative ideas, approaches
 - Including enthusiasm of trainees and early-stage investigators

Opportunities and Innovation Fund
Diversity Supplements
Junior Investigator Pilot Clinical Trials
NOFO for Graduate Students and Post-docs



What's common to these questions? (3 of 4)

- Require large, diverse cohort or multi-center intervention trial
 - Product of effective collaboration
 - Whole greater than sum of parts
 - Science of Team Science



How has ECHO been addressing these scientific questions?

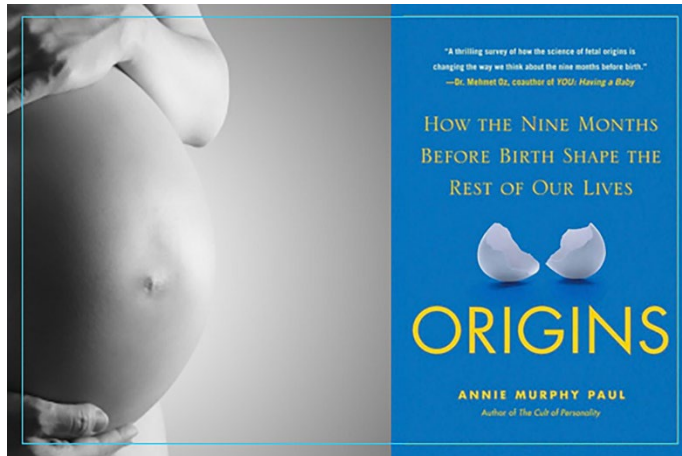


ECHO Mission

Enhance the health of children for
generations to come



A good start to life...



...can last a lifetime



...and over generations



5 Key Pediatric Outcomes With High Public Health Impact

PRE-, PERI-
AND POSTNATAL



UPPER AND
LOWER AIRWAY



OBESITY



NEURO-
DEVELOPMENT



POSITIVE HEALTH



From birth through adolescence

Observational & Intervention Research

ECHO Cohort
&

ECHO IDeA States Pediatric Clinical Trials Network



ISPCTN Overall Goals

- Provide access to state-of-the-art clinical trials among rural or underserved children in IDeA states
- Build pediatric research capacity in IDeA states
 - To conduct clinical trials
 - To compete for future funding



ISPCTN and Rural Health

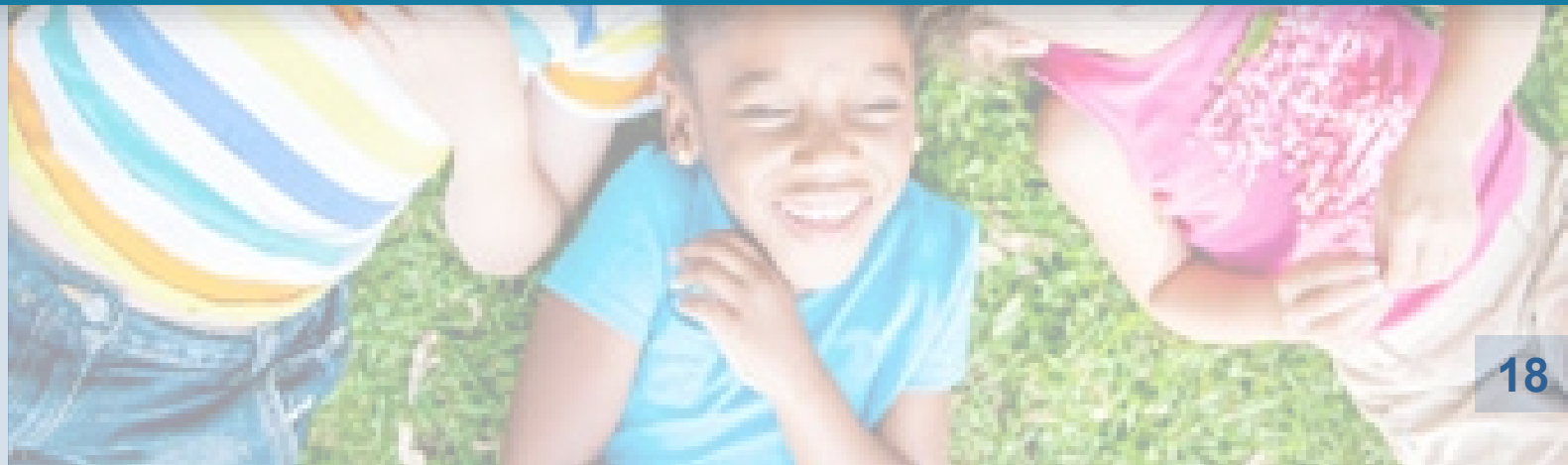
- More than a quarter (27.6%) of ISPCTN clinical trial participants live in rural settings
- ISPCTN trials address issues that disproportionately affect rural communities
 - Indoor air quality
 - Treatment of obesity far from specialists
 - Opioid crisis





ECHO Science

Mitigating Neonatal Opioid Withdrawal Syndrome (NOWS)



ECHO's Response to the Opioid Epidemic

- **Accelerating Clinical Trials for Neonatal Opioid Withdrawal Syndrome (ACT NOW)**

- From no standard of care to evidence base for best practices



Jittery

Fussy

Tremors

Hard to console

Poor sleep

Poor feeding

Long hospital stays

Long-term neurodevelopment?



[Athenahealth.com](https://www.athenahealth.com) 2019 08 16



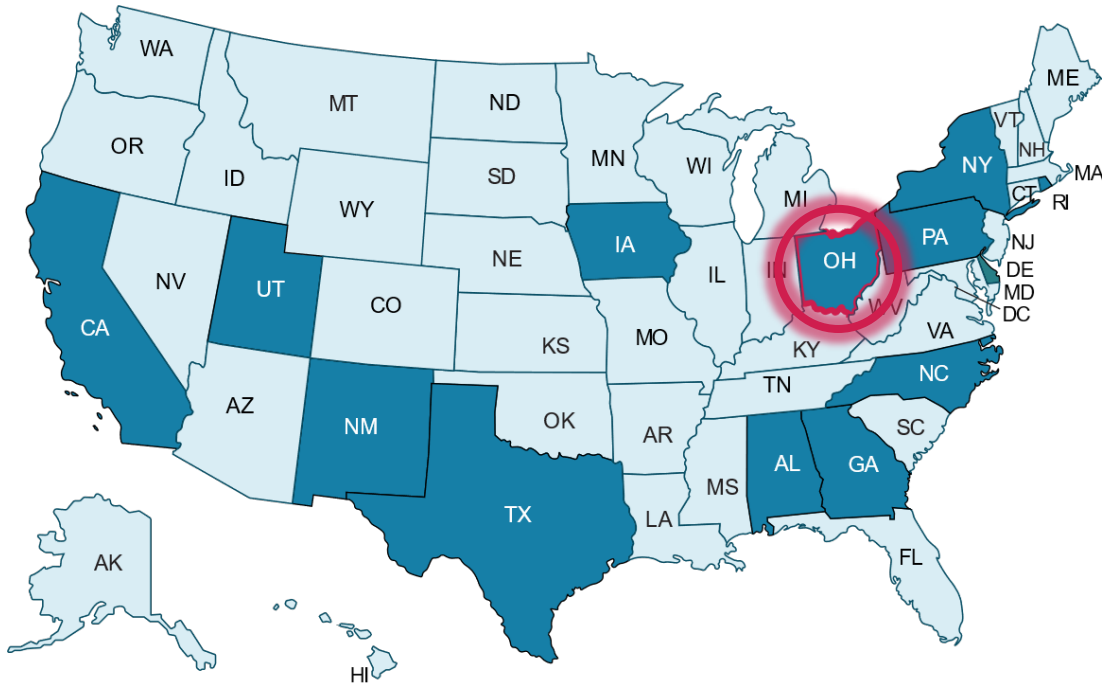
[Kidspot.com.au](https://www.kidspot.com.au) 2019 08 16





