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National Children's Study
Federal Advisory Committee (NCSAC) 9th Meeting
March 4–5, 2004
Holiday Inn Select
Bethesda, MD

This meeting was held in conjunction with the National Children's Study, which is led by a consortium of federal agency partners: the U.S. Department of Health and Human Services (including the National Institute of Child Health and Human Development [NICHD] and the National Institute of Environmental Health Sciences [NIEHS], two parts of the National Institutes of Health, and the Centers for Disease Control and Prevention [CDC]) and the U.S. Environmental Protection Agency (EPA).

Welcome
Review Agenda, Meeting Goals and Objectives

Donald Mattison, M.D., NCSAC Chair, NICHD, NIH, DHHS

Dr. Mattison welcomed National Children's Study Advisory Committee (NCSAC) members and other participants to the ninth meeting of the NCSAC. The stated goals of this meeting were to:

- Focus on the transition from National Children's Study (Study) planning to implementation
- Establish a specific set of goals and objectives for the June 2004 NCSAC meeting
- Determine the status of work products submitted to date by the Working Groups, including current proposed hypotheses, measures of exposures and outcomes pilot studies, and workshop reports
- Determine the activities required to finalize these products
- Consider measurements of healthy development
- Discuss timelines for phasing out or reconfiguring various Working Groups
- Discuss an appropriate response to the President's Council on Bioethics' request to include an assessment of artificial reproductive techniques as part of the Study.

Jan L. Leahey, NCSAC Executive Secretary, NICHD, NIH, DHHS, provided an overview of NCSAC administrative issues. Ms. Leahey said that the NCSAC's 10th meeting will be held June 28–29, 2004, in the Washington, DC, area. The minutes for the NCSAC eighth meeting have been posted to the Study's Web site. To date, there have been no comments on these minutes. Ms. Leahey asked participants to forward briefing materials and other information to the Program Office to keep the Study Web site current. Ms. Leahey listed the following action items for the meeting:

- Recommendations on Working Group work products
- Determine where individual Working Groups stand
- Determine what additional products are needed
- Determine what the NCSAC can do to facilitate getting those products
- Discuss future schedule and activities of the NCSAC and Working Groups.

Program Office Update
Study Timelines, Institute Updates

Peter C. Scheidt, M.D., M.P.H., National Children's Study Director, NICHD, NIH, DHHS

Dr. Scheidt summarized the major events and activities since the last NCSAC meeting in December 2003:

- **Program Office Staffing.** Dr. Scheidt listed the following full-time staff members who joined in the fall of 2003:
  - Ruth A. Brenner, M.D., M.P.H., protocol development leader
  - Sarah S. Knox, Ph.D., behavioral scientist
  - Warren Galke, Ph.D., data management/clinical coordinating center project officer
  - Marion J. Balsam, M.D., partnerships/project officer.

  Current part-time/detailed scientists in the Program Office include:
  - Kenneth Schoendorf, M.D., M.P.H.
  - Carole A. Kimmel, Ph.D.
  - James J. Quackenboss, M.S.
  - Rebecca Brown, M.P.H., M.E.M.
  - Lester R. Curtin, Ph.D.

  Three new part-time/detailed scientists have joined the staff since December 2003:
  - Terry Cox, M.D., Ph.D., epidemiologist, neuro-opthalmologist, biostatistician
  - Terry Dwyer, M.D., M.P.H., protocol development, cohort and epidemiological studies specialist
  - Tracey Thomas, P.H.D., biomarker specialist.
- **Contracts.** Battelle, technical support contractor for the Study Program Office, is currently assigned the following tasks:
  - Provide background information for the Study sampling strategy
  - Identify developmental measures in four domains for the Study
  - Develop a sample protocol for the Practice Based Research Network (PBRN) feasibility study
  - Perform power analyses for social environment hypothesis
  - Review extant databases for the Study
  - Review literature and write a white paper on measurement of housing quality.

  The information technology (IT) system for the Study is being developed by a consortium of Booz Allen Hamilton Inc. (project lead); RTI; Battelle; and Levine, Fricke, and Sanz. These contractors are involved in the following tasks:
  - Defining the IT requirements for recruitment and enrollment
  - Identifying mechanisms for questionnaire data collection
  - Identifying mechanisms for electronic capture of clinical data.

  Dr. Scheidt explained that the electronic capture of clinical data is important for the success of the Study. However, because of the diversity of information sources and disparities in medical records systems, electronic data capture will be challenging.

  The Program Office anticipates contractual procurements for the following:
  - Clinical/data coordinating center (concept clearance approved and currently under development)
  - Repository (sources-sought announcement made and responses received)

- Vanguard centers.

- **Pilot Studies.** Dr. Scheidt noted that there about 30 pilot studies that are currently ongoing for the Study. He listed the following recent and upcoming workshops and dates:
  - Rurality Workshop, March 2, 2004
  - Sampling Design Workshop, March 21–22, 2004
  - Possible Roles for Inclusion of the Study of Cancer Workshop, tentatively April 2004
  - Questionnaire and Diary-Based Methods for the Early Assessment of Asthma-Related Health Outcomes Workshop, tentatively May 27, 2004
  - Assessing Dietary Intakes and Patterns in Women and Children, tentatively spring 2004
  - Day-Specific Probabilities of Conception and Prospective Pregnancy Studies Workshop, tentatively May 2004
  - Measurement of Maternal and Fetal Infection and Inflammatory Responses Workshop, date to be determined
  - Gene Expression and Behavior Workshop, date to be determined
  - Social Environment Measures Workshop, date to be determined.
- **Protocol Development.** Dr. Scheidt explained that as the Program Office engages in protocol development, the Study is entering a new phase. Elements of the protocol will become part of the scope of work for procurements. Because of this, there are potential problems with possible contractors or competitors regarding possible conflicts of interest, "inside track" information, and procurement integrity. Dr. Scheidt listed the following implications for the protocol phase of the Study:
  - Findings and proposals about Study design and measures (that is, protocol elements) can be shared with Working Groups and NCSAC.
  - Conversely, protocol elements cannot be shared with Working Groups and NCSAC ahead of other potential contractors.
  - To protect Working Groups and NCSAC, communication about the evolving protocol must be in the public domain.
  - Therefore, the Working Groups and NCSAC will have limited interaction with the Interagency Coordinating Committee (ICC) and the Program Office.
  - There will be reduced intensity of Working Group and NCSAC activities.
- **Partnership Development.** Dr. Scheidt briefly discussed partnership development with the Foundation for the National Institutes of Health:
  - A memorandum of understanding is being prepared.
  - Implementation of specific partnerships will depend on funding for the full Study.
  - The Program Office is exploring cosponsorship of congressional briefings with the American Chemical Council, the Children's Environmental Health Network, and other organizations.
- **Proposed Expansion of the Study.** Dr. Scheidt explained that the proposal to expand the adult component of the study is still under consideration and will continue to be explored. While decisions about funding with Congress and the current administration are in progress, the Study will continue as it has. The National Human Genome Research Institute and other institutes engaged with the adult component will continue to address conceptual questions and relationships with other adult genetic studies. When funding for the Study is clarified, the proposed three-generational study will be given more detailed consideration.

- **Funding Status Update.** Dr. Scheidt briefly discussed the status of funding for the Study. For fiscal year 2004, the total funding required is approximately $26 million. However, to date, only $12 million has been allocated for fiscal year 2004. According to Dr. Scheidt, the Study is ready for launching. With funding, the Study will start collecting data beginning with participant enrollment in 2006. The funding needs for fiscal year 2005 are $27 million. The President's budget request for fiscal year 2005 of the Study contains approximately $12 million. Dr. Scheidt noted that the total projected costs for the Study—$2.7 billion spread over 25 years—have not changed.

In a question-and-answer session, Dr. Scheidt addressed the following issues and concerns:

- **Calculation of Economic Benefits of the Study.** Although no formal calculation of the economic benefits has been performed, many experts familiar with the Study believe that the overall economic benefits will be enormous. The costs benefits from a single year could possibly pay for the entire study.
- **Fiscal Year 2006 Budget.** The projected budget needs for fiscal year 2006 is approximately $70 million, assuming vanguard centers begin enrolling participants by the end of 2006.
- **Quality Assurance.** Although there is not a specific quality assurance component stipulated for the vanguard centers, quality assurance is part of the procurement process, and activities of the vanguard centers are heavily laced with quality assurance requirements.
- **Enrollment of Vanguard Centers.** Vanguard centers will be enrolled through competitive procurements. However, caveats to the competitive process are sampling needs and geographic requirements. Participant enrollment may require stratification, and there may be requirements for certain types of data collection. Vanguard centers may not be exclusively academic centers. Centers may be private hospital systems, state health entities, or federal entities (for example, Native American areas). Optimum linkages with communities will be highly encouraged as part of the requirements for selection. Although the study protocol may have certain rigid elements, flexibility will be included to incorporate input from communities.
- **Study Advocates.** Because Study consortium partners are federal agencies, they cannot lobby Congress directly for Study funding. Study partners and allies such as the Foundation for the National Institutes of Health and the American Chemistry Council can, however, keep Congress informed on the Study efforts. There is no current need to lobby Congress for increased funding. Those involved in the Study will continue to cultivate advocates for the Study. Fiscal year 2005 is the first year for which appropriations will be required to implement the Study.
- **Procurement Processes.** Some of the pros and cons of various funding mechanisms such as requests for applications, requests for proposals, and P30 grants were mentioned. Other issues and concerns in the procurement process include ethics, the use of human research subjects, advice from the Office of Management and Budget, consent issues, internal review boards, data ownership, and publishing.
- **Budget Allocation.** Because of the amount of funding allocated to the Study, health science researchers have expressed concern about potential impact on budget allocations for investigator-initiated research. Although additional funding is required to begin the Study, this should not affect funding for other research. The Study will create a large database for potential use to researchers and will eventually create more opportunities for a vast program of research.

Update on Protocol Development

Ruth Brenner, M.D., National Children's Study Program Office, NICHD, NIH, DHHS

Dr. Brenner described the Program Office's role in protocol development; defined the Study protocol; described the processes, issues, and challenges in this effort; and presented a timeline for continued protocol development. At this time, the Program Office is:

- Drafting the text of the Study protocol
- Overseeing and coordinating development of operational manuals
- Working with the contracting office to develop relevant procurement documents.

According to Dr. Brenner, the background, goals, and objectives of the Study protocol will outline the science in a precise manner. The Study design and methods will describe:

- Who the Study will be enrolling (that is, sampling) as participants
- When and where participant contacts will occur
- What will occur when participants are contacted
- Limited information on how data will be collected (details on data collection will appear in the operational manuals).

Dr. Brenner explained that the Study protocol is not a detailed operational manual, which will be developed at a later date. The protocol will address the appropriate issues of human subjects in research, including descriptions of:

- The benefits and risks of Study participation
- Confidentiality policies and regulations
- Consent and assent policies and regulations.

The protocol will also address appropriate issues regarding the handling and processing of data, including data analyses and data sharing and dissemination.

Dr. Brenner listed the following "givens" about what the Study protocol will involve:

- Environmental influences on child health and development
- Environment broadly defined
- Enrollment of approximately 100,000 children
- Enrollment during or before pregnancy
- Follow-up for 21 years
- National in scope.

Dr. Brenner commented that the protocol is driven by the focus of the Study—the infant/child, not the mother or family. She briefly described the guidelines for protocol development. The Program Office and protocol development team are developing a unified Study protocol that is:

- Hypothesis-driven
- Focused enough to be a cohesive document
- Broad enough to cover all relevant exposures and outcomes.

The process of protocol development is derived from a complex collaboration among hypotheses, workshops, pilot studies, and other reports and documents. The draft protocol will

then be submitted for federal input and comments. The draft protocol will be modified, revised, or refined in response to the feedback from federal entities. The next step in the process is to submit the protocol as a public document and to invite additional input and comments.

The current major issues for protocol development, and the resources for addressing them, include the following:

- Sampling strategy
  - Westat document
  - Battelle document
  - Sampling design workshop (March 21–22, 2004)
- Timing of enrollment
  - Same materials as cited for sampling strategy
  - Publications
  - Other documents
- Participant burden (for example, the number of blood draws)
  - Focus groups
  - Pilot studies (PBRN)
- Ethical issues (for example, will there be a central internal review board or multiple internal review boards?)
  - Workshop (June 2003)
  - Working Group recommendations.

The current challenges for protocol development include reviewing, synthesizing, and integrating all of the materials prepared to date for the Study. The solution to this challenge, Dr. Brenner said, is to organize these materials into manageable "bites." Program Office staff members are dividing up the workload, with different members focusing on different areas. Another challenge for protocol development is the limitations on who can provide input to the process. The Program Office is prohibited from seeking input from outside the federal government. The solution to this challenge is to rely heavily on expertise with the federal government.

The current strengths for protocol development include:

- Voluminous study documents
- Expertise within the Program Office
- Full-time senior scientific staff and their areas of expertise:
  - Marion J. Balsam, M.D., pediatrics, health care management
  - Ruth A. Brenner, M.D., M.P.H., pediatrics, epidemiology
  - Warren Galke, Ph.D., environmental epidemiology
  - Sarah S. Knox, Ph.D., behavioral sciences
  - Peter C. Scheidt, M.D., M.P.H., general pediatrics
- Part-time senior scientific staff and their areas of expertise:
  - Terry Cox, M.D., Ph.D., neuro-opthalmology, biostatistics
  - Carole A. Kimmel, Ph.D., development toxicology
  - James J. Quackenboss, M.S., environmental exposures
  - Kenneth Schoendorf, M.D., M.P.H., pediatric epidemiology
- Temporary senior scientific staff and their areas of expertise:

– Terry Dwyer, M.D., M.P.H., pediatric epidemiology.

The projected timeline for protocol development is as follows:

- 2004 Circulate draft protocol to federal experts
- 2004–2006 Ongoing public comment and revision
- 2004–2005 Release initial requests for proposals
- 2005–2006 Selection of vanguard study sites
- 2006 Initial phase of vanguard sites
- 2007+ Additional sites added.

In concluding her presentation, Dr. Brenner reminded meeting participants that children are the focus of the Study. In a question-and-answer session, Dr. Brenner addressed the following issues:

- **NCSAC Assistance to the Program Office.** Dr. Brenner reiterated that one of the challenges for the Program Office is the extent to which it can ask for help, assistance, and input from various groups and organizations, particularly those outside the federal government. The NCSAC can best assist the Program Office by making sure that the Working Groups have answered all questions posed to them, that they submit all work products in a timely manner, and that they define and submit their lists of exposure and outcome measurements.
- **Composition of Expertise.** A participant recognized that the Study design is an integral part of the science and that it is important to have scientific expertise among the protocol development team. However, the participant suggested that the team might be lacking in the area of social sciences. In response to this comment, Dr. Scheidt acknowledged that the current protocol development team is a "skeleton crew" that depends on input from many sources. There are plans to recruit social scientists to the team, and the Program Office expects its staff to increase in numbers when current hiring restrictions are lifted.

Report from Joint ICC/NCSAC Executive Committee

Judith A. Graham, Ph.D., NCSAC Member and Chair of the Executive Committee, American Chemistry Council

Dr. Graham reported that the Joint ICC/NCSAC Executive Committee met three times since the NCSAC's eighth meeting in December 2003. During those meetings, the Executive Committee focused on the agenda for the current meeting and drafted a schedule for receiving and reviewing the Study strategic plan, which includes all activities and actions for 2004. The draft schedule lists the goals and expected outputs of the upcoming meetings; it also specifies the responsibilities of the NCSAC in this process. Dr. Graham explained that the NCSAC needs to "look downstream" at these future meetings in an effort to make the schedule more realistic. The NCSAC also needs to coordinate its efforts with the Working Groups and synchronize with other Study entities. Dr. Graham asked NCSAC and ICC members to provide input on the draft schedule, particularly the feasibility of the dates.

According to Dr. Graham, the strategic plan is basically a management plan that describes the "who, what, when, and where" of Study activities. The process of moving from Study planning to implementation is complex, and therefore, the strategic plan is complex. Dr. Graham

discussed her outline of the draft strategic plan, which was provided to meeting participants. She provided an overview of upcoming events and activities of the NCSAC and other Study entities, including the ICC, Working Groups, and Program Office. Dr. Graham reiterated the goals of the current meeting and described her vision of goals and objectives of the NCSAC's June 2004 meeting.

During a brief open discussion of the strategic plan, a participant commented on the sequence of Study events, suggesting that the development of the protocol and study design needs to "mesh" and that other activities listed in the strategic plan also need to "mesh."

Exposure to Chemical Agents Working Group

P. Barry Ryan, Ph.D., NCSAC Member, Emory University

Dr. Ryan reported on the activities of the Exposure to Chemical Agents Working Group. He introduced the co-chairs and members of this Working Group and noted that the Working Group has been very active over the past 18 months. Dr. Ryan became NCSAC liaison to this Working Group in August 2003. To date, the Exposure to Chemical Agents Working Group has proposed four hypotheses, refined hypotheses during meetings in 2002 and 2003, participated in workshops in 2003 and 2004, prepared background information for a pilot investigation, responded to all ICC questions and comments, and identified relevant measures of exposures and outcomes.

Over the last 6 months, the Working Group has been actively working to complete draft sections of its white paper. Working Group members held a working meeting in October 2003 to draft sections of the white paper, and they have been having routine conference calls to provide updates on progress. A review draft of their white paper was recently provided to Dr. Ryan, and he recommend that it be forwarded to the ICC and Program Office for review and comment. The Working Group has discussed having a contractor work with the draft white paper to develop a consolidated outline and revise the paper and tables. Dr. Ryan discussed the possibility of using the RTI contract for this with Carole A. Kimmel, Ph.D., National Center for Environmental Assessment, EPA, and Pauline Mendola, Ph.D., Office of Research and Development, EPA. Drs. Ryan, Kimmel, and Mendola are currently drafting a work assignment and government cost estimate before seeking approval from the Pilot Study Committee and the ICC.

The primary focus of this white paper is the measurement and analysis of exposures to environmental pollutants and biological agents for the Study. The completed document will be approximately 200 pages and will contain the following sections:

- Introduction
- Relevant chemical and biological agents for different study hypotheses, with listings of specific hypotheses and exposure measurements needed to assess them
- Methods for measurement of exposures and candidate environmental chemicals and aeroallergens, with discussion of measurement methods strengths and weaknesses by pollutant class
- Methods for measurement of chemicals in biological media, including a comprehensive overview and review of biological monitoring state of the art

- Survey collection instruments for use in the Study and evaluation of exposure-related questionnaire instruments
- Study design issues related to exposure measurements for the Study, including an assessment of where exposure fits into the Study.

Drs. Ryan and Graham have reviewed the draft white paper, and the Working Group is currently seeking direction from the NCSAC via feedback through their liaison. Specifically, the Working Group requests input, through hypotheses and thematic Working Groups, on the specific pollutants and time periods of exposures. The Exposure to Chemical Agents Working Group will then be able to provide a more focused response in the white paper. Although the document is still in the review process, the Working Group expects to complete the white paper by the end of March 2004.

In a question-and-answer session, Dr. Ryan addressed the following issues:

- **Important Chemical Exposures.** A participant expressed concern that the Working Group's hypotheses seemed to be missing important chemical exposures, particularly chemicals that might affect reproduction and testicular function. The participant mentioned metal compounds, volatile organic compounds, and chlorinated compounds. Dr. Ryan explained that there is a historical account of the chemical exposures that the Working Group considered; chemicals that were not listed in Dr. Ryan's presentation may have discussed and considered.
- **Exposure Assessments.** Dr. Graham expressed her concern about chemical exposures that may have been left out because of lack of expertise in health toxicology. George P. Daston, Ph.D., Proctor and Gamble Company, emphasized the importance of performing cumulative exposure assessments. Dr. Ryan commented that the Working Group is attempting to identify and address all appropriate chemical exposure assessments.
- **Publication Review.** Dr. Mattison asked whether groups outside the Study would review the Working Group's white paper. Dr. Ryan briefly discussed peer-reviewed publications. Other Working Groups could certainly serve as part of the review process, which would enhance cross-Working Group activities.
- **Multiple Chemical Exposures.** Several participants suggested that the clustering of chemical exposures, the correlations of certain exposures such as lead, and the interactions of these exposures should somehow be incorporated into the Study measures. Dr. Ryan replied that there might be a need to expand on this idea and to seek advice from other Study entities.

Repository Working Group

Mark Cosentino, D.P.M., Ph.D., Repository Working Group Co-Chair, Science Applications International Corporation

Dr. Cosentino explained that the meeting goal is to complete the transition from Study planning to implementation. To accomplish this goal, the Study design logistics need to be:

- Discussed
- Flexible/expandable
- Decided on
- Communicated to Working Groups
- Factored into contract applications

- Continuously upgraded as needed.

Dr. Cosentino said that the Study must begin to address logistical design issues, including communication, data sharing, and the handling and processing of samples and specimens. The following logistical design issues need to be discussed and decided:

- Study database design
  - A single unified system?
  - Several stand-alone systems?
  - Several stand-alone systems but federated?
- Information that needs to be tracked in real time
  - Subject-relevant
  - Sample collection
  - All sample shipments
  - Vial location at the repository and testing sites
  - Test results
- Specimen identification format and label design
- The type, quantity, and storage configuration of specimens needed to answer the hypotheses
- Determine specimen sharing between hypotheses
- Regional/satellite repositories
- Specimen processing at repositories or regional laboratories
- Quality assurance/quality control—centralized or regional?
- Need stable contractors that will plan for the future.

Dr. Cosentino emphasized the importance of minimizing contractor turnover during the Study. He said that specific contractual terms can help protect the Study against contractor turnover. He suggested that contracts include specific terms about source code ownership. Because some repositories may also be performing tests, testing labs and vanguard centers will need to coordinate their efforts and integrate their information systems. Other issues regarding specimens include shipping, tracking, processing, and storage configurations. Dr. Cosentino warned that managing the database may be one of the more challenging aspects of the Study. He emphasized that the logistical design needs to be flexible and expandable, yet have built-in safeguards to ensure contractor stability.

Recommendation: Dr. Costentino recommended that the Study establish a Logistical Working Group to address the logistical design issues.

In a question-and-answer session, Dr. Cosentino addressed the following issues:

- **Specimens.** Given the anticipated large number of specimens for the Study (speculated to be on the order of 2–20 billion), the anticipated costs of freezers simply to store the large number of specimens are great (speculated to be on the order of $40 billion over the 21-year Study).
- **Procurement.** Procurement issues for the logistical design were briefly discussed.

Assisted Reproductive Technologies

Donald J. Dudley, M.D., NCSAC Member, University of Texas Health Sciences Center at San Antonio

Dr. Dudley explained that the President's Council on Bioethics had approached several individuals involved in the Study to discuss an assessment of assisted reproductive technologies (ART) as a possible component of the Study. As a result of these discussions, O. Carter Snead, General Counsel of the President's Council on Bioethics, presented an overview of the Council's preliminary findings on ART in the United States. This presentation was given at the NCSAC's December 2003 meeting in Atlanta, Georgia. At that time, the NCSAC recommended that the Council contact the Reproductive Medicine Network to discuss a possible longitudinal study of the health and developmental impacts of ART on children born with their aid. In addition, the NCSAC Executive Committee agreed to seek input from the Fertility and Early Pregnancy, Birth Defects, and Health Services Working Groups. Subsequently, the Executive Committee formally requested the Fertility and Early Pregnancy Working Group to:

- Identify the need for further studies of ART on child health
- Explore implications of several alternatives to examine ART within the Study and as a parallel adjunct to the Study.

Dr. Dudley said that the response to the Executive Committee's request began with a review of a hypothesis submitted by the Fertility and Early Pregnancy Working Group. A recent meta-analysis on ART was reviewed, and discussions were held with the following subject matter experts:

- Phyllis Leppert, M.D., Ph.D.
- Dorrie Lamb, Ph.D.
- Jim Segars, M.D.
- Robert Brzyski, M.D., Ph.D.
- Germaine M. Buck, Ph.D.

Dr. Dudley characterized the Fertility and Early Pregnancy Working Group's hypothesis on ART as follows:

- Primary outcomes: intrauterine growth retardation, birth defects
- Other outcomes: preterm birth, mortality, cost/financial burden, quality of life
- Strong rationale for this hypothesis
  - Justification for large sample size
  - Scientific merit
- No sample size calculation
- No consideration of potential oversampling needs
- Some consideration of control groups.

Dr. Dudley described the findings from a recent meta-analyses titled Perinatal Outcomes of Singletons and Twins After Assisted Conception: A Systematic Review of Controlled Studies (Helmerhorst et al., *British Medical Journal*, 2004 Jan 31;328(7434):261):

- 25 studies reviewed; 17 controlled; studies published 1985–2002
- Of the singletons, 5,361 conceived via ART, compared with 7,038 spontaneous births
  - Very preterm (<32 weeks), relative risk = 3.27 (ART)

  - Preterm (<37 weeks), relative risk = 2.04 (ART)
- Of the twins, 3,427 conceived by ART, compared with 3,429 spontaneous births
  - Very preterm (<32 weeks), relative risk = 0.95
  - Preterm (<37 weeks), relative risk = 1.07
- Birth weight of singletons
  - <1,500 grams, relative risk = 3.00 (ART)
- Birth weight of twins
  - <1,500 grams, relative risk = 0.89
  - <2,500 grams, relative risk = 1.03
- SGA in singletons: relative risk = 1.40–1.46
- SGA in twins: no difference
- Perinatal mortality:
  - Singletons: 1.68 ART (skewed by one study)
  - Twins: 0.58

Dr. Dudley noted that this recent meta-analysis had problems with matched cohort studies (one study dominated and three had different control groups) and that matching for GA was questionable. Dr. Dudley listed the following meta-analysis conclusions:

- Shift emphasis from achieving pregnancy to normal outcomes
- Consider any multiple pregnancy as a failure of ART technology
- Narrow the gap in perinatal outcomes from assisted pregnancies.

The consensus opinion from the subject matter experts who were consulted is as follows:

- No study on ART ongoing in the United States
- Not all ART is the same
- Unclear whether the Study is the best design
  - 1 percent of pregnancies are by ART (2 percent in the future)
- Indications for ART are varied
- Adjust for cause of infertility (data are difficult to acquire)
- Necessity for oversampling?

Dr. Dudley briefly discussed a comparison of the elements of epidemiological methods of the Study and those required for studying the effect of ART on child health. Based on this comparison, Dr. Dudley suggested that the Study might not necessarily offer the best circumstances to best address the concerns of the President's Council on Bioethics. However, Dr. Dudley offered three possible courses of action:

- Decline consideration
- Accept as hypothesis and develop
- Reconsider: Fertility and Early Pregnancy and Study Design Working Groups determine
  - Power calculation
  - Need for oversampling
  - Effect on Study overall.

In a question-and-answer session, Dr. Dudley addressed the following issues and concerns:

- **Risk of Prematurity.** There is a greater risk of prematurity among twins, and there is a greater chance of twins with ART.
- **Study Design.** Given that the Study seeks to examine a representative sampling of the U.S. population, the current study design may not be able to answer the questions that the President's Council on Bioethics is asking. Dr. Daston commented that incorporating the ART hypothesis would require a marked alteration of the study design. To this end, Study entities could provide the necessary statistical background in order to make a wiser recommendation.
- **Additional Resources.** At this time, it is not clear whether inclusion of the ART hypothesis would bring additional resources to the Study.
- **Conception Data.** Although the Study will attempt to collect data on the circumstances of conception (to the extent possible), it is very difficult to collect information on the indications for ART, which often involve very private issues. Participants acknowledged that there is an interest in the long-term effects of ART but emphasized that the Study does not offer an ideal design to collect data on ART outcomes and is not conducive to investigating ART. The Study will attempt to capture data on ART, if possible. A participant noted that the Study cannot adequately or scientifically address rare outcomes.
- **Preconception Study Enrollment.** Enrolling a preconception subgroup is still being considered. The Sampling Design Workshop will examine this issue, and the NCSAC will make a recommendation on the preconception subgroup during their June 2004 meeting.
- **Pending Legislation.** Dr. Dudley commented that the discussion on ART might be moot because of legislation sponsored by Senator Lamar Alexander to study preterm births. According to Dr. Dudley, an amendment to Senator Alexander's bill directs the Study to examine the effects of ART on child health. The bill's current status was not known, nor was it known whether funding will be provided for the ART mandate.

Recommendation: The NCSAC recommends that a full study of ART not be included as a component of the National Children's Study. However, the lack of a full study does not preclude the collection of data on ART or the ability to explore questions that can be answered by those data, as they exist. The NCSAC recommends that Study entities seek a dialogue with the President's Council on Bioethics to further discuss the scientific issues of studying the effects on ART on child health. This discussion would identify the challenges of implementing a full study of ART within the Study and explain the types of outcomes that are achievable with the Study's anticipated sample size.

Defining Positive Health

Deborah A. Phillips, Ph.D., NCSAC Member, Georgetown University

Dr. Phillips reminded the participants that the consensus from the last NCSAC meeting was to include measures and definitions of positive health as a component of the Study. In the present meeting, she suggested that participants focus their discussions on the status of measures of exposures and outcomes, particularly identifying what may be missing. Dr. Phillips noted, as an example, that neurodevelopment was one of the thematic areas that had "fallen through the cracks." Although neurodevelopmental outcomes have now been included, they need to be expanded and refined. Dr. Phillips urged participants to assess the work done to date and to

determine where Study activities are headed. She briefly discussed some of the upcoming Study workshops and proposed that the Study form an ad hoc working group to advise on issues concerning positive health. The NCSAC seeks additional input to help craft the hypotheses on positive health outcomes regarding neurodevelopment for the next NCSAC meeting in June 2004.

Dr. Phillips presented an overview of a proposed conceptual approach and hypotheses that were developed by Neal Halfon, M.D., Ph.D., University of California, Los Angeles, and Paul Wise, M.D., M.P.H., Boston University. The approach and hypotheses were summarized in an 8-page document that was distributed to participants. Drs. Halfon and Wise explained that their focus was not to resolve ongoing tensions between different analytical frameworks and potential etiologic pathways, but rather to develop proposed hypotheses that reflect an approach while making use of the best science available, in a manner that responds purposefully to the specific, practical requirements of the Study.

Historically, health has been defined within three evolving contexts:
- Negative
- Normative
- Positive.

Positive health was initially defined as simply a lack of negative health; then it was viewed in light of what was considered normative. In 1948, the World Health Organization defined positive health as "a state of physical, mental, and social well-being, not merely the absence of disease or infirmity." Dr. Phillips provided a composite of recent definitions of positive health:

> Health is the extent to which an individual or group is able, on the one hand, to develop and realize aspirations and satisfy needs, and on the other hand, to develop the capacities that allow them to change and cope with the environment.

Some of the proposed components of positive health include:
- Character
- Spirituality
- Virtues
- Hope
- Satisfaction
- Social engagement
- Sense of purpose.

