



The National Children's Study: Implications for Birth Defects Programs

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention
National Institutes of Health

U.S. Environmental Protection Agency

Overview



- Why the NCS was proposed
- How the NCS was planned
- What the NCS proposes to accomplish
- Status of the NCS implementation
- Some implications for birth defects programs
- Perspectives from one study center
- Discussion



President's Task Force



- 1998 Task Force on Environmental Health and Safety Risks to Children
- Charge – Develop strategies to reduce risk of environmental exposures to children
- Co-chairs
 - Secretary HHS
 - Administrator USEPA
- Members
 - 7 more cabinet officers
 - Senior staff
- Many risks not clear or quantified



President's Task Force (continued)



- Need for a longitudinal study of effects of environmental exposures (broadly defined)
- Consultation January 2000 endorsed Study:
 - large, bold
 - multiple agencies
 - public private partnerships
 - new money would be required



Rationale



- Converging factors
 - Increased vulnerability to environmental exposures in children in general
 - Exposures to some agents have caused serious developmental effects – lead, alcohol
 - Known current exposures of high frequency – pesticides, phthalates, violence, etc.
- Existing studies limited in size & scope
- Study needed to identify effects or assure safety
- Longitudinal design to infer causality with multiple exposures and multiple outcomes



PL 106-310: Children's Health Act of 2000



- (a) PURPOSE - ... to authorize NICHD to conduct a national longitudinal study of environmental influences (including physical, chemical, biological, and psychosocial) on children's health and development.
- (b) IN GENERAL - The Director of NICHD shall establish a consortium of representatives from appropriate Federal agencies (including the CDC and EPA) to:
 - (1) plan, develop, and implement a prospective cohort study, from birth to adulthood, to evaluate the effects of both chronic and intermittent exposures on child health and human development; and
 - (2) investigate basic mechanisms of developmental disorders and environmental factors, both risk and protective, that influence health and developmental processes...



Study Concepts



- Hypothesis driven
- Exposure begins with pregnancy
- Power to study high priority conditions (n~100,000)
- Gene environment interaction
- Consortium of Federal Agencies
- Public-private partnerships
- National resource for future studies



Planning Process for the NCS



- Interagency Coordinating Committee: NICHD, NIEHS, CDC, EPA
 - Federally Chartered Advisory Committee*
 - Expert Working Groups
 - Hypotheses
 - Measures/methods
 - Workshops*
 - Literature reviews/white papers*
 - Pilot Studies*
 - Program Office Staff
 - Study investigators (CC and Study Centers)
- * Findings on website: nationalchildrensstudy.gov



Examples of Hypothesis-defining Questions



- Does impaired maternal glucose metabolism during pregnancy cause obesity in children?
- Is maternal subclinical hypothyroidism associated with environmental exposure to endocrine active agents and with subsequent neurodevelopmental disabilities?
- Do pre- and post-natal exposures to endocrine-active environmental agents alter age at onset, duration, and completion of puberty?
- How is asthma incidence and severity influenced by the interaction of early life infection and air quality?



Priority Health Outcomes/Exposures



Priority Exposures	Examples
Physical Environment	Housing quality, neighborhood
Chemical Exposures	Pesticides, phthalates, heavy metals
Biologic Environment	Infectious agents, endotoxins, diet
Genetics	Interaction between genes and environment
Psychosocial milieu	Family structure, socio-economic status, parenting style, social networks, exposure to media and violence



Priority Health Outcomes	Examples
Pregnancy Outcomes	Preterm, Birth defects
Neurodevelopment & Behavior	Autism, learning disabilities, schizophrenia, conduct and behavior problems
Injury	Head trauma, Injuries requiring hospitalizations
Asthma	Asthma incidence and exacerbation
Obesity & Physical Development	Obesity, diabetes, altered puberty



Summary



- The National Children's Study is a longitudinal study of environmental factors and children's health in the U.S.
- A public health project unprecedented in terms of
 - Planning (interagency, public-private partnerships)
 - Scope (environment defined broadly)
 - Size (~100,000 US children)
 - Follow-up (21 years)
- A unique opportunity to study major public health issues using a life-stage approach