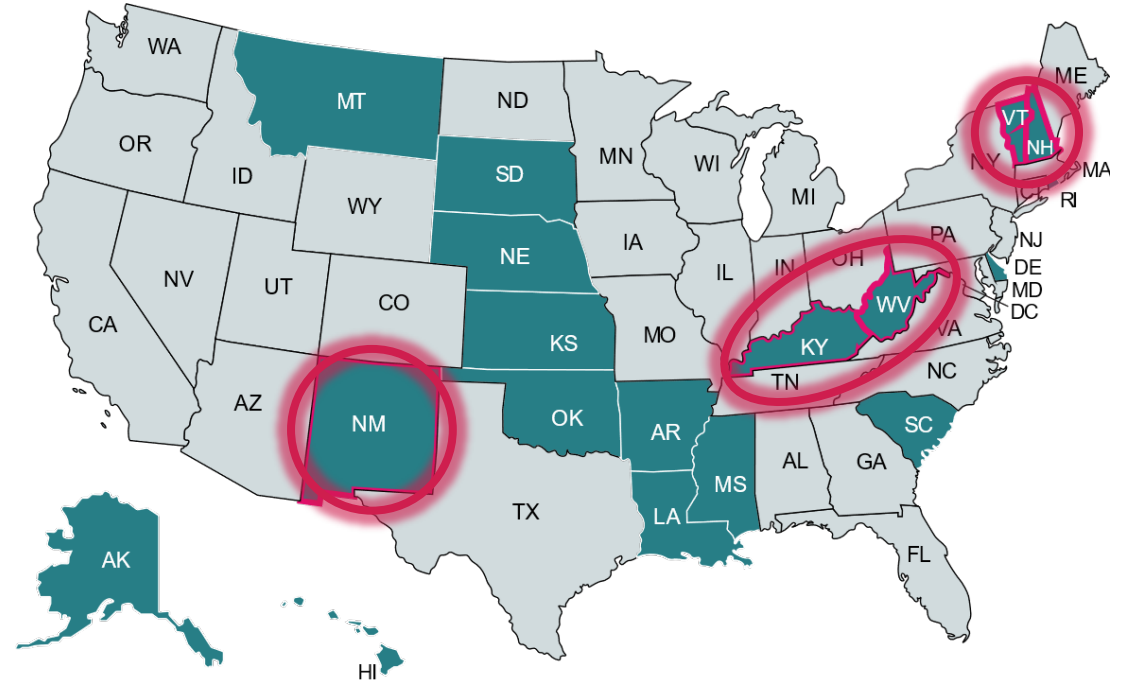
The ACT NOW Partnership

NICHD's Neonatal Research Network (NRN)



- Started in 1986
- 15 sites, mainly urban
- Many sites do not have high prevalence of NOWS

ECHO's IDeA States Pediatric Clinical Trials Network (ISPCTN)



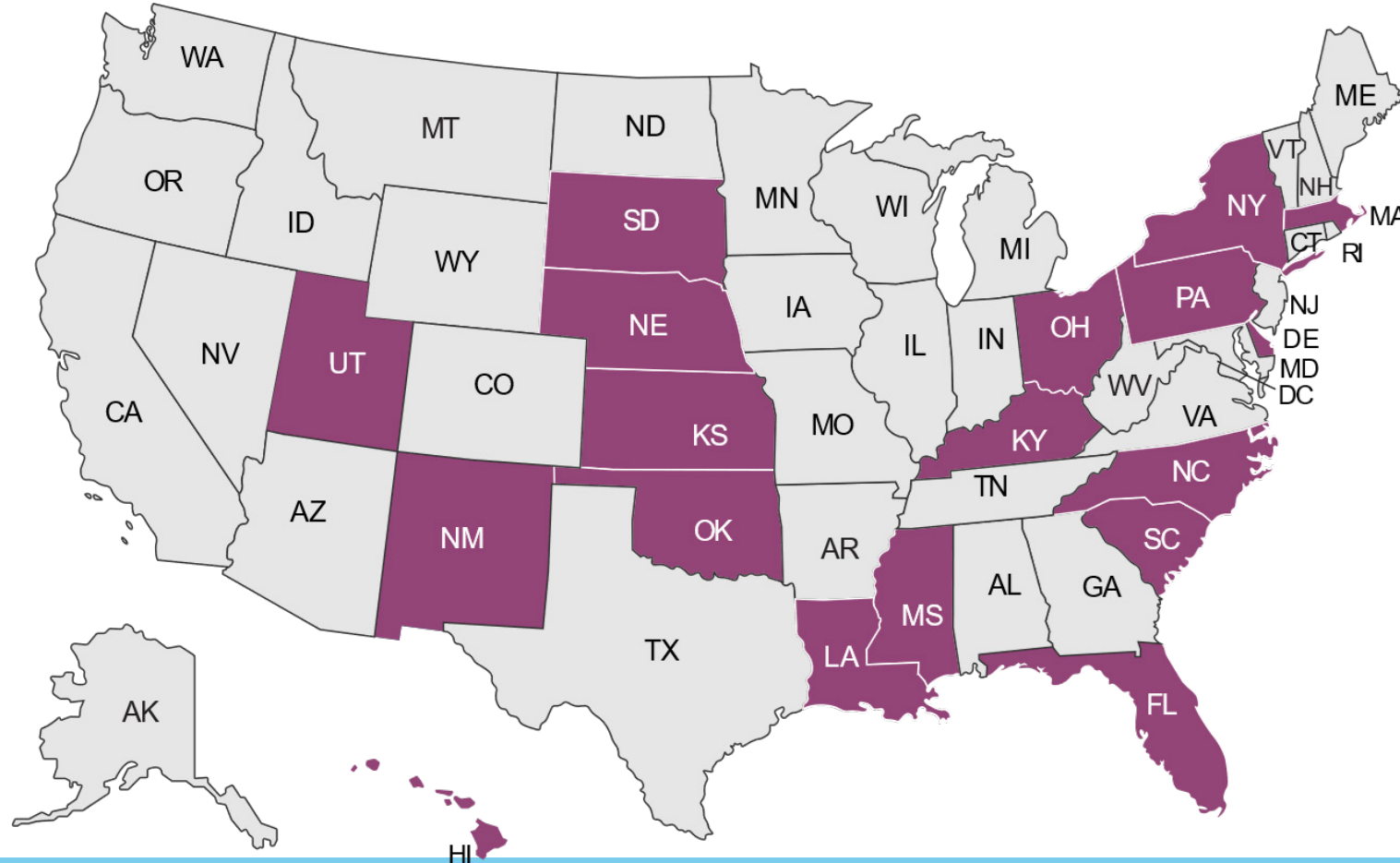
- Started in 2016
- 18 sites, mostly rural
- Sites overlap with areas of high prevalence of NOWS



