



THE NATIONAL CHILDREN'S STUDY

December 8, 2010

Marion J. Balsam, MD
Research Partnerships Program Director

National Children's Study
Eunice Kennedy Shriver National Institute of
Child Health and Human Development

The National Children's Study



- Congressionally mandated - authorized by the Children's Health Act of 2000
- Led by NICHD in collaboration with CDC, USEPA, NIEHS...
- Largest long-term study ever conducted in the U.S. concerning environmental effects on child health and development; unprecedented in scope and complexity
- Environment broadly defined: chemical, biological, physical and psychosocial-cultural environments
- Gene-environment interaction and gene expression



Rationale for the National Children's Study



- Numerous conditions/outcomes with suspected, but as yet unproven, environmental contributors: autism, diabetes, birth defects, premature birth, learning disabilities...
- Exposures of concern but with uncertain impact: pesticides, plasticizers, media violence...
- Children are more vulnerable to certain exposures because of their metabolism, behavior, developmental phases...
- Life-course (longitudinal) design is key to linking multiple exposures with multiple outcomes over time



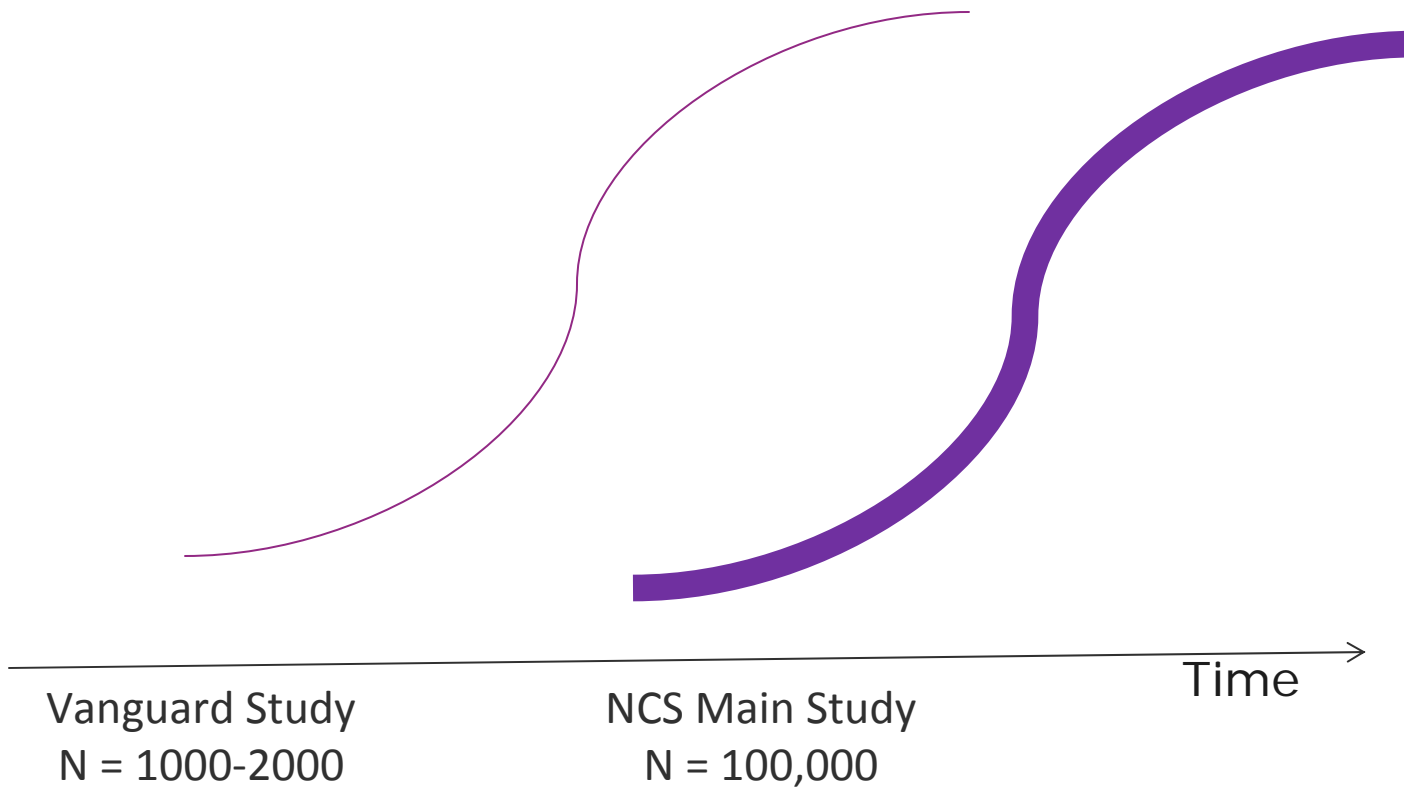
Key Concepts for the NCS



- Longitudinal study of 100,000 children from before birth to age 21
- National sample generalizable to the U.S. population
- Clustered in segments within 105 locations in the U.S.
- Contracted Study Centers for data collection
- Enroll pregnant women and those likely to become pregnant, ages 18-49
- Vanguard Study and Main Study will run in parallel
 - Vanguard (pilot) Study: methodology
 - Main Study: exposure/outcome linkages
- Public-use data sets



Vanguard Study-Main Study Relationship



Phased Implementation: The Current Vanguard Phase



- A platform to evaluate procedures and resource requirements, to inform an evidence-based Main Study
- Study recruitment (alternate strategies)
- Logistics and operations
- Study visit choreography and assessments (~250: laboratory assays, physical measures, tests, questionnaires...)

From the perspectives of

