

4. AIMS AND HYPOTHESES

4.1 Specific Study Aims

The National Children's Study has several broad aims. These aims will be served through a program of current, carefully designed research questions and the creation of a resource for future research questions. The specific aims of the Study are:

- (1) Determine the presence or absence of effects, both harmful and helpful, related to the timing, frequency, magnitude, and duration of specific chemical, physical, biological, and psychosocial exposures in children's environments from preconception to adulthood.
- (2) Determine possible environmental contributions to, or causes of, specific diseases and conditions of children, including, but not limited to, prematurity and other outcomes of pregnancy, neurological and developmental disorders, psychiatric and behavioral disorders, altered physical development and sexual maturation, obesity and insulin resistance, asthma, and injuries.
- (3) Determine how genotypic variation and mechanisms, and the interaction of genes with environmental factors, influence disease risk and developmental trajectories in children.
- (4) Serve as a national resource for future studies of child health and development by providing a rich database and repository of environmental and biological samples and information that can be used to address future questions and hypotheses.

4.2 Core Hypotheses

The rationale for a large longitudinal study with multiple classes of exposure, outcome, and genetic measures to address the Study aims has been described. These aims are the sum of specific hypotheses examining how environmental and genetic factors may affect children's health and development. Thus, the NCS can be best understood as a broad program of research comprising multiple separate and overlapping hypothesis-driven studies, each requiring this proposed design and size.

The NCS planners recognize that framing hypotheses is essential to guide study planning and to assure that important questions can be addressed. Nonetheless, not all important or answerable questions are necessary or even possible to state. However, in planning the Study a standard was established that a supporting hypothesis must be required for inclusion of measures or design elements in the Study. Within broad priority exposure and outcome areas, the NCS has framed 28 well-defined core hypotheses to fulfill its aims to ascertain whether exposures to environmental factors either adversely or positively affect the health and development of children and whether certain health conditions of children result from environmental exposures.

To derive the core study hypotheses, the NCS relied on the expertise and input of a Federal advisory committee (National Children's Study Advisory Committee [NCSAC]), its working groups, and the general public. Within priority areas, many hypotheses were proposed by working groups and other entities and then considered by the NCSAC, which made recommendations concerning their relevance

and prioritization. Ultimately, the NCS Interagency Coordinating Committee¹ established the core Study hypotheses (see Table 4-1). A more detailed listing by priority outcome area appears in Appendix A-1. Fully documented and referenced hypotheses across different priority areas are found in Appendix A-2. These hypotheses identify relevant environmental exposures including physical, chemical, biologic, and psychosocial factors that affect the identified priority outcomes, including pregnancy outcomes, neurodevelopment and behavior, injury, asthma, obesity and growth, child health and development, and reproductive development. Many hypotheses also take into consideration the vital impact of gene-environment interactions or the effect of access to health care services on health and well-being. The potential avenues of investigation are too numerous to cite, but a number of specific study questions have been developed to assure that key measures are obtained, and that the sample of participants and the study design are adequate to address the questions. Acknowledging that science evolves, this list of hypotheses is expected to change as additional existing hypotheses are refined, omissions of important questions are identified, and other hypotheses become outdated.

¹ The Interagency Coordinating Committee is comprised of senior Federal staff scientists assigned since 2000 to lead the development of the NCS on behalf of the lead Agencies supporting the NCS: the Department of Health and Human Services, National Institute of Child Health and Human Development, National Institute of Environmental Health Sciences, Centers for Disease Control and Prevention, and the U.S. Environmental Protection Agency.

Table 4-1. Hypothesis Topics of the National Children's Study

<ul style="list-style-type: none">■ Birth defects from impaired glucose metabolism■ Increased risk of preterm birth from intrauterine exposure to mediators of inflammation■ Increased risk of fetal growth restriction, preterm birth, birth defects and developmental disabilities in children born through assisted reproductive technologies■ Maternal subclinical hypothyroidism and neurodevelopmental disabilities/adverse pregnancy outcomes■ Non-persistent pesticides and poor neurobehavioral and cognitive skills■ Prenatal infection and neurodevelopmental disabilities■ Gene-environment interactions and behavior■ Prenatal and perinatal infection and schizophrenia■ Family influences on child health and development■ Impact of neighborhood and communities on child health■ Impact of media exposure on child health and development■ Social institutions and child health and development■ Influences on healthy development■ The role of prenatal maternal stress and genetics in childhood asthma■ Exposure to indoor and outdoor air pollution, aeroallergens, and asthma risk■ Dietary antioxidants and asthma risk■ Social environmental influences on asthma disparities■ Early exposure to structural components and products of microorganisms decreases the risk of asthma■ Environmental exposures interact with genes to increase the risk of asthma and wheezing in children■ Obesity and insulin resistance from impaired maternal glucose metabolism■ Obesity and insulin resistance from intrauterine growth restriction■ Breastfeeding associated with lower rates of obesity and lower risk of insulin resistance■ Fiber, whole grains, high glycemic index and obesity and insulin resistance■ Genetics, environmental exposures, and type 1 diabetes■ Repeated mild traumatic brain injury and neurocognitive development■ Behavioral exposures, genetics, and childhood or adolescence onset aggression■ Antecedents and resiliency to traumatic life events in childhood■ Hormonally active environmental agents and reproductive development