Eat, Sleep, and Console for Neonatal Opioid Withdrawal

A Randomized Controlled Trial

26 Hospitals
in 18 States



Eat, Sleep, and Console Trial

Background and Objective

- Neonatal opioid withdrawal syndrome (NOWS)
 - Follows *in utero* opioid exposure
 - Opioid epidemic → high incidence of NOWS
 - If symptomatic enough, clinicians treat with replacement opioids
- Substantial variation in management of NOWS
 - No evidence-based standard of care
- Effectiveness and safety of new approach vs. usual care
 - Simpler assessment—Eat, Sleep, Console
 - Prioritize non-pharmacologic care, e.g., holding, swaddling, rocking
 - Caretaker involvement/empowerment



Eat, Sleep, and Console Trial Study Design

- Stepped wedge cluster randomized trial
 - Randomly allocated 26 hospitals to transition from usual care to Eat, Sleep, Console care at designated time
- Whole of practice change
 - Trained ~5000 nurses
- Led by 3 Early-Stage Investigators



Eat, Sleep, and Console Trial Short-term Outcomes



The NEW ENGLAND
JOURNAL of MEDICINE

Outcome	Adjusted Analysis (95% CI)†		
	Usual Care	Eat, Sleep, Console	Absolute Difference
Mean time until medical readiness for discharge — days‡	14.9	8.2	6.7 (4.7 to 8.8)
Percent who received pharmacologic therapy§	52.0	19.5	32.5 (25.9 to 39.0)

Did not find differences in safety outcomes through 3 months of age



Neurodevelopmental & Behavioral Follow Up

- 2-year follow up ongoing
 - Further inform safety of ESC care approach
 - Infant and family wellbeing and neurodevelopment
 - Anticipate completion summer 2024



Washington State Requires ESC Implementation by January 2025

State agencies announce changes in policy and best practices for infants and parents affected by substance use at birth

For immediate release: June 26, 2023 (23-087)

Contact: [DOH Communications](#)

Change incorporates “Eat, Sleep, Console” model of care for substance-exposed infants

OLYMPIA – The Washington State Department of Children, Youth, and Families (DCYF), in conjunction with the Department of Health (DOH), the Health Care Authority, and the Washington State Hospital Association, have updated state requirements and best practices that aim to improve the health of infants and parents affected by substance use at birth.

If there are no safety concerns, state policy now allows substance-exposed infants to receive voluntary wrap-around services without being reported to Child Protective Services. All hospitals should update policies to align with [state policy](#) and train staff no later than Jan. 1, 2025, to comply with federal requirements.

“While hospitals are still required to report cases where there is a safety concern for the child, not all families that have a child with prenatal substance exposure require child welfare intervention. We still want to connect these families with community-based services and resources that will support the family’s needs, reduce risks, and increase protective factors,” said DCYF Secretary Ross Hunter.

Updated requirements also include best practices for the clinical care of mothers/birth parents who need withdrawal/stabilization care at birth, as well as for infants being monitored or treated for withdrawal.

For years, the Finnegan Neonatal Abstinence Scoring Tool was the primary model of care for treating substance-exposed infants. However, a growing body of research shows infants treated using the Eat, Sleep, Console (ESC) model of care experience shorter hospital stays and are less likely to receive medication to treat neonatal opioid withdrawal symptoms. Eat, Sleep, Console prioritizes parental involvement and non-pharmacological care such as cuddling, swaddling, rooming-in with parents, chest/breastfeeding, and a quiet, dark room. The announced change formally recognizes Eat, Sleep, Console as the new best practice for birthing hospitals, and states medications and NICU admissions should no longer be the first line of treatment for infants exhibiting withdrawal symptoms.

“The opioid and overdose epidemic is disrupting the lives of a growing number of families in our state,” said Tao Sheng Kwan-Gett, MD, MPH, Chief Science Officer at DOH. “These changes will help every baby born in Washington get the healthiest start possible.”

The [DOH website](#) is your source for a healthy dose of information. [Find us on Facebook](#) and [follow us on Twitter](#). Sign up for the DOH blog, [Public Health Connection](#).

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Eat, Sleep, Console Trial

Achieving ECHO mission through informing policy and clinical practice



ISPCTN Today and in the Future

- Only NIH multi-center trial network focused on rural or underserved children
 - Advisory Council approved concept for 3rd 5-year cycle
- Studies within ISPCTN—and now with outside funding—reflect capacity building
- Part of NIH ecosystem of clinical trial networks to inform policy, program, practice



Observational & Intervention Research

ECHO Cohort

&

ECHO IDeA States Pediatric Clinical Trials Network



All 50 states, DC, PR



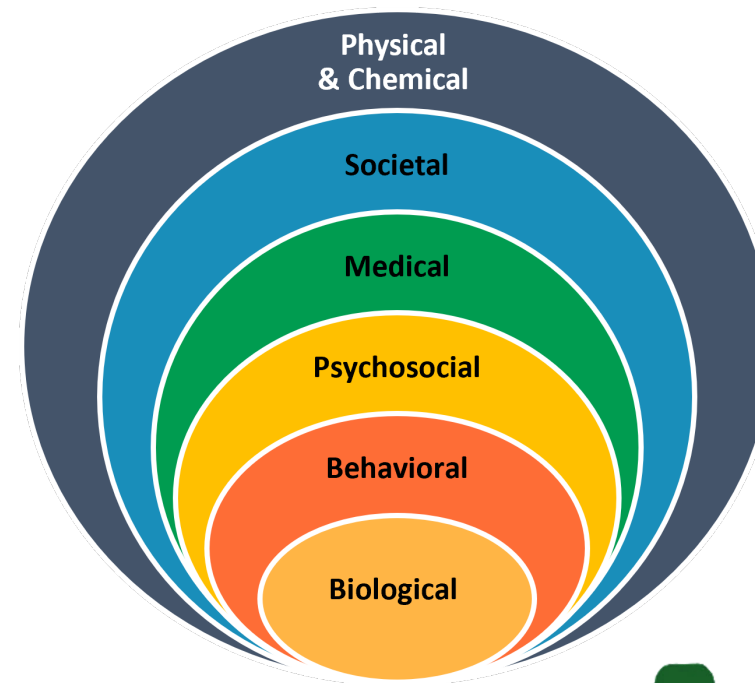
ECHO Cohort Overall Scientific Goal

Answer **solution-oriented questions** about effects
of
broad range of **early environmental exposures**
on
child health and development