Dr. Phillips said that the primary goal of a positive health outcomes hypothesis is to reframe the central elements of this complex field to meet the specific, practical requirements of the Study. The specific objectives are to:
- Develop an analytic approach to identify the critical determinants of optimal health in children who do not have known health problems
- Assess whether approaches to address positive health could be helpful in elucidating the critical determinants of optimal health outcomes in children with known, serious health conditions.

Special considerations for the positive health outcomes hypothesis include:

- The impact of developmental modulation
- The requirement for predictive capacity in the context of development.

According to Drs. Halfon and Wise, the first challenge to creating analytical strategies is a direct reflection of the developmental cadence of childhood. Factors that influence child health at 1 year of age may take on a very different form than those that affect a 4-year-old child. The second challenge reflects the inherent quality of positive health measures in children that they are often fundamentally referenced to later outcomes. Most positive health measures are "tilted forward" and convey a predictive or speculative element to any effort to assess positive health in a longitudinal cohort.

In response to these considerations, Dr. Halfon and Wise propose that the development hypothesis not depend on the adoption of any particular definition of positive health. Moreover, they propose that the effort to generate hypotheses not be directed at identifying a comprehensive list of factors determining positive child health. Their proposed approach focuses on the designation of a highly focused set of capabilities that generally reflect a broad array of child capabilities. Identification of selected "sentinel capabilities" would help ground the hypothesis generation and facilitate the search for appropriate measurement instruments.

The characteristics of the sentinel capabilities would conform to the following requirements:

- Capacity to transform potential into functioning
- Reflect generic pathways of effect
- A strong consensus that they relate directly to essential elements of positive health
- Relate to critical transition points in childhood
- Evidence exists to suggest important genetic and environmental determinants
- Relevant measurement tools available.

Drs. Halfon and Wise proposed two sentinel capabilities and two corresponding hypotheses.

Capability 1: School readiness is a measure of a child's capacity to respond to challenges and opportunities presented by entering the formal education process.

School readiness includes:

- Physical/motor development
- Cognitive development
- Social and emotional development
- Language development
- Approach to learning.

School readiness hypothesis: School readiness will be influenced by the character of family work patterns.

Several school readiness subhypotheses were also proposed:

- Genetic and biological variations will influence the impact of parental work on school readiness.
- Preschool childcare will mediate and modify the role of parental work in altering school readiness trajectories.
- Exposure to media will influence school readiness and will be related to parental work patterns.

Capability 2: Antecedents of positive and negative health behaviors appear in adolescence; positive health behaviors include patterns of avoidance of tobacco, alcohol, and illicit drugs.

Positive health behaviors in adolescence hypothesis: Positive health behaviors will be influenced by the level and content of exposure to media.

Several positive health behavior subhypotheses were also proposed:

- Biological and genetic differences alter susceptibilities to the influence of media on the development of positive behaviors.
- Family relationships, routines, and practices mediate the influence of media on the development of positive health behaviors.
- Schools and peer-group relationships modify media effects on positive health behaviors.

In a question-and-answer session, Dr. Phillips addressed the following issues and concerns:

- **Self-Regulation.** A participant noted that adolescent self-regulation appears to be defined by the absence of negative behaviors. Dr. Phillips explained that interest is in how self-regulation affects outcomes, not necessarily behaviors.
- **Media Effects.** Positive health can be considered in the context of "freedom," that is, transforming opportunity into positive outcomes. Media effects can have both positive and negative outcomes. The purpose of including media effects was to simplify, not trivialize, the assessment of this exposure and allow the Study to assess media effects across fields and disciplines.
- **Racism.** Because positive outcomes tend to be mostly political and economic in nature, a participant asked how racism could be assessed in the context of positive health. Dr. Phillips acknowledged that mechanisms to assess racism are currently unknown. She suggested that the Study could perform characterizations of media exposure, including violence and portrayals of values and racism. Christine A. Bachrach, Ph.D., NICHD, NIH, DHHS, emphasized the importance of assessing the content of media exposure. To this end, media data could be collected, archived, and content analyzed at a later time.
- **Adverse Events.** The collection of data on adverse events such as law enforcement encounters and violent or aggressive encounters with peers will overlap with activities of other Working Groups. Dr. Wise stressed that activities on positive health will coordinate with other Working Groups to assess functional outcomes and to implement data collection efficiently.
- **Measurement Issues.** Capturing infant and early childhood positive outcomes may prove challenging. Issues such as attachment are heavily tilted forward to older ages. Outcomes such as attachment, attentional issues, and language development will be considered under the concept of school readiness. Dr. Wise noted that measures of negative outcomes in

infancy and early childhood need to be examined, and he asked for input from all Working Groups. He also asked for input on proximal measures of exposures that contribute to sentinel capabilities. Barry S. Zuckerman, M.D., Boston University School of Medicine, commented that although there are more concrete measures for older children, there are some measures in early childhood that may carry through life, such as mutually satisfying parent-child relationships. Among the more practical measures of positive health for infants and toddlers are physical measures such as finger pointing by age 12 months. Barbara R. Foorman, Ph.D., University of Texas Health Science Center at Houston, explained that measurements have to start early in infancy and should cover all of the important domains; the Study must collect the right measures at the right ages. Assessments of newborns might be performed, but the measures for this assessment have not yet been determined.

- **Cultural Sensitivity.** Positive health approaches need to retain a culturally sensitive component to capture differences in measuring success. Dr. Wise said that he and Dr. Halfon recognized the need to reflect cultural diversity when assessing positive health outcomes. Although there may be many arenas to reflect the cultural diversity of success, there seems to be a consensus across cultures that school readiness and the avoidance of addictive behaviors are important positive health outcomes.

Reports from the Working Group Liaisons

NCSAC liaisons provided presentations to the full NCSAC on the status of various Working Group products—what is needed to complete their work, whether the Program Office can provide assistance, and when the outstanding work products will be completed. For Working Groups that have completed their assignments and tasks, the NCSAC liaison indicated when the Working Group should be thanked and disbanded. These Working Groups were asked to provide general recommendations concerning their findings to Duane Alexander, M.D., Director, NICHD, NIH, DHHS; the Program Office; and the ICC.

- **Asthma Working Group.** Stephanie J. London, M.D., Dr.P.H., NIEHS, NIH, DHHS, reported that the Working Group is sponsoring a workshop in May 2004. The workshop will address questionnaire and diary-based methods for the early assessment of asthma and will consider outcome measurements and biomarkers. The workshop results will be reported at the September 2004 NCSAC meeting. The Working Group is coordinating with the Exposure to Chemical Agents Working Group, but has not yet developed specific hypotheses to address multiple interactions such as chemical exposures, diet, and genetic variables.
- **Birth Defects Working Group.** Dr. Daston, NCSAC liaison to the Birth Defects Working Group, reported that, since December 2003, this Working Group had completed several conference calls; he said that the Working Group would convene one more face-to-face meeting. The Working Group is:
  - Refining and attending to the final details for its hypothesis
  - Addressing the ICC's questions
  - Examining lists of potential exposures developed by other Working Groups
  - Developing its own list of potential exposures.

  Dr. Daston concluded that the Working Group has basically accomplished its tasks and assignments and fulfilled its responsibilities.

- **Community Outreach and Communication Working Group.** Willa M. Doswell, R.N., Ph.D., University of Pittsburgh School of Nursing, stated that the guidance document would be completed in approximately 2 to 3 weeks. Dr. Doswell listed the following request-for-proposal criteria:
  - Community listening sessions
  - Outreach strategies
  - Community profiles to recruit
  - Community leaders
  - Community outreach advisory board.

  Dr. Doswell said that the Working Group would continue to formalize outreach and communication strategies. She explained that the Working Group's recommendations would be incorporated into the guidance document and that specific strategies would follow.
- **Development and Behavior Working Group.** Dr. Foorman stated that this Working Group would participate in the Gene Expression and Behavior Workshop to be held in June 2004. The goal of this workshop is to discuss the environment and windows of vulnerability. There is the possibility of another related workshop sometime in the near future. The Working Group will be working closely with contractor Battelle in an effort to list measures of key outcome domains. A main focus of exposures will be chemicals. Participants briefly discussed the idea that this Working Group might evolve into two Working Groups, one involved with positive health and the other involved in neurodevelopment. There was a brief discussion of whether to consider reproductive outcomes of chemical exposures. A participant suggested developing a matrix relating various exposures to brain outcomes. Through such a matrix, researchers could systematically pose a series of questions to develop a comprehensive list of tests. Dr. Mattison explained that the Fertility and Early Pregnancy Working Group would address exposures and outcomes related to reproduction and endocrine function. However, he agreed that the matrix might prove worthwhile, and he highly encouraged collaboration across Working Groups.
- **Fertility and Early Pregnancy Working Group.** Lucina Suarez, Ph.D., Texas Department of Health, reported that the Working Group had completed its assigned tasks and achieved its goals, to date. This successful Working Group will complete its responsibilities by the end of June 2003. Answers to the ICC's questions will appear in the Working Group's white paper.
- **Gene-Environment Interactions Working Group.** M. Anne Spence, Ph.D., University of California, Irvine Medical Center, explained that the Working Group is drafting responses to two questions from the ICC. The first question involves critical influences in disease development. Critical influences are those with biologically important outcomes such as diabetes and obesity. The Working Group will continue to identify which genes need to be assessed and will develop a list of candidate genes for the Study. The ICC's second question concerns the possible gathering of data on siblings, particularly twins. The Working Group will analyze the pros and cons of including siblings and report its findings in the near future. Dr. Spence said that the Working Group would be ready for "sunsetting" when the Study sampling design is finalized. Dr. Gaston commented that the level of knowledge about human genetics is increasing and that more genes will be identified as factors in disease. Dr. Spence noted that because of this issue, the Working Group would periodically reexamine topics in gene-environment interactions; it will update hypotheses and make recommendations as necessary.

- **Health Disparities and Environmental Justice Working Group.** Loretta Jones, M.A., Healthy African American Families, reported that the Working Group would explore measures of racism in an upcoming workshop, develop a list of concrete measures, and report its findings at the June NCSAC meeting. This Working Group may possibly be incorporated into the Social Environment Working Group.
- **Health Services Working Group.** Although there are modified hypotheses for five domains, more specificity is needed. The Sampling Design Workshop will help identify the measures that will serve as covariants. The measures identified will be described and discussed in a subsequent white paper.
- **Immunity, Infections, and Vaccines Working Group.** William J. Rodriguez, M.D., Ph.D., Center for Drug Evaluation and Research, U.S. Food and Drug Administration, DHHS, reported that the Working Group has drafted nine hypotheses and is currently planning a workshop on fetal infection and inflammatory responses. Outcomes under consideration include obsessive-compulsive and bipolar disorders. The Working Group would like to integrate its hypotheses with the activities of other Working Groups. The Working Group will wait until its workshop in spring 2004 is completed before considering a timetable for "sunsetting."
- **Injury Working Group.** Dr. Zuckerman explained that the Working Group's submitted hypothesis was not accepted by the NCSAC and that the Working Group was perplexed as to why it was not accepted. The Working Group asked for specific guidance from Dr. Zuckerman and the NCSAC. In its efforts to draft an acceptable hypothesis, the Working Group developed, and Dr. Zuckerman presented, the following aims, hypotheses, and subhypotheses concerning injury:
  - **Aim 1:** Identify the predictors of physical abuse of children in the first 3 years of life.
  - **Hypothesis 1:** Marital/relationship violence during pregnancy or in the first year of a child's life will lead to increased incidence of physical abuse of the child by age 3.
    - Parent psychopathology (for example, depression, anxiety, post-traumatic stress disorder) and neighborhood factors (higher crime index, increased joblessness, increased poverty, and high family mobility) will further increase the likelihood of physical abuse.
  - **Aim 2:** Identify the consequences of physical and sexual abuse.
  - **Hypothesis 2a:** Chronic physical abuse will result in altered cortisol levels, increased likelihood of post-traumatic stress disorder, chronic depression, and oppositional defiant disorder, and impaired developmental functioning (including cognitive, social, and emotional development).
  - **Subhypotheses on physical abuse:**
    - Chronic physical abuse will result in more severe outcomes (listed above) than will single incidents of physical abuse.
    - The relationships between physical abuse and its adverse consequences are exacerbated by environmental (for example, household lead, pesticides) and community (high rates of poverty, exposure to or witnessing of violence, unemployment, family mobility, and childcare burden) factors.
    - Exposure to media violence increases the likelihood of adverse outcomes in the presence of environmental and community factors.

  - Of those children who experience physical abuse, those with the genetic disposition will develop chronic depression or oppositional defiant disorder.
  - The quality and duration of intervention programs will decrease the likelihood of the above adverse outcomes.
- **Hypothesis 2b:** Chronic sexual abuse will result in altered cortisol levels, increased likelihood of post-traumatic stress disorder, and impaired developmental functioning (including cognitive, social, and emotional development).
- **Subhypotheses on sexual abuse:**
  - Outcomes of sexual abuse will be modified by the developmental age of the child at the start of the abuse and the duration of the abuse.
  - The relationship between sexual abuse and its adverse consequences will be exacerbated by community factors including high rates of poverty, exposure to or witnessing of violence, and the childcare burden in the home.
  - The quality and duration of intervention programs will decrease the likelihood of the just-mentioned adverse outcomes.

Dr. Zuckerman said the Working Group requests specific feedback on these aims, hypotheses, and subhypotheses. In a subsequent discussion, a participant questioned whether these were testable hypotheses. Dr. Scheidt reiterated the criteria for Study hypotheses. He explained that the more narrow and specific a hypothesis becomes, the less interesting and compelling it is. Hypotheses need to be sufficiently broad and within the context of the Study's 100,000-subject sample size. A participant asked how physical abuse will be defined and how it will be measured. Dr. Daston commented that because injury is one of the most concrete outcomes, the Study must be able to adequately and appropriately further the understanding of injury. Legal and ethical issues concerning abuse, neglect, and intervention may prove to be particularly challenging within the context of the Study. Most states have strict reporting requirements for suspected physical abuse. Another challenge will be determining cognitive and behavioral outcomes as related to severity of traumatic head and brain injury. Dr. Zuckerman noted that the Working Group is focusing on three areas: aggression, physical abuse, and physical injury. Dr. Dudley questioned whether families that are susceptible to abuse are likely to be enrolled in the Study, and if they are, the probability that such families will be lost to follow-up. Participants agreed that high-risk families must be included in the Study. Participants also discussed the following topics:

- Impact of contact sports
- Power calculations
- Continuous effects versus threshold effects
- Data collection issues
- Cultural norms for physical abuse and violence.

- **Medicine and Pharmaceuticals Working Group.** Dr. Graham said that the Working Group had identified best practices and compiled answers to the ICC's questions. The Working Group proposed a pilot study on drug coding and is planning a workshop on this topic to finalize the details. The Working Group has essentially completed its activities and will gladly serve as future consultants.
- **Nutrition, Growth, and Pubertal Development Working Group.** This Working Group was formed after most of the other Working Groups were formed, and it will have a role in the Study as the protocol is further developed. To date, the Working Group has completed

activities that it was asked to perform. The Working Group has planned or completed workshops on the following topics:

- Physical activity
- Dietary intake methods
- Body composition
- Early markers of puberty.

The Working Group is assessing several promising new technologies as they are developing the framework for body composition measures. Because of the rapidly evolving research on candidate genes related to delayed sexual development, early markers of pubertal development will be reevaluated in several years, perhaps in 2010. Priorities in measuring exposures and outcomes will be reassessed as the protocol continues to evolve. The Working Group is planning an upcoming workshop on body composition.

- **Pregnancy and the Infant Working Group.** Dr. Dudley reported that Working Group issued the request for proposal for the pilot study on three-dimensional ultrasound analysis. Remaining issues include data transmission, storage, and retrieval. RTI will help address these issues. The Working Group completed its hypotheses and developed a list of exposure and outcome measures. The stress hypothesis needs some refining. Subhypotheses may be developed, and there are questions concerning sample size and instruments to measure stress. Dr. Dudley said that the Working Group is close to completing its activities.
- **Repository Working Group.** Dr. Cosentino stated that the Working Group has fulfilled its responsibilities and is ready for "sunsetting." Dr. Cosentino expressed his desire to have this Working Group evolve into a new Working Group on logistics to help address contract issues.
- **Social Environment Working Group.** Linda M. Burton, Ph.D., Pennsylvania State University, reported that the Working Group developed its hypothesis and has responded to the ICC's questions. The Working Group is concerned about how it will integrate its activities with those of other working groups. The Working Group participated in both Media Effects and Rural Children Workshops. Upcoming endeavors include addressing emerging themes developed from the Sampling Design Workshop, including an assessment of home-scale diary methods. Dr. Burton stated that the Working Group has delivered its work products. However, the Working Group will continue to help develop appropriate measures of social environment issues for other Working Groups. Dr. Burton recommended that the Working Group remain empanelled to review data and make recommendations concerning future social issues. Because investigators cannot predict what social environment issues will be important and relevant to the Study 20 years from now, new hypotheses may be developed as data on developmental phases is produced.

Overview of the Department of Health and Human Services Initiative on Electronic Medical Records

Carolyn M. Clancy, M.D., Chair, Council on Applications of Health Information Technology (CAHIT), and Director, Agency for Healthcare Research and Quality (AHRQ), began her presentation by saluting all of the people who are involved with the planning and implementation of the Study, which she described as a large and ambitious endeavor. The purpose of Dr. Clancy's presentation was to describe CAHIT and explore how AHRQ could collaborate with

the Study for mutual benefit. Personnel from the two organizations had been sharing information, and these discussions led to the question: How might AHRQ relate to the Study?

CAHIT was formed in June 2003, under the direction of DHHS Secretary Tommy G. Thompson. CAHIT is an internal DHHS deliberative body whose purpose is to:

- Create synergy within DHHS
- Coordinate activities across DHHS agencies
- Improve quality and safety for a variety of research activities
- Provide an efficient and accurate method for gathering information
- Promote timely exchange of information about DHHS activities and opportunities
- Serve as primary forum for identifying and evaluating activities and investments that complement private sector initiatives
- Make recommendations to the Secretary to create strategic opportunities to enhance applications of health information technology in U.S. health care.

Dr. Clancy described health information technology as a network to connect and allow communication across health care entities. A national health information infrastructure would serve as a paperless, electronic health care and medical system. Such health information technology applications can:

- Support clinical care and its coordination, as well as research activities
- Improve health care quality and patient safety measurement
- Improve data accuracy and reliability (no more handwritten charts, units and conversions, weight-based dosing for children).

Dr. Clancy cautioned that health information technology systems require local health information infrastructures such as the Indianapolis hospitals system and the Santa Barbara health care data exchange. These systems require unified standards to facilitate networking and information sharing.

Because of the low penetration of information technology in U.S. medical systems, health information technology has an opportunity to improve several areas, including:

- Electronic health and medical records
- Computerized decision support systems (guideline-based prompts)
- Patient-physician communication (e-mail, patient portals)
- Smart cards
- Community-level data sharing and integration
- Computerized prescription order entry
- Web-facilitated research.

In the future, health information technology may create wearable data collection technologies to reduce patient burden.

According to Dr. Clancy, health information technology issues focus on increasing the use and effectiveness of electronic medical records. Information technology experts will have to become involved to develop appropriate health care and medical systems. Dr. Clancy noted that an electronic research infrastructure could be one of the Study's legacies. Other issues include:

- Privacy and confidentiality
  - Health Insurance Portability and Accountability Act regulations
  - Beyond—identity theft
- A thousand flowers blooming—need interconnectivity
- Standards and platforms
  - HL7 (a standard for information exchange between medical applications; an abbreviation of "Health Level Seven," seventh OSI layer protocol for the health environment)
  - SNOMED (Systematized Nomenclature of Medicine, the universal health care terminology that makes health care knowledge usable and accessible wherever and whenever it is needed)
- Cost
  - Short-term capital investment
  - Long-term savings/efficiencies?
- Research-practice connection.

Dr. Clancy listed two topics for discussion:
- The Study is a strategic opportunity for CAHIT.
- CAHIT is a strategic opportunity for the Study.

Dr. Clancy offered the following as “some initial ideas”:
- Paperless records
- Link different data collection efforts
  - A laptop or personal digital assistant (PDA) for every child
- Dynamic and quick access to data
  - Research papers
  - Identify needs for more rigorous studies
  - Identify opportunities for improvement
    - Toxic exposures
    - Disparities in health care
    - Quality improvements
- Leave systems behind for participating
  - Communities (coordination within and across sites)
  - Research participants (smart cards)
- Quick future study expansions and adaptations.

In a question-and-answer session, Dr. Clancy addressed the following issues and concerns:
- **Information Technology Vendors.** Vendors that use Web-based applications on HL7 platforms are able to communicate between systems through open architecture. Study vendors will need to build local systems that interact with each other. The Study will provide opportunities for a consortium of vendors, but long-term commitments will be necessary. The magnitude of the Study will help identify and promote a unified health information system.
- **Use of Technology.** A participant noted that most commercial information technology products are geared toward adults and may have limited adaptation to children and pediatric medicine. Physicians and medical researchers will use electronic medical records if the electronic systems are effective and efficient. Veterans Affairs systems and Medicare

demonstrations have proven the effectiveness of electronic systems. Data sharing, registries, and network-to-network communication systems (for example, from hospital to hospital) will validate the use of electronic medical records.

- **Legal Issues.** A key underpinning for electronic data exchange is a series of legal agreements between entities. These agreements help to ensure that no data are shared without permission. Other legal issues concern consent, confidentiality, privacy, and misuse of data.
- **Data Abstraction.** Because of the great amount of data that will be generated by the 40 Study centers, much information will have to be abstracted to facilitate information exchange and sharing. An information system will have to be planned and implemented and will require input from technical experts. The data will vary in complexity and will need to include not only medical records but also information on social environment and other exposures.
- **Systems Development.** The Study's information system will have two domains: the research infrastructure and the medical/health care infrastructure. Issues for this system include capturing data in electronic medical records and gathering information during subject enrollment. The Study provides an opportunity to develop an important information system, which may, in itself, be a major contribution to continuing research.

Update on Sampling Design Workshop

James J. Quackenboss, M.S., ICC Member, Office of Research and Development, EPA

Mr. Quackenboss began his presentation by listing the members of the Sampling Design Workshop Planning Committee:

- Lester R. Curtin, Ph.D., National Center for Health Statistics, CDC, DHHS (Study Program Office)
- Jonas H. Ellenberg, Ph.D., Westat (Study Design Working Group)
- Robert T. Michael, Ph.D., University of Chicago (NCSAC)
- James J. Quackenboss, M.S., Office of Research and Development, EPA (ICC)
- P. Barry Ryan, Ph.D., Emory University Rollins School of Public Health (NCSAC)
- Peter C. Scheidt, M.D., M.P.H., NICHD, NIH, DHHS (National Children's Study Director and ICC)
- Sherry G. Selevan, Ph.D., Office of Research and Development, EPA (ICC)
- Frank E. Speizer, M.D., Harvard School of Public Health (Study Design Working Group).

To plan and prepare for the Sampling Design Workshop, the planning committee identified documents needed to inform sampling decisions, including background white papers and design options. White papers were developed by Battelle under a contract with the Study Program Office. The design options paper was reviewed and revised by the planning committee and sent to the workshop panel. The workshop panel was selected in collaboration with panel chair David Savitz, Ph.D., University of North Carolina, Chapel Hill. Workshop participants were identified and invited.

To inform the sampling design deliberations during the workshop, Battelle wrote a white paper titled "Initial Sampling Design Options for the National Children's Study and Criteria for Evaluation." This white paper (published in September 2003) addresses the definitions, design

elements, and range of design options for the Study. It identified the following questions and issues for developing the sampling design:

- Advantages and limitations of alternative sampling methods for the Study
  - Internal and external validity: level of detail and generalization
- Recruitment and retention for the Study
  - Rates and their impact on design selection
- Measures for Study core hypotheses
  - Design requirements and burden.

A second white paper titled "Family of Designs (Hybrids) for the Study," which was produced by Battelle and Westat, addressed the following issues:

- Multiple sampling frames to provide coverage of target populations, possibly including
  - National probability-based sample
  - Center-based (patients and MSA sample)
- Organizational structure(s) and their existing relationships with potential participants
- Selection methods/criteria for:
  - Groupings (for example, geographic areas, clinics, centers)
  - Individuals.

Battelle's sampling design options report suggested the following tasks:

- Identify critical measures for Study priority outcomes and current hypotheses
- Assess design options for:
  - Recruitment and long-term retention rates
  - Estimated costs for the Study
  - Power to test selected hypotheses
    - Exposure-outcome relationships
    - Different life stages
    - Given estimated retention rates.

The criteria to evaluate Study sampling design options include:

- Ability to satisfy "givens"
  - Engage communities
  - Specialized measures
  - Prenatal recruitment (with some preconception)
- Scientific merit
  - External validity (probability basis)
  - Population diversity; range of exposures
  - Internal validity (measures, confounders, covariates)
  - Power (in unweighted and weighted analyses)
  - Resource for future (standardization, data access)
- Costs (relative to sample sizes, power, and measures).

Mr. Quackenboss explained that the Study Sampling Design Workshop format will be similar to the format of a National Institutes of Health Consensus Development Conference. The format will include:

- An impartial panel of experts to discuss issues and trade-offs
- Debate informed by documents and presentations from different viewpoints.

The 2-day workshop will be held March 21–22, 2004. On the first day, participants will discuss the Battelle designs and white papers, and additional speakers may be included. On the second day, the workshop panel will deliberate and report its findings.

The Study Sampling Design Workshop expert panel consists of the following people:

- David Savitz, Ph.D., University of North Carolina, Chapel Hill (Chair)
- Scott Zeger, Ph.D., Johns Hopkins Bloomberg School of Public Health (Co-Chair)
- Jean Golding, Ph.D., University of Bristol
- Barry Graubard, Ph.D., National Cancer Institute, NIH, DHHS
- Graham Kalton, Westat
- Michael Kramer, McGill University
- Anne R. Pebley, Ph.D., University of California, Los Angeles
- John Spengler, Ph.D., Harvard University
- Clarice R. Weinberg, Ph.D., NIEHS, NIH, DHHS.

The tentative speakers for the Sampling Design Workshop include the following people:

- Battelle design team
  - Warren Strauss, John Menkedick, and Jeff Lehman (Battelle employees)
  - Louise Ryan, Harvard University
  - Colm O'Muircheartaigh, University of Chicago and National Opinion Research Center
  - Alan Zaslavsky, Harvard University
- Alternative perspectives on Study sampling needs
  - Mark Klebanoff, M.D., M.P.H., NICHD, NIH, DHHS (ICC)
  - Robert T. Michael, Ph.D., University of Chicago (NCSAC)
  - Christine A. Bachrach, Ph.D., NICHD, NIH, DHHS (Social Environment Working Group)
  - Germaine M. Buck, Ph.D., NICHD, NIH, DHHS (Fertility and Early Pregnancy Working Group)
  - Nigel Paneth, M.D., M.P.H., Michigan State University (Study Design Working Group).

The proposed next steps and timetable for the Sampling Design Workshop include:

- Workshop reports to the ICC, NCSAC, Sampling Design Working Group, and other interested Working Groups by the end of April 2004
- NCSAC receives the findings from the Working Groups; NCSAC members are assigned to review and discuss key questions and issues by the end of May 2004
- NCSAC prepares written advice for the ICC and NICHD Director by the end of June 2004
- The ICC and NICHD Director make decisions on sampling design and pilot studies by the end of July 2004
- Study Program Office implements feasibility/pilot studies by the end of August 2004.

In a question-and-answer session, Mr. Quackenboss addressed the following issues and concerns:

- **Community Involvement.** Community leaders and community researchers are essential to the success of the Study. Mr. Quackenboss acknowledged the importance of community involvement and noted that community experts will participate in the Sampling Design Workshop.
- **Consensus Process.** A participant asked whether the Sampling Design Workshop would generate a single decision or recommendation through a formal consensus. Dr. Scheidt explained that the Federal Advisory Committee Act prohibits advisory committees from implementing a formal consensus process; that is, an advisory committee cannot, by vote, give advice to the federal government. The expert panel of the Sampling Design Workshop will present its findings—including pros and cons, costs and benefits, and any trade-offs—to the NCSAC. The ICC will also assess the workshop's findings.
- **Information Sharing.** Because of its size and complexity (approximately 200 pages of detailed findings), the Battelle report will not be distributed to the NCSAC prior to the Sampling Design Workshop. Workshop participants will assess the accuracy and validity of the report and make the appropriate interpretations of the facts presented by Battelle. The purpose of the workshop is to determine those elements that are relevant and important and to address the high-level issues and concerns. After the workshop findings are presented to the NCSAC, there will be sufficient time to digest and interpret the information before the NCSAC ultimately advises the federal government on the appropriate sampling design.

Update of the Health Disparities and Environmental Justice Working Group Workshop

Rueben Warren, D.D.S., Dr.P.H., Working Group Co-Chair, CDC, DHHS

Dr. Warren began his presentation by naming the Working Group's other co-chairs: Charles Lee, EPA, and Kristine O. Suozzi, Ph.D., Bernalillo County Environmental Health Department. Dr. Warren explained the Working Group's intent to balance the voice and influence of non-federal group members with those of federal members. At this time, a major charge for the Working Group is to not let the racism hypothesis overcome all of the Working Group's other responsibilities. The intent of the upcoming workshop is to specifically focus on measures and outcomes of racism.

Dr. Warren explained that public health experts have only recently considered the concept of racism as a factor in health disparities. He described the literature that brought this issue into the domain of public health. Researchers and public health experts are still struggling to explain the gaps in morbidity and mortality data for different racial and social groups in the United States (that is, is it race or racism?).

The Working Group's workshop on racism will bring together experts in the field to examine the issues surrounding the measurement and outcomes of racism. The Working Group will distill the findings of the workshop, develop a hypothesis on racism, and integrate their findings into other Working Groups' activities. The Working Group will develop a list of core measures and draft a preliminary list of presenters and other participants prior to the workshop. The Working Group

will deliberate on the measures and present the findings at the NCSAC's June 2004 meeting. Names of potential participants—both individuals and organizations—should be submitted to Dr. Warren.

NCSAC Open Forum

Donald Mattison, M.D., NCSAC Chair, NICHD, NIH, DHHS (Moderator)

Dr. Mattison reminded the NCSAC that their role during the transition from Study planning to implementation is clearly outlined in advisory committee meeting materials that were distributed prior to the meeting. He drew particular attention to the goals and responsibilities for the NCSAC June meeting (listed in Tab 5, page 3, of the meeting binder). A primary focus during the June meeting will be to discuss the findings of the Sampling Design Workshop. Dr. Mattison emphasized that the NCSAC needs to finalize its recommendations on Study themes, hypotheses, and measures during the June meeting.

Dr. Michael proposed that, in preparation for the June meeting, NCSAC members list and prioritize their visions of, aspirations for, and objectives of the Study. Dr. Michael offered the following questions:

- What are people hoping that the Study will accomplish, achieve, or produce?
- What are the expectations for the Study?
- Which children are the main focus of the Study?
- What are the Study priorities?
- Which hypotheses are most important?
- What do Study investigators want to know?
- What outcomes are most important?