- Acceptability: impact on participants and study infrastructure; scalability; informative value
- Feasibility: technical performance, reliability, validity
- Cost: personnel/resources, level of effort, \$\$\$



Vanguard Study Content



- Minimal visit configuration: focus is methodology
- Limited cohort size
- Recruitment, operations and study visit assessments
- Formative Research:
 - Focused methodological studies initiated and funded by the NCS
- Supplemental Methodological Studies:
 - Focused methodological studies initiated, planned, implemented and funded from '**outside**' of the NCS planning process



Recruitment Strategy



- Household recruitment: 7 original Vanguard Centers, deployed January and April 2009
- 30 new Vanguard Locations, 3 groups of 10 each to test alternate strategies: deployment planned in 2010
 - Provider based recruitment
 - Enhanced household method: intensive/professional outreach
 - High-Low: two tier comparing high vs low intensity efforts
- Primary outcome measures:
 - Recruitment and retention (through the birth visit)
 - Associated costs
 - Demographic characteristics
 - Any potential bias inherent in any of the strategies



Supplemental Methodological Studies (Vanguard Phase)



- Modular focused studies initiated from outside the NCS protocol planning process
- Pertain to feasibility, acceptability or cost of a methodological aspect, to inform the Main Study
- Integrates with the Vanguard phase, involving
 - NCS participants
 - NCS biospecimens or environmental samples
- Funded from 'outside' the NCS
- Instructions and application: on the NCS website under the 'Research' tab



Planning the Main Study



- Core protocol: Exposure-outcome relationships and gene-environment interaction
 - Cohort large enough to study uncommon conditions with important public health impact
 - Analyses of entire cohort, sub-studies, case control studies...
- Adjunct Studies: Opportunities to leverage the NCS
 - Modular, focused studies integrated with Main Study
 - Address areas of investigator or community interest
 - Complement the Main Study protocol
 - A good 'fit' with the NCS without excessive burden
 - Initiated/funded from 'outside' the NCS appropriation