Broad Range of Early Environmental Exposures

From
society
to
biology



ECHO Cohort Status

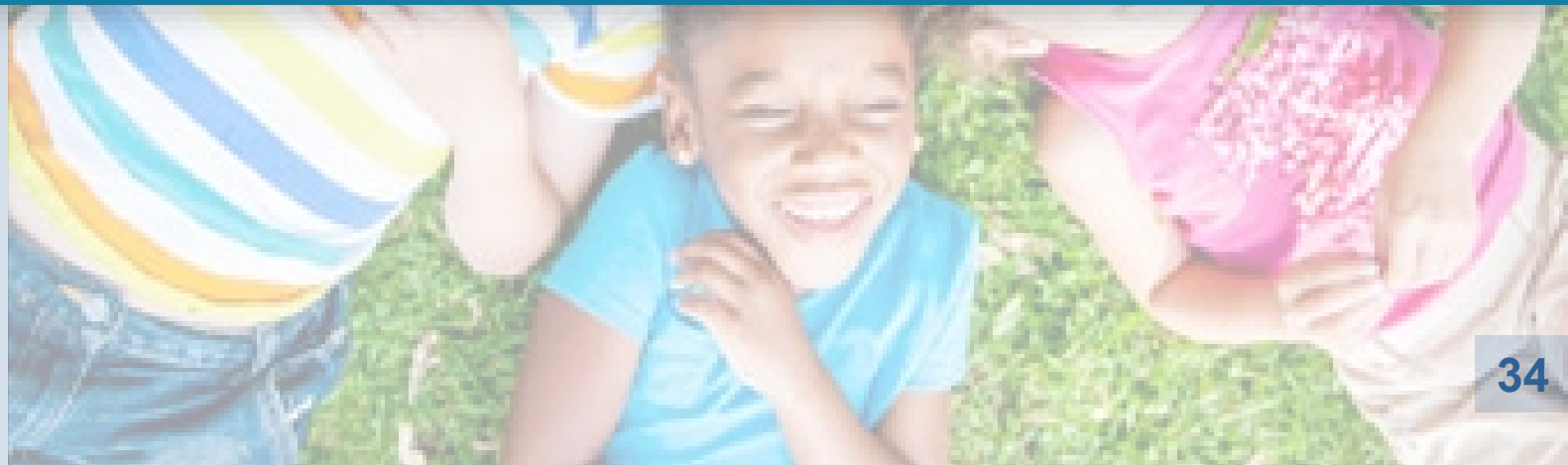
- Harmonized data from 107,000+ participants from ~70 pre-existing, ongoing longitudinal maternal-child studies
 - ~65,000 children
 - ~>30,000 active follow up
 - Extant assay data
 - ~55,000 newly assayed biospecimens
 - 100,000+ biospecimens in biorepository
- >1400 publications
 - >130 collaborative multi-award
 - Median relative citation ratio ~85th %ile





ECHO Science

Explaining asthma incidence & disparities



Disparities in Asthma Incidence

- Most research on frequency of asthma focused on prevalence, not incidence
 - Incidence data can reveal more about etiology



[JAMA Pediatr.](#) 2021 Sep; 175(9): 1–9.

PMCID: PMC8129904

Published online 2021 May 17. doi: [10.1001/jamapediatrics.2021.0667](https://doi.org/10.1001/jamapediatrics.2021.0667)

PMID: [33999100](https://pubmed.ncbi.nlm.nih.gov/33999100/)

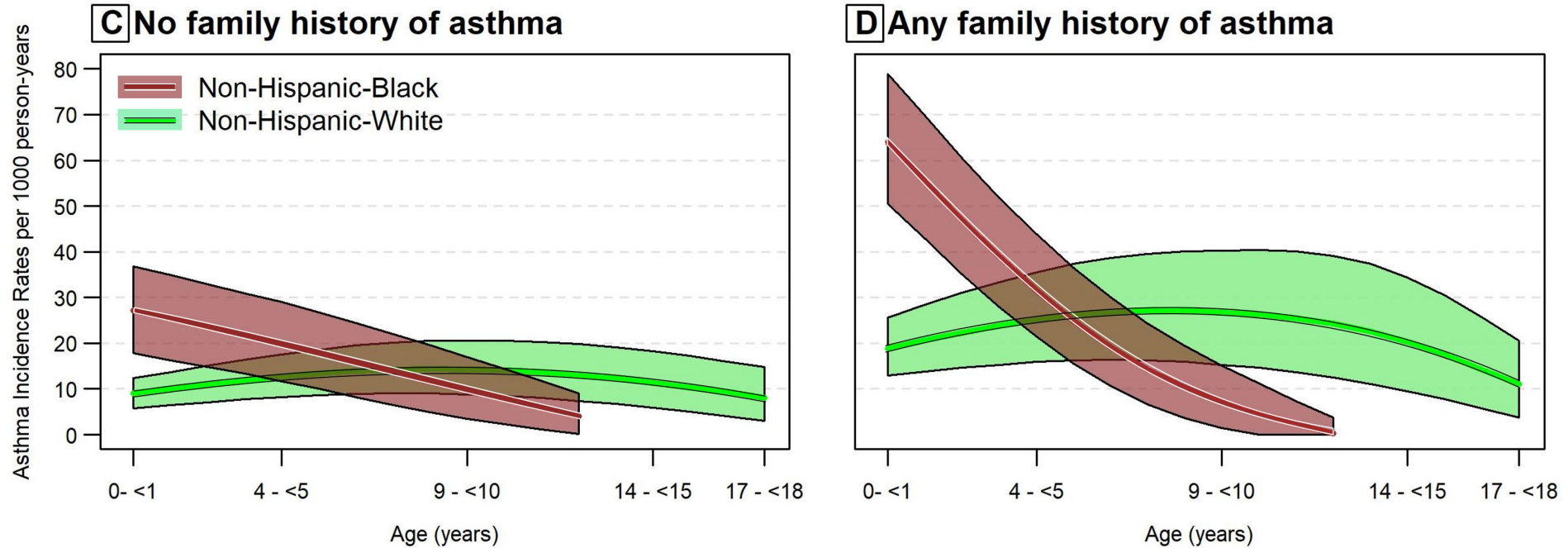
US Childhood Asthma Incidence Rate Patterns From the ECHO Consortium to Identify High-risk Groups for Primary Prevention

[Christine Cole Johnson](#), PhD, MPH,¹ [Aruna Chandran](#), MD, MPH,² [Suzanne Havstad](#), MA,¹ [Xiuhong Li](#), MAS,² [Cynthia T. McEvoy](#), MD, MCR,³ [Dennis R. Ownby](#), MD,¹ [Augusto A. Litonjua](#), MD, MPH,⁴ [Margaret R. Karagas](#), PhD,⁵ [Carlos A. Camargo, Jr](#), MD, DrPH,⁶ [James E. Gern](#), MD,⁷ [Frank Gilliland](#), MD, PhD,⁸ and [Alkis Togias](#), MD⁹, for the Environmental Influences on Child Health Outcomes (ECHO) collaborators

JAMA Network



Black Children Had Higher Asthma Incidence than White Children But Only in Early Childhood



32 ECHO Cohort sites, N = 12,471



Asthma Incidence

- Higher risk of asthma among Black children in early childhood
- Suggests prenatal determinants of disparities in asthma risk
- Air pollution is one such potential determinant
 - Socially patterned

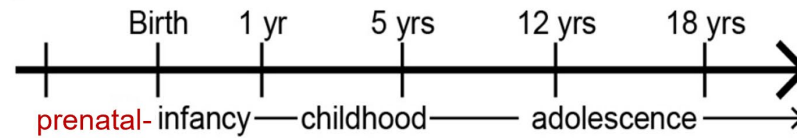


Place- & Time-based Exposures

1) Collect Addresses and Data



2) Construct Individual Residential Timelines



3) Geocode Addresses (lat/long coordinates)