Answering these questions will provide the proper perspective for the Study's focus, and within this context, the NCSAC will be able to assess and interpret the finding of the Sampling Design Workshop and make its recommendation on sampling design.

Action Item: NCSAC members will send their lists of answers to Dr. Michael, who will compile them and report the findings to the NCSAC at the June meeting.

In an open discussion, participants recognized the possibility of additional hypotheses emerging in the future as the Study gathers and analyzes data. However, they acknowledged that a set of measure must be proposed at this stage of the Study to frame discussions on sampling design strategies. Establishing the measures will help guide both hypotheses and protocol development. Dr. Mattison suggested that each NCSAC member prepare a matrix of exposures and outcomes. Weighting the priorities of exposures and outcomes will enhance the discussions of sampling design. Dr. Scheidt explained that the matrix should help determine whether measures of exposures and outcomes are sufficient to address the Study hypotheses.

Action Item: NCSAC members will develop a matrix of Study exposures and outcomes, with weighted priorities, and present them at the NCSAC June meeting.

Participants acknowledged the importance of the Study hypotheses and their role in generating scientific credibility for Study findings. The hypotheses provide a scientific method to define Study boundaries and create a tool to allocate resources. Because important exposure and outcome measures will help develop future hypotheses, the Study design will need to remain flexible.

Action Item: Prior to the June meeting, NCSAC members need to provide written comments on:
- Revised theme description and core hypotheses (from the ICC)
- Sampling Design Workshop report
- Study strategic plan
- Any additional input from Working Groups on measures.

Action Item: Prior to the June meeting, Working Group liaisons need to provide the following from their respective Working Groups:
- Critiques and comments on the ICC's hypotheses
- Sets of measures of exposures and outcomes
- Answers to the ICC's and NCSAC's questions.

NCSAC Members

Donald R. Mattison, M.D., NCSAC Chair, NICHD, NIH, DHHS
Jan L. Leahey, NCSAC Executive Secretary, NICHD, NIH, DHHS
David C. Bellinger, Ph.D., Boston Children's Hospital
Linda M. Burton, Ph.D., Pennsylvania State University
George P. Daston, Ph.D., Proctor and Gamble
Willa M. Doswell, R.N., Ph.D., University of Pittsburgh School of Nursing
Donald J. Dudley, M.D., University of Texas Health Sciences Center at San Antonio
Alan R. Fleischman, M.D., New York Academy of Medicine
Barbara R. Foorman, Ph.D., University of Texas Health Science Center at Houston
Judith A. Graham, Ph.D., American Chemistry Council
*Fernando A. Guerra, M.D., M.P.H., San Antonio Metropolitan Health District
Loretta Jones, M.A., Healthy African American Families
*Shiriki Kumanyika, Ph.D., M.P.H., University of Pennsylvania School of Medicine
Philip J. Landrigan, M.D., Mount Sinai School of Medicine
*Grace LeMasters, Ph.D., University of Cincinnati
Roderick Joseph A. Little, Ph.D., University of Michigan
Robert T. Michael, Ph.D., University of Chicago
Deborah A. Phillips, Ph.D., Georgetown University
P. Barry Ryan, Ph.D., Emory University Rollins School of Public Health
M. Anne Spence, Ph.D., University of California, Irvine Medical Center
Lucina Suarez, Ph.D., Texas Department of Health
*Daniel J. Swartz, Children's Environmental Health Network
Barry S. Zuckerman, M.D., Boston University School of Medicine

*Did not attend.

ICC Members

Amy Branum, M.S.P.H., National Center for Health Statistics, CDC, DHHS
*Adolfo Correa, M.D., Ph.D., National Center on Birth Defects and Developmental Disabilities, CDC, DHHS
Sarah A. Keim, M.A., NICHD, NIH, DHHS
Woodie Kessel, M.D., M.P.H., Office of the Secretary, DHHS
Carole A. Kimmel, Ph.D., National Center for Environmental Assessment, EPA
Mark Klebanoff, M.D., M.P.H., NICHD, NIH, DHHS
Pauline Mendola, Ph.D., Office of Research and Development, EPA
*Sheila A. Newton, Ph.D., NIEHS, NIH, DHHS
James J. Quackenboss, M.S., Office of Research and Development, EPA
Peter C. Scheidt, M.D., M.P.H., NICHD, NIH, DHHS
Kenneth C. Schoendorf, M.D., M.P.H., National Center for Health Statistics, CDC, DHHS
Sherry G. Selevan, Ph.D., Office of Research and Development, EPA
*Marshalyn Yeargin-Allsopp, M.D., National Center on Birth Defects and Developmental Disabilities, CDC, DHHS

*Did not attend.

Observers and Other Participants

Gerry G. Akland, M.S.
Teneshia G. Alston, NICHD, NIH, DHHS
Tye E. Arbuckle, Ph.D., Environmental Health Science Bureau, Health Canada
Christine A. Bachrach, Ph.D., NICHD, NIH, DHHS
Tina Bahadori, Sc.D., American Chemistry Council
Marion J. Balsam, M.D., NICHD, NIH, DHHS
Adelaide Barnes, M.A., NICHD, NIH, DHHS
Arthur M. Bennett, M.E.A., B.E.E., NICHD, NIH, DHHS
Ruth A. Brenner, M.D., M.P.H., NICHD, NIH, DHHS
Davis Bu, Ph.D., Booz Allen Hamilton Inc.
Leni Buff, NICHD, NIH, DHHS
Audrey Burwell, Office of the Secretary, DHHS
Carolyn Clancy, M.D., Agency for Healthcare Research and Quality, DHHS
Mark Cosentino, D.P.M., Ph.D., Science Applications International Corporation
Ben P. Daughtry, R.Ph., M.B.A., FACHE, Dynport Vaccine Company
Elizabeth A. Davis, NICHD, NIH, DHHS
Diane Dennis-Flagler, M.P.H., CDC, DHHS
Virginia DeSeau, NICHD, NIH, DHHS
Leslie J. DiFonzo, Booz Allen Hamilton Inc.
Denise Daugherty, Ph.D., Agency for Healthcare Research and Quality, DHHS
Pam Smeder Douglas, Booz Allen Hamilton Inc.
Terence Dwyer, M.D., Ph.D., NICHD, NIH, DHHS
Jonas H. Ellenberg, Ph.D., Westat
Alexa Fraser, Ph.D., Westat

Warren Galke, Ph.D., NICHD, NIH, DHHS
Anoop Ghuman
Lynn R. Goldman, M.D., M.P.H., Johns Hopkins University
William D. Grubbs, Ph.D., Science Application International Corporation
Doris B. Haire, American Foundation for Maternal and Child Health
Melissa Hardt, Oracle Corporation
Mary L. Hediger, Ph.D., NICHD, NIH, DHHS
John H. Himes, Ph.D., M.P.H., University of Minnesota
Jamie Hui, Booz Allen Hamilton Inc.
Anne E. Imrie, Science Application International Corporation
Raffael Jovine, Ph.D., Booz Allen Hamilton Inc.
Sarah S. Knox, Ph.D., NICHD, NIH, DHHS
Danuta Krotoski, Ph.D., NICHD, NIH, DHHS
William F. Lawrence, M.D., M.S., Agency for Healthcare Research and Quality, DHHS
Rebecca T. Leeb, Ph.D., CDC, DHHS
Stephanie J. London, M.D., Dr.P.H., NIEHS, NIH, DHHS
William Lyman, Ph.D., Wayne State University
Stephen Marcus, Ph.D., National Cancer Institute, NIH, DHHS
Ellen L. Marks, RTI International
John R. Menkedick, M.S., Battelle Memorial Institute
Luke P. Naeher, Ph.D., University of Georgia
Maryam Naserghodsi, NICHD, NIH, DHHS
Haluk Ozkaynak, Ph.D., M.S., EPA
Susan Pagliaro, NICHD, NIH, DHHS
Nigel Paneth, M.D., M.P.H., Michigan State University
Sherri L. Park, NICHD, NIH, DHHS
Layna McConkey Peltier, Capitol Health Group
Bobbie Peterson, M.S., McKesson BioServices
Pat Phibbs, Daily Environment Report
Barbara J. Porter, B.S., National Institutes of Standards and Technology, U.S. Department of Commerce
Nancy Potischman, Ph.D., National Cancer Institute, NIH, DHHS
Jonathan Radow, The Blue Sheet
Jerry D. Rench, Ph.D., RTI International
William J. Rodriguez, M.D., Ph.D., Center for Drug Evaluation and Research, U.S. Food and Drug Administration, DHHS
Marquette Roher, NICHD, NIH, DHHS
Beth D. Roy, Social and Scientific Systems, Inc.
Lee Salamore, American Chemistry Council
Gary D. Sandefur, Ph.D., University of Wisconsin, Madison
Kathy Schneider, Ph.D., Iowa Foundation for Medical Care
Julie A. Schoenborn, M.B.A., Brady Corporation
Paul J. Seligman, M.D., M.P.H., Center for Drug Evaluation and Research, U.S. Food and Drug Administration, DHHS
Christine Shreeve, Ogilvy Public Relations Worldwide
Anita Singh, Ph.D., Food and Nutrition Service, U.S. Department of Agriculture

David C. Songco, NICHD, NIH, DHHS
Paul D. Sorlie, Ph.D., National Heart, Lung, and Blood Institute, NIH, DHHS
Catherine Y. Spong, M.D., NICHD, NIH, DHHS
Paul Swidersky, B.Sc., Quality Associates, Inc.
Mary Jane Teta, Dr.P.H., Exponent, Inc.
Hale Vandermer, Ph.D., Native American Management Services, Inc.
Ann M. Vinup, Learning Disabilities Association of American
Diane K. Wagener, Ph.D., RTI International
Rueben C. Warren, D.D.S., Dr.P.H., M.P.H., CDC, DHHS
Robin M. Whyatt, Ph.D., Columbia University
Cathy Spatz Widom, Ph.D., University of Medicine and Dentistry of New Jersey
Marian Willinger, Ph.D., NICHD, NIH, DHHS
Paul Wise, M.D., M.P.H., Boston University
Edward Tin Wong, Science Applications International Corporation
Robert H. Yolken, M.D., Johns Hopkins University Medical Institutions

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

May 4, 2004
Date

Donald Mattison, M.D.
Chairperson
National Children's Study
Federal Advisory Committee

National Children's Study
Advisory Committee 10th Meeting

June 28–29, 2004
Holiday Inn Select Old Town
Alexandria, VA

Meeting Objectives of the June 2004 NCSAC Meeting:

The primary purpose of the June National Children's Study Advisory Committee (NCSAC) meeting will be for NCSAC members to establish a series of recommendations concerning the overall sampling design for the National Children's Study. Throughout the meeting, the NCSAC members will listen to and participate in a series of discussions concerning sampling design strategies from the Sampling Design Subcommittee and the Program Office. Objectives of the meeting will be for members to:

- Review and comprehend the background material outlining the various sampling design options
- Discuss the information and Executive Summary produced at the March Sampling Design Workshop
- Answer a series of questions posed by the National Children's Study Program Office
- Agree to a series of recommendations that will be provided to the Director, NICHD.

Additional goals of the meeting will be to:

- Hear updates regarding protocol development
- Review revised hypotheses; and,
- Determine feasibility or impact of joining the AGES Study
- Discuss the changing role of the NCSAC and WGs as the Study moves into the implementation phase.

Agenda

Monday, June 28

8:00 a.m.–8:05 a.m.	**Welcome** *Don Mattison, M.D.* *Chairperson, NCSAC*
8:05 a.m.–8:30 a.m.	**Introduction** **Review and Comments on Minutes from Last Meeting** **Review of Agenda and Modifications** **Goals of the Meeting** **Action Items** ▪ **Recommendation Concerning Sampling Design** ▪ **Recommendation Concerning Impact of AGES to the Study**
8:30 a.m.–9:30 a.m.	**Program Office Update** **Staffing, Protocol Development, Institute Updates** *Peter Scheidt, M.D.* *National Children's Study Director*
9:30 a.m.–9:45 a.m.	**BREAK**
9:45 a.m.–10:15 a.m.	**Overview of Sampling Discussion** *Peter Scheidt, M.D.* *National Children's Study Director* *Don Mattison, M.D.* *Chairperson, NCSAC*

	Introduction of Sampling Session Facilitator, Brook Rolter *Don Mattison, M.D.* *Chairperson, NCSAC*
	Overview of Sampling Process *Brook Rolter* *Sampling Facilitator*
10:15 a.m.–10:45 a.m.	**Summary of Sampling Design Workshop** **(Goal: to provide the NCSAC adequate background information)** *David Savitz, Ph.D.* *Professor and Chair, Department of Epidemiology* *University of North Carolina School of Public Health* *Sampling Subcommittee Panel Chair*
10:45 a.m.–11:30 a.m.	**Program Office: Sampling** **"Thoughts of the Program Office"** *Ruth Brenner, M.D.* *National Children's Study Program Office*
11:30 a.m.–12:00 p.m.	**Technical Background Relating to Sampling Issues** *Warren Strauss*, *Sc.M.* *Program Director, Battelle*
12:00 p.m.–12:30 p.m.	**Presentation of the ICC's Questions** *Peter Scheidt, M.D.* *National Children's Study Director*
12:30 p.m.–1:30 p.m.	**LUNCH ON OWN**
1:30 p.m.–3:00 p.m.	**Discussion of the Sampling Strategy** *Brook Rolter* *Sampling Facilitator*
3:00 p.m.–3:15 p.m.	**BREAK**
3:15 p.m.–4:15 p.m.	**Discussion of the Sampling Strategy (continued)** *Brook Rolter* *Sampling Facilitator*
4:15 p.m.–5:00 p.m.	**Closing Discussion: Sampling "Assignments"** **(Goal: clarifying "what" NCSAC will provide)** *Brook Rolter* *Sampling Facilitator*
5:00 p.m.–5:30 p.m.	**Update of Human Genome Institute "AGES" Study** *Alan E. Guttmacher, M.D.* *Deputy Director* *National Human Genome Research Institute, NIH*
5:30 p.m.	**Adjourn** *Don Mattison, M.D.* *Chairperson, NCSAC*
6:30 p.m.–9:00 p.m.	**Dinner: NCSAC Members** **Gadsby's Tavern Restaurant** **Alexandria, VA**

Tuesday, June 29

8:30 a.m.–11:00 a.m.	**Sampling Discussion (continued)** *Brook Rolter* *Sampling Facilitator*
9:00 a.m.–10:00 a.m.	**NCSAC "Assignments" Reports and Discussion** *TBD*
10:00 a.m.–10:15 a.m.	**BREAK**
10:15 a.m.–11:00 a.m.	**Sampling Discussion Wrap-Up and Recommendation** *Brook Rolter* *Sampling Facilitator*
11:00 a.m.–11:45 a.m.	**Discussion of Positive Health Framework** *Deborah Phillips, Ph.D., NCSAC Member* *Chair, Department of Psychology* *Georgetown University*
11:45 a.m.–1:00 p.m.	**LUNCH ON OWN**
1:00 p.m.–1:15 p.m.	**Presentation of Revised Hypotheses**
	Physical Environment *Don Mattison, M.D.* *Chairperson, NCSAC*
1:15 p.m.–1:45 p.m.	**Social Environment** *Linda Burton, Ph.D., NCSAC Member* *Professor and Director* *Center for Human Development and Family Research in Diverse Contexts* *Pennsylvania State University*
1:45 p.m.–2:15 p.m.	**Injury** *TBD*
2:15 p.m.–2:30 p.m.	**Report from Joint ICC/NCSAC Executive Committee** *Judith A. Graham, Ph.D., NCSAC Member and Chair of the Executive Committee* *Senior Scientist and Senior Director* *Long-Range Research Initiative, American Chemistry Council*
2:30 p.m.–2:45 p.m.	**BREAK**
2:45 p.m.–3:30 p.m.	**Discussion Regarding Future of the NCSAC** **Discussion Regarding AGES** *Don Mattison, M.D.* *Chairperson, NCSAC*
3:30 p.m.–4:00 p.m.	**NCSAC Open Forum**
4:00 p.m.–4:15 p.m.	**Closing Announcements** *Don Mattison, M.D.* *Chairperson, NCSAC*
4:15 p.m.	**Adjourn**

DEPARTMENT OF HEALTH & HUMAN SERVICES National Institutes of Health

National Institute of Child Health
and Human Development

MEMORANDUM

DATE: May 20, 2004

TO: Duane Alexander, M.D.
Director, NICHD

FROM: National Children's Study Federal Advisory Committee

SUBJECT: Request from O. Carter Snead, Esq.

This memo has been prepared in response to the request from O. Carter Snead to the Federal Advisory Committee of the National Children's Study (NCSAC) on December 16, 2003 regarding the effects of assisted reproductive technology (ART) on child health. In this request, he referred to a draft report where it is noted, "… an ideal vehicle for this study is the National Children's Study now being planned….". In his presentation to the NCSAC, he asked that we consider the possibility of utilizing the NCS to study the effects of ART on child health outcomes. In brief, the Advisory Committee strongly supports the capture of information regarding the use of ART to achieve pregnancy in those women recruited for this study and will recommend that this information be included in the study protocol currently being developed. The remainder of this memo outlines the process we took to arrive at this conclusion and further recommendations to you and the President's Council on Bioethics.

In response to Mr. Snead's request, the NCSAC has reviewed the issue in considerable detail. We have reviewed the original hypothesis regarding ART and child health outcomes proposed by the Fertility and Early Pregnancy (FEP) Work Group and a recent meta-analysis on ART in relation to child health outcomes published in the British Medical Journal. In addition, several experts in the area were consulted by telephone or conference call, including Phyllis Leppert, M.D., Ph.D., of the National Institute of Child Health and Human Development (NICHD), Dorrie Lamb, Ph.D., of Baylor College of Medicine, James Segars, M.D., of NICHD, Robert Brzyski M.D., Ph.D., past president of the Society for Assisted Reproductive Technology (SART), and Germaine Buck, Ph.D., of NICHD.

The original hypothesis proposed by the FEP Work Group focused on the primary outcomes of intrauterine growth restriction (IUGR) and birth defects. These outcomes are the least studied of the potential complications of ART and more important than previously appreciated. Other outcomes proposed for study include birth outcomes (preterm birth) and cost and burden to the family. The proposal included a strong rationale for including the hypothesis in the study and the justification for a large sample size, but no power calculation or sample size consideration. Because the low overall frequency of ART and the low rates of primary outcomes (birth defects, LBW) in an unselected sample would not have sufficient power, we considered that the effect of ART on child health ideally require a study specifically designed for this problem, and the hypothesis was not advanced further.

The meta-analysis by Helmenhorst et al ("Perinatal outcome of singletons and twins after assisted conception: a systematic review of the literature"; British Medical Journal on line publication, doi:10.1136/bmj.37957.560278.EE, January 23, 2004) surprisingly showed that there was a higher incidence of preterm births among singletons conceived through ART (relative risk of 3.27), with no increase in the rate of preterm births among twins (when compared with spontaneous conceived twin pregnancies). Notably, there was less perinatal mortality among twins conceived with ART (RR 0.58) when compared to spontaneous twin conceptions. One should remember that twinning is far more common with ART conceptions than with spontaneous conceptions and hence the burdens to the health care system consequently greater. Also, this meta-analysis has some limitations, including the predominance of one relatively large study from Belgium (in which the authors used three different control populations for different aims in the study).

In discussions with the experts above, a consensus opinion included the following points:

1. This problem is indeed important, but there are currently no studies in the United States with requisite power on-going or planned.
2. As currently designed the National Children's Study likely does not have the appropriate study design to answer the question definitively. Even assuming 1% ART conceptions in the US, only 1000-1500 such conceptions would result in the NCS sample. This sample size likely would not be sufficient to study this problem adequately.
3. To achieve the needed power to address this problem using the NCS, over sampling of specific populations would likely be necessary.
4. Not all ART is the same. There are different techniques utilized to achieve conception, and an adequate study of ART effects on child health would need to account for these different techniques.
5. The indications for ART are varied, as there are a number of reasons for infertility in couples. Study results would need to be adjusted for cause of infertility, and this information is often difficult to acquire.

Given these caveats, the NCSAC recommended that the circumstances regarding the conception, including ART, be recorded for each child enrolled in the study. This information will provide helpful data that may lead to important insights. Also, the NCSAC did not recommend that over sampling for the purposes of studying ART on child health should occur, unless additional resources for required sampling and measures were available. However, the NCSAC feels that the NCS could serve as a control population for a study specifically designed to address the effects of ART on child health given the current plan for a representative population sample. The NCSAC advises you to consider using the current funding mechanisms in NICHD to develop a study specific for the study of ART on child health. If you wish, we will request that the FEP Work Group readdress this problem and develop guidelines for such a study with specific consideration of sample size issues.

The NCSAC is most appreciative that the President's Council on Bioethics made this request and recognizes the scientific value of the NCS, and we hope that we have addressed this request in a satisfactory manner. Representatives from the NCS and NCSAC would be pleased to attend a subsequent meeting of the President's Council on Bioethics to elaborate on our response should you feel the need.

Guidance: Each hypothesis will be given a maximum of 15 minutes for review and discussion. The primary review should be no longer than 5 minutes. The secondary reviewer should add only new information or discrepancies in view point. Any additional time will be used for questions and discussion. Prior to the meeting, each reviewer should provide a brief written review addressing the hypothesis from the following perspectives:

- Relevance to a national study of environmental impacts on health of children at various life stages
- Contemporary nature of hypothesis and analytic approach proposed
- Benefit of including hypothesis in study
- Cost of including hypothesis in study (number of environmental samples needed, number of biological samples needed, information needed from individual and families)
- Rating for each hypothesis (one of three groups);
    - Recommend - the NCS should include this as a core hypothesis
    - Consider- while it may not meet the criteria of a core hypothesis, this proposal should be given consideration if sufficient resources are available
    - Not Recommended at this Time - this should not be considered as core or potential secondary hypothesis at the present time

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Assignments – June 2004 Meeting

WG Hypothesis	Work Group	Primary	Secondary
The Social Environment and Children's Health and Development. Overview	Social Environment	Linda Burton	David Bellinger
Media Hypothesis Social Environment	Social Environment	Deb Phillips	Loretta Jones
Built Environment and Physical Activity in Children	Physical Environment WG	Phil Landrigan	Bob Michael
Child Maltreatment Hypotheses (21 May 2004)	Injury	David Bellinger	Willa Doswell
Unintentional Injury Hypothesis (25 May 2004) Cathy Spatz	Injury	Lucina Suarez	Phil Landrigan
New Unintentional Injury Hypothesis January 25, 2004 Fred Rivara	Injury	Grace LeMasters	Judy Graham

Initial Proposal for Core Hypothesis\Question
Please limit your response to 2-3 pages

I. Proposed Core Hypothesis\Question – include what is the primary outcome associated with this hypothesis:

II. Workgroup(s) – collaboration across workgroups is encouraged:

III. Contact Person for Proposed Core Hypothesis\Question (include phone and email):

IV. Public Health Significance - please address the following issues to the extent possible for both the exposure and outcome:
- Prevalence/incidence
- Morbidity
- Quality of Life
- Mortality
- Economic burden to individual, family, community, etc
- Social burden to individual, family, etc.
- Perceived importance – how is answering this hypothesis going to improve the health and development of children.
- Preventability / Malleability

V. Justification for a large, prospective, longitudinal study
- Time sequencing
- Need for repeated measures (e.g. change in exposure, cumulative exposure, etc)
- Justification for sample size of approximately 100,000 based on one or any of the criteria below. Be as specific as possible – include power calculation if at all possible)
    - Need to study subgroup exposures, susceptible subgroups
    - Need to study multiple overlapping exposures
    - Need to study interactions
    - Does this hypotheses have such a rare exposure/outcome or low relative risk that it would require investigation using the entire cohort of 100,000.

VI. Scientific Merit - please address the following issues to the extent possible:
- What theory supports the hypothesis?
- Current scientific understanding
    - Non-human experimental data support the hypothesis
    - Non-human experimental data support the hypothesis at exposure levels experienced by humans
    - Human data supporting the hypothesis
- How will answering this hypothesis\question advance our understanding

VII. Potential for innovative research
- New findings
- New technologies

Initial Proposal for Core Hypothesis\Question
Please limit your response to 2-3 pages

VIII. Feasibility - please address the following issues to the extent possible:

- Critical period for exposure and outcomes
- Sampling needs: targeted groups or settings, special strategies, sample size (provide power calculations if possible), special subgroups of interest, etc
- Contact – if more than one contact is needed, frequency and timing of the recontact
- Measurement tools for assessing exposures or outcomes: questionnaires, educational or psychological testing, medical diagnosis or clinical assessments, biological specimens, interviews.
  - For each measurement tool:
    - Have the measurement tools been demonstrated to be valid and reliable in the population in which NCS will use them?
    - Is specialized expertise and equipment needed?
    - Is there sufficient capacity to measure these factors on a large scale?
    - What are the estimated costs of the measurements?
    - What are the risks associated with these measurements?
    - Are there other ethical considerations associated with these measurements, e.g. reporting issues, etc.?
    - What are the burden to the participant and family associated with these measurements?
- Community Involvement
- Other burden to the participant and family associated with this hypothesis not covered in the measurement tool section.

Individual Hypothesis Review Form

Hypothesis # _____ Date Received: _____

Title:_____

Work Group or Organization: _____

	Strengths	Weaknesses
Relevance to a national study of environmental impacts on health of children at various life stages		
Contemporary nature of hypothesis and analytic approach proposed		
Benefit of including hypothesis in study		
Cost of including hypothesis in study (number of environmental samples needed, number of biological samples needed, information needed from individual and families)		
Recommend - the NCS should include this as a core hypothesis		
Consider- while it may not meet the criteria of a core hypothesis, this proposal **should be given consideration** if sufficient resources are available		
Not Recommended at this Time - this should not be considered as core or potential secondary hypothesis at the present time		

Reviewer: _____ Date: _____

Primary: _____ Secondary: _____

The Social Environment and Children's Health and Development.

Overview

Expanded and Updated
June 1, 2004

The Social Environment Working Group (SEWG) submitted a set of seven hypotheses for consideration by the National Children's Study Advisory Committee in May 2003. The Working Group also included an "Overview" document that summarized the hypotheses.

This expanded and updated Overview document contains two additions:

1. In response to questions from the ICC, a section on power analyses has been integrated (see pp. 24-29). These power analyses provide examples of six specific hypotheses that could not be tested in the absence of the National Children's Study. The hypotheses chosen are a sampling of similar hypotheses that require large sample sizes to test. Four of the six power tests yield N's of approximately 75,000 or higher, and all require N's of 40,000 or higher. No existing data base is large enough to permit testing of any of the examples given.
2. The Overview summarizes an eighth hypothesis now being submitted by the Working Group (pp. 10-11). This hypothesis was developed through a SEWG-initiated workshop on media exposures and children's healthy development. The new hypothesis documents is being forwarded to NCSAC for the June 2004 meeting. It proposes that children's media exposures be tracked by the NCS and a set of hypotheses relating media exposures to various health and developmental outcomes be tested.

Remaining questions raised by the ICC about the SEWG hypotheses focused on recommended measures. SEWG provided a large set of measures to the NCSAC at the March 2004 meeting. Final additions to this set will be completed this summer.

3. The Social Environment and Children's Health and Development.

Overview

Introduction

The social environment in which a child is raised has a profound influence on his or her health and development. The social environment sometimes affects child health directly, and sometimes indirectly through influencing children's exposures to the physical and biological environments. The characteristics of a child's family affect the quality of care giving and level of material resources (including nutrition, housing, and medical care) available to the child. Family resources and behaviors are in turn affected by the characteristics and social norms of people in the child's community and the family's social networks. Formal institutions, such as childcare services, schools, health services, religious organizations, social service agencies, and even the media, are also important. Some of these institutions directly affect the quality of care children receive, whereas others affect the knowledge and behaviors of the child and his or her family members. Finally, the resources available to families and communities are affected by policies and programs—such as health insurance programs, income support programs, and housing policies—in place where the child lives.

The Social Environment Working Group has prepared a series of eight proposals for core hypotheses that are concerned with the social environment. Six of these proposals are structured around different aspects of the social environment. The topics of these six proposals are: families and households; socioeconomic status; neighborhoods and communities; formal institutions; public policy; and media. The last two are integrative proposals on asthma and obesity. These illustrate how all of the different aspects of the social environment combine to influence specific health outcomes in childhood. Although the eight proposals are on different topics, they share many common elements. They rely on an overlapping set of measures of the social environment, and many issues related to methodology, measurement, and sampling needs are common across the proposals.

This document provides an overview and synthesis of the eight proposals. Section II defines the different elements of social environment, discusses their public health significance, and summarizes the hypotheses in the eight proposals. Section III turns to measurement issues, and discusses different mechanisms for data collection, sampling needs, and measures of different aspects of the social environment. It includes a summary table of measures of the social environment that we believe are critical to the success of this study.

The definition and public health significance of the social environment

A. <u>What is the social environment?</u>

The "social environment" is defined broadly, to include demographic, economic, political, legal, organizational, cultural, and familial factors that affect the resources available to children and their experiences as they develop. We have categorized the social environment into six inter-related domains: families and households; socioeconomic status; social

networks and social support; neighborhoods and communities; formal institutions; public policy, and media:

Families and households: Family resources and family processes are important for child health and development. For example, the presence or absence of fathers or father figures, and the availability of supportive members of kin and non-kin networks—influences both the quality of care children receive and the economic resources available to children. A key family process is parenting. Parents have a profound influence on their children through their knowledge of and ability to implement health behaviors—such as the provision of appropriate medical care and a healthy environment—as well as their ability to provide their children with secure attachments and an emotionally supportive environment.

Socioeconomic Status: Socioeconomic status includes income, education, employment opportunities, and job characteristics. A family's financial status affects its ability to live in a safe and healthy environment, and to provide children with a variety of goods and services—including medical care, nutrition, and childcare—that affect their health and development. The education levels of adults in a family are related to health knowledge (for example, the ability to follow medical protocols) and behaviors (for example, smoking and drug use) that affect children's health. The characteristics of parents' jobs, for example the degree of stress or uncertainty produced by jobs, may have indirect effects on child wellbeing.

Neighborhoods and communities: Neighborhoods and communities provide resources that are important to children. These resources include the level of income in the community, and the quality of community organizations such as schools, recreational facilities, commercial outlets, public services, religious organizations, and employment opportunities. Communities are characterized by social processes that determine the degree of social interaction, crime levels, and political activity. There is a close connection between the physical and social environments in neighborhoods and communities. For example, communities that have higher incomes and more effective community and political organizations may be better positioned to create and maintain physically healthy environments. Structural characteristics of neighborhoods, such as age, racial and ethnic composition, population density, and housing stocks, have an impact on social processes and the resources available to neighborhood residents.

Formal institutions: Formal institutions include schools, childcare facilities, youth development programs, organized recreational activities, law enforcement and justice programs, social services, religious institutions, and the media. Many of these formal institutions, in particular childcare facilities and schools, directly influence the quality of care children receive and their social and cognitive development. Other institutions operate indirectly, by influencing the way caregivers and other individuals interact with children, or by shaping important neighborhood or community characteristics that impinge on children's development.