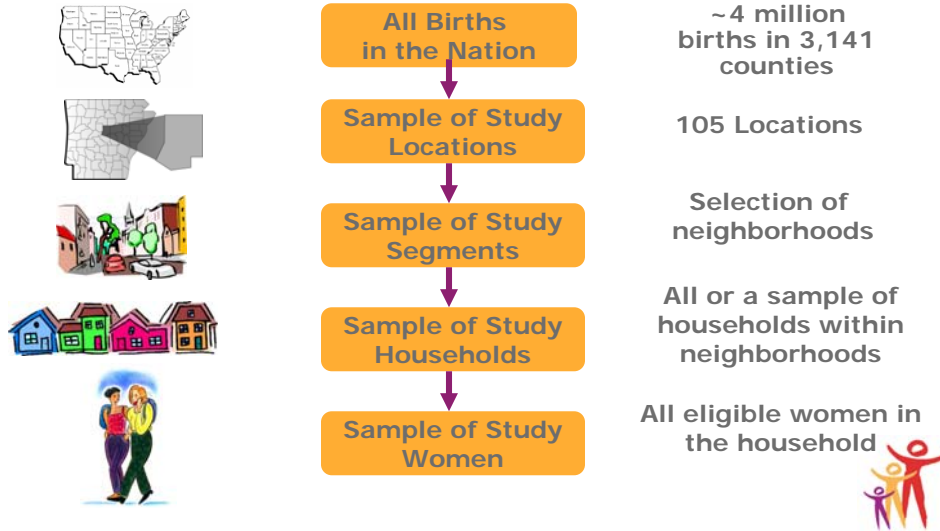
Sampling and Center strategies



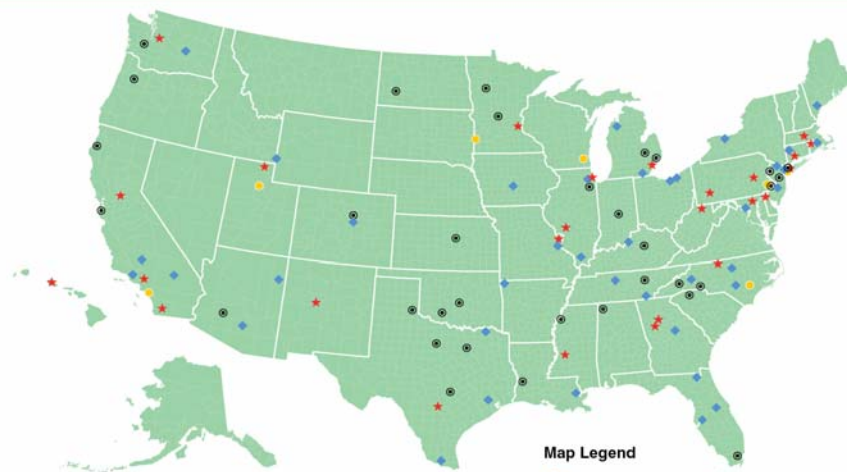
- National probability sample important
 - Exposure-outcome relationship representative of the U.S. population
 - Important exposures with varied and unknown distributions are not missed
 - Clustered for community attributes & logistics
- Centers of Excellence important
 - Broad scientific input
 - Community engagement and identity
 - Measures require center based expertise and facilities
- Probability sample by Centers
 - Unique combination
 - Requires flexibility and adaptation of center to the scientific design
 - Requires support and guidance by coordinating center



National Children's Study Sample



National Children's Study Locations



- Map Legend**
- ◆ 2008 Locations
 - ★ 2007 Locations
 - Vanguard Locations
 - 2009-2010 Locations



October 2008

Current Status of Study Centers and Locations



- 36 Centers plus Coordinating Center
- 105 Study Locations
 - 37 Wave One Locations (37 PSUS)
 - 36 Wave Two Locations (38 PSUS)
 - 32 Wave Three Locations (35 PSUS)
 - 15 Wave three locations awarded as contract options
 - 17 Wave three locations un-awarded
 - Wave three options to be exercised in the future, pending availability of funds
 - Wave three un-awarded locations to be included in a future procurement, pending availability of funds



Who will be enrolled?