4) Assign Exposures

- Neighborhood indices
 - Opportunity
 - Social vulnerability
 - **Air pollution**
 - Built environment

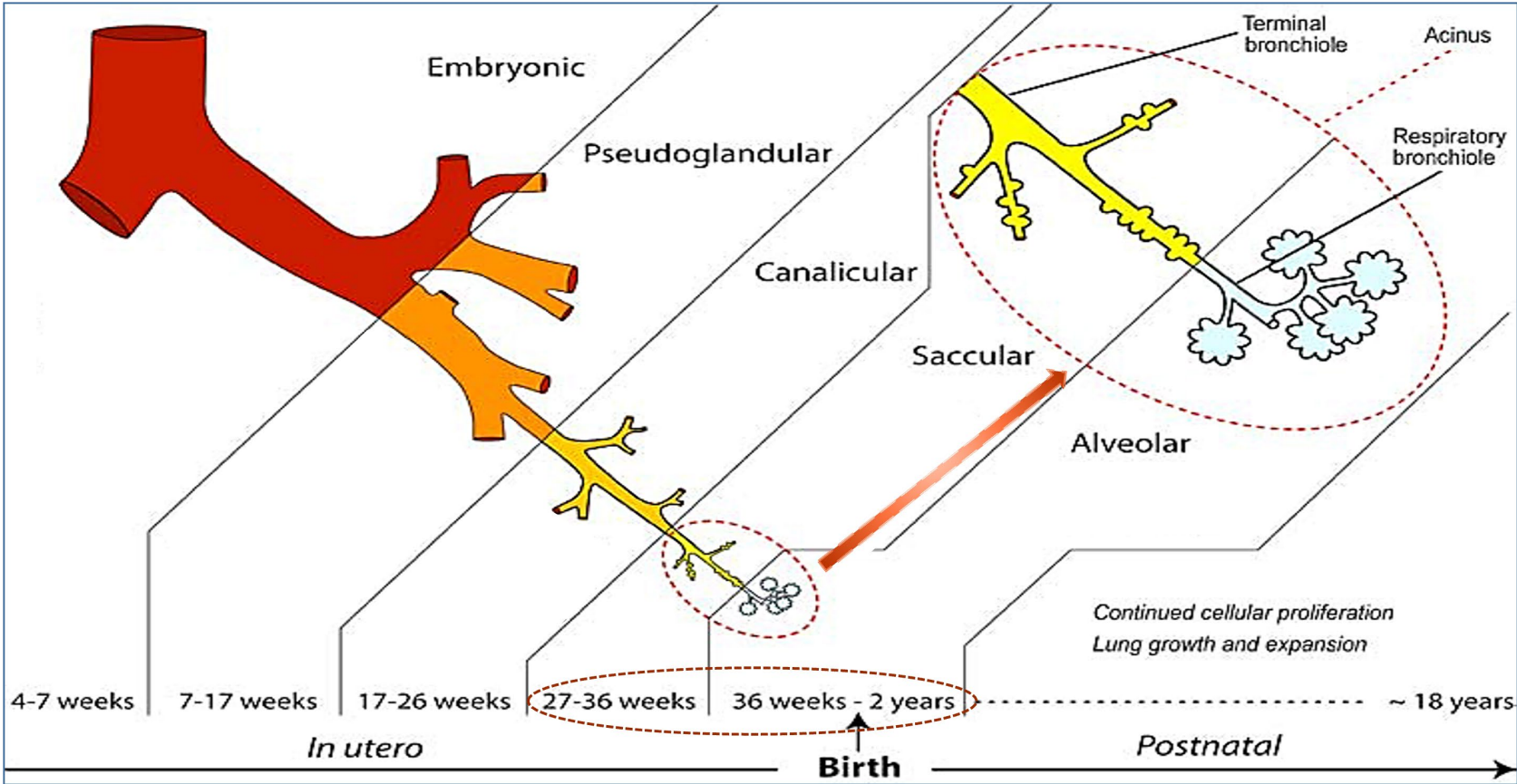


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Satellite &
Ground
Monitoring

Critical Windows for Air Pollution and Airways Outcomes

Late pregnancy?



ECHO Studies Suggestive

- Mid- to late- pregnancy exposure to PM_{2.5} associated with childhood wheeze and asthma
- Risk of asthma highest among children exposed to *ultra-fine particles* late (vs. earlier) in pregnancy



Take Away Messages

- Childhood asthma related to prenatal air pollution exposure
 - Later pregnancy—critical period
 - Small particles—may lead to new regulations
 - May help explain early childhood racial differences in asthma incidence





ECHO Science

Reducing childhood obesity

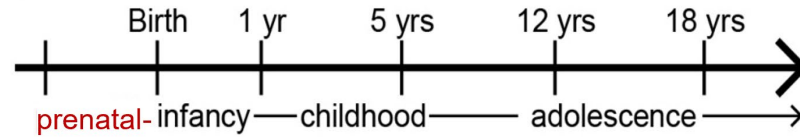


Place- & Time-based Exposures

1) Collect Addresses and Data



2) Construct Individual Residential Timelines

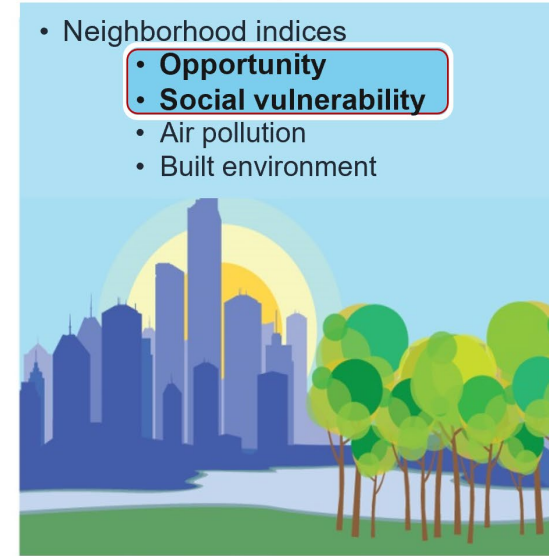


3) Geocode Addresses (lat/long coordinates)



4) Assign Exposures

- Neighborhood indices
 - **Opportunity**
 - **Social vulnerability**
 - Air pollution
 - Built environment



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Satellite &
Ground
Monitoring

Census Tract-Level Neighborhood Opportunity

- Child Opportunity Index (COI)
 - 29 indicators of neighborhood conditions important for children’s health
 - Three domains
 - Education; health and environment; social and economic
 - Higher scores: more favorable neighborhood opportunities