Public policy: Virtually every aspect of the social environment is influenced by public policy. We focus on policies that diminish or buffer risks to health and development.

These include income support and safety net programs, including both cash and in kind benefits, food stamps, WIC, and medical insurance; child care and education policies; housing; and transportation. These policies affect the level and nature of resources availability to families or to their communities.

Media: Electronic and interactive media comprise a major part of children's lives, even at very young ages. The presence in the media of images inimical to children's healthy development - including violence, substance use, risky sex, and certain kinds of advertising – raises important public health questions about media exposures. Media exposures also provide stimuli for positive learning and development. However, except in a few areas, scientific research on the impact of media exposures is very limited. We focus on a variety of media exposures, including TV, video games, computer and internet use, and others, from birth through adolescence.

Another aspect of the social environment that cuts across all of these domains is the shared meanings and norms associated with racial or ethnic identity. In families, neighborhoods, and institutions, whether minority status is viewed as a disadvantage and/or a source of strength matters for children's development. When public policies or institutions discriminate against racial or ethnic minorities, and when communities are divided by racial tensions, all residents, including children, are affected.

B. Public Health Significance

The importance of the social environment is best illustrated by the disparities in children's health and development across socioeconomic groups within the United States. By nearly any measure, disadvantaged children have worse health and developmental outcomes than do others. Poorer children are more likely to develop a variety of serious chronic health problems, including heart conditions, vision and hearing disorders, and diabetes (Newacheck, 1994); to have more hospitalization episodes; to experience accidental injuries and accidental deaths; to develop obesity in adolescence; to develop emotional problems, such as depression; and to adopt "risky" behaviors, such as smoking, drug and alcohol use, and early sexual activity, in adolescence.

These disparities are not simply the result of children in poverty being at heightened risk of poor outcomes relative to all other children. Instead, there is a clear income gradient: for many outcomes, health and development improve continuously as socioeconomic status improves. This is illustrated in the following table, which shows a set of selected health outcomes for children at different levels of family income:

Income quintile	Fraction in excellent or very good health	Average annual hospital episodes (ages 1-17)	Percent with asthma	Percent with heart condition	Percent with hearing problem	Percent with mental retardation	Percent 5.5 lbs or less at birth
1 (poorest)	0.66	0.048	7.2	2.3	2.1	2.2	9.6
2	0.77	0.039	5.9	2.3	1.9	1.4	7.8
3	0.84	0.034	5.6	1.9	1.8	0.9	6.5
4	0.87	0.032	6.0	2.0	1.6	0.9	5.4

5 (richest)	0.90	0.025	6.4	1.7	1.3	0.7	4.8

Notes: The first 6 columns are based on samples of children from the 1986-1995 NHIS. The children are aged 0-17 unless otherwise noted. The information on birth weight is from the 1988 Child Health supplement of the NHIS, which collected information on one child aged 0 to 17 in each household with children.

Similar patterns are seen if children are categorized by measures of the social environment other than income. For example, children are more likely to be in excellent or very good health if their mothers have more education and if they live in two-parent households. There are also pronounced differences in health outcomes for children across racial and ethnic groups. Although these bivariate relationships do not provide information on the underlying causal mechanisms that relate various aspects of the social environment to children's health and development, they underscore the importance of the social environment.

Children's health varies over geographic space as well as along socioeconomic gradients. The table below illustrates substantial variation in indicators of infant, child, and adolescent health among four states and four large cities, chosen on the basis of their diversity with respect to the percent of children living in poverty. All of the indicators show substantial variation by place. In some cases, this variation parallels variation in child poverty but in others it does not. For example, Miami has the highest rate of child poverty of the four cities, but the lowest infant mortality rate and a moderate proportion of youth who fail to wear seatbelts. Like the statistics on income gradients above, these data cannot speak to why place matters for child health, and it cannot disentangle the effects of place from the effects of population characteristics such as race, ethnicity, and income. They do tell us that children across the United States experience different levels of health depending on where they live.

		Four States		
Indicator	UT	DE	MO	MI
% of children in poverty	12.0	15.0	21.0	30.0
Infant mortality rate	5.8	7.8	6.9	10.6
Child death rate	27.0	25.0	32.0	36.0
% high school students:				
current cigarette use	8.3	24.2	28.5	23.6
rarely/never wear seatbelts	7.5	14.9	19.8	24.5
		Four Cities		
	San Francisco	Dallas	Philadelphia	Miami
% of children in poverty	18.0	27.0	30.0	44.0
Infant mortality rate	6.8	10.9	14.5	5.3
% high school students:				
current cigarette use	13.3	17.8	15.8	16.9
rarely/never wear seatbelts	8.7	8.5	34.5	18.1

Notes: Data on % in poverty, infant mortality rate, child death rate from Annie E. Casey Foundation, Kids Count Data Book 2000 and City Kids Count. Data on high schools students from Centers for Disease Control

and Prevention, MMWR 51(SS-4), Youth Risk Behavior Surveillance - United States, 2001. States and cities chosen on the basis of data availability and to provide a distribution of areas with respect to the % of children living in poverty.

Rural-urban differences are also consequential for health. In general, children from suburban areas enjoy better health than children living in the inner cities of metropolitan areas. Relatively little is known about the influence of urban vs. rural residence on child health and development in the contemporary United States, because most research has been conducted in urban areas. However, national data reveals important differences (see table below). Adolescents living in rural areas are most likely to smoke while those living in the central cities of large metropolitan areas are least likely. Infant mortality rates are lowest in the fringe counties of large metropolitan areas. Death rates for children and young adults are highest in rural counties. Homicide rates are highest in central cities while death rates for suicide and unintentional injuries are highest in rural areas.

	Metropolitan counties			Nonmetropolitan counties	
	Large central	Large fringe	Small	With city >=10,000	No city >=10,000
Infant mortality rate	7.5	6.1	7.5	7.7	7.7
Death rate, persons 1-24	44.5	35.4	41.7	46.2	58.5
% smoking, youth12-17	11.0	15.9	16.1	15.2	18.9
Homicide rates	11.5	3.9	6.4	5.2	5.4
Suicide rates	13.2	12.6	15.2	16.5	18.0
Death rates, unintentional injuries	31.2	29.1	36.5	44.6	54.1

Source: Eberhardt, et al. , 2001

The Case of Asthma: Asthma, the third-ranking cause of hospitalization among U.S. children under 15 years of age, provides a useful example of the role of the social environment in health. Although, as shown in a previous table, the reported overall prevalence of asthma does not uniformly decrease with income, the prevalence of severe asthma does decrease with income. Asthma death rates are highest in areas with higher concentrations of poor people and minority residents (particularly African Americans). Racial differences in asthma are independent of socioeconomic status. Asthma mortality and hospitalizations vary across regions, cities, and even within cities. Rates of asthma are high in central urban areas, but evidence indicates that rates are nearly as high in some rural areas.

How does the social environment contribute to differences in children's asthma outcomes across locations, income groups and ethnic groups? The observed patterns of outcomes are likely the result of complex interactions between genetic predispositions, aspects of the physical environment, and characteristics of the social environment. Socioeconomic status may affect whether children live in areas where they are exposed to environmental risk factors such as air pollutants or allergens; whether they have access to medical care for asthma treatment; and whether their families are equipped to follow medical protocols for asthma. The expression and severity of asthma may also be affected by psychosocial stress experienced by children and their families. (For example, both wheeze and asthma among

children has been related to parenting problems and family stress.) Stress that exacerbates asthma may be increased by living in violent or poor communities or having unstable sources of income, and may be ameliorated by public policies that address these situations.

The complex mechanisms though which the social environment affects asthma are also likely to affect other childhood health outcomes. Existing research on childhood obesity, for example, highlights the "causal web" of social factors, including parenting, peer influences, food pricing and availability, and opportunities for physical activity that, together with genetic predispositions, affect a child's chance of becoming obese.

Hypotheses

The Social Environment Working Group has developed six proposals that contain testable hypotheses on how different aspects of the social environment affect children's health, and two "integrative" proposals that illustrate how the interplay of different aspects of the social environment affect two important childhood health problems, asthma and obesity. The hypotheses contained in these proposals are summarized as follows:

1. Family and Households

Pathways to specific child health and development outcomes are directly influenced, mediated, and/or moderated by family resources and processes.

Example Hypotheses: The following hypotheses are examples of the many implied by the role of family resources and processes in child health and development. Specific examples of more general hypotheses are given in the family hypothesis document.

- Family structures, including parental unions, household composition, and living arrangements affect child outcomes. The extent to which changes in family structure affect child outcomes stems in part from the nature and stability of family structures.

- Families' social networks may have positive or negative influences on child health and development, by providing (or limiting) access to instrumental and/or emotional support for either child or adult family members, by placing demands on parents' time for helping others, by providing (or limiting) access to information and health-supportive resources, by exposing children to positive or abusive relationships, or by supporting healthy or unhealthy norms for health-related behaviors.

- Family socioeconomic status (e.g., income, wealth, parents' education and occupation and other human capital) influences the health and development of children by ameliorating the effects of risk factors associated with family structure, process, physical and mental health, and family identity.

- Children with less healthy parents are likely to be in poorer health themselves, in part because of shared genetic predispositions but also because of poorer quality parenting and compromised access to resources. The more household family members that are in poor health, the more likely a child is to experience physical and mental health problems.

- Racial/ethnic minority families and their children are likely to have higher morbidity and mortality than whites from the same disease conditions, in part because they experience greater disparities in health care and because of differences in acquiring health knowledge and engaging in health-promoting lifestyles. At the same time cultural risk or protective factors associated with minority status (e.g., supports for health-protective behaviors among first-generation immigrants, knowledge and use of alternative medical practices, norms supporting antisocial behaviors or delay of appropriate health care) will contribute to variability in the health experiences of racial/ethnic minorities.

- Parental investments in health advocacy and help-seeking behaviors on behalf of their children contribute to better physical and mental health outcomes in children.

- Families' interactions with and involvement of their children in community institutions, including child care, schools, and religious organizations, influence children's health and development both directly, and indirectly through the formation of social networks.

- Parental monitoring of children’s activities will enhance health and development.

- Parental promotion of healthy lifestyle behaviors through teaching and modeling will influence children’s exposure to toxins and infectious agents, reduce the likelihood of injury, and reduce the level of morbidity from diseases.

- Children who are exposed to negative family dynamics will display more problematic health and developmental outcomes.

2. Income, Socioeconomic Status

Socioeconomic gradients in child health and developmental outcomes may be explained by multiple pathways involving health behaviors, parenting, social resources, stress, and the reciprocal effects of health on socioeconomic status:

- More highly-educated parents may make better use of medical information that protects their children’s health, or may be more able to follow medical protocols.

- Higher incomes may enable parents to choose less-hazardous living environments; to provide their children with better nutrition; or to access and purchase a greater quantity and higher quality of medical care.

- Stress associated with low income, low job status, unemployment, and social inequality may undermine parenting behaviors that promote children's health and development.

- Higher socioeconomic status may facilitate access to social resources (e.g., diverse social networks, family stability, and "social capital") that provide access to health information and services, buffer stress, and improve material well-being.

- The association between parents' socioeconomic status and children's health may arise because of common genetic or environmental influences linked to both poor health and status.

- Poor childhood health may adversely affect family economic status.

3. Community and Neighborhoods

Where one lives affects exposure to social, physical, psychological, and environmental factors that increase the risk of developing health problems such as asthma and decreased access to protective resources.

- Neighborhood and community characteristics that negatively influence the health of the mother during pregnancy – including poverty, poor housing quality, poor health care access, norms and policies that encourage smoking, and low levels of social interaction and support – increase the likelihood that the fetus will develop characteristics that predispose it to heightened susceptibility to health problems later in life.

- Neighborhood and community characteristics that contribute to environmental hazards– including poverty, poor housing quality, norms and policies that encourage smoking, low levels of political mobilization or collective efficacy, and high levels of crime and violence – increase the incidence and severity of childhood health problems, such as asthma, and complicate their management.

- Neighborhood and community characteristics that contribute to stress – including stressors such as poverty, unemployment, crime and violence, and poor housing quality, and the absence of stress-buffering resources such as social supports and access to health care and other institutions– increase the incidence and severity of childhood health problems, such as asthma, and complicate their management.

- Collective efficacy in neighborhoods reduces the incidence of high risk behaviors among children and adolescents, such as smoking, drinking, and drug use.

4. Formal Institutions

The interactions between children and families and the formal institutions in their communities influence children's health and development.

- The physical and social environments of non-parental child care settings influence child health and cognitive and social functioning. Variations in the quality of child care affect child outcomes. Child care influences are mediated through family influences.

- Children's participation in schools affect social, emotional, and physical development. Provision of health services and of curricula and programs targeted toward health promotion directly impact on children's health and mental health outcomes. Child, family, and community factors interact with structural and functional aspects of schools to shape child development.

- Family participation in religious organizations during early and middle childhood (ages 3-10) results in better emotional health and fewer health-compromising behaviors during middle adolescence (ages 14-15). These effects are stronger in female children, ethnic minority and immigrant families, and impoverished areas, and when the religious organizations provide effective mechanisms for integrating adolescents into the life of the religious community.

5. Policy

Public policy directly affects child health and development by providing access to resources and facilities and indirectly by its influence on other social environmental variables.

- Policies and programs that buffer families from risks, instability, and hardship have positive effects on child health/development.

- Variations in policies and programs by state and by size of community contribute to child health differentials across place.

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6. Media

The amount, type, content and context of media exposure from infancy through adolescence influence brain and neurological development; cognitive and social development, risk behaviors factors related to injury, substance use, sexual health; and obesity and other aspects of physical development. Effects and effect sizes will differ with timing of and cumulative amount of exposure and in different populations with differing vulnerabilities.

- Media exposure contributes to obesity and other nutrition related disorders (bulimia/anorexia, Type II diabetes) through three mechanisms:
    a) Sedentary behavior due to displacement of physical activity;
    b) Increased intake of nutritionally poor (high fat, sodium, and/or sugar content) food due to advertising exposure as well as food intake during media use;
    c) Distorted body image as a consequence of exposure to idealized human images
- Media devices (e.g., handheld video games, joysticks, keyboards, light guns, mouse) that are used for extended periods of time leads to increased risk of repetitive strain injuries and musculoskeletal disorders.

- Mature brain function and architecture (neuronal development and death of unneeded neurons) are altered by exposure to audiovisual media (any/ amount of exposure to screen media) during a critical developmental window between birth and 2 years of age. This will be reflected in long-term cognitive, attentional, and behavioral outcomes.

- Exposure of children to educational media content enhances the development of cognitive skills and increases academic achievement. These effects are maximized:
  a) in the developmental period of 2-5 years;
  b) where other sources of cognitive support and stimulation are minimal;
  c) where English is not the first language; and
  d) when children are exposed to same-ethnic models in the media.

- Amount, nature, and context of exposure to sexual content in entertainment media predicts beliefs about sexual norms and practices, early onset of sexual activity, greater number of sexual partners, increased frequency of sexual activities, and less frequent use of condoms and other protection. Through these outcomes, it also predicts higher incidence of unplanned pregnancy and sexually transmitted diseases.

7. Obesity

Economic, cultural, social, and policy characteristics of the social environment, along with characteristics of the physical environment, influence the development of obesity from conception to adulthood. These factors operate largely through influences on family and social network resources and processes that affect behaviors related to energy balance (diet, activity, and inactivity).

- Programs that connect low-income women to early prenatal care and social environmental influences that support the management of maternal hyperglycemia during pregnancy reduce the risk of accelerated fetal growth and the child's subsequent risk of childhood obesity.

- Support for breastfeeding in the work environment and kin/nonkin networks of new mothers will contribute to lower rates of obesity through increasing the probability of breastfeeding and the duration of breastfeeding. These factors partially mediate the influence of socioeconomic status on breastfeeding and obesity.

- Parenting behaviors influence the timing of adiposity rebound and changes in adiposity during childhood through their effects on children's diet and physical activity/inactivity. Parenting behaviors are a function of the family's food and physical environments, family resources (structure, parental education and income), and norms and beliefs supported through kin and nonkin networks.

- The influence on obesity of non-family factors, including peer and media norms for thinness or body shape, access to and promotion of energy-dense foods, and opportunities for physical activity in schools and communities, increases with increasing age and intensifies after puberty. Social interaction with peers influences physical activity/inactivity and diet, and is in turn adversely influenced by obesity in children and adolescents. Sociocultural influences on diet and physical activity differ by race, ethnicity, and gender.

8. Asthma

Disparities in the prevalence, severity, and effective management of asthma by race and socioeconomic status are explained, in part, by social environmental factors and processes that influence exposure to physical environmental risk factors, psychosocial stress, and health-related behaviors.

- The relationship between socioeconomic status, race/ethnicity, and asthma incidence and morbidity is explained, in part, by socially determined differential exposure to physical environmental risk factors (i.e., diesel-related air pollutants, allergens) and psychosocial stress. These effects are moderated by policies and programs that buffer the effects of economic disadvantage on families.

- Economic, cultural, and social features of the local area influence: (1) exposure to stressful life conditions and events; (2) the availability of social ties that provide informational, emotional and instrumental resources to individuals and families; and (3) shared norms influencing health behaviors. These, in turn, influence outcomes including immunological functioning in the child, the likelihood that the child will develop asthma, and asthma severity and management.

Measuring the social environment

1. Methods of data collection

Social scientists employ a variety of data sources and data collection techniques in measuring the social environment. Specific measurement approaches adopted in any study

depend on the constructs to be measured, the populations and geographic areas under study, required precision, and the resources available to the study. Data collection methods employed in existing studies of social environmental influence include:

Household surveys

Household surveys are the most common data collection method for measuring many aspects of the social environment. Household surveys can be used to obtain information on household structure and demographics; income, employment, and other socioeconomic characteristics; characteristics of social networks in which the children's parents and the child are engaged; household members' perceptions of community and neighborhood characteristics; the family's engagement with different formal institutions; and the family's knowledge and use of different publicly-provided programs. Much of this information can be obtained through telephone surveys. However, some information on the family or household—for example, the quality of parenting, or characteristics of the physical environment in the child's home—require in-home visits.

Several important design issues related to the use of household surveys in longitudinal studies require attention:

- *Definition of household*. Data from the 2000 Census highlight the increasing diversity and complexity of households. The fraction of "unmarried partner" households rose from 3.5% to 5.2% from 1990 to 2000. The fraction of households headed by unmarried females rose from 6.6% to 7.2% over this time period. The fraction of households that are multi-generational (either grandparent-parent-child or grandparent-child) households was 3.7% in 2000 (no figures from 1990 are available in recent reports.) Children's living arrangements reflect this complexity: only about 70% of children under 18 lived with two parents in 2000, and of these, an estimated 2 out of 5 no longer lived with biological parents who were married to each other. Household surveys must capture this complexity, by collecting information on the complete set of individuals living in a child's household rather than just the child's biological parents. At the same time, adults who do not live in the household—for example, absent fathers and grandparents—are often important to the child's health and development, and it is important to collect information on their contact and relationship with the child, and the degree to which they provide financial or other support.

- *Choice of respondent*. No one family member is the best source of information on all survey items, and different family members may give systematically different information. For example, data from the National Health Interview Surveys indicates that, on average, fathers report their children as being in better health and having fewer doctors' visits than do mothers. Most child health surveys collect information from the child's "primary caregiver", typically the mother. However, if the child's primary caregiver is not the primary earner in the family, or if the household contains multiple earners, the primary caregiver may not provide accurate or comprehensive information on the family's economic status. Similarly,

the mother may not be able to report accurately on the father's or other family members' relationship with the child. We recommend collecting information on income, employment, and job characteristics from each of the adult household members, and on family relationships and processes from all family members significantly involved in caregiving. At a minimum, the child's mother and father should be surveyed separately. If a significant caregiver is not present in the household, efforts should be made to locate him or her and collect relevant information. The focal child should be included in providing data at a developmentally appropriate stage.

Administrative data on individuals

Administrative data sources can be used to supplement the information obtained in household surveys, and are useful for information that is difficult for family members to remember accurately (for example, use of medical care services, or earnings histories), or may be difficult for family members to discuss (for example, involvement with child protective services or the juvenile justice system.) Gathering administrative data can be difficult: it requires the agreement of the respondents as well as the cooperation of agencies that hold data, and also requires carefully-constructed safeguards for the confidentiality of the respondents. However, several large studies have developed methods for merging administrative data with household survey data, and making these combined data sources available to researchers in a way that protects confidentiality.

Existing data on state and local characteristics

The collection of regional and local information at various levels of aggregation is critical to studying the effects of the social environment. Although the household-level survey will collect information on perceptions of the local environment and the respondent's participation in programs, it will not necessarily capture true neighborhood characteristics or actual program availability. Relying on reports of household members can result in erroneous conclusions. One problem is that the knowledge and use of programs may be endogenous to children's health—so that, for example, parents of sick children are more likely to know about or use local health services. If so, it would not be surprising to find that health and the availability of health services *as reported by the parent* are negatively correlated, even if health services have beneficial effects on the population. A related problem is that respondent's perceptions of their neighborhoods may be colored by their own health—so that, for example, depressed parents may be more likely to report their neighborhoods to lack cohesion or to produce stress. In this case, the effects of parental depression on child wellbeing may be incorrectly attributed to neighborhood characteristics.

Information on local areas is available from a variety of existing sources, detailed below. Measures vary in the type and size of geographic unit for which they are available (e.g., states, metropolitan areas, school districts, census block groups). Where possible, the unit and level of aggregation should be selected based on theory. For example, many policies are formulated at the state level and should be measured at the state level; however the

processes that produce criminal activity and the effects of crime on individuals mainly occur within smaller areal units such as the local neighborhood and its surrounding areas. Some constructs should be measured at multiple levels of aggregation. For example, the economic well-being of the population influences resources available for programs and public services at the state and county levels, as well as norms and social processes within neighborhoods. Thus, measures of areal income should be collected at the state, county, census tract and block group level.

Sources of information on local areas:

Policy and program information. Many policies that affect children's lives are implemented at the state level (even if they are fully or partially federally funded.) These include: TANF rules, including generosity of payments, time limits, and work requirements; Medicaid and SCHIP generosity and eligibility rules; child support enforcement provisions; and laws surrounding definitions of and reporting requirements for child abuse and neglect, and policies that affect the disposition of child maltreatment cases. Information on policies and programs can be collected from states. In some cases (e.g., TANF, tobacco-related policies) existing databases summarize current policy and policy changes.

- *Census data*. Many characteristics, such as income levels, racial and ethnic diversity, neighborhood segregation, proportion of single parent families, and housing characteristics, can be constructed from decennial Census data for block groups, census tracts, counties, metropolitan areas, and states. These data cannot be used to follow changes in neighborhood characteristics over short periods of times. However, plans to replace the 2010 Census Long Form with an ongoing survey (the American Community Survey) will provide more frequent small area estimates at the county and census tract levels, but will provide no data at the block group level.

- *Administrative and other data for geographic areas*. Some data sources, such as crime reports, can be obtained at the county level. School characteristics are collected at the level of the school district, which are usually but not always within counties. Data on the size, (other characteristics) of specific schools are available through an existing data base collected by Quality Education Data, Inc., (QED), and the National Center for Education Statistics provides individual school-level information on many variables in their Common Core of Data. Data on health care facilities and utilization are also available at the local level. Others, such as characteristics of medical services, are available at the level Data on religious adherence is available from nongovernmental organizations. The number and characteristics of businesses and social service organizations is available from InfoUSA and the locations of these are often available in GIS databases. Real estate and rental prices are available from real estate data bases. A wealth of data from administrative and other sources is available in many communities, but additional research is necessary to identify potential gaps in these information sources and issues that might arise in accessing them. The SEWG will propose a pilot study to conduct this research.

Linking this diverse set of areal information to the child- and family-level data is no small task. A basic requirement is to obtain specific information on the geographic location of the child, ideally through use of a geographic positioning system (GPS) device that provides exact geographic coordinates for the child's residence. Existing data on defined areal units can be linked by matching geographic coordinates. In addition, alternative approaches can be adopted that are not based on pre-defined geographic units. For example, the number of recreational sites or health care facilities within a given radius of the individual's home can be coded.

Most existing studies create datasets that combine measures of state and local characteristics linked to survey data on individual respondents. An alternative approach is to *not* attempt to collect the information on local areas, but instead to provide researchers with individual respondents' geographic identifiers and allow them to collect and link appropriate areal data. However, this approach has several serious shortcomings. The first is that the provision of geographic identifiers compromises confidentiality. The second is that, because different researchers will inevitably use different measures and methods of merging, the ability to compare results across studies is compromised. Providing a standard set of contextual data requires more work on the part of the organization conducting the study, but avoids these problems. A "middle ground" approach is to provide a basic set of contextual measures to all researchers, and set up a secure procedure that investigators may use to link other contextual measures to the individual survey data without compromising confidentiality.

Direct observation

Another innovative approach employed by recent studies of neighborhood and community effects has been to collect systematic data on area characteristics through the use of inventories completed by trained observers (Pebley, 2002) and through a technique, called systematic social observation (Sampson and Raudenbush, 1999) based on videotaping and coding the characteristics of public spaces. These techniques permit the assessment of characteristics that are not available, or unreliably measured, in existing records. For example, they have been used to measure the physical condition of neighborhoods (conditions of streets, traffic, presence of trash and garbage, land use, condition of buildings, graffiti) and social characteristics (loitering, gang activity, presence of prostitutes, homeless, or drug dealers, public intoxication, presence of children, police, use of multiple languages).

Other observational studies include studies that assess child developmental outcomes through direct observation, observation of interactions between children and caretakers, and direct observation of the physical and social characteristics of schools, day-care centers, and medical facilities.

Community ethnography, observation, and other methods

Ethnography is a set of methods used to provide an in-depth understanding of the cultural understandings that pattern individual behaviors and experiences in daily life in the context of historical, social, economic, and physical opportunities and constraints. Culture, as a model "of and for reality" (Geertz, 1973) operates in the background of daily life and behavior, and so is difficult to study directly. The methods of ethnography are flexible and varied, and may include direct observation, in-depth interviews, key informant interviews, textual analysis, focus groups, and surveys. The essence of ethnography is in this flexibility, and in the commitment to go beyond the collection of individual facts about individual lives to get at the shared understandings, expectations, and values that profoundly influence individuals' view of the world (and therefore their behavior) and the social dynamics of communities or groups.

Ethnography is expensive, and necessarily undertaken mainly in small-scale studies. However, it can provide invaluable insights when properly integrated into larger-scale studies. The flexibility of ethnographic approaches permits the discovery of new facts and relationships that investigators may miss altogether if they rely solely on pre-designed measurement protocols. Insights derived from ethnography may clarify the interpretation of study findings by clarifying the meaning of events to individuals. Ethnography can also provide direct measurement of hard-to-measure constructs such as cultural norms.

Furthermore, ethnographic methods can often be employed selectively to address specific measurement needs. For example, independently conducted community surveys might collect data on local attitudes and values and the extent and quality of social interaction and political participation among area residents (e.g., PHDCN). [In some studies, local area estimates of such measures are derived by aggregating the responses of the primary study participants; however the aggregate measures thus derived are not truly independent of the study participants and may give misleading results for the reasons given above.] Key informants in community institutions (religious organizations, day care centers) may be asked to provide information about the ways in which their institutions function (e.g., Laumann et al), or teams can be sent to observe the operation of these institutions (e.g., NICHD Day Care Study). In-depth interviews can be conducted with a subsample of families. Local media outlets can be monitored for content that could influence health (e.g., advertising of alcohol or tobacco, news stories about physician malpractice or side effects of drugs, etc.). Mapping, using geographic information system (GIS) data, can be used to examine how individual's daily lives unfold over physical space.

A three-tiered approach: Household surveys, existing state and local data, and selected in-depth local studies

The Social Environment Working Group believes that an ideal approach to measuring the social environment would consist of three "tiers" of measurements. The first tier is survey data on the child, household, and key family members as well as family resources and process, social support networks, ties to community institutions, and knowledge/use of social programs and public policy. The second is the collection and integration of existing information on the local areas in which study participants live (states, counties, neighborhoods, etc.). This tier of measurement should include as much data as possible

that is relevant to the goals of the study, and the set of identifiers collected by the study should include the geographic coordinates of participants' residence.

The third tier of measurement should include a small sample of local communities selected for intensive measurement. The goals of the study should guide the criteria for selecting these communities; illustrative criteria might include diversity by rural/urban status, racial and ethnic composition, income levels, and the presence or absence of environmental hazards. Participants in these communities would follow identical protocols to participants in the overall study (the two tiers of data described above) but a variety of additional measurement strategies would be implemented as well to provide greater depth and coverage in the measurement of the social (and perhaps physical) environment. These measurement strategies could include:

- Community surveys of values, attitudes, and social processes
- Observational studies of schools, religious organizations, and day care centers
- In-depth studies of the implementation of public policies and programs, and the enforcement of laws (housing violations, child welfare systems)
- Geographic mapping of participants' social, work, and institutional contacts and resources
- Monitoring of media content for health-related influences
- Measurement of global social networks in schools at selected grades
- In-depth interviews with families and extended family members; in-home observation of family process

These intensive measurement strategies are necessary for testing some of the Working Group's hypotheses, and highly desirable for others. For example, to adequately test hypotheses about the impact of child care quality on child outcomes, observation of provider-child interaction among children in child care would be conducted to measure dimensions of quality of care that cannot be adequately captured by other means. Measuring the influence of peers on children's behavior cannot be accomplished without assessment of global social networks, because ego-centered reports on peers are biased by the child's own attitudes and behaviors. The most important influence of public policies on asthma etiology and severity may reside in policy implementation (e.g., of housing codes and housing subsidies), which may not be adequately documented in available administrative records.

2. Longitudinal Design

a. .Need for a longitudinal study

An important feature of the social environment is that it is not static. Many children will experience changes in family structure over their lives, as their parents' marital status and/or living arrangements change. Children who move experience changes in their neighborhoods; and, for those who do not move, neighborhood characteristics may change over time. Economic status changes due to changes in economic cycles, employment, family structure, and life cycle stage. And, characteristics of the institutions and policies that affect children vary over time.

It is also likely that the effects of different aspects of the social environment vary at different ages—so, for example, neighborhood characteristics may become increasingly important as children grow older—and may have cumulative effects on children over time. For example, evidence indicates that health disparities between poorer and better-off children become increasingly large as children become older. Some social environmental effects may be most important during specific critical periods, for example, care-giving during infancy, and may have latent effects that express themselves at a later stage of development.

For these reasons, longitudinal data collection is essential for research on the effects of the social environment on the health and development of children. Many if not most features of the social environment cannot be reliably reported retrospectively. Longitudinal data are needed to track changes in the social and family environment, and variation across children in their "exposures" to different aspects of the social environment over time.