Priority Exposures and Outcomes



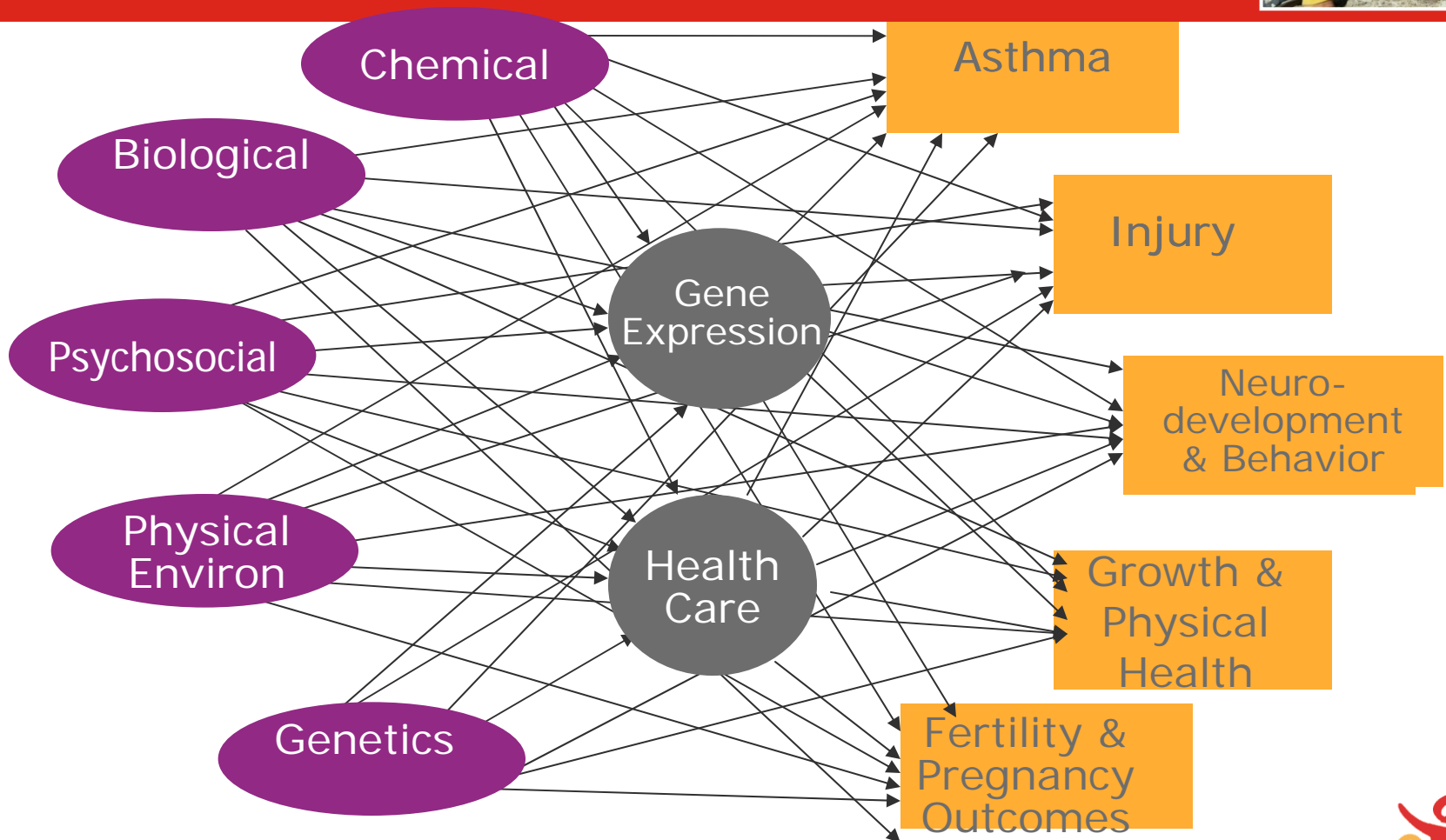
Priority Exposures	Examples
Physical Environment	Housing quality, neighborhood...
Chemical Exposures	Pesticides, flame retardants, heavy metals, plasticizers...
Biological Environment	Nutrition, infections, endotoxins, intra-uterine environment...
Genetics	Interaction between environmental factors and genes...
Psychosocial-cultural Milieu	Families, socio-economic status, cultural institutions, social networks...