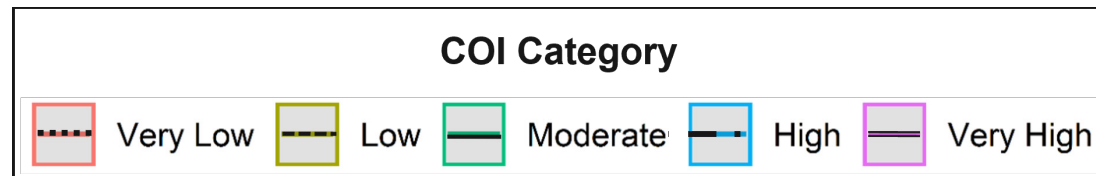


Residence in higher opportunity neighborhoods promotes lower obesity in children

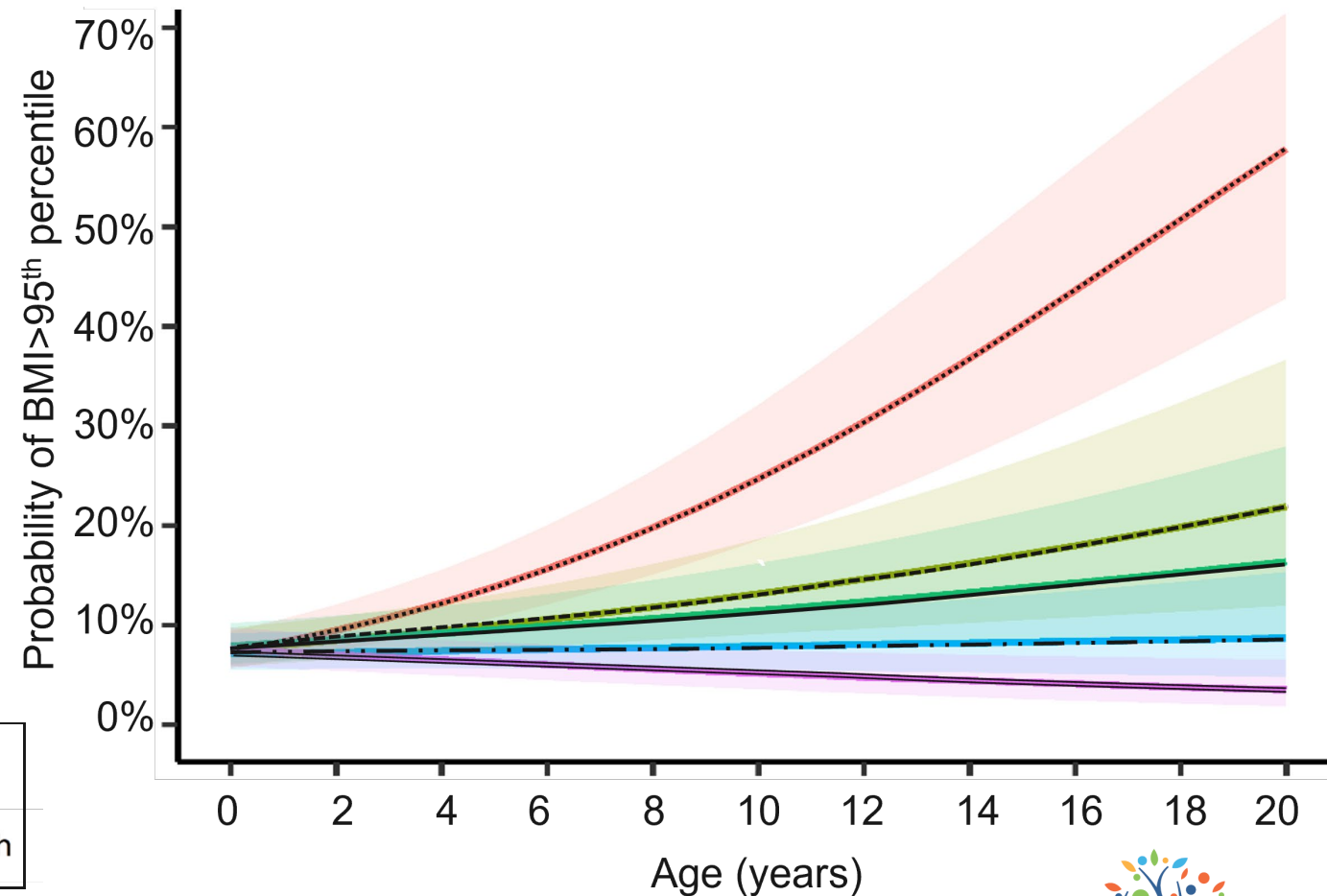
- Higher Child Opportunity Index predicted lower trajectories of mean BMI and risk of obesity across childhood and adolescence

- COI at birth better predictor than was COI later in childhood

54 ECHO Cohort sites; 20,677 children



COI at Birth and Risk of Obesity



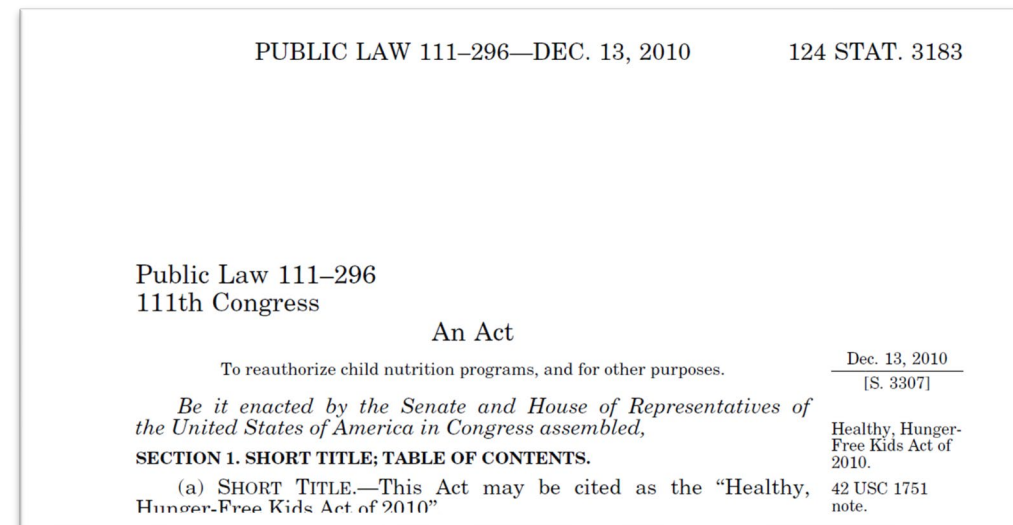
Take Away Messages

- Neighborhood factors predict BMI trajectory and obesity risk
 - Independent of individual and family sociodemographic factors
- Associations stronger with exposure at birth (vs. later)
 - Sensitive period?
- Associations stronger with outcome at later ages
 - Cumulative effect of opportunity?
- Supports community-level interventions to prevent obesity
 - Starting early in the life course