Longitudinal data are also required because the relationship between many social environmental factors and health and development is *reciprocal.* For example, ill health can result in a change in availability of social support, and lack of social support can undermine health. Preserving the correct temporal sequence between exposure and outcomes is essential for inferring causality, and for understanding the ways in which health and social factors influence each other over the course of development.

b. Periodicity of measurement

Because the social environment changes over time, surveys need to be administered at multiple points over the course of childhood. The frequency and timing of measurements depend on the independent variables and the hypothesized timing of critical exposures and effects. We recommend developing a comprehensive "baseline" data collection to measure family, household, and area characteristics. Household survey data should be updated in a series of annual or bi-annual surveys that gather information on items (such as parental employment status, income, use of social and medical services, social networks, and family process) that vary across years and for which subjects can be expected to have poor recall over longer frequencies. Neighborhood, community, and policy characteristics should also be updated on a regular basis. Specific requirements for periodicity by measure require further study by the Social Environment Working Group.

Sampling and Design Requirements

1. *Probabilistic sampling of a nationally-representative population*

The Social and Environment Working Group strongly supports the use of a probability sampling to obtain data that are representative of a cohort of US children (including children born on US military bases and children born to incarcerated or homeless mothers). One approach is to follow the lead of the Early Childhood Longitudinal Study – Birth

Cohort study, which implemented a national probability sample of births based on vital registration. Recruitment of a probability sample of mothers giving birth in hospitals and birthing centers is another alternative (though at the cost of slightly less population coverage), one that has been used successfully in a current NICHD study.

Biases resulting from reliance on nonprobability sampling would undermine the validity of the study in a number of ways:

- The descriptive findings of the study would not be generalizable to any known population, and in fact the sample may systematically underrepresent individuals most at risk for adverse outcomes. This would be true if, for example, participants are selected from the population of women who receive prenatal care.
- The substantive findings of the study, e.g., measuring the impact of exposure A on outcome X, could be seriously compromised. One potential problem is failure to find effects due to insufficient range in either the dependent or independent variables (because participants have been systematically excluded in ways correlated with those variables); another is the potential for failing to identify, and account for, important conditional effects. For example, if A influences X in some groups or under some conditions but not others, then the relative representation of the groups/conditions in the study population will influence the overall estimate of the effect.
- Other major data sources on health, such as the National Health Interview Study, the Medical Expenditure Panel Study, and the NHANES, are based on nationally representative probability samples. The comparability of results across studies requires the use of similar sampling methods.

We recognize that a sample drawn from the population of births rather than from a population of pregnant women will make it difficult to study the effects of the pre-natal environment on birth outcomes and later childhood health. If it were feasible, the ideal sampling method would be to randomly sample women of child-bearing age, and track them into and through pregnancy. However, no complete list currently exists that could provide a sampling frame for a probability sample of soon-to-be-pregnant women. Such a frame could be constructed by starting with an area probability sample, screening to select a sample of women, and monitoring them until they become pregnant. The sample of women could be selected to maximize the potential yield of pregnancies by oversampling those women with characteristics associated with an impending pregnancy (there is a solid literature on such characteristics in the field of demography). However, this method would be costly. While it would be less costly to construct a frame of service providers that would yield a sample of pregnant women, such a frame would systematically exclude women who fail to have contact with providers. Many women, primarily young, single, and poor, identify pregnancy late and have contact with health or social services even later. Those who are late in recognizing pregnancy and getting care are systematically different than those who are early with regard to important social and psychological factors.

An alternative would be to combine methods, e.g., combine a sample of births with an area sample of women screened for the likelihood of impending pregnancy; combine an area sample with a probability sample based on a provider frame; or other similar combinations. The key is to base at least some substantial portion of the sampling plan on probability methods and a comprehensive sampling frame.

2. *Stratification and clustering*

A simple random sample of the population, in which all children have equal probability of being sampled, will result in relatively small groups of children from some types of communities and ethnic groups, making it difficult to study health problems in these populations. It will undoubtedly be desirable to oversample some types of communities and populations. Rural communities are generally not adequately represented in national probability samples. It will be important to oversample diverse types of rural communities that pose special risks to child health and development. These include agricultural communities (because of pesticide use and other occupational safety issues); impoverished rural communities (because of poor access to health care and other social services, high incidence of high risk factors like obesity and diabetes, and siting of environmental contaminants); and perhaps high growth rural communities in recreation and leisure (because these are places of future growth and development). Impoverished communities generally and minority, immigrant, and migrant labor populations are other likely targets for oversampling. All decisions on oversampling should be made with an eye to the adverse impact of weights on statistical precision.

A related issue is the need to have an adequate number of U.S. states represented in the sample. The working group has several hypotheses regarding the effects of variations in state-level public policies on child outcomes. Measuring the effects of these policies requires variation in the policy environment, something that can only be achieved by having a large number of states with variation in the policy environment.

A final issue is the need to design the sample to optimize the modeling of multi-level effects on health. There are a variety of sampling issues in the design of datasets that will be used to identify neighborhood and community effects. The degree of clustering within neighborhoods, and stratification to ensure adequate variability in the independent variables are two such issues.

3. Changes over time

The collection of a longitudinal cohort study poses special challenges. A major difficulty is keeping track of research subjects after they have moved. Although it is costly to track movers, the Working Group strongly recommends that movers be followed wherever they go. There are two reasons for tracking subjects who change location. First, those who move are not a random sample of the population of interest and, by restricting the sample to those who do not move the sample will become less and less representative of the underlying population over time. Second, a growing body of literature is documenting that residential mobility is consequential for children's health and development. Data from the Current Population Survey show that one in five U.S. children under 6, and one in three poor

children, change residences annually. On the one hand, movement from harmful to safer environments has been shown to improve child health and behaviors; on the other hand, high levels of residential instability disrupt social ties and contribute to poorer developmental outcomes. Further, issues of residence and mobility are central to the goal of estimating the effects of environmental influences on health outcomes. The risk of exposure to toxins, bad schools, or high-crime neighborhoods is confounded with the social and economic disadvantage that limits residential choice for many residents of inner cities and poor rural communities. The study will need to address the selection processes that result in people living where they live in order to accurately measure the impact of these exposures.

Another issue concerns changes in the population of children due to international migration. Data from the 2000 Census indicate that 3.9% of children (those aged 17 or less) were not native born, i.e. were born outside of the United States. Immigrant children have special health concerns, and this study will be unable to measure or analyze health problems among immigrant children if it is based solely on a sample of births. One way to deal with this problem is to add, at regular intervals, "refresher" samples of immigrant children who are of the same age as those in the original sample, so that the sample continues to be representative of all children in the U.S. who are members of the same birth cohort.

A final issue concerns the use of a single cohort of children who were born around the same time. In a single cohort study, period effects (e.g., a recession, a change in social policy) are experienced at the same time by all participants. Changes in outcomes that follow such "shocks" cannot be distinguished from maturational effects unless another cohort born at a different time period is available for comparison. The working groups recommends consideration of a multi-cohort design to enable analysts to distinguish the effects of maturation from period change. This could be accomplished by introducing new cohorts to the study at regular (e.g. 5-year) intervals or (less ideally) by recruiting the sample from multiple cohorts over a shorter time interval.

4. Sample size

Power analyses for example hypotheses are presented in the following section. Here, we address the general requirement for a large sample, which follows from many features of the hypotheses and the general character of social environmental effects.

- Testing the *multi-level* nature of social environmental effects demands a hierarchical data structure with sufficient numbers of observations at each different level (e.g., community, neighborhood, family, child) to allow analysts to appropriately model contextual influences. Moreover, there must be sufficient variability at higher levels (e.g., geographic, environmental, economic, cultural, and policy variability) and within levels to adequately power hypotheses concerning multi-level effects.

- Studying *multiple pathways* involving the social environment, community and family processes, and child development patterns require a large, diverse sample that can represent different types of family and household structures, care-giving patterns, community characteristics, and children who have different developmental and health experiences (i.e., low birth weight; physical and mental disability; temperament; turbulent family experiences; etc.).

- Socioenvironmental effects on child health are often multidimensional, that is, not reducible to the effect of a single dimension or factor. For example, different dimensions of socioeconomic status—indexed by the education, labor force status, source-specific incomes, and other attributes of one or both parents—may vary in the relative strength of their effects, both over time and across population subgroups. A large sample is essential to estimate these complex effects. Similarly, examining multiple, *overlapping* exposures (e.g., family social support versus peer group social support; neighborhood income vs. access to recreational facilities; policies that support family income vs. provide health care) requires a sufficiently large sample size to power such analyses.

- Testing interactions (e.g., cross-level interactions between community characteristics and individual characteristics; or gene-environment interactions) demands a large sample size. Such interactions are likely to be extremely common in social environmental pathways. For example, research suggests that early prenatal care may have less influence on birth outcomes in poor neighborhoods; job programs will have differential effects depending on the availability of child care subsidies; peer influence will have a different effect on weight-control patterns in African American and white adolescents. Examining the differential impacts of social environmental factors on population subgroups (e.g., women, Mexican immigrants, low SES groups, rural families) requires a large enough sample to represent these groups.

- Many important aspects of the social environment require large samples by virtue of their own characteristics or because of the outcomes they influence. For example, use of social welfare programs tends to be episodic, affects only a small proportion of the population at any given point in time, and varies greatly by social, spatial, and demographic characteristics. Only a very large sample will have sufficient power to enable investigation of small incidence of program use across different social groups in different locations. Many of the health conditions that are associated with economic status in childhood are rare. Data from the National Health Interview Study indicate that epilepsy, diabetes, and kidney disease are all associated with low income, but affect only a very small fraction (1% or less) of children. Even relatively “common” conditions such as asthma and obesity affect small enough fractions of children that large samples are required for analyses that involve separating children into groups classified by race, region, or gender.

Regardless of the samples sizes are required to evaluate the hypotheses presented by the Working Group, it is remains necessary to collect valid and thorough measures of social

environmental influences on health and development in the National Children's Study. Social environmental effects and the effects of rare exposures in the physical environment are not independent of each other. In an observational study, analysts will be unable to disentangle the causal effects of physical environmental hazards on children's health without complete measurement of correlated social environmental effects. As we hope this document and the accompanying hypotheses illustrate, these effects are complex and not easily captured in a few simple measures. Furthermore, the effects of physical environmental hazards will be affected by the ways in which families, neighborhoods, and policy-makers respond to them. Measurement of the social environment is necessary to a complete and valid discovery of the influence of physical threats to children's health.

5. *Power analyses*

The purpose of this section is to illustrate ***some*** of the social environment hypotheses that require sample sizes in excess of those currently available for research on child health and well-being. The National Children's Study would enable us to test these hypotheses.

Power analyses are presented below for six *specific* hypotheses that correspond to general hypotheses proposed by the Working Group. Required sample sizes are at or above approximately 75,000 for four of the six and above 40,000 for all six. The power analysis for hypothesis 4 was completed by Dr. Steve Rust of Battelle under an NCS pilot study project. All others were calculated by Dr. Gary Sandefur using the methods employed by Dr. Rust.

All power tests assume that the sample would be a simple random sample. This is unlikely to be the case, so the estimated sample sizes may be under- or over-estimates of what would be needed with other types of sampling designs. In general, clustered sample designs increase required sample sizes relative to simple random samples. In addition, the estimated sample size would be an overestimate if the sampling design results in over-sampling some of the socioeconomic characteristics used in the power analyses and it could be an underestimate if the sampling design results in a sample that is under-representative of the population distribution of certain characteristics.

1. <u>The Impact of Income and Socioeconomic Status</u>

General Hypothesis:

The association between higher incomes and child health and well-being is in part due to the higher quality of life that parents may purchase with their income. Higher incomes may enable parents to choose less-hazardous living environments; to provide their children with better nutrition; or to access and purchase a greater quantity of medical care.

The Role of Race and Ethnicity:

Given that the relationships between risk factors and outcomes vary with race and ethnicity, the association between income and health outcomes is likely to vary with race

and ethnicity. This is because of cultural and other differences across racial and ethnic groups. The National Children's Study provides an opportunity to explore racial and ethnic differences in the relationship between income and various health outcomes. One important racial and ethnic group in the United States is the Mexican American group. This group continues to grow in size and importance due in large part to continuing immigration from Mexico to the United States.

Specific Hypothesis:

Mexican American children whose families have incomes below the poverty line will be 1.5 times as likely to develop asthma as Mexican American children whose families have incomes above the poverty line.

Assumptions:

1. 15.6 percent of the NCS will be Mexican American children (NCHS, 2003a).
2. Approximately 30 percent of Mexican American children are poor. (U. S Census Bureau, 2002a).
3. The number of children in any subgroup of the NCS cohort having asthma at age 10 follows a binomial distribution.
4. Approximately 6 percent of children have asthma at age 10 (NCHS, 2003b).

Power Requirements:

1. .05 significance level in a two-tailed test for an odds ratio of 1.5 (poor children = .087, non-poor children = .06)
2. Power = .90

Required Sample Size

- 1944 poor Mexican American children
- Total of 6480 Mexican American children
- Total of 41,538 children in the NCS

2. Community and Neighborhoods

General Hypothesis:

Neighborhood and community characteristics that negatively influence the health of the mother during pregnancy—including poverty, poor housing quality, poor health care access, norms and policies that encourage smoking, and low levels of social interaction and support—increase the likelihood that the fetus will develop characteristics that predispose it to heightened susceptibility to health problems later in life.

Specific Hypothesis:

The incidence of depression during childhood for individuals whose mothers during pregnancy lived in severely distressed neighborhoods is higher than that for individuals whose mothers during pregnancy lived in other types of neighborhoods.

Assumptions:

1. A severely distressed neighborhood is one characterized by three of the following four characteristics: a poverty rate in excess of 27.4 percent, the percentage of families with children headed by a woman is 37.1 percent or more, the percentage of high school dropouts is 23 percent or more, and the percentage of males 16-64 detached from the labor force is 34 percent or more. In the 2000 Census, 7.7 percent of children lived in neighborhoods that were severely distressed (Annie E. Casey Foundation, 2003).
2. The number of children in any subgroup of the NCS cohort at age 21 who develops depression follows a binomial distribution.
3. According to Birmaher et al. (1996) up to 2.5 percent of children and up to 8.3 percent of adolescents suffer from depression. We focus for the purposes of this power test on childhood depression, which may be more likely to be related to conditions during pregnancy than is adolescent depression.

Power Requirement:

1. .05 significance level in a two-tailed test for an odds ratio of 1.5 (socially disorganized neighborhoods= .037, other neighborhoods= .025)
2. Power = .90

Required Sample Size

- 4331 children whose mothers lived in severely distressed neighborhoods during pregnancy
- 56,247 children in the NCS

3. <u>Formal Institutions</u>

General Hypothesis:

The physical and social environments of non-parental childcare settings influence child health and cognitive and social functioning. Variations in the quality of childcare affect child outcomes. Childcare influences are mediated and moderated by family influences.

<u>Specific Hypothesis:</u>

Children experiencing family day care during the preschool years are more likely than those in center-based day care to become overweight; this effect is stronger among children of single mothers than among children of married mothers.

This is an interaction hypothesis that explores how family structure and type of day care interact to influence becoming overweight. Center-based care is thought to have advantages over other forms of day care for cognitive development, but little research has

explored the impact of forms of day care on eating habits and obesity. Because center-based care is closely regulated it should be more likely to consistently provide nutritious meals and snacks than less formal child care arrangements. Therefore, we hypothesize that children of single mothers who are in family day care during the preschool years are more likely to become overweight than children of single mothers who are in center based day care. The association between type of day care and being overweight will be smaller among children of married mothers. This is because married mothers have more time and other resources to counter the effects of less organized child care facilities than do single mothers.

Assumptions:

1. Around 22 percent of children age 5 and under are living with single mothers (Census Bureau, 2002b).
2. Approximately 51.2 percent of children of single mothers had a parent employed full time (Casper and Bianchi 2002).
3. About 10 percent of children of working single mothers are primarily in family day care (National Research Council, 2003).
4. Approximately 15 percent of children and adolescents between the ages of 6 and 19 are overweight (CDC, 2002).
5. The number of children in any subgroup of the NCS that become overweight follows a binomial distribution.

Power Requirement:

1. .05 significance level in a two-tailed test for an odds ratio of 1.5 (center based care = .15, .209 in family based care)
2. Power = .90

Required Sample Size:

- 883 children of working single mothers in family day care
- 8830 children of working single mothers
- 17,246 children of single mothers
- 78,391 children in the NCS

4. <u>Policy</u>

General Hypothesis:

Policies and programs that buffer families from risks, instability, and hardship have positive effects on child health/development.

<u>Specific Hypothesis</u>:

Average intelligence scores at age 10 for children maltreated at age 5 are different for children who live in states with strong policies affecting the investigation and

substantiation of child maltreatment cases vs. children who live in states with weak policies affecting the investigation and substantiation of child maltreatment cases.

Assumptions:

1. 0.489 percent of all children are maltreated at age 5 (Children's Bureau, 2001).
2. The average (Wechler Scale) intelligence score at age 10 for children maltreated at age 5 who live in states with strong policies affecting the investigation and substantiation of child maltreatment is 100.
3. The standard deviation of intelligence scores (Wechler Scale) is 15.
4. 50 percent of maltreated children live in states with strong policies affecting the investigation and substantiation of child maltreatment cases.

Power Requirement:

1. .05 significance level (weak states = 95, strong states = 100)
2. Power = .90

Required Sample Size

- 379 children who at age 5 were maltreated and lived in states with strong policies affecting the investigation and substantiation of child maltreatment cases
- 77,506 children in the NCS

5. <u>Media</u>

General Hypothesis (a):

The higher the levels of exposure to violent media, the greater the risk of aggressive behavior.

<u>Specific Hypothesis (a):</u>

Children who are in the top quintile of exposure to violent media will be 1.5 times more likely to experience a firearm injury during the period from birth to age 21 than are children who are less exposed to violent media.

Assumptions:

1. Approximately 24 per 100,000 children are injured by a firearm each year (Centers for Disease Control, 2001). Over the course of the NCS, approximately 504 children (0.5%) will be injured by a firearm between the ages of 0 and 21.
2. Exposure to violent media is associated with increased risk of involvement in a broad range of aggressive behaviors (Paik and Comstock, 1994), thereby increasing children's exposure to violence and violent situations. An increased risk of firearm injuries is one of several potential outcomes of this increased overall exposure.
3. Virtually all children experience some exposure to violent media prior to age 10; those in the top quintile of exposure are considered most at risk of long term effects (Lefkowitz et al, 1977).

Power Requirement:

1. .05 significance level for a difference in odds of 1.5 (top quintile = .008, other quintiles = .005)
2. Power = .90

Required Sample Size:

- 14,914 children who are repeatedly exposed to violent media
- 74,570 children in the NCS

General Hypothesis (b):

Exposure of children to educational media content enhances the development of cognitive skills and increases academic achievement. These effects are maximized where English is not the first language.

Specific Hypothesis (b):

Children from non-English speaking families regularly exposed to English-language educational programming during the preschool years will be 1.5 times more likely to be school ready than children from non-English speaking families who are not regularly exposed to English-language educational programming.

Assumptions:

1. According to the ECLS-K, children from families where English is not the primary language constitute 9% of all children in the United States (NCES, 2000).
2. Approximately 15% of preschool children from non-English speaking families are regularly exposed to English-language educational programming (Based on data from the Kaiser Family Foundation (1999; 2003)).
3. Only about 12% of children from non-English-speaking families have mastered school readiness tasks such as recognizing word-ending sounds (NCES, 2000).

Power Requirement:

1. .05 level of significance for a difference in odds of 1.5, (17% of children who are regularly exposed to English language educational programming will be school-ready relative to 12% of those who are not exposed to English language educational programming)
2. Power = .90

Required Sample Size:

- 1036 children who are regularly exposed to English-language educational programming among children from non-English-speaking families.
- 6906 children from families where the primary language is not English
- 76,740 children in the NCS

B. Measures

The following tables provide *preliminary* lists of variables that are required to test the Working Group's hypotheses. The first table contains information that can be obtained from household surveys. The second contains information that can be obtained from administrative and other data sources. We do not include measures of the child's health here, since we anticipate that health measurement will be the focus of many of the other working groups. The Working Group has supplied additional detail on how and how often these variables are to be collected.

Table 1: Measures from Household Surveys

Variable/scale
Child and family characteristics
Demographic variables: age, gender, marital status, relationship to child of each household member (family structure)
Race, ethnicity, and migration: race, ethnicity, place of birth, migration history (including residence 5 years prior to initial interview), legal immigration status (if born outside of the U.S.); language spoken.
Religious affiliation, beliefs, attitudes, practices
Education levels of household members: Highest grade attained, whether currently in school or a job training program.
Employment status of household members
Job characteristics of household members: work hours, annual earnings and bonuses, occupation, industry, benefits (health insurance, maternity/paternity leave, breastfeeding supports, child care, flextime), perceptions of job stress.
Household division of labor, time use (time spent in child care, meal preparation, housekeeping, outdoor maintenance, etc. by primary caretakers of child)
Characteristics of parents living out of the household: age, gender, education, employment status, job characteristics, frequency and nature of contact with child
Unearned income of each household member: cash and in-kind public transfers (TANF, WIC, food stamps), child support receipt, other private transfers (gifts from relatives and friends), asset income, other income.
Food Expenditure (Panel Study of income Dynamics measure)

Housing Expenditure. Monthly expenditures on owned or rented housing and utilities.
Medical Care Expenditure. Out-of-pocket expenses for medical and dental care.
Child Care Expenditure. Monthly expenditure on child care for sample child and other children in the household.
Assets: Financial assets, home equity, ownership of major durables
Housing characteristics: Type of structure (single-family, duplex, townhouse, apartment, trailer); number of rooms; quality of housing (safety of environment for children, crowding, noise levels, cleanliness of home); whether publicly provided or subsidized housing.
Mobility: Number of moves during past year; reasons for moves; locations of places lived in the past year.
Economic stress: Utility shut-offs; debt problems and bankruptcy; food security (CPS measure).
Current mental health of household members: stress, depression and anxiety, drug and alcohol use
Mental health history of household members:: history of mental health disorders, drug and alcohol use.
Current physical health of household members: body weight and height, current self-assessed health status, reports of current physical health problems and chronic conditions; current pregnancy
Physical health history of household members: history of health problems and onset of chronic conditions.
Family Process
Relationships among household adults: domestic violence and measures of family conflict.
Parental discipline: Conflict tactics scale (???)
Monitoring and supervision
Cognitive stimulation: selected items from HOME and other scales.

Family warmth, closeness
Family meal environments: meals eaten at home or away from home; parenting practices directed at eating; child feeding questionnaire (Birch, et al., 2001)
Breastfeeding practices: Frequency, problems with.
Parenting practices related to physical activity: Frequency of television viewing, video and computer use, outdoor play. (note: additional measures of media use included with the Media hypothesis)
Health behaviors: Whether child receives regular medical checkups; whether child receives proper dental care (checkups, toothbrushing, put to bed with bottle); use of age-appropriate car restraints (seat belts or car seats); exposure to second-hand smoke; put to sleep on back (for infants)
Social ties
Parents' social networks and social support: Some subset of the following scales: the Social Network Index (Berkman and Syme, 1979); New Haven EPESE Network Assessment (Seeman and Berkman, 1988), Glass et. Al. 1997); Social support scale (Lin et.al. 1979); Perceived Social Support Scale (Blumenthal et.al. 1987); Medical Outcomes Study Social Support (Sherbourne and Stewart, 1991); Interpersonal Support Evaluation List (Cohen and Hoberman, 1983).
Children's social networks (ego-centered)
Social Institutions
Parent's knowledge of social services: Knowledge about local social service programs (visiting nurse programs, breastfeeding support programs, parenting programs, nutrition counseling.) Knowledge of eligibility for WIC, Medicaid and SCHIP, TANF.
Use of local programs: Use of local social service programs (visiting nurse programs, breastfeeding support programs, parenting programs, nutrition counseling.)

Participation with local institutions: Affiliation and participation with religious institutions, religious education programs, voluntary associations (e.g., PTA, civic groups).
Child Care: Frequency and duration of time child spends in child care, by setting. Kinds of child care used (care provided by relatives, friends, in a home-based or center-based daycare) over the past year. Child care expenses; use of public subsidies.
Neighborhood Characteristics
Social capital: Some subset of the following scales: the Collective Efficiacy scale (Sampson et.al, 1997); Community Social Capital Benchmark Survey (Putnam, 2001); Australian Social Capital Assessment Tool (Bullen and Onyx, 1998); and the World Bank Social Capital Assessment Tool (Krishna and Shrader, 1999). These measure the extent of social ties within the local area that can be used to achieve common ends.
Norms and attitudes (e.g., relevant to behavior, upkeep of housing, parenting)
Perceptions of neighborhood: crime, safety, helpful neighbors, etc.
Geographic location of residence using GPS device.

Table 2: Information from Administrative and Other Data Sources

Administrative Data on Families and Individuals
Medicaid/SCHIP Records: number of visits, health conditions treated
Social Security earnings records—earnings history of primary income earners in child's family
Child Protective Services records: Whether the child or any family members have been reported to child protective services. If so, disposition of the report.
Death records: Date and cause of death for children and family members who are deceased.
Local Characteristics
Economic structure (percent of jobs in service, manufacturing sectors, etc.)

Land use
Population density
Transportation systems (availability of public transportation, street conditions, traffic)
Problem conditions (safety hazards, noise, odors, pollution)
Socioeconomic status (education, income, occupation of neighborhood residents)
Racial/ethnic composition and residential segregation
Health status of population (presence of infectious agents, % disabled)
Employment opportunities
Voting and political participation
Crime rates
Direct observation of community physical and social characteristics, using LAFANS Inventory or Systematic Social Observation
Local Institutions
Community organizations: Presence, location, and quality of organizations, including health services, schools, recreational facilities, and religious institutions.
Commercial establishments: Presence and accessibility of grocery stores, pharmacies, fast food restaurants, other.
School characteristics, including structural features (makeup of student population, staffing, teacher pupil ratio, funding per pupil, average class size) and functional features (peer norms, school climate, instructional focus, extracurricular activities); school climate (student engagement and attachment to school, achievement, motivational influences, peer interactions, aspirations); school facilities, including exposure to hazardous conditions.
Health-related characteristics of schools: availability of health and mental health personnel; formal linkages between schools and community health providers; health promotion curricula, programs and policies; access to healthy and unhealthy foods, requirements for and availability of physical education classes.

children, continuity in relationships, curriculum, attitudes and values of staff .
Policies and Programs
Medicaid, SCHIP, WIC (state eligibility policies and regulations)
Child support: policies and enforcement
Health policies: policies directed toward tobacco control and other health and environmental concerns
Housing-related policies, e.g., zoning, housing codes, public housing programs
Child care: subsidies and subsidized services; regulation
School health programs and school policies
Local and state governmental expenditures on education, health, welfare, transportation, housing.

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Media Hypothesis
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Proposed Media Core Hypothesis

I. Proposed Core Hypothesis

The amount, type, content and context of media exposure from infancy through adolescence influences brain and neurological development; cognitive and social development, risk behaviors factors related to injury, substance use, sexual health; and obesity and other aspects of physical development. Effects and effect sizes will differ with timing of and cumulative amount of exposure and in different populations with differing vulnerabilities.

Examples of specific sub-hypotheses (developed in Section VI):

Media exposure contributes to obesity and other nutrition related disorders (bulimia/anorexia, Type II diabetes) through three mechanisms:

- *Sedentary behavior due to displacement of physical activity;*
- *Increased intake of nutritionally poor (high fat, sodium, and/or sugar content) food due to advertising exposure as well as food intake during media use;*
- *Distorted body image as a consequence of exposure to idealized human images*

Media devices (e.g., handheld video games, joysticks, keyboards, light guns, mouse) that are used for extended periods of time leads to increased risk of repetitive strain injuries and musculoskeletal disorders.

Mature brain function and architecture (neuronal development and death of unneeded neurons) are altered by exposure to audiovisual media (any/ amount of exposure to screen media) during a critical developmental window between birth and 2 years of age. This will be reflected in long-term cognitive, attentional, and behavioral outcomes.

Exposure of children to educational media content enhances the development of cognitive skills and increases academic achievement. These effects are maximized:

a) in the developmental period of 2-5 years;
b) where other sources of cognitive support and stimulation are minimal;
c) where English is not the first language; and
d) when children are exposed to same-ethnic models in the media.

Amount, nature, and context of exposure to sexual content in entertainment media predicts beliefs about sexual norms and practices, early onset of sexual activity, greater number of sexual partners, increased frequency of sexual activities, and less frequent use of condoms and other protection. Through these outcomes, it also predicts higher incidence of unplanned pregnancy and sexually transmitted diseases.

II. Workgroups

Social Environment Working Group, in collaboration with participants in the NCS Workshop on Media Effects on Child Health and Development[1]

III. Contact persons for proposed core hypothesis/question

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IV. Public Health Significance

There now exists an overwhelming body of evidence indicating that electronic and interactive media comprise a major part of children's lives, even at very young ages. A recent study published by the Kaiser Family Foundation revealed that American children between the ages of 2 and 18 spend an average of 5 hours and 29 minutes each day using media; about 2 hours and 46 minutes of this time is spent watching television (Kaiser Family Foundation, 1999). Over two-thirds of children under the age of two use screen media, spending an average of 2 hours and 5 minutes each day with television, videos, computers, or video games (Kaiser Family Foundation, 2003). These recent findings have concerned many in the public health community because America's youngest children are immersed in this electronic culture and there is not a clear understanding of how this level of media exposure impacts child health and development. Despite the absence of scientific evidence, the American Academy of Pediatrics has recommended that children under two not watch any television at all and that children over two be limited to one to two hours of educational screen media a day (1999).

Many claims exist regarding the impact of the mass media, and especially the newer, more interactive, electronic media, on the health and development of American children. Some suggest that media constitutes a developmental risk factor, while others point to opportunities for enhancing children's positive development (Mares, 1996). Certainly, the presence in the media of many potentially noxious images has been well documented:

- Results from the National Television Violence Study from 1994-1997 revealed that 2 out of 3 television programs contained violence at a rate of about 6 acts per hour. Therefore, the average child who watches about 2 hours of television daily will see about 10,000 violent acts per year (NTVS 1998).
- Recent studies have found that 70% of episodes on primetime television feature alcohol use (Christensen, Henriksen, Roberts, 2000). Likewise, 85% of the top grossing movies between 1988-1997 have depicted characters using

[1]A list of workshop participants is included in Appendix A. Special thanks to Adelaide Barnes, who drafted the hypothesis; Ellen Wartella, David Bickham, Allison Caplovitz, and David Bickham, who organized the workshop; and Dale Kunkel, Carole Pardun, Vicky Rideout, Victor Strasburger, Elizabeth Vandewater, Ellen Wartella, and Barbara Wilson who provided comments on drafts of the hypothesis.

tobacco (Sargent, Tickle, Heatherton et al., 2001). In addition there is a significant amount of alcohol advertising in youth-oriented magazines and in TV shows popular among young people.

- Content analyses indicate that depictions of and talk about sex are an extremely common element on television, including those shows most watched by youth: among the top 20 TV shows for teen viewers, more than eight in ten (83%) include sexual content, including nearly half (49%) that contain sexual behaviors and one in five (20%) that depict or imply sexual intercourse (Farrer & Kunkel, 2002; Kaiser Family Foundation, 2003).