Priority Health Outcomes	Examples
Pregnancy Outcomes	Birth defects, preterm delivery... EARLY RESULTS
Neurodevelopment and Behavior	Autism, learning disabilities, behavioral problems, schizophrenia...
Injury	Head trauma, injuries requiring hospitalization...
Asthma	Asthma incidence and exacerbation...
Obesity and Physical Development	Obesity, diabetes, altered pubertal development, etc.



Associations and Interactions: The Scope of the Study



Study Components Under Consideration



- Home visits, NCS clinic visits, day care site and school visits
- Diaries, self-administered questionnaires, interviews
- Interim telephone contact between visits
- Demographic, historical, occupational, cultural information
- Clinical event data collection: diagnoses and interventions
- Physical assessments: anthropometrics, fetal ultrasound, video/photos
- Neuro-developmental, behavioral, mental health assessments
- Nutritional assessments
- Physical activity assessments
- Biological specimen collection/analyses
- Environmental sample collection/analyses



Potential Laboratory Collections - Mother, Father, Child



BIOSPECIMENS:

Blood Placenta Urine Cord/Cord blood Breast Milk
Saliva Meconium Hair/Nails

Clinical analytes include:

metabolic, endocrine, reproductive, nutritional, infectious,
genetic, inflammatory, immunological...

Environmental toxicants: pesticides, volatile
organic compounds, flame retardants, cotinine,
plasticizers, heavy metals, etc.

ENVIRONMENTAL SAMPLES:

Soil Water Indoor Air Dust
Pollutants and environmental toxins



Proposed Biomonitoring for Chemical Agents



Blood	Polychlorinated biphenols (PCBs), persistent and non-persistent pesticides, polybrominated diphenyl ether (PBDE), perfluorinated compounds, flame retardants; perchlorate; lead, mercury, cadmium; bisphenol A (BPA)...
Urine	Alkyl phenols, mercury, speciated arsenic, perchlorate, phytoestrogens, halogenated phenols (pentachlorophenol/PCP), phthalates, atrazine, organophosphates, carbamates, pyrethroids, dithiocarbamates (EBDC/ETU), cadmium...
Breast milk	dioxins/furans; organochlorine pesticides; PCBs...
Meconium	cotinine, organophosphate metabolites...
Nails	mercury (organic, inorganic)...
Hair	cadmium, cotinine, mercury, nicotine...



Proposed Environmental Measures



- Indoor Air: metals, volatile organic compounds, carbonyls, nitrous oxide, ozone...
- House Dust: allergens, endotoxins, mold, inorganics/metals, semi-volatile organic compounds (SVOCs), pesticides (pyrethroids)...
- Tap Water: disinfection byproducts, volatile organic compounds...
- Soil: SVOCs (Pesticides – organophosphates, carbamates, pyrethroids)...



Mental Health and Neuro-development: Autism and Learning Disabilities



- Mental health and neuro-development are amongst the highest NCS priorities
- Considerations include study visit assessments regarding:
 - Mental health, depression, anxiety
 - Perceived stress, social support, family relationships, child rearing practices, domestic violence
 - Neuro-development: Bayley Scales of Infant Development; Ages and Stages Questionnaire...
 - Child attachment, temperament, socio-emotional competence, behavior
 - Autism: screening tools such as the M-CHAT (Modified Checklist for Autism in Toddlers) and other recommendations from the Autism Speaks Advisory Panel report of Sept 2010



What Do We Expect the NCS to Mean to Children's Well-Being?



- Identify environmental factors which influence health, development and behavior as well as resiliency
- Contribute to the understanding of gene-environment interaction
- Gather evidence-based data to guide decisions about healthcare, health policy and research methodology pertaining to children's physical and mental health
- Achieve economic benefits through cost avoidance
- Ultimately to improve health and well-being
- Resource for future research



Contact Information



- For information about the NCS:
www.NationalChildrensStudy.gov
- E-mail: ContactNCS@mail.nih.gov

Marion Balsam, M.D.
Research Partnerships Program Director
The National Children's Study