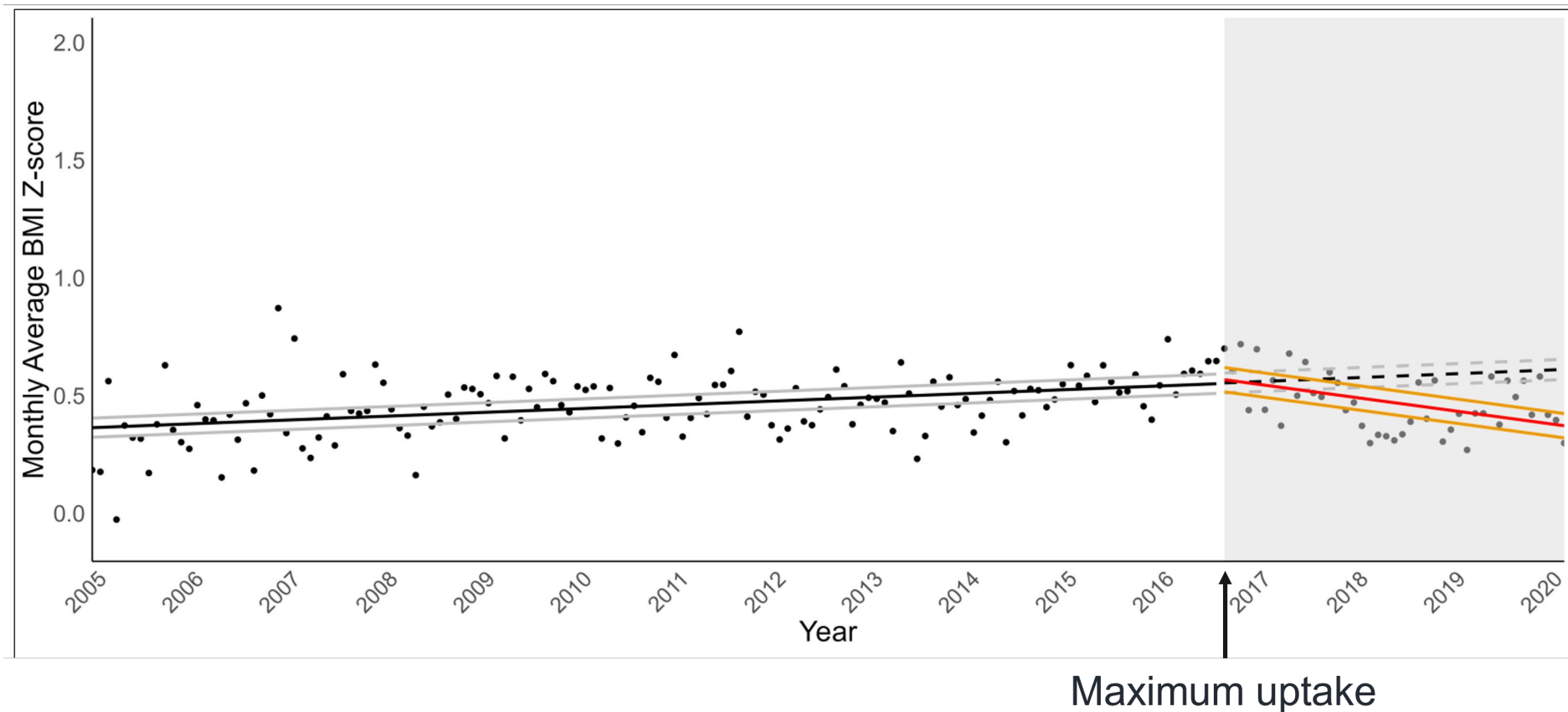
ECHO Addresses Effects of Natural Experiments

- Healthy, Hunger-Free Kids Act 2010
 - Set nutrition standards for National School Lunch, Breakfast, and Smart Snacks Programs
 - 10s of millions of children across U.S.
 - Previous study suggested HHFKA associated with better dietary quality
 - Effect on obesity rates?



Decrease in BMI After Implementation of Healthy, Hunger-Free Kids Act

50 ECHO cohorts—14,121 children ages 5-18 years—26,205 measurements



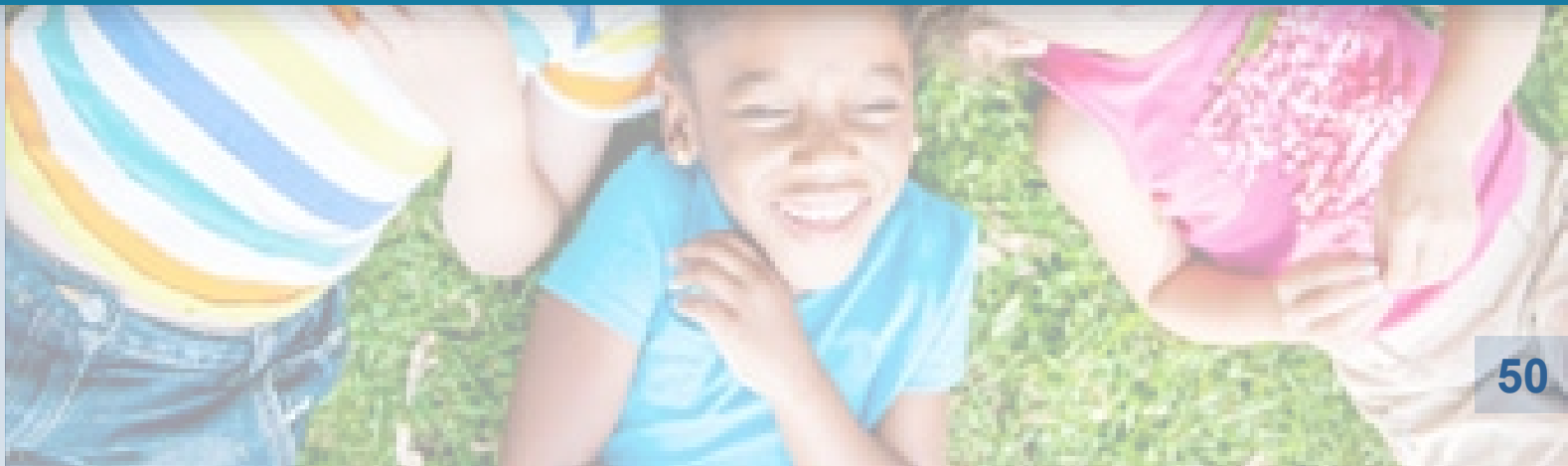
Take Away Messages

- Decrease in BMI in first few years following full implementation of Healthy, Hunger-Free Kids Act
 - Reversal of trend during decade before program implementation
- National policies like HHFKA can have widely beneficial effects
 - Salutary effect on children from lower-income families





Future of the ECHO Cohort



ECHO Cohort—Promise of Second 7 Years

Sep 2023 – May 2030

- Extend and expand the ECHO Cohort to further investigate the influences of a broad range of early exposures from society to biology, *including the preconception period*, on child health.
 - Standardized data and biospecimen collection protocol
- Large, diverse cohort from preconception through adolescence
 - Follow up >30,000 kids
 - Recruit >30,000 new pregnancies
 - Postpartum = preconception