Given the ubiquitous presence of media in children's lives, it is of great importance to document: a) what aspects of contemporary media have negative (or positive) influences on development; b) at what ages they have those effects; and c) what individual and familial aspects of younger children put them at risk (or opportunity) for such developmental pathways.

The outcomes for which media effects are hypothesized are central to the health and development of children and to the priorities of the National Children's Study. These include brain and neurological development; cognitive and social development, risk behaviors factors related to injury, substance use, sexual health; and obesity and other aspects of physical development. Specific hypotheses proposed in these areas, and the scientific rationale for each, are discussed under Scientific Merit (Section VI).

The public health importance of media effects is perhaps best illustrated with the case of exposure to violence. A substantial body of evidence now exists to support the existence of media effects on violence (Bushman & Huesmann, 2001; National Television Violence Study, 1996; see discussion in Section VI). Violence takes a serious toll on children and youth. Each year more than 20,000 children and adolescents are either killed or injured in firearm-related incidents. In 1998, 3,792 young persons under age 20 died as a result of firearm-related injury in the United States, accounting for 7% of all deaths in this age range (National Center for Health Statistics). For every child who died from a firearm related injury in 1996-1998, more than four others sought care in an emergency department for a firearm related injury. During 1996-1998, the annual number of visits to the emergency department for firearm injuries among young people under age 20 averaged about 18, 400. While not attributing the firearm violence solely to media violence, the likelihood that media violence contributes to the problem is well established.

Although the effects of media on other outcomes, including obesity, neurodevelopment, and risky behaviors such as sex and substance use, have not been as conclusively documented, the potential impacts are large:

- About one in ten preschool children, and 15% of school-aged children are overweight, proportions that have risen dramatically in the last two decades (Kaiser Family Foundation, 2004).

- By the time they graduate from high school, 61% of youth have had sexual intercourse, and one in five (22%) have had four or more partners (CDC, 2002).
- Approximately 900,000 teenage girls become pregnant and four million teens contract a sexually transmitted disease each year (National Center for Health Statistics, 2001; American Social Health Association, 1998).
- Half of all new HIV infections in this country occur among people under age 25 (CDC, 2001).
- About 3 to 5 percent of children are diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) (NIMH).
- Half of high school seniors use alcohol and a substantial part of the minority population smokes or uses other illicit drugs (Monitoring the Future).

Because media influences are so widespread and have wide-ranging potential impacts, even small effects of media on children's health and development can have large public health impacts.

V. Justification for a large, prospective, longitudinal studies

The design of the National Children's Study makes several major advances in media research possible. Much of the prior work on media effects has been cross-sectional, rather than longitudinal, making it difficult to assess the role of media in growth and development over time. While some important exceptions exist (e.g., research on the effects of violent television viewing; Huesmann & Eron, 1986; Anderson and his colleagues' work on educational television viewing; Anderson, Huston, Schmitt, Linebarger, & Wright, 2001; and the PSID Child Development Supplement Data, CDS I & II, http://psidonline.isr.umich.edu/CDS/), little is known about how media use affects children over extended periods of time. No existing research has the capacity to study the effects of media exposures on children's health and development starting at birth. In addition, most of the longitudinal studies conducted to date have relied on convenience samples, locally random samples or some combination of the two. Data drawn from such samples obviate researchers' ability to assess the prevalence of phenomena and differences in impacts across different population groups.

The importance of longitudinal data in media research is underscored by the challenges inherent in understanding the impact of exposures that become increasingly a function of personal choice as development proceeds. A correlation between exposure to media violence and aggressive behavior in a sample of adolescents conveys no information about possible causal pathways unless one also has information on the prior developmental trajectories of media preferences and exposures and predispositions and behaviors related to aggression. Because it begins at or before birth, the National Children's Study is unique in offering an opportunity to (briefly) measure the effects of media exposures that are controlled by parents, and not children. The potential of these early exposures to influence trajectories of both development and later media consumption can be explored, and these early exposures can be used in causal modeling of media effects later in childhood. An optional embedded experiment, described in

Section VII, would provide further purchase on causal inferences regarding media effects.

Many hypotheses about the effects of media on development and health do not require a sample size of 100,000. However, the large sample offers unprecedented and important advantages. A large sample will allow the detection of small effects resulting from media exposures across which, as noted above, can have substantial public health implications because of children's widespread exposure to media. In addition, a large sample size will permit the testing of complex interactions between media exposures and other risk and protective factors. Healthy development depends on a wide variety of environmental resources, but environmental resources may be, to a greater or lesser extent, interchangeable in their ability to provide children the experiences necessary to healthy development (Horowitz, 2000). Thus, in a family that provides little cognitive stimulation to a child through reading, toys, or parental interaction, children may be able to obtain some of the experience they need for cognitive development through exposure to educational media. In such a family, media exposure would have a strong influence on cognitive development. However, in a family where other stimuli are available, the effect of media exposure may disappear or be reduced. Testing such interactions require increasingly larger sample sizes as the complexity of the interaction increases.

Another type of interaction involves the tradeoffs between media use and other aspects of children's lives. There is some evidence that media use replaces familial interactions (Vandewater, Bickham, & Lee, 2003), and it may also replace social interactions with peers. These social interactions are a key component of young children's development. The NCS may be used to examine the effects of complex patterns of media use and other activities in order to understand such tradeoffs and their impact on development.

Examples of specific hypotheses that require a large sample size include:

1. Media and Aggressive Behavior: *Children who are in the top quintile of exposure to violent media prior to age 10 will be more likely to experience a firearm injury during the period from birth to age 21 than are children who are less exposed to violent media.*

Assumptions:

A. Approximately 24 per 100,000 children are injured by a firearm each year (CDC, 2001). Over the course of the NCS, approximately 504 children (0.5%) will be injured by a firearm between the ages of 0 and 21.
B. Exposure to violent media is associated with increased risk of involvement in a broad range of aggressive behaviors (Paik and Comstock,1994), thereby increasing children's exposure to violence and violent situations. An increased risk of firearm injuries is one of several potential outcomes of this increased overall exposure.

C. Virtually all children experience some exposure to violent media prior to age 10; those in the top quintile of exposure are considered most at risk of long term effects (Lefkowitz et al, 1977.)

Power requirement:

A. .05 significance level for a difference in odds of 1.5 (top quintile = .008, other quintiles = .005)
B. Power = .90

Required Sample Size:

- 14,914 children who are repeatedly exposed to violent media
- 74,570 children in the NCS

2. Media and Cognitive Development: *Children from non-English speaking families regularly exposed to English-language educational programming during the preschool years will be 1.5 times more likely to be school ready than children from non-English speaking families who are not regularly exposed to English-language educational programming.*

Assumptions:

A. Children from families where English is not the primary language constitute 9% of all children in the United States. (Early Childhood Longitudinal Study-Kindergarten Cohort, http://nces.ed.gov/pubs2000/2000070.pdf)
B. Approximately 15% of preschool children from non-English speaking families are regularly exposed to English-language educational programming. (This proportion is estimated based on data from Kaiser Family Foundation, 1999; 2003).
C. About 12% of children from non-English-speaking families have mastered specific school readiness tasks (operationalized as recognizing word-ending sounds; Early Childhood Longitudinal Study-Kindergarten Cohort, http://nces.ed.gov/pubs2000/2000070.pdf)

Power Requirement:

A. .05 level of significance for a difference in odds of 1.5, (17% of children who are regularly exposed to English language educational programming will be school-ready relative to 12% of those who are not exposed to English language educational programming)
B. Power = .90

Required Sample Size:

- 1036 children who are regularly exposed to English-language educational programming among children from non-English-speaking families.
- 6906 children from families where the primary language is not English
- 76,740 children in the NCS

VI. Scientific Merit

In this section, we present specific hypotheses along with the scientific rationale for each. The hypotheses fall into five overarching areas of interest, and are ordered roughly in relation to the level of existing evidence supporting the hypothesized associations: behavioral development, social development, physical development, and neurodevelopment. Hypotheses about media depictions of minorities and other population groups are also advanced. Each of the hypotheses below could be further elaborated into many others that would be highly specific as to measures of exposure and outcome.

BEHAVIORAL DEVELOPMENT

Media exposure may affect children's behavioral development through a number of pathways. First, media may influence children's perception of normal (and abnormal) social behavior, social reality, and cultural norms (Strasburger 1999). People who are heavy viewers of television are most likely to believe that it depicts the real world, or that the real world should conform to television's pattern of portrayals (Gerbner, et al., 2002). Second, Bandura's social learning theory (Bandura, 2001) suggests that children learn behavior by watching attractive adult role models, both in real life and vicariously through the media. Finally, desensitization theory suggests that young people exposed to certain types of graphic media depictions (e.g., sex and violence) may become less reactive to these stimuli, and, in the case of violence, more indifferent to the plight of others (Molitor & Hirsch, 1994; Mullin & Linz, 1996).

Aggressive and Violent Behaviors

There is ample research illustrating that media violence, especially repetitive exposure, is unhealthy for children and adolescents (see Bushman & Huesmann, 2001; Cantor, 2001). The effects of violent media on children's attitudes and behaviors are well documented (see Bushman & Huesmann, 2001, for a review). Results from the National Television Violence Study from 1994-1997 revealed that 2 out of 3 television programs contained violence at a rate of about 6 acts per hour. Therefore, the average child who watches about 2 hours of television daily will see about 10,000 violent acts per year (NTVS 1998). The study concluded the following:

1. Viewing television violence contributes to antisocial behavior.
2. Three primary effects arise from viewing televised violence:
    a. Learning of aggressive behaviors and attitudes;
    b. Desensitization to violence;
    c. Fear of being victimized by violence.
3. Not all violence poses the same degree of risk of these harmful effects (Villani, 2001).

Perhaps the most convincing evidence that exposure to media violence significantly contributes to hostile and violent behavior is provided by the meta-analysis

by Paik and Comstock (1994). This report analyzed over 200 correlational and experimental studies and involved more than 1000 comparisons between violent media and control groups. The study provided results revealing that repetitive exposure to violence is associated with increased levels of antisocial behavior ranging from trivial (reenacting violence seen against toys) to serious (actual criminal acts). Likewise, there is a range of behaviors exhibited in between such as recognizing violence as an acceptable solution to a problem and increased feelings of hostility (Cantor 2000).

Existing longitudinal studies suggest that there is a direct relationship between media violence and violent behavior. In 1963, Eron and his colleagues studied 875 year olds in New York primarily to determine how child-rearing practices might lead to aggression. A re-analysis of a cohort of 460 subjects at age 19 revealed that the relationship between TV violence and aggressive behavior was highly significant.

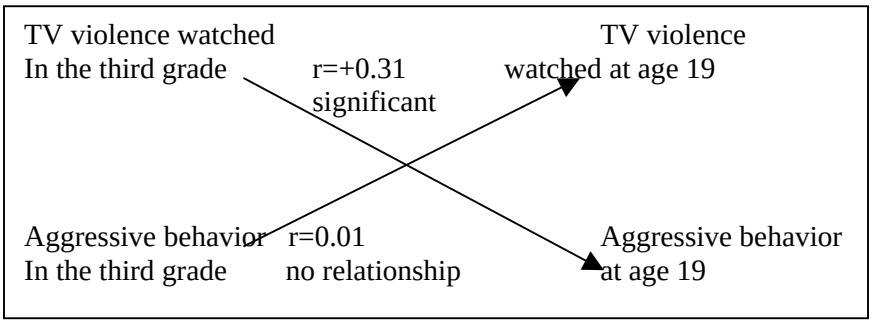

Figure 1. Effect of television viewing and aggressive behavior in children in the third grade and the same effects 10 years later. Television viewing at the young age affects aggressive behavior. (Lefkowitz et al, 1977).

These researchers concluded that the children acquired attitudes about violence in their formative years. Once these attitudes were learned, they were often permanent (Huesmann et al. 2003, Wilson et al., 2002).

There have been no opportunities to study the relationship between media violence and subsequent behaviors on a large cohort of children. Studying this particular phenomenon in the National Children's Study would provide the opportunity to examine effects over a long period of development and the moderating influences of other environmental and developmental factors on the effects of exposure to media violence.

<u>Hypotheses</u>:
The context and amount of violent media (including TV, DVD/video, interactive media) to which children are exposed, influences the risk of aggressive behavior and desensitization (including acceptance of violence). This effect is moderated by:

a) earlier age of exposure,
b) developmental delay and/or brain injury,
c) violence in the home,
d) poverty, and

e) by early adolescence, peer group aggression.

Heavy exposure to news and other "realistic" media violence increases the propensity for children to experience chronic fear and anxiety. This effect is increased by:

a) living in a high-crime area,
b) predisposition for anxiety, and
c) personal experience with victimization.

Exposure to Drugs and Alcohol

Alcohol, drug abuse, and smoking all pose significant health risks to American adolescents. Content analyses indicate that portrayals of smoking, drug use, and alcohol consumption continue to pervade popular media, including television, music videos and movies (Roberts and Christensen, 2000). Recent research demonstrates a strong association between young adolescents' exposure to smoking in movies and subsequent initiation of tobacco use. The effect was strongest in adolescents whose parents did not smoke (Dalton, et al., 2003)

Hypothesis:
Exposure to media portrayals (including advertising) of alcohol, tobacco, and illicit drugs predicts beliefs about substance use norms and practices, early onset of substance use, and increased substance use. The relationship between exposure and substance use is moderated by:

a) nature of media portrayal (pro- or anti- substance use message)
b) genetic predispositions to substance use
c) individual sensation seeking/risk-taking
d) exposure to substance use in family members
e) exposure to substance use in peer group
f) access to substances in community, e.g. presence of bars, liquor/tobacco outlets, drug dealers
g) state/local policy governing penalties for selling alcohol or tobacco to minors.

Sexual Health

Little is known about how sexual media content affects teens' developing sense of sexuality and sexual behavior (Huston, Wartella, & Donnerstein, 1998). A few experimental studies have found some differences in sexual knowledge and attitudes between control groups and groups who were exposed to TV sexual content (Bryant & Rockwell, 1994; Greenberg, Linsangan, & Soderman, 1993), and music videos (Greeson & Williams, 1986) in laboratory settings, but none of these have included measures of sexual behavior. Correlational studies of naturally occurring media use have found small relationships between exposure to music videos and attitudes about premarital sex,

especially for females (Strouse, Buerkel-Rothfuss, & Long,1995), and between TV viewing and initiation of sexual intercourse (Brown & Newcomer, 1991).

Although recently initiated longitudinal studies are examining correlations between exposures to sexual content and behavioral outcomes in adolescence, none of these is able to assess exposures occurring prior to adolescence, when media-use preferences and patterns may be established. Increasing heterogeneity in media portrayals of sexual behavior underscores the importance of considering the content and context of exposures in assessing outcomes. For example, television shows that address the consequences of sexual behavior may have a different effect than shows that portray sexual behavior divorced from its consequences.

Hypothesis:
Amount, nature, and context of exposure to sexual content in entertainment media predicts beliefs about sexual norms and practices, early onset of sexual activity, greater number of sexual partners, increased frequency of sexual activities, and less frequent use of condoms and other protection. Through these outcomes, it also predicts higher incidence of unplanned pregnancy and sexually transmitted diseases.

SOCIAL DEVELOPMENT

Prosocial Behaviors

Evidence of the effects of prosocial media content (e.g., sharing, showing empathy, etc.) has been best demonstrated in the area of children's educational programs (Friedrich & Stein, 1973, 1975). Shows such as *Sesame Street* and *Barney* have been successful in eliciting specific types of prosocial behaviors when those behaviors were modeled in the program. We expect that the more consistently children are exposed to prosocial content across media (e.g., television, computer and video games, websites), the more they will behave in prosocial ways.

As in the case of other outcomes, the effects of media on social development are likely to reflect complex interactions involving individual predispositions and other environmental factors. For example, exposure to media modeling prosocial behaviors may be most likely to result in prosocial behavior in the child when media influences are reinforced by parental modeling. Child temperament may also modify the impact of media exposures on behavior.

Hypotheses:

Children who are exposed to a consistent diet of prosocial media content early in their development are more likely to demonstrate prosocial behaviors and to select prosocial media content over the course of development.

Children who are at constitutional risk and vulnerable (e.g., ADHD) will be more likely to demonstrate favorable development outcomes (i.e., be more prosocial and less antisocial) when they have grown up in stable homes where prosocial media are frequently shown.

Children who are at constitutional risk and vulnerable (e.g., ADHD) will be more likely to demonstrate unfavorable developmental outcomes (e.g., delinquency) when they grow up in homes where coercive discipline techniques are used and there is more exposure to antisocial than to prosocial media.

PHYSICAL DEVELOPMENT

Obesity

There is some evidence that children's media use is linked to their weight status (Dietz & Gortmaker, 1985; Kaiser Family Foundation, 2004). There are several possible processes underlying this relationship. First, media use may be a component of a sedentary lifestyle. If this is the case, children who participate in activities that require low levels of energy will also use media more often. Second, media use may be accompanied by concurrent snacking. This may be especially true for television use and movie watching in theatres. If this occurs, children who watch television more will eat more and will more likely become obese. Third, advertising for prepared foods, high-calorie foods and fast-food restaurants are common elements of television programming (roughly 75% of all food advertising money is spent on television advertising). The effects of these commercials on children's eating habits are well documented. Thus, it is possible that electronic media encourages higher caloric intake among children (Kunkel, 2001; Horgen et al, 2001).

In its recent review of scientific literature, the Kaiser Family Foundation (2004) concluded that, although some association between obesity and media use has been established, the reasons for the association are still poorly understood. Exposure to food advertising and its effects on the formation of food preferences appears to be a likely mechanism, but this pathway has not been definitively established and other pathways cannot be definitively ruled out. The NCS provides a means of testing alternative hypotheses about this important link.

<u>Hypotheses</u>:
Media exposure contributes to obesity and other nutrition related disorders (bulimia/anorexia, Type II diabetes) through three mechanisms:

- Sedentary behavior due to displacement of physical activity;
- Increased intake of nutritionally poor (high fat, sodium, and/or sugar content) food due to advertising exposure as well as food intake during media use;
- Distorted body image as a consequence of exposure to idealized human images

The relationship between media exposure and BMI is moderated by genetic predispositions.

The association between media use and obesity may be a function, in part, of reduced opportunities of overweight and obese children for activities that replace media use. In other words, overweight children may use media more because they have fewer friends and fewer opportunities for engaging in activities outside the home. By examining trajectories of media use and BMI within the National Children's Study, some purchase on this possibility may be obtained.

Hypothesis:
The correlation between media use and obesity is the result of the causal effect of obesity on increased sedentary activities, including media use.

Musculoskeletal Risks

It is possible that computer and electronic game use poses musculoskeletal risks for young users. Various reports suggest that concern is warranted based on results of ergonomic analyses of classroom computers (Gillespie, 2002). In recent years, computers, televisions, video games, and related devices have become progressively ubiquitous and essential aspects of home, school, and work life. Therefore, it is important that the impact of these media is investigated and plans be developed to limit or prevent possible adverse effects.

Hypothesis:
Media devices (e.g., handheld video games, joysticks, keyboards, light guns, mouse) that are used for extended periods of time leads to increased risk of repetitive strain injuries and musculoskeletal disorders. These effects may be cumulative, especially when the content reinforces repetitive motion and sustained use, and when the ergonomics of the device are not appropriate for children.

Visual Acuity

Visual demands at young ages are thought to contribute to myopia and eyestrain. However, it is also possible that being exposed to media that project active visual images might enhance or facilitate specific aspects of development, such spatial skills or visual acuity. An in-depth, longitudinal study is necessary to verify the effects of such media use.

Hypotheses:

Children who are heavier users of media that involve immersion in virtual environments – and to a lesser extent, videogames – will be at increased risk for problems in visual development (e.g., development of visual accommodation).

Children who are heavier users of portable media (e.g., video games, small screens on cell phones) are at an increased risk for developing myopia and other eyesight problems.

NEURODEVELOPMENT

Brain and Neurological Development

Little is known about how early childhood electronic media use affects brain development. While research with children older than three has not found that television viewing interferes with attention span formation, language acquisition, or intellectual activity (see Anderson, 1998; Anderson & Collins, 1988; Huston & Wright, 1997 for reviews), there has yet to be a systematic exploration of these effects in infants and toddlers. Furthermore, little is known about how new forms of electronic media, especially interactive media and electronic toys, might affect brain development. It is possible that these media have the negative effects that were predicted for television viewing.

Scientists believe that exposure to audiovisual media during the critical developmental window between birth and 2 years of age will adversely affect mature brain function and architecture through effects on neuronal development. However, no scientific evidence currently exists to affirm or support this position. Current theorizing suggests that both direct interaction of very young children with screen media and distractions caused by exposure to background media may affect neurodevelopment.

Increasingly, TV programs and videos are being made for children under 2 years of age. Prime examples are *Teletubbies* and the *Baby Einstein* series of videos. While these programs and videos are claimed to be educational for infants and toddlers, recent studies have indicated that infants and toddlers under 2 show either no learning or only very limited learning from video as compared to equivalent live demonstrations (Barr & Hayne, 1999; Kuhl, Tsao & Liu, 2003; Mumme & Fernald, 2003; Schmitt & Anderson, 2002; Troseth & DeLoach, 1998). If children under 2 learn little from television, then time spent watching TV is taken away from other potentially more valuable activities such as active play or interactions with other family members – activities basic to neurodevelopment. There is some correlational evidence indicating that substantial exposure to TV is associated with poorer cognitive and language development (Carew, 1980; Gottfried, 1984; Nelson, 1973). Because TV was not the focus of these studies, however, it is possible that other factors associated with heavy TV use, such as lower parent education, may be responsible for these findings.

Much of very young children's exposure to media occurs indirectly, during use by other family members. Anderson and Evans (2001) hypothesized that background television might have deleterious effects on very young children by distracting them as they play or interact or by distracting others in the family, especially parents. Such distractions may make it difficult for very young children to organize their behavior and may reduce the amount and quality of interactions with parents. Preliminary evidence

that background television has a disruptive influence comes from a study reported by Evans et al., (2003). They compared 1-, 2-, and 3-year-olds' play behavior with and without a television set playing an adult game show in the background. Play episodes were about half as long when the TV was on, suggesting that sustained play became fragmented in the presence of TV.

It is unclear, at this point, what are the long-term implications of media exposure on neurobehavioral development. NCS provides a unique opportunity to determine the extent to which both the amount of viewing, and the extent of cognitive interaction the child has with media during this period, are associated with alterations in neurodevelopment. Answering causal questions about the effect of early-life media exposure would be further facilitated by embedding an optional intervention experiment, as described in Section VII.

> Hypothesis:
> Mature brain function and architecture (neuronal development and death of unneeded neurons) are altered by exposure to audiovisual media (any/ amount of exposure to screen media) during a critical developmental window between birth and 2 years of age. This will be reflected in long-term cognitive, attentional, and behavioral outcomes.

Cognitive Development and Academic Achievement

Research has also found that educational television can lead to positive cognitive outcomes and abilities in their viewers (for a review, see Bickham, Wright, & Huston, 2001), including enhanced pre-literacy and reading skills. These abilities have been found to translate into long-term educational achievement (Anderson et al., 2001). Paradigmatic of educational effects are those attributed to *Sesame Street* which is the longest-running educational TV program as well as the program that has been most studied. Early evaluations indicated that its preschool viewers learned the intended educational content (Ball & Bogatz, 1970; Bogatz & Ball, 1971). Later studies indicated that, the more children viewed *Sesame Street*, the better were their vocabularies (Rice, Huston, Truglio & Wright, 1990), the better prepared they were for school (Wright, Huston, Scantlin & Kotler, 2001; Zill, Davies & Daly, 1994), and that positive associations with academic achievement were traceable through high school (Anderson, Huston, Schmitt, Linebarger & Wright, 2001). All these studies were correlational in nature.

The importance of educational media for children's cognitive development may vary depending on the other resources supporting cognitive growth in the home. Children from low-SES families may benefit more from exposure to educational programming. Similarly, children growing up in families where English is not the primary language may gain more from exposure to English-language programming, with differences appearing in language abilities important for school readiness. Such children may respond differently to media that provides educational content in culturally-consonant ways.

Hypotheses:

The relationship between media use and cognitive development and academic achievement is due to content and time spent with media.

Exposure of children to age-appropriate educational media content enhances the development of cognitive skills and increases academic achievement. These effects are maximized:
a) in the developmental period of 2-5 years;
b) where other sources of cognitive support and stimulation are minimal;
c) where English is not the first language; and
d) when children are exposed to same-ethnic models in the media.

SUBGROUP DEPICTIONS

Television and video games targeting adults and general audiences often present gender roles and ethnic minorities in stereotypical ways (Dietz, 1998; Entman & Rojecki, 1998; Signorielli, 2001). Young children who are exposed to such depictions may be more likely to have views that correspond to traditional gender and race stereotypes. In addition, Social Learning Theory suggests that children are more likely to learn from role models that they perceive as positive, and as similar to themselves (Bandura, 1986). Thus, the inclusion and portrayal of media characters belonging to different gender, racial, ethnic, religious, or socioeconomic subgroups may interact with the child's own subgroup identification in determining the effect of media on the child.

Hypotheses:

Positive or negative portrayals of gender/race/ethnic/sexual orientation/disabled groups in the media is related to the formation of stereotyped social expectations.

Viewer identification with groups portrayed intensifies the influence of stereotypical attributions on social and behavioral development.

VI. Potential for Innovative Research

The design of the National Children's Study provides opportunities for innovation not available in current studies of media effects:

- The large cohort of children, together with the measurement of social, psychological and biological development, makes possible the examinations of complex interactions involving multiple aspects of the child's social environment, biological predispositions, and media use.
- The longitudinal design beginning from birth or before provides an unparalleled ability to address causal questions regarding the effect of media

exposures on children. The addition of a small experimental component (see Section VII) would further expand this ability.

- The types of media to which children are exposed will continue to expand and change dramatically over the years of the NCS. Much existing research focuses almost exclusively on television. While television will continue to be a central medium in children's lives, the proliferation of new media is a ripe area for new research.
- The majority of existing research is focused on school age children and adolescents; and very young children are often excluded. However, as noted above, recent research (Jordan & Woodard, 2001; Rideout, Vandewater, & Wartella, 2003) indicates that from infancy through preschool, children spend a fair amount of time using electronic media. The NCS provides a unique opportunity to study both the short-term and long-term effects of early exposures to media.

VII. Feasibility

Critical periods for exposure and outcomes

The first two years of life are thought to be critical for media effects on neurodevelopment. The preschool years are key ages for cognitive development and the development of other abilities necessary for school readiness. Social development may be affected by the media throughout childhood. Engagement in risk behaviors is likely a function of exposures throughout childhood and adolescence. Media use may affect physical development at any time but these effects may be most pronounced during early childhood.

Sampling needs:

No special needs. See below for sampling strategies for an embedded experimental design.

Contact:

Outcomes and exposures must be measured at regular intervals throughout the child's life. We recommend a schedule that would collect media measures at ages 1, 2.5, 5, 8, 11, 14, 17, and 21.

Measurement tools:

To test the proposed hypotheses, three major design components are recommended for the NCS:

- Track, at intervals, household media behavior and media consumption by the target child and in the child's home. Diary methods have been used to collect this information in numerous studies of media consumption, including some involving youth (detailed examples are included in Appendix B). Specific approaches are detailed below.
- Collect and archive samples of the media consumed by youth for later analysis.

- Embed a randomized experiment within the NCS, whereby a small randomly selected group of participating families is invited, at enrollment, to modify their media use behavior. This is described in further detail below.

Tracking household media behavior and child's use:

- Inventory all media equipment, including portable devices, in the child's homes, noting location (e.g., TV in child's bedroom).
- Include questions about household media behavior in periodic interviews. Relevant measures include parental media use, attitudes towards media use, rules and routines involving media (e.g. TV on at mealtimes, time limits or content limits for children's viewing).
- At intervals during the child's life, collect diary information on the child's media use. As an example, diary collection could be undertaken at ages 1, 2.5, 5, 8, 11, 14, 17, and 21. Supplement diary information with questions about the child's most-watched show, and, at some ages, questions on whether the child incorporates media characters into play or imitates viewed behaviors.
- Types of media use to be recorded include television, videos, video games, computer games, internet, books, and music. Types and measurement tools will require updating periodically to reflect new technologies and the child's developmental stage. For example, instant-messaging on the internet and cell phones become important later in childhood.
- Diary reports will ascertain, for television, the time periods during which television was viewed and the specific shows viewed. It will also ascertain whether the child was alone, with friends or siblings, or with an adult; and other simultaneous activities such as eating or doing homework. Ideally, the diary will be collected for a full week, although some experts believe that collection over a random weekday and a random weekend day during the week may be adequate.
- For other forms of media, time periods spent with each type and appropriate measures of content (e.g., names of video games) will be collected. Some work is underway to develop appropriate measures of non-TV media consumption; some piloting may be necessary.
- The potential for tracking the child's or household's media use through electronic monitoring should be explored. Arbitron devices can record whether the television is on and what is being shown. These should be considered for a subsample of households at least during the first two years of life. These devices do not measure whether any specific person is watching the television, and thus have limited value for understanding media effects based on content. However, new technologies are being developed by Nielson that may allow more precise monitoring. These devices are worn on the body and track the radio signals of electronic devices. These should be explored and piloted if deemed promising for the NCS. Such technologies could, if cost-efficient, replace the need for diary data**.**
- Some collection of media use in child care and school settings is also desirable.

Collection of Media Samples

- Diary information on specific media segments (shows, videos, etc) viewed by participants should be compiled on a regular basis and a random sample of segments identified for collection and archiving. The sampling procedure should ensure a nearly 100% probability that the most popular media shows, games, etc. are represented in the archive. This could be achieved with a random sample and an appropriate sampling ratio.
- The archive should be maintained by the National Children's Study and made available to researchers for analysis. Researchers would be expected to obtain funds to conduct the appropriate content analysis, and to donate the results of the content analysis back to the archive within one year of its completion.

Embedded Experimental Design

- The embedded experimental design is proposed as a means of addressing selection issues in media research. Because individuals exert considerable control over their media consumption, their exposures to specific media types and content reflect their predispositions and interests. This problem compromises the ability to draw causal inferences concerning the effects of media on child health, development, and behavior. The longitudinal design of the NCS provides substantial purchase on this problem, but an embedded experiment would provide far more definitive evidence about media effects.
- The experiment will study the effects of intervention in media exposure for a group of children from zero to five years of age. Two groups of parents would be recruited to follow a "best practice" regime with respect to their children's exposure to media. A comparison group, taken from the National Children's Study, would consist of children who did not receive the intervention.
- The first intervention group will have an intervention that lasts from birth to 24 months of age. The intervention will be designed to minimize exposure to screen media consistent with the recommendation of the American Academy of Pediatrics. Parents will be asked to limit their own media use when the child is present. Experimenters will provide written materials in support of the American Academy of Pediatrics recommendations and periodic telephone calls will be made to help maintain motivation for compliance.
- The second intervention group will have an intervention that lasts from birth to 60 months of age. For the first two years the intervention will be the same as for the first group. From 24 to 60 months of age the intervention will be designed to restrict media use to a weekly maximum, and within that maximum, to content that is explicitly designed to be educational and prosocial. Parents will be asked to avoid the child's exposure to general entertainment and especially violent content. Parents in this group will receive TV program as well as interactive software information that will help them choose an optimal media diet.
- Children for the experimental groups will be randomly chosen from participants in the National Children's Study. Parents will be offered incentives to comply with the intervention. In order to gain maximum compliance with best media

practices, it is recommended that the children be first-borns. Parents without older children are generally more able to control the media environment than are parents who have children with established media consumption habits.