- Household recruitment
 - Women who are in the first trimester of pregnancy
 - Women who are planning a pregnancy
 - Women of child bearing age who are not planning pregnancy but could become pregnant during the enrollment period
- Supplemental recruitment
 - Prenatal care providers
 - Community based recruitment of eligible women





Schedule of Visits – Core Protocol



**Preconception (high probability) - one face to face visit,
phone follow-up**

1st Trimester	3 years
2nd Trimester UTZ	5 years
3rd Trimester	8 years
Delivery Visit	12 years
6 months	16 years
12 months	20 years

 Clinical Setting
 Home



Data Collections



- Interview and history
- Cognitive measures
- Serology and medical data
- Housing and living characteristics
- Family and social experiences
- Neighborhood, community, and school characteristics
- Environmental samples: air, water, dust from home, day care, school
- Biomarkers: blood, breast milk, hair, tissue, etc.
- DNA



Environmental and Biomarker Laboratory plans



- Central Repository – RFP posted, review complete, award anticipated in March 2009
- Environmental Laboratory Capacity
 - Solicitation for interim E Lab contract(s) in early 2009 off GSA schedule – award anticipated in March/April
 - Full and open solicitation 2010
- Biomarker Laboratory
 - MOU in place for NCEH/CDC biomarker analyses
 - Commercial biospecimen labs as necessary



Laboratory Pilot Studies



- Environmental samples
 - Prescreening of collection materials
 - Stability of samples
 - Preparation of samples
 - Analysis of samples
- Biospecimens
 - Development and characterization of QC pools
 - Prescreening of collection materials
 - Stability of biospecimens
- Prevalence of early environmental biomarkers in first 500 NCS mothers and infants
- Digital Microfluidics technology for biospecimen analyses comparison with conventional methods



NCS: A Platform for Adjunct Studies



- Involve a portion of the NCS cohort – participants and/or their collected samples – from one or more locations, to address additional or in-depth questions
- Examples
 - Genomic analysis for targeted gene-environment interactions
 - Functional neuro-imaging of exposed subjects for mechanism of effect on child development
- Funding: R01 or other grant; public private partnership (foundation, industry,...)...
- Review and approval process established at NCS Program Office



Use and access to data



- Planned analyses of core hypotheses by community of NCS investigators
- Public use data sets for respective phases of the Study by level of confidentiality as soon as possible
 - Totally anonymous limited data set with open access
 - De-identified with requirements for access
 - Restricted to use in specific location with safeguards
- For Federal programs and missions



Current status of the NCS



- **September 2008** - Award Wave II Locations and Centers
- **October 2008** – OMB approval for the Pilot of full protocol
- **September-November 2008** – IRB approvals for Pilot at the starting VCs
- **January 2009** – Full Pilot begins enrollment for Group I Vanguard Locations – Duplin Co., NC, Queens, NY
- **April 2009** – Full Pilot begins enrollment for Group II Vanguard Locations (remaining VC Locations)
- **July 2010** – Begin Full Study all Wave I & VC Locations
- **July 2011** – Begin Full Study all Wave II Locations
- **July 2012** – Begin Full Study all Wave III Locations



Status of Funding



- FY00–6: \$50m from existing budgets of lead agencies
 - Infrastructure: Study plan, Coordinating Center, Vanguard Centers
 - Scientific development: 30 workshops, 20 scientific reviews, 19 pilot studies; hypotheses, exposure and outcome measures, protocol
- FY07: \$69m appropriated
 - Prepare to recruit/enroll at Vanguard Centers
 - Information Management System
 - Establish 2007 Study Centers
- FY08: \$110.9m appropriated
 - Begin recruitment in Vanguard Centers
 - Prepare for recruitment in 2007 Study Centers
- FY 09: \$193 m requested
- To conduct the full Study: FY08–34 ~ \$3.2 B projected



Contact Information



- Check the Web site: <http://NationalChildrensStudy.gov>
- Join the listserv (via the Web site) for news and communication
- Contact us at ncs@mail.nih.gov or 301.594.9147
- CDC contacts: Marshalyn Yeargin-Allsopp (mxy1@cdc.gov); Adolfo Correa (aic8@cdc.gov), Amy Branum (ZVL5@cdc.gov), Mary Mortensen (zeo5@cdc.gov)