ECHO Cohort

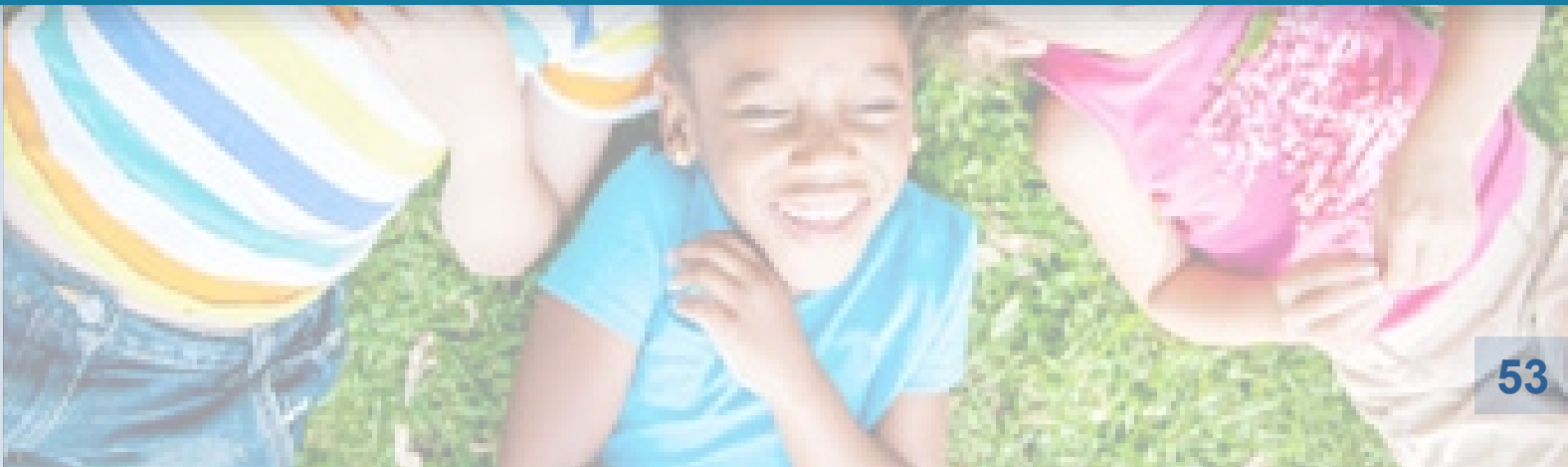
Potential Expanded/New Scientific Opportunities

- Health disparities and health equity
 - Early origins of disparities, which widen from childhood onwards
- Health trajectories
 - Identifying early critical periods
- Natural experiments or health crises
 - COVID follow-up, ready for next crisis
- Exposure to novel chemicals
 - Pregnant women and children exposed to many uncharacterized
- Biological pathways
 - Epigenetics, metabolomics, exposomics
- Social determinants of health
 - E.g., stress biology
- Resilience, reversibility
 - Puberty as sensitive period
- Media use
 - Pros and cons
- Preconception exposures
 - Social factors, behaviors, weight change, chemicals, etc.





ECHO as Nationwide Resource



Nationwide Research Resource

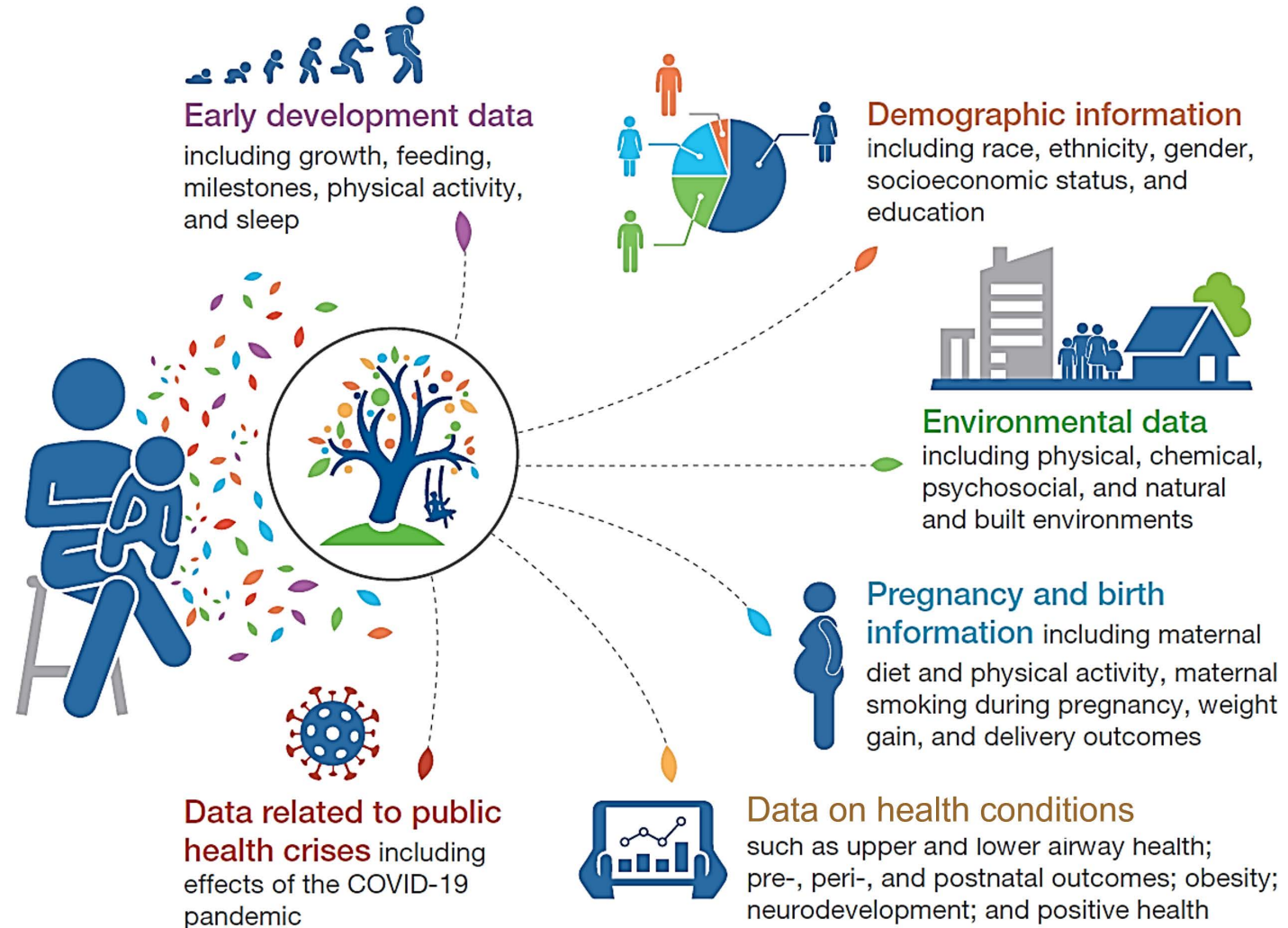
- Sharing protocols across NIH studies
 - Common data elements
- Controlled-Access Public Use Database
 - De-identified data on NICHD Data and Specimen Hub
 - Cohorts: Deposited at regular intervals
 - ISPCTN: Deposited after each trial
 - Access requests undergo administrative review
 - Funding opportunities to incentivize use



Nationwide Research Resource

Available ECHO Cohort Data on DASH

- Data from >60,000 participants
- >40 user requests to date



Overall Summary/Conclusions

- ECHO is a major investment in understanding early environmental influences on child health
- 5 key pediatric outcomes
- ECHO Cohort filling evidence gaps on long-term influences of prenatal and early childhood factors
 - Sample size, diversity, generalizability
 - New: preconception phase
- IDeA States Pediatric Clinical Trials Network addressing how to change practice and programs for rural or underserved kids
- US nationwide research resource





Questions and Discussion