- A control, or comparison, group will be chosen from the larger National Children's Study sample. The control group sample will be precisely matched to the characteristics of the experimental groups.
- Children in all three groups would participate in the National Children's Study protocol until age 21. All would have media use and outcomes assessed according to the standard protocols developed for the larger Study.
- Multi-level model equations will be employed to estimate the influence of time-varying covariates and to take account of rate of change due to individual age and rate of change due to developmental stage. It is anticipated that the intervention will take place over a five year period and that the children in the intervention sample will be followed at least for an additional 3 years (up to age 8) in order to assess the longer term effect of the intervention. Thus, based on estimating a 3 (experimental group) x 2 (gender) x 8 (time) factorial design, power analyses indicate that in order to detect a small effect size (f = .05) for tests performed at a=.05, with power=.90, and estimating 20% attrition, a total sample of N = 6108 is required for the intervention study (2036 in each group). If the goals of the intervention study were limited to content-related effects, with larger effect sizes estimated from the literature, then a smaller total sample would be required. If the effect size were .10, a total sample of 1512 (504 per group) would be needed, whereas if the effect size were .15 a sample size of 730 (244 per group) would be required. Finally, if the approximate effect size observed in the content effects literature were used, .25, then a sample of 300 (100 per group) would be appropriate.

A full description of the proposed experiment and its rationale is included in Appendix C.

Appendix A

National Children's Study Media Workshop Participants:

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Appendix B[2]

MEASURES OF MEDIA USE AND ACCESS

A) ***The Panel Study of Income Dynamics Child Development Supplement (PSID-CDS)***

1997 Wave

Media Use: Primary Caregiver Child Questionnaire

1. Think for a moment about a typical weekday for your family. How much time would you say (CHILD) watched television and videos on a typical weekday, either in your home or elsewhere?

2. Now think for a moment about a typical weekend day for your family. How much time would you say (CHILD) watched television and videos on a typical weekend day, either in your home or elsewhere?

Media Use: Time Diary

Headers for this diary

1. What did your child do?
2. Time began
3. Time end
4. If watching TV, was that a video tape or TV program,?
5. If TV, video, computer games, what was the name of the (program/video/game) child was (watching/playing)?
6. Where was child?
7. Who was doing the activity with child?
8. Who (else) was there but not directly involved in the activity?
9. What else was child doing at the same time>

2003 Wave

Media Use: Child Questionnaire

1. How often did you use each of the following in the last month?
   [Scale (1-5) = *Never, Once or twice in the last month, about once a week, 2 or 3 times a week,*
   almost every day, every day]
   a.) Handheld game system
   b.) Video game system
   c.) A computer to play games
   d.) A computer to do other things besides play games

2. Have you ever used the internet?

3. How often did you use the internet for any of these in the last month? *(Scale = Never, One or twice in the last month, about once a week, 2 or 3 times a week, almost every day, every day)*
   a.) To visit websites
   b.) To use email
   c.) To use a chatroom or instant messenger

[2] Special thanks to Elizabeth Vandewater for providing this compilation.

d.) To do research for school work
e.) To shop
f.) To play games

4. What is your favorite website?

Media Use: Self-Administered Computer Program

1. What do you like to do for fun?
    a. Read books
    b. Play or hang out with my friends
    c. Play board games like Monopoly
    d. Talk on the phone
    e. Play with my family
    f. Do homework
    g. Play sports
    h. Watch television

2. In the last three months, how much of your money did you spend on
    a. Music CDs or cassette tapes for yourself?
    b. Computer or video games for yourself?
    c. Magazines or books that are not for school for yourself?

Media Use: Time-Use Diary

Headers for this diary:

1. What did your child do?
2. Time Began
3. Time Ended
4. If watching TV was that a tape or TV program?
5. If TV, video, computer games: What was the name of the (program/video/game/book) child was (watching/playing/reading)?
6. Where was the child?
7. Who was doing the activity with the child?
8. Who (else) was there but not directly involved in the activity?
9. What else was the child doing at the same time?

Computer Use: Household Questionnaire

1. How often did {child} use the computer(s) in your home last month?
   [Scale (1-5): *Not in the past month, One or two times in the past month, About once a week, Several times a week, Every day*]

Media Access: Household Questionnaire

1. Do you have a working TV in your house?
2. About how many hours is the TV on in your home each day? [Range: 0-24]
3. How many working televisions are in your home?
4. Is there one in your child's room?
5. How many televisions have cable or satellite service?
6. How many videogame systems (e.g., Sega Dreamcast, Nintendo, Sony Playstation) that your child could use do you have in the home?
7. How many working computers are there in the home that your child could use?
8. How many of the computers in your home have an Internet connection?
9. How many cell phones does your family own?

B) ***National Longitudinal Survey of Youth (NLSY), 1997***

Description: Nationally representative sample of approximately 9,000 youth (12 to 16 years old), who were first interviewed in 1997 and have been interviewed on an annual basis. In addition to the NLSY97's main focus on educational and labor market experiences, these data include information on youths' relationship with parents, dating, sexual activity, onset of puberty, expectations, time-use, alcohol and drug use, and criminal activity. One of the youths' parent(s) was also interviewed in 1997.

Questionnaire on Time Use

1. In a typical [school week/work week/week] did you spend any time watching TV?
    a. In that week, on how many weekdays did you spend time watching TV?
    b. On those weekdays, about how much time did you spend per day watching TV?
2. In a typical [school week/work week/week], did you spend any time reading for pleasure?
    a. In that week, on how many weekdays did you spend time reading for pleasure?
    b. On those weekdays, about how much time did you spend per day reading for pleasure?
    c. Approximately, how much total time did you spend reading for pleasure on the weekend?

Media Use obtained using a self-administered computer program

In the past month, has your home usually had a computer?

C) ***Michigan Study of Adolescent and Adult Life Transitions (MSALT)***

Description: The purpose of this study was to investigate the impact of changes in classroom and family environments on adolescents' achievement-related beliefs, motives, values, and behaviors. In 1983, a sample of sixth graders, their teachers, and their parents were drawn from 12 public school districts located in middle-income communities in southeastern Michigan; it included approximately 3,248 adolescents; 95% of the teachers (representing 143 classrooms), and 72% of the parents asked to participate. School districts were selected where the adolescents would experience the traditional junior high school transition as they moved from the sixth to the seventh grade. During the first two years of this study, adolescents filled out extensive questionnaires in their math classrooms two times in the sixth grade and two times in the seventh grade. During the same testing periods, teachers and parents completed their own questionnaires. To date, there have been 9 waves of data collected.

Child Questionnaire (1996 and 2000):

1. Think about the kinds of things you usually do after school and on weekends. About <u>how many hours each week</u> do you <u>usually</u> spend on these activities (check one line for each activity):
   (*Scale:* None, 1 hour or less, 2-3 hours, 4-6 hours, 7-10 hours, 11-15 hours, 16-20 hours, 21 or more hours)
    a. Talking to friends on the phone
    b. Reading for fun
    c. Watching television
    d. Using a computer at home (for example, internet, AOL)

D) ***The New Hope Child and Family Study***

Youth Interview (9 to 17 years old), 1994

1. Ok, for the last school year I would like to know how often you did some activities. No one does all of these activities, but you may have done some of them. We'll use this card to help you answer these questions. Your answer choices are *never, less than once a month, about every month, about every week, about every day*
    a. Play video games
    b. Use a computer, including the internet
    c. Read a book or magazine you didn't have to for school

2. We've just been talking about how you've spent your time during the school year. Now let's talk about what you've done during the summer. We'll be using this card again. Your answer choices are *never, less than once a month, about every month, about every week, about every day*
    a. Play video games
    b. Use a computer, including the internet
    c. Read a book or magazine you didn't have to for school

3. Now I have some questions about your TV viewing. We're still talking about your time during the school year. This time we'll use this card. Your answer choices are none, less than one hour, one to two hours, two to three hours, three or more hours.
    a. On a typical school day, that is, Monday through Friday, how many hours do you spend watching TV or videotapes
        i. Before noon
        ii. Between noon and about 6 in the evening?
        iii. From about 6 in the evening until you go to bed?
    b. On a typical weekend day, that is, Saturday or Sunday, how many hours do you spend watching TV or videotapes
        i. Before noon
        ii. Between noon and about 6 in the evening?
        iii. From about 6 in the evening until you go to bed?

E) ***Sloan Study of Youth and Social Development***

Description: Conducted at the University of Chicago between 1992 and 2000, this longitudinal study of adolescent development used multiple methods to examine career and social development among youth from middle- and high school through college.

Student Questionnaire (2000)

1. During the school year, how many hours per day (count weekends too) do you USUALLY spend

doing the following activities? [Scale(1-7)*: None, less than 1 hour, 1-2 hours, 2-3 hours, 3-4 hours, 4- 5 hours, over 5 hours*]

a. Playing video games
b. Watching TV and videotapes

F) ***Teen Media: The mass media and adolescents' sexual health***

Teen Questionnaire
[Scale (1-6)*: Never, Once a week or less, Two or three times a week, Almost every day, At least once every day, Almost all the time I'm not in school*]

1. How often do you watch TV Monday through Fridays during the school year?
2. How often do you watch TV on Saturdays and Sundays during the school year?
3. How often do you watch TV through the week during the summer months?
4. How often do you listen to music Monday through Fridays during the school year?
5. How often do you listen to music on Saturdays and Sundays during the school year?
6. How often do you listen to music through the week during the summer months?
7. How often do you go on the Internet Monday through Fridays during the school year?
8. How often do you go on the Internet on Saturdays and Sundays during the school year?
9. How often do you go on the Internet through the week during the summer months?

[Scale (1-5): *Never, Every other month, once a month, a few times a month, once per week*]

10. How often do you go to movies in the theater?
11. How often do you watch movies at home?

[Scale (1-5): *Never, once a month or less, about once a week or less, a few times a week, everyday*]

12. How often do you read or look at magazines?
13. Please check which newspapers you read.

G) **National Household Education Survey (NHES)**

From 1999 data collection
1. On average, about how many hours of television or video tapes does child watch at home each weekday, that is, Monday through Friday? How about

a. Before 8 a.m.?
b. Between 8 a.m. and 3 p.m.?
c. Between 3 p.m. and dinner time?
d. After dinner time?

2. How about on Saturday and Sunday? How many hours does child watch television or video tapes at home on…

a. Saturday?
b. Sunday?

H) ***Early Childhood Longitudinal Study (ECLS)***
Description: The Early Childhood Longitudinal Study, Kindergarten Class of 1998-99 (ECLS-K) is an ongoing study that focuses on children's early school experiences beginning with kindergarten and following children through fifth grade. The ECLS-K provides descriptive information on children's status at entry to school, their transition into school, and their progression through fifth grade. The longitudinal nature of the ECLS-K data also enables researchers to study how a wide range of family, school, community, and individual variables interact with early performance in school.

From all waves of data collection (fall and spring of kindergarten 1998-1999, fall and spring of first grade 1999-2000, spring of third grade 2002):

During the past week, on average how many hours of television or video tapes did child watch at home each weekday, that is, Monday through Friday? How about…

a. Before breakfast?
b. Between breakfast and dinner time?
c. After dinner time?

Computer Use (Scale: Yes/No)

- Have home computer child uses
- Frequency child uses computer (*Never, Once or twice a week, 3 to 6 times a week, Every day*)
- Use computer to learn skills
- Use computer to learn drawing
- Child uses computer for Internet

MEASURES OF MEDIA CONTENT

A) *The Topeka Study*

- Viewing was measured with diaries maintained by parents for 1 week in the spring and 1 week in the fall for 2 years.
- Viewing by all members of household was recorded in 15-minute intervals from 6:00 a.m. to 2:00 a.m. for each day.
- If children were in regular day care, their viewing was recorded by the caregiver
- Parents instructed to record as a "viewer" anyone who was present for more than half of the 15-minute interval in which the television was turned on
- Validity assessed by examining errors in diaries (e.g., wrong program title for time and channel listed)

B) National Household Education Survey (NHES), 1993

Description: The National Household Education Surveys Program (NHES) provides descriptive data on the educational activities of the U.S. population and offers researchers, educators, and policymakers a variety of statistics on the condition of education in the United States. The NHES surveys cover learning at all ages, from early childhood to school age to adulthood.

1) Please tell me whether child watches any of the following television programs once a weel or more, either at home or someplace else
    a. Sesame Street
    b. Mr. Rogers' Neighborhood
    c. Barney and Friends
    d. Reading Rainbow

2) Before starting kindergarten/first grade, did child watch *Sesame Street* either at home or someplace else, at least once a week for a period of three months or more? [Yes/No]

C) ***Early Childhood Longitudinal Study—Kindergarten Cohort (ECLS-K)***

Data on content collected Spring 2000
During this week, did child watch… [Yes/No]

a. Children's programs such as those on Nickelodeon or the Disney channel, or programs such as Sesame Street, Reading Rainbow, or Magic School Bus?
b. Cartoons?
c. Children's videos or movies?
d. Educational programs designed for a general audience, such as those on the Discovery or Learning Channel or programs such as National Geographic or NOVA?
e. Sports?
f. Situation comedies or sit-coms that come on in the evening, including re-runs?
g. Soap operas?
h. Talk shows?
i. News shows or news channels?

D) ***Sloan Study of Youth and Social Development***

Description: Conducted at the University of Chicago between 1992 and 2000, this longitudinal study of adolescent development used multiple methods to examine career and social development among youth from middle- and high school through college.

1. Think about the different kinds of TV shows you usually watch. How often do you watch the kinds of shows listed below each week? (*Scale:* Every day, several times a week, once a week, less than once a week)
    a. Soap operas
    b. Sitcoms
    c. Dramas
    d. News
    e. PBS/Discovery or History channels
    f. Movies/movie channels
    g. Music videos (MTV, VH1 etc.)
    h. Sports
    i. Talk shows

E. Kaiser Family Foundation Measures

<http://www.kff.org/entmedia/1535-index.cfm>

Appendix C[3]

Proposal for an Intervention Experiment as part of the National Children's Study

Overview

The Working Group on Media Effects on Child Health and Development met on January 22 and 23, 2004 in Austin, Texas. The Working Group developed hypotheses concerning a variety of media effects on children. During discussions of how these effects would be interpreted in the context of the National Children's Study, the possibility of an intervention experiment was raised. This document briefly outlines the rationale and method for such an experiment.

This is a draft proposal to study the effects of intervention in media exposure for a group of children from zero to five years of age. A group of parents would be recruited to follow a "best practice" regime with respect to their children's exposure to media until the age of five years. The comparison group would be taken from the National Children's Study but would consist of children who did not receive the intervention. While there are multiple purposes for such an intervention experiment, a main purpose for present purposes is to determine whether associations with media use that are found in the National Children Study are due to media self-selection effects or are due to the media themselves. For example, consider the possibility that children who watch educational television such as *Sesame Street* have better cognitive development and school achievement. Is this result due to the curriculum of *Sesame Street*, or is it due to the fact that children who are eager to learn choose to watch *Sesame Street*? If it is the latter case, the positive association of *Sesame Street* viewing and cognitive development would be due to media self-selection. If, on the other hand, an intervention study following best practice found that children who were encouraged to watch educational television showed enhanced cognitive development and school achievement compared to controls, then it could be concluded that selective exposure to educational media played a causal role in this enhancement.

Background

Exposure to media during early childhood is thought to have a variety and range of effects. These effects may be distinctly different from infancy to age 2 years as compared to effects for preschool children older than 2. This distinction is reflected in the hypotheses of the media working group as well as in the recommendation by the American Academy of Pediatrics that children under 2 have minimal or no exposure to electronic screen media. Because of these concerns, the two phases of early childhood will be considered separately, and the outcomes of interest will be somewhat different. The focus in this draft document is on television since that is the medium to which young children are most exposed.

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[3] Thanks to Daniel R. Anderson, Michael Rich, and Elizabeth A. Vandewater for drafting this intervention proposal.

Infants and toddlers. Of greatest concern for children in this developmental stage is the possible effects of media use on neurobehavioral aspects of development such as attentional skills.

Most exposure to media in very young children is likely as part of the background home environment as older siblings and parents watch TV and use computers and game machines. While the average American home with children has a TV in use about 6 hours a day, on the average, children under 3 actively view TV, in the sense of paying attention, about an hour (Rideout, Vandewater & Wartella, 2003). During much of the remaining time, television is present as background stimulation. Schmitt, Woolf and Anderson (2003) reported that, in the presence of a TV set in use, 2-year-olds spent 39% of their time engaged in social interactions with other family members and 32% playing with toys. Anderson and Evans (2001) hypothesized that background television might have deleterious effects on very young children by distracting them as they play or interact or by distracting others in the family, especially parents. Such distractions may make it difficult for very young children to organize their behavior and may reduce the amount and quality of interactions with parents. Preliminary evidence that background television has a disruptive influence comes from a study reported by Evans et al., (2003). They compared 1-, 2-, and 3-year-olds' play behavior with and without a television set playing an adult game show in the background. Play episodes were about half as long when the TV was on, suggesting that sustained play became fragmented in the presence of TV.

Increasingly, however, TV programs and videos are being made for children under 2 years of age. Prime examples are *Teletubbies* and the *Baby Einstein* series of videos. While these programs and videos are claimed to be educational for infants and toddlers, the producers provide no evidence that they are.

In contrast, a number of recent studies have indicated that infants and toddlers under 2 show either no learning or only very limited learning from video as compared to equivalent live demonstrations (Barr & Hayne, 1999; Kuhl, Tsao & Liu, 2003; Mumme & Fernald, 2003; Schmitt & Anderson, 2002; Troseth & DeLoach, 1998). These latter studies make claims that TV is educational for children under 2 somewhat dubious.

If children under 2 learn little from television, then time spent watching TV is taken away from other potentially more valuable activities such as active play or interactions with other family members. There is some correlational evidence indicating that substantial exposure to TV is associated with poorer cognitive and language development (Carew, 1980; Gottfried, 1984; Nelson, 1973). Because TV was not the focus of these studies, however, it is possible that other factors associated with heavy TV use, such as lower parent education, may be responsible for these findings.

In summary, the evidence, while somewhat meager, indicates that television use may be a possible risk factor for early neurobehavioral development. Recognizing this possibility, the American Academy of Pediatrics recommended that children under 2 have no exposure audiovisual electronic media. It is unclear, at this point, what are the

long-term implications of media exposure on neurobehavioral development. The intervention experiment described here would provide definitive new evidence.

Preschool Children. For 2- to 5-year-old children, the impact of media use on three developmental outcomes becomes particularly salient: 1) Pre-literacy and literacy skills, 2) Pro- and anti-social behavior, and 3) Physical activity and diet. All three early childhood outcomes are known to have important implications for trajectories of healthy development as children age.

From age 2 to 5 years children begin to attend to a much wider range of programming, so that overall attention to TV at home greatly increases (Anderson, Lorch, Collins, Field & Nathan, 1986). This increase in attention is related to a greatly increased ability to comprehend TV during the preschool years (e.g., Smith, Anderson & Fischer, 1985). Consequently, it is possible for television content to influence preschool children's behavior, knowledge, and skills. This influence can be both good and bad.

Among the presumed good effects are those associated with educational and prosocial content. Paradigmatic of educational effects are those attributed to *Sesame Street* which is the longest-running educational TV program as well as the program that has been most studied. Early evaluations indicated that its preschool viewers learned the intended educational content (Ball & Bogatz, 1970; Bogatz & Ball, 1971). Later studies indicated that, the more children viewed *Sesame Street*, the better were their vocabularies (Rice, Huston, Truglio & Wright, 1990), the better prepared they were for school (Wright, Huston, Scantlin & Kotler, 2001; Zill, Davies & Daly, 1994), and that positive associations with academic achievement were traceable through high school (Anderson, Huston, Schmitt, Linebarger & Wright, 2001). All these studies were correlational in nature; although all used statistical controls to help eliminate alternative interpretations of their findings, none could conclusively attribute cause and effect relationships to *Sesame Street* viewing. It is possible that through self-selection, *Sesame Street* viewers are the kind of children who simply become better students.

Other kinds of content are associated with distinctly different results. Exposure to prosocial content, that is, content that teaches and models positive social behavior, is associated with prosocial behavior in children. Exposure to violent content is associated with an increase in aggressive behavior and with poorer school achievement (for reviews see Huston & Wright, 1997). Although there are experiments showing short-term causal relationships of behavior to prosocial or violent TV content, all studies that relate media exposure to real-world measures, such as arrest records, are correlational. It is possible that media self-selection can account for these findings. Again, conclusive experimental evidence is largely lacking.

Time spent with media may also play a role in the development of childhood obesity. Television, along with other sedentary behaviors, may contribute to obesity by competing with more physically active behaviors. It is also possible that television viewing may contribute to increased caloric intake, either through setting the occasion for eating, or increases in consumption in response to food-related advertising.

Regardless of the specific mechanism involved, studies examining the relationship between television viewing and obesity in children and adolescents have consistently found weak associations between the two phenomena (Robinson & Killen,

1995). Dietz & Gortmaker (1985) reported a small but significant relationship between television viewing and obesity. They report that the prevalence of obesity in a large epidemiological sample of adolescents 12-17 increased 2% for each additional hour of television watched.

However, ensuing studies have been unable to reliably reproduce this link. Robinson and Killen (1995) found that while television viewing was associated with increased dietary intake in a large (*N* = 1,912) sample of ninth graders, it was only weakly associated with body mass index, and only among White boys. Robinson et al. (1993) found that baseline hours of television viewing were not associated with either baseline or longitudinal change in body mass index in a large (*N* = 971) sample of sixth and seventh grade girls. McMurray et al. (2000) found that there was no relationship between television or video game use and body mass index in a sample of 2389 adolescents ages 10-17 once the influence of socioeconomic status and ethnicity were controlled. Finally, Durant, Baranowski, Johnson and Thompson (1994) also found no relationship between body mass index and television watching in a longitudinal sample of young children (ages 3-4). On the other hand, it is worth noting that in the sole existing experimental intervention study, Robinson (1999) found that compared to a control group, elementary school children who received classroom curriculum designed to reduce television use over 128 months showed significant relative decreases in body mass index, television viewing and eating meals in front of the television (though there were no differences in high-fat food intake or moderate-to-vigorous physical activity). Overall, this "mixed bag" of findings seems to suggest that *some* relationship between children's media use and weight status exists—the problem is this it is impossible tell exactly what that relationship is or for whom it is strongest.

Thus, the widely held conviction that media use plays a causal role in childhood obesity is not well-supported by existing evidence and urgently requires further empirical evaluation. It is possible that media use is related to obesity because it encourages inactivity, increased food consumption, or both. However, it seems equally plausible that obesity may lead to more sedentary activity, including increased media use. Only an experimental study with a longitudinal prospective design will allow us to disentangle the direction of effects in this area.

In summary, there is substantial evidence that media content as well as time spent with media have important effects on preschool children, effects that in some respects, are traceable through high school. The evidence, however, is largely correlational, as will be most of the evidence from the longitudinal National Children's Study. In order to to conclude that the associations of outcomes with media exposure that are revealed in the National Children's Study are causally due to media, an intervention experiment would help clarify the issue.

Design

Three groups are proposed. The control, or comparison, group will be chosen from the larger National Children's Study sample. This group will have media use and outcomes assessed according to the standard protocols developed for the larger Study. The control group sample can presumably be precisely matched to the characteristics of the experimental groups.

There will be two experimental groups that differ by the length of the intervention. The first, or infant intervention group will have an intervention that lasts from birth to 24 months of age. The intervention will be designed to minimize exposure to screen media consistent with the recommendation of the American Academy of Pediatrics.

The second group will have an intervention that lasts from birth to 60 months of age. For the first two years the intervention will be the same as for the first group. From 24 to 60 months of age the intervention will be designed to restrict media use to a weekly maximum, and within that maximum, to content that is explicitly designed to be educational and prosocial. Ideally, following the intervention periods, the children would participate in the National Children's Study protocol until age 21.

Method

The interventions will involve exhortations to parents to follow recommended best media practices for two or five years, depending on group. Ideally, the children for the experimental groups will be randomly chosen from participants in the National Children's Study. In order to gain maximum compliance with best media practices, it is recommended that the children be first-borns. Parents without older children are generally more able to control the media environment than are parents who have children with established media consumption habits. That said, because parents will be asked to minimize children's exposure to any screen media for the first two years, parents will consequently be asked to limit their own media use when the child is present. Experimenters will provide written materials in support of the American Academy of Pediatrics recommendations and periodic telephone calls will be made to help maintain motivation for compliance.

Following the infancy period, the five-year group will be exhorted to allow selective media exposure, under a maximum amount of time, to screen media content that is prosocial and educational in nature, avoiding general entertainment and especially violent content. Parents in this group will receive TV program as well as interactive software information that will help them choose an optimal media diet.

In every other respect, it is proposed that the two-year and five-year intervention groups be treated exactly the same as other participants in the National Children's Study. The outcome measures of the larger study will become the outcome measures of the experiment.

Sample Size Required

On the basis of existing literature, we estimate that the effect sizes for attentional skills infants and toddlers, and pre-literacy skills and behavioral outcomes in preschoolers, should all range from small to moderate. For example, in their meta-analysis Paik & Comstock (1994) found an effect size of violent television content on anti-social behavior of .31. Mares and Woodard (2001) found a slightly smaller effect size (.27) for pro-social programming on positive behavior. Though there is no existing meta-analysis on the relationship between educational content and literacy skills, there is a large body of literature demonstrating a consistently positive relationship between the two. The relationship between media use and obesity has proven more problematic and more difficult to reproduce. Though no meta-analysis exists in this area, we would expect that the effect size for this relationship would be quite small, requiring larger samples to detect.

Multi-level model equations will be employed to estimate the influence of time-varying covariates and to take account of rate of change due to individual age and rate of change due to developmental stage. It is anticipated that the intervention will take place over a five year period and that the children in the intervention sample will be followed for an additional 3 years (up to age 8) in order to assess the longer term effect of the intervention. Thus, based on estimating a 3 (experimental group) x 2 (gender) x 8 (time) factorial design, power analyses indicate that in order to detect a small effect size (f = .05) for tests performed at a=.05, with power=.90, and estimating 20% attrition, a total sample of ***N* = 6108** is required for the intervention study (2036 in each group). If the goals of the intervention study were limited to content-related effects, with larger effect sizes estimated from the literature, then a smaller total sample would be required. If the effect size were .10, a sample of **1512** would be needed, whereas if the effect size were .15 a sample size of **730** would be required. Finally, if the approximate effect size observed in the content effects literature were used, .25, then a sample of **300** would be appropriate.

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MEMO

To: National Children's Study Advisory Committee
From: Social Environment Working Group
Subject: Design of NCS
Date: June 1, 2004

The Social Environment Working Group wishes to endorse the attached memo from Arleen Liebowitz and Duncan Thomas of UCLA. As noted in earlier communications, we believe that the design of the study to include siblings would add important scientific leverage.

The National Children's Study
The role of family and socio-economic status

Arleen Leibowitz and Duncan Thomas
UCLA

10 May 2004

One of the goals of the National Children's Study (NCS) is to pin down causal effects of environmental exposure on child health and development. For many of the biological mechanisms that are of central interest, the cohort design is ideally suited for this task. However, for social, economic and family factors, identifying causal mechanisms has proved to be very difficult and a cohort design is not well suited for this task. Yet, identification of the causal mechanisms underlying social and economic behaviors is extremely important for science and policy, since these are factors that public policy could potentially alter.

Take, as an example, the relationship between whether a child's parents are married through the child's first few years of life. The literature suggests that children of married parents are at lower risk of poor health and cognitive development. If this effect is causal, then policies should be designed to increase the probability parents remain married. If, however, the correlation reflects other choices that are not measured in the NCS, then married parents is simply a marker for those behaviors. These might be, for example, greater investments in the marriage and in the family. In that case, keeping parents married when they do not also make these investments may have no beneficial effects on child health and development.

Similar issues arise with co-residence of parents and other family helpers, with working parents and with family resources. In all cases, there are behavioral choices of parents and other family members which play a potentially important mediating role and which not only affect child outcomes but are affected by child outcomes. These relationships can also be very complex. For example, a mother may choose to work part-time (or not at all) in order to look after a child that is not developing well. Or she might choose to work more in order to pay for special schooling and professional help for that child.

Identifying the causal mechanisms underlying associations between social and economic behaviors and child outcomes is key for designing policies that are likely to work.
There are a number of approaches that can be taken:

1. A modeling approach would measure the broad social and economic environment to which all family members in a cohort are exposed and use those characteristics to predict behaviors. This approach can document correlations, but can not identify causal mechanisms since this approach can not be used to identify exogenous variation in variables, such as mother's employment, that affect child well-being. That approach has not been very successful in the child development literature. Its validity rests on assumptions that are seldom likely to be satisfied in the complexity of family life.

2. Lacking the ability to experimentally assign some parents to a happy marriage, and others to divorce, we can use statistical methodologies to obtain "quasi-experimental" results. One way to do that is to design the NCS so that a sibling can serve as a within-family "control" for the target child. In that way, parent and family behaviors that are time invariant can be held constant and differences in child outcomes between siblings can be related to other factors (such as marital status, employment status or income) that vary between siblings. This is much like the approach of comparing outcomes for identical twins (or siblings) which geneticists used before genetic factors could be directly measured.

Following the second approach suggests that not only should each target child in NCS be assessed thoroughly, but that the entire household unit in which the target child resides should also be assessed. Capturing the economic and social environment of the household and family is important in order to measure the relationships between child outcomes and the behaviors and resources of all family members. By contrasting outcomes of a target child with those of a sibling, it is possible to sweep out a good deal of the unobserved behaviors of parents and family life, and with plausible assumptions about the time invariance of these behaviors, measure the causal effect of those behaviors on child outcomes. Let us return to the example of whether parents are married. Say a target child is born in 2006. Say a sibling is born in 2008. In 2009, the parents divorce and the mother lives with the two children. By following the target child and the sibling, it is possible to trace the life course of the target child (who experienced married parents for three years) with a sibling (who experienced married parents for only one year). If the parental behaviors did not change in the year before divorce, by comparing outcomes of the target child with outcomes of the sibling (at the time when he or she is the same age as the target child), it is possible to assess the impact of parental separation on child outcomes. This type of comparison necessarily abstracts from birth order effects, which would need to be modeled using data on families that remained intact throughout their childrens' early years.

A practical advantage of collecting sibling data is that it can reduce the costs of data collection because there are fixed costs associated with each child that will be shared among siblings. These include, for example, the cost of contacting parents, collecting information from them and collecting information from siblings. In a longitudinal survey, it is key that attrition be kept to a minimum. The costs of re-contacting each respondent will be substantially reduced in a design that follows siblings. Moreover, this design would provide a cost-effective means of collecting pre-pregnancy data on mothers of later birth-order children. This design also provides for the collection of information on step-siblings and foster children and interpreting the relationships between socio-economic characteristics and the outcomes of these children. A disadvantage of this plan is that the effective sample size will be lowered due to the correlation in outcomes between siblings. However, if some of the rare outcomes are not correlated within families, this may not be an important concern given the planned sample size of 100,000 children.

Controlling family background and socio-economic characteristics by exploiting sibling comparisons does not mean we can avoid measurement of the social environment. What it means is that these characteristics no longer only play the role of confounding factors in the analyses which soak up some of the correlations between, say, birth-weight and school readiness. Rather, these family, social and economic characteristics become potentially powerful inputs into the analytical structure of the study and substantially enrich the range of hypotheses that can be tested with these data. This is important not just for science but because it is feasible to design policies that affect marriage and divorce, non-marital and teenage pregnancy, living arrangements, work and earnings and health insurance coverage. Knowledge of the causal effect of these factors on child outcomes is critical if such policies will be effective. It would be a tremendous opportunity lost for both scientific research and policy if the design of NCS precludes addressing these important questions.

MEMO

To: National Children's Study Advisory Committee
From: Social Environment Working Group
Subject: Comments on ICC Hypotheses
Date: June 1, 2004

This memo responds to a request made by Dr. Graham at the March, 2004 NCSAC meeting. Dr. Graham requested comments from the Working Groups about the set of Core Hypotheses developed by the ICC.

The members of the Social Environment Working Group (SEWG) have based their comments on a document entitled "Improving Children's Environmental Health with High Quality Science: Formulating Hypotheses and Study Design-List of Priority Outcomes and Core Hypotheses for the National Children's Study" dated December 1, 2003. The document clearly states that "a manageable set of core hypotheses cannot alone convey the true breadth of the Study, nor do they, alone, assure the collection of data necessary to address the full range of topics to be covered by the Study." Recognizing the validity of this disclaimer, members of the SEWG believe that, as currently constituted, the core hypotheses are too narrow to adequately represent the scope and vision of the NCS.

We believe that the core hypotheses should reflect the central mission of the study, to understand the impact of environment on children's health and development. Given this mission, all of the core hypotheses should relate one or more aspect of the environment to specific health or developmental outcomes. This is not currently the case. Recognizing that there may be disciplinary differences in how "environment" is conceptualized, we count only seven hypotheses that clearly refer to factors that exist independent of the individual child or pregnant woman, and five more that refer to infection (a common but not inevitable result of exposure to infectious agents). While some scientists might view "diet" as an environmental factor, dietary intake is actually a behavior, and one that becomes increasingly choice-driven as children develop.

Naturally, our primary concern is the limited acknowledgment of the social environment as a determinant for the priority outcomes in the proposed hypotheses. The text in the document properly acknowledges the role of the social environment and states that "[t]here is substantial public health concern about the impact of the quality of the environment on child health and development but surprising little research to help policy makers determine which environmental factors are harmful, harmless, or helpful." However, this emphasis on children's environments in general and their social environments in particular is not evident in the core hypotheses.

We argue that the social environment is strongly associated with each of the five priority outcomes. That is, there is ample evidence suggesting that various aspects of the social environment impact the physical and mental health of mothers, the timing of first intercourse, age of conception, the risk of pre-term birth and low birth weight,

neurodevelopmental trajectories, behavioral problems, the risk of injury, the onset and subsequent burden of asthma, the risk of obesity, and physical development. Thus:

> *We urge the ICC to position the social environment more centrally in hypotheses addressing* ***each*** *of the core priority outcomes of the National Children's Study.*

It is the position of the SEWG that the social environment is a fundamental cause of health and well-being among infants, children, and adolescents. Link and Phelan (1995) have made this case convincingly for socioeconomic status, one of the domains of the social environment. The nearly monotonic relationship between socioeconomic status and health (both morbidity and mortality) is an established finding across a number of disciplines. This relationship is evident regardless of the compositional characteristics of the study (e.g., age, gender, or race), the operationalization and measurement of socioeconomic status (e.g., income, education, occupation, and wealth), or the temporal or physical setting of the study. The factors that mediate the relationship between socioeconomic status and health evolve over time. As new risks emerge, individuals and families in relatively advantageous socioeconomic positions have greater access to information about the risks as well as greater resources that they can mobilize to protect their health. In short, although the proximate causes of disease may change, socioeconomic status remains a consistent and fundamental cause of illness, functional limitations, and death.

> *Because the social environment is a fundamental cause of health which may o*perate through a varied and evolving set of mediating processes, understanding its effects on health will require the NCS to adequately measure both social environmental causes and mediating processes. The hypotheses should incorporate both types of causes.

The proposed core hypotheses do a better job of highlighting proximate causes of health such as diet, exercise, and psychological stress than they do of highlighting fundamental socioeconomic or other social environmental causes. Indeed, several of the core hypotheses propose the ascertainment of psychological stress as a major predictor (e.g., obesity, pregnancy outcomes, asthma, and neurodevelopment). However, stress is not in and of itself an environmental factor. Aspects of both the physical and social environments can contribute to stresses experienced by individuals, and various sociodemographic characteristics (e.g., lower social class, ethnic minority status, gender) may predispose individuals to particular forms of chronic life stress. However, not all individuals respond to environmental challenges in the same way. Environmental effects on health mediated by psychological stress cannot be adequately studied without rigorous attention to the systematic characterization of the social environmental influences, as well as the stress response itself. These influences, and their relation to stress and behavioral mediators, should be incorporated in the core hypotheses.

The large sample size proposed for the NCS provides a unique opportunity to explore interactions among both physical and social environmental factors as well as genetic factors. Consensus holds that it is more likely the case that gene-by-gene, gene-

by-environment, and environment-by-environment interactions are the crucial determinants of differential morbidity and mortality. From the perspective of health disparities, members of the SEWG strongly contend that differential exposure to both social environmental factors and physical environmental toxins that co-vary with SES will be critical determinants in the causative pathways of disease. That is, subjects who are exposed to toxins that are more highly prevalent in lower social status communities (psychological stress, smoking, aeroallergens, diesel exhaust) and carry genetic variants that have causal effects but also modify the host response to the social and physical environments will have the greatest increased risk of disease. We encourage those constructing the core hypotheses to represent such complex influences on health.

A further reason for improving attention to social environmental influences within the NCS core hypotheses is the potential power to manipulate such influences through policies. For example, policies designed to improve access to health care, enforce child support payments, and affect the quality of child care have direct implications for children's health. However, not all policies are equally effective, and research that examines the intended and unintended effects of specific policies can provide a valuable resource for policymakers. Attention to this aspect of the social environment will enable the NCS to add this audience to other potential beneficiaries of the results of the study.

Another concern regarding the core hypotheses is the absence of hypotheses pointing to positive developmental outcomes, despite the goals of the study to examine developmental as well as health outcomes. A separate group has developed hypotheses related to healthy development and the NCSAC has repeatedly endorsed the addition of a new outcome domain related to healthy development. We also endorse such an addition.

In summary, the core hypotheses of the National Children's Study require greater attention to a broad range of environmental exposures and developmental outcomes if they are to truly reflect the mission of the study. We particularly stress that the social environment plays a central role in developmental trajectories of nearly all aspects of children's lives. The immediate social environment shapes exposure to known health risk factors and it facilitates access to important resources. The accurate operationalization and subsequent measurement of the social environment is paramount to our understanding of the progression of disease and or subsequent resiliency in the face of otherwise risky profiles. We encourage those responsible for finalizing the set of "core hypotheses" for the NCS to consider the hypotheses listed in the attached document. Most of these hypotheses have been previously suggested by the Social Environment Working Group (SEWG) and recommended by the NCSAC. A few are additional hypotheses generated since the SEWG last submitted its hypotheses.

Reference

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Attachment

Hypotheses Concerning Social Environment Exposures

Pregnancy outcome:
Rates of joblessness and the proportion incarcerated among local area males of similar race and socioeconomic status increase the probability of preterm delivery. These relationships are mediated by marital status, unintended pregnancy, and maternal stress.

Neighborhood and community characteristics that negatively influence the health of the mother during pregnancy – including poverty, poor housing quality, poor health care access, norms and policies that encourage smoking, and low levels of social interaction and support – increase the likelihood that the fetus will develop characteristics that predispose it to heightened susceptibility to health problems later in life.

First generation and more recent Mexican immigrants experience lower rates of infant mortality in part because of their stronger social ties within ethnic communities that share norms for physical activity, healthy dietary habits, and other behaviors.

Neighborhoods characterized by high levels of social disorganization and a shortage of affordable housing increase the exposure of neighborhood residents to stressors such as criminal victimization and eviction; these are most likely to cause stress and increase the likelihood of adverse pregnancy outcomes among unmarried, poor, and unemployed women.

Among women who work during pregnancy, those with low-control jobs and negative relations with co-workers are less likely to experience stress - and poor pregnancy outcomes - if they have positive relationships with the baby's father and with parents.

Among poor women who become pregnant while unmarried, the experience of stress during pregnancy (and resulting poor birth outcomes) is less likely in states with generous/favorable TANF policies (e.g., higher benefits, fewer barriers to eligibility, simpler administrative procedures for accessing benefits).

Neurodevelopment and Behavior:
Among employed women with similar salary levels, those whose employer provides health insurance, paid maternity leave, and adequate sick leave will be less likely to experience stress during and after pregnancy and less likely to give birth to a child who later develops cognitive or neurobehavioral problems.

Over the first three years of life, children born to unmarried or cohabiting parents are more likely than children born to married parents to exhibit sub-optimal functioning of stress-responsive biological regulatory systems, inferior levels of emotional regulation, and behavioral problems in the form of externalizing and internalizing behaviors, in part because of increased instability in family relationships.

The outcomes of prematurity will depend on family SES. Middle-class premature infants face fewer long-term risks and learning problems than do premature infants born into low SES households. Family processes, including factors such as household management, parenting, and family climate, mediate this relationship.

Children of depressed mothers will receive parenting that is less warm, supportive, and consistent than children of non-depressed mothers, and will be more likely to exhibit internalizing and externalizing disorders during childhood and adolescence.

Children from families that participate in shared religious activities throughout pre-adolescence are more likely, in adolescence, to have friends who refrain from risk behaviors, and to refrain from such behaviors themselves.

Children who experience family violence, maltreatment, and/or neglect face a higher likelihood of expressing genetic predispositions to depression and schizophrenia.

[Adaptation of a policy hypothesis]: Low-income children in localities with more generous TANF provisions will have higher cognitive functioning at age 5, controlling for educational level of mother and parental marital history.

Stress associated with low income, low job status, unemployment, and social inequality may undermine parenting behaviors that promote children's positive development.

Family participation in religious organizations during early and middle childhood (ages 3-10) results in better emotional health and fewer health-compromising behaviors during middle adolescence (ages 14-15). These effects are stronger in female children, ethnic minority and immigrant families, and impoverished areas, and when the religious organizations provide effective mechanisms for integrating adolescents into the life of the religious community.

Children's participation in schools will affect social, emotional, and physical development. Provision of health services and of curricula and programs targeted toward health promotion will directly impact on children's health and mental health outcomes. Child, family, and community factors interact with structural and functional aspects of schools to shape child development.

Variations in the quality of child care affect children's cognitive and social functioning. Child care influences are partially mediated through family influences.

Variations in policies and programs by state and by size of community contribute to child health differentials across place. (more specific version?:low-income children in localities with more generous TANF provisions will have higher cognitive functioning at age 5, controlling for educational level of mother and parental marital history.)

Social relationships that are abusive contribute to the onset of depression and other mental health problems, and adversely affect physiological function. In parents, these effects result in impaired parenting.

Among children placed in protective custody , the prevalence of depressive symptoms (measured by a CES-D score of over 16) by age 21 will be higher among those placed in foster care compared with those placed with relatives.

Among children age 5 living with two biological parents, those whose parents engage in high levels of physical conflict(upper decile on the Physical Assault Subscale of the Conflict Tactics Scale (Straus et al, 1996)) will have lower levels of salivary cortisol than those whose parents engage in low (lower decile) levels of conflict .

Children living in states with strong policies affecting the investigation and substantiation of child maltreatment cases will have higher intelligence scores at age 10 than children living in states with weak policies; this effect will be mediated by children's experience of parental maltreatment prior to the age of 10.

Among children carrying the DRD2 subtype of the dopamine receptor, those who at age five lived in census tracts characterized by high levels of neighborhood collective efficacy will be less likely to have received a diagnosis of schizophrenia by age 21 than those who lived in census tracts characterized by low levels of collective efficacy.

Among children carrying two copies of the short allele of the 5-HTT promoter polymorphism, those who at age five lived in census tracts characterized by high levels of neighborhood collective efficacy will be less likely to have received a diagnosis of dpression by age 21 than those who lived in census tracts characterized by low levels of collective efficacy.

Injury

Children whose parents monitor their activities at home and in their neighborhoods will experience fewer injuries.

Automobile-related injuries will be lower in families in which parents consistently fasten their own seat belts while driving and ensure that their children are protected by appropriate restraints.

Children who experience family violence, maltreatment, and/or neglect are more likely to be victims of severe injury or death.

Asthma

The relationship between socioeconomic status, race/ethnicity, and asthma incidence and morbidity is explained, in part, by socially determined differential exposure to physical environmental risk factors (i.e., diesel-related air pollutants, allergens) and psychosocial

stress. These effects are moderated by policies and programs that buffer the effects of economic disadvantage on families.

Economic, cultural, and social features of the local area influence: (1) exposure to stressful life conditions and events; (2) the availability of social ties that provide informational, emotional and instrumental resources to individuals and families; and (3) shared norms influencing health behaviors. These, in turn, influence outcomes including immunological functioning in the child, the likelihood that the child will develop asthma, and asthma severity and management.

Neighborhood and community characteristics that contribute to environmental hazards– including poverty, poor housing quality, norms and policies that encourage smoking, low levels of political mobilization or collective efficacy, and high levels of crime and violence – increase the incidence and severity of childhood health problems, such as asthma, and complicate their management.

Neighborhood and community characteristics that contribute to stress – including stressors such as poverty, unemployment, crime and violence, and poor housing quality, and the absence of stress-buffering resources such as social supports and access to health care and other institutions– increase the incidence and severity of childhood health problems, such as asthma, and complicate their management.

Social ties that provide instrumental and/or emotional support to families and children help to prevent the onset of asthma and to facilitate its management.

Obesity and Physical Development

Programs that connect low-income women to early prenatal care and social environmental influences that support the management of maternal hyperglycemia during pregnancy reduce the risk of accelerated fetal growth and the child's subsequent risk of childhood obesity.

Support for breastfeeding in the work environment and kin/nonkin networks of new mothers will contribute to lower rates of obesity through increasing the probability of breastfeeding and the duration of breastfeeding. These factors partially mediate the influence of socioeconomic status on breastfeeding and obesity.

Parenting behaviors influence the timing of adiposity rebound and changes in adiposity during childhood through their effects on children's diet and physical activity/inactivity. Parenting behaviors are a function of the family's food and physical environments, family resources (structure, parental education and income), and norms and beliefs supported through kin and nonkin networks.

The influence on obesity of non-family factors, including peer and media norms for thinness or body shape, access to and promotion of energy-dense foods, and opportunities

for physical activity in schools and communities, increases with increasing age and intensifies after puberty. Social interaction with peers influences physical activity/inactivity and diet, and is in turn adversely influenced by obesity in children and adolescents. Sociocultural influences on diet and physical activity differ by race, ethnicity, and gender.

First generation and more recent Mexican immigrants experience lower rates of obesity in part because of their stronger social ties within ethnic communities that share norms for physical activity, healthy dietary habits, and other behaviors.

Asthma prevalence at age 10 will be lower among second generation Mexican immigrant children as compared to 3rd and higher generation Mexican immigrant children.

National Children's Study Workshop
Addressing Rural Children in the National Children's Study
March 1–2, 2004
Holiday Inn Select
Bethesda, MD

This meeting was held in conjunction with the National Children's Study, which is led by a consortium of federal agency partners: the U.S. Department of Health and Human Services (including the National Institute of Child Health and Human Development [NICHD] and the National Institute of Environmental Health Sciences [NIEHS], two parts of the National Institutes of Health, and the Centers for Disease Control and Prevention [CDC]) and the U.S. Environmental Protection Agency (EPA).

Background

Co-Chairs: Daniel Lichter, Ph.D., Ohio State University, and Ann Tickamyer, Ph.D., Ohio University

Rural populations comprise one fifth of the nation, yet are often neglected in research and the public consciousness. Rural children face unique challenges to healthy development associated with poverty; spatial and social isolation; inadequate health, educational, commercial, and social service infrastructure; and unique environmental hazards. The National Children's Study (Study) provides an unprecedented opportunity to learn how these challenges influence the health and development of rural children, and what can be done to improve their lives. However, to realize this potential, careful attention must be given to rural populations in the design of the Study. This workshop explored how the Study can contribute to a better understanding of the health and development of rural children.

The Study has a clear responsibility to address the unique health and developmental challenges of rural children, but doing so will require careful thought and planning. Rural populations are typically poorly represented in national studies because their dispersion makes them more difficult to sample and interview. These sampling issues need to be identified, and creative solutions to them advanced. Rural environments are highly diverse, and sampling strategies must be theoretically guided to capture those environments of greatest interest to the Study. In addition, rural children may experience different threats to health and development, and different protective influences, than children in urban or suburban settings; measurement protocols for the Study must be designed to encompass these influences.

This workshop was designed to cast a spotlight on rural children and to identify what the Study needs to do in order to effectively address their health and development. The purposes of the workshop were to:

- Highlight the importance of rural children's health issues and identify high-priority questions for the Study relevant to the health and development of children.
- Address methodological challenges in designing the Study so that it can address these issues effectively, including informing alternative sample design approaches currently under consideration.

Overview of the National Children's Study

Marshalyn Yeargin-Allsopp, M.D., CDC, DHHS

The Rural Workshop began the evening of March 1 with an orientation to the Study given by Dr. Yeargin-Allsopp, a member of the Study's Interagency Coordinating Committee. Dr. Yeargin-Allsopp discussed the Study's origins in the President's Task Force on Environmental Health and Safety Risks to Children. Planning for the Study was mandated in the Children's Health Act of 2000 (PL 106-310), which called for a national longitudinal study of environmental influences on children's health and development. She then described the involvement of multiple agencies in development of the Study.

Dr. Yeargin-Allsopp outlined the major concepts of the Study:

- It will be a national, high quality, longitudinal study of 100,000 children, their families, and their environment.
- Environment is broadly defined to include chemical, physical, behavioral, social, and cultural aspects.
- The design includes a common range of environmental exposures, less common outcomes, and gene-environment interactions.
- State-of-the-art technology will be used for tracking, measurements, and data management.
- Extensive public-private partnerships are planned.
- Data collected will be a national resource for future studies.

The Study will examine five different priority outcome areas: pregnancy outcome; neurodevelopment and behavior; asthma; injury; and obesity and physical development. Examples of some exposures that the Study might measure include:

- Environmental samples of air, water, dust, and soil
- Exposure biomarkers and genetic factors in blood, breast milk, hair, tissue, and urine
- Information on occupation, diet/nutrition, medicines, supplements, and herbals
- Housing and living situations, family and social experiences, and neighborhood and community characteristics.

Demographic Overview of Children in Rural America

Leif Jensen, Ph.D., Pennsylvania State University, and William O'Hare, Ph.D., The Annie E. Casey Foundation

Dr. Lichter began the second day of the workshop by introducing Dr. Jensen and Dr. O'Hare, who provided participants with an overview of the demographics of rural children. Dr. Jensen's presentation focused on three topics, including the definition of "rural," comparisons of rural and urban children, and migration between rural and urban settings. Dr. O'Hare's presentation addressed poverty and diversity among rural children and public policy issues relating to rural children.

Dr. Jensen explained differences among various concepts of "rural." Ecological concepts define rural based on the distribution of people across space and identify as rural areas with low and sparsely settled populations. Economic/industrial concepts define rural areas as those in which farming or other extractive industries are more likely to occur. Sociocultural concepts define

rural areas as locations where people adhere to a set of values that differ from residents of more urban areas. Dr. Jensen said that the most commonly used definitions of "rural" are the ecological ones.

Dr. Jensen next discussed operational methods for defining "rural." The most commonly used operational definition of "rural" is as a nonmetropolitan area. To explain the meaning of nonmetropolitan, Dr. Jensen began by describing metropolitan areas as counties that have one or more urbanized areas with a population of 50,000 or more, plus surrounding counties with economic ties as determined by commuting patterns. All other areas are considered to be nonmetropolitan. He said that many people use the terms "rural" and "nonmetropolitan" interchangeably. However, according to the definition used by the U.S. Census Bureau, "rural" means areas of open country or settlements with fewer than 2,500 people. Dr. Jensen pointed out that the definitions of "nonmetropolitan" and "rural" overlap.

Because nonmetropolitan areas encompass many types of places, researchers have refined that definition in various ways. Mr. Calvin Beale, a senior demographer at the Economic Research Service (ERS), U.S. Department of Agriculture, developed a nine-category, rural-urban continuum that blends metropolitan and rural definitions, taking into account metropolitan status, size of settlements, and adjacency to metro areas. Another method to operationalize "rural" uses urban influence codes. These incorporate micropolitan areas—nonmetropolitan counties that have an urbanized area of 10,000 or more—plus the surrounding areas tied through commuting patterns. The ERS uses codes that include county typologies (for example, by persistent poverty or the most common industrial or economic activity).

Dr. Jensen said that nonmetropolitan counties outnumber metropolitan counties by almost 2:1 and cover more land, but they contain less than 20 percent of the U.S. population. They are distributed throughout the country, but a band exists from the northern plains south into Texas. He then showed a map that indicated the number of counties that changed categories over time.

Dr. Jensen noted that the definition of "rural" has implications for the Study, because rural areas are heterogeneous and the full array of types of rural areas needs to be included in the Study sample. He stressed that it would be unacceptable to only define rural as nonmetropolitan, because that large category includes children from areas that are fairly urban to those that are extremely rural. It is important for the Study to include as much geographic specificity as possible (for example, by collecting Global Positioning System readings for every place the child lives), and to provide rural-urban continuum codes and urban influence codes.

Dr. Jensen discussed the reasons why the Study should include rural children. Fourteen million children live in nonmetropolitan areas in the United States, and 15.4 million children live in rural areas. Children in rural and nonmetropolitan areas are important to study because they have less access to quality services and institutions (for example, schools and health care).

Dr. Jensen then provided a brief demographic overview of the differences between children in nonmetropolitan areas and those in metropolitan areas. He pointed out that nonmetropolitan children are:

- Concentrated in the Midwest and the South

- More likely to live in a home that is owned rather than rented
- More likely to be White (20–25 percent of Whites are nonmetropolitan) or American Indian (close to 50 percent are nonmetropolitan)
- More likely to be covered by Medicare or Medicaid but less likely to be covered by other health insurance than metropolitan children.

Nonmetropolitan children are as likely to be living with both parents as metropolitan children, but central-city children are less likely to be living with both parents. Fewer children in nonmetropolitan areas are rated as having "excellent" health than children living in metropolitan areas.

Dr. Jensen said that 15 percent of children in the U.S. moved between 2002 and 2003. Approximately 50 percent of families that moved stayed within the same county. The most common movement was within metropolitan areas, and the next most common move was within nonmetropolitan areas. Of the children who moved to an area in a new category, nonmetropolitan to metropolitan moves were twice as common as those in the other direction. The trend during the twentieth century has been migration from rural to urban areas, except for the 1970s and the 1990s when that flow was reversed. Over the last 5 decades, many young adults have left rural areas for education, employment, and social opportunities in urban areas.

Dr. O'Hare continued the presentation with a discussion of child poverty, racial and ethnic diversity, and public policy. In 2000, child poverty rates were 15 percent in metropolitan areas, 18.5 percent in micropolitan areas, and 21.2 percent in rural areas. Child poverty is higher in nonmetropolitan areas for all racial groups except Asian Americans. Further, the gap between child poverty in metropolitan and nonmetropolitan areas is growing.

Dr. O'Hare noted that three institutions contribute to whether children are likely to be poor:
- Work (if parents work, children are less likely to be poor)
- Education (the higher the educational level of parents, the less likely children are to be poor)
- Marriage (children who live with two parents are less likely to be poor than those who live with single parents).

These three factors affect children in both metropolitan and nonmetropolitan areas, but they are more effective in preventing poverty for children living in metropolitan areas.

Dr. O'Hare said that rural child poverty is highest in Appalachia (mostly White), the Northern Plains (mostly American Indian), the Rio Grande Valley (mostly Hispanic), and the Southern Delta region (mostly Black). The overlay of race and region is very important to consider when studying rural children who live in poverty. A key finding is the major distinction between urban child poverty and rural child poverty based on the regionalization of child poverty by race.

There are 382 persistently impoverished counties in the U.S. (poor every census from 1959 to 1999) with poverty rates of 20 percent or higher. Almost all of these counties are nonmetropolitan. There is a large overlap between persistently poor counties and the racial distribution of poor children. Of the 50 counties with the highest child poverty rates (defined as

having more than 43 percent of the children being poor), 48 are nonmetropolitan with high numbers of minority children. Of the 48 counties:

- Twenty-four are Black majority
- Nine are American Indian majority
- Eight are Hispanic majority
- Seven are White majority.

Dr. O'Hare discussed the relevance of federal policies for rural children. He explained that poor rural children are more likely to be in working families, thus policies that are aimed at the working poor disproportionately affect the rural poor. These include policies related to the Earned Income Tax Credit, the minimum wage, childcare subsidies, health insurance for low-income adults and their families, and low-income housing programs. He explained that devolution—the shifting of power to the states—increases the importance of measuring social policies at the state level. Compared to their urban counterparts, poor rural families usually live in states with lower per capita incomes, fewer services and institutional resources, and less supportive policies and benefits for low-income families. As a result, these families are less likely to get cash public assistance.

Dr. O'Hare stressed two implications of his comments for the design of the Study. First, the sample should capture the different subgroups of the rural population, defined in terms of race and region of the country. Second, it will be important to design the Study to provide representation at the state level as much as possible so that the effects of state-level policies on children's health and development can be studied.

During discussion following the presentations, James J. Quackenboss, M.S., EPA, said he is interested in state representation in the Study but sample sizes required in states are something to consider. He emphasized that the Study is being designed to answer questions about relationships between social, demographic, behavioral, and environmental exposures and relatively rare health outcomes. He said that a large sample is necessary to assess rare outcomes, and there may be difficulties when dealing with small populations. Nevertheless, some environmental information may possibly be summarized at a state level.

Janet Bokemeier, Ph.D., Michigan State University, explained that a large number of rural children change schools within a year, and this can have an impact on interventions. In addition, recent trends towards the consolidation of rural schools have taken children out of smaller, local schools and moved them to larger schools at great distances from home. These developments may have profound impacts on their activities and development.

In response to a question about rural/urban differences in children's health and well-being, Dr. O'Hare said that a book to be released in fall 2004 will compare state-level data on child well-being in city and rural populations on 10 census-based indicators. He added that a special report on measures of child well-being, which is published every year, will include a set of rural measures, and it will soon be available on the Population Reference Bureau Web site.

Key Aspects of Rural Environments Relevant to Children's Health and Development

During the next portion of the workshop, three breakout groups—focused on chemical exposures, physical health and development, and mental health and development—considered the following questions:

- What are the most important questions for the Study to answer about rural children?
- What are the questions about the health and development of children that are unique to rural children?
- What is it about rural settings that produce different (negative or positive) health and developmental outcomes in children?
- What characteristics, exposures, and processes are especially characteristic of rural settings and how do they affect children?

The groups were asked to consider the five focal areas of the Study: pregnancy outcome, neurodevelopment and behavior, asthma, injury, and obesity and physical development.

Following their deliberations, members of the breakout sessions reported back to the larger group.

Haluk Ozkaynak, Ph.D., M.S., EPA, summarized the discussions of the Chemical Exposures Breakout Session. The group considered several types of rural/urban differences that could affect differences in chemical exposures and their impact on children. Rural areas may differ not only in the prevalence of various toxins, but also in behavioral and climatic patterns which affect the extent of exposure and its impact. The group noted many factors that produce differences in chemical exposures for rural children, including:

- Outdoor and indoor environments
- Commuting in cars
- Daily behaviors that depend on community and social context
- Exposures to environmental tobacco smoke and parental use of alcohol
- Methods of cooking and heating (increased emissions of particulates, PAHs, and nitrogen oxides)
- Environmental factors (houses with lead paint, pesticides in water and air)
- Mitigating factors (more fresh air, less lead in gas, and less exposure to motor vehicle exhaust)
- Compositional differences in outdoor air pollution (particulate matter, gases, sulfur dioxide, nitrogen dioxide, ozone, volatile organics, and metals)
- Compositional differences in indoor air
- Differences in climate (hot moist air in the South can increase mold and mildew and affect the atmospheric formation of acids, metals, and other toxic pollutants)
- Grasshopper effect from pesticides blown by the wind to neighboring areas
- Regional differences due to crops, grain dust, dry or moist air, pollen, and water sources
- Crop and livestock interactions
- Dietary differences
- Greater proportion of time spent outdoors (perhaps with a greater ingestion of outdoor soil but lower exposure to indoor dust)

- More physical activity (children allowed more freedom of movement)
- Caregiving provided more often by family and friends, rather than a daycare setting
- Presence of toxic dumps and Superfund sites
- Water sources (runoff from fields with pesticide application or biological waste runoff from animals on farms)
- Occupation of parents.

Dr. Ozkaynak said that rural preschool children might be exposed to urban environments when accompanying their parents who work in urban employment centers. He added that rural children sometimes are exposed to poor housing conditions such as mobile home dwellings, which have a higher potential for mildew, mold, and formaldehyde. These can increase the chances for infections, respiratory problems, and exacerbation of asthma. Older homes in rural communities may have lower indoor pesticide concentrations than urban homes, but higher outdoor concentrations may be present due to greater numbers of home gardens and nearby agricultural fields.

Dr. Ozkaynak suggested that the Study relate sources and concentrations of exposures to ensuing health effects while accounting for the relationships among exposures, genetic factors, and individual predispositions. The group recommended that exposures may be evaluated collectively for certain groups with similar exposure characteristics, rather than individually. However, the group also expressed the concern that some proposed sampling methods might not adequately incorporate rural communities if sampling rates are driven by large primary sampling units (PSUs) or areas with high population densities.

Christine Bachrach Ph.D., NICHD, NIH, DHHS, summarized the report of the Physical Health and Development Breakout Session. She said that rural children have worse overall health and higher mortality rates than do urban children, however, data that show the extent of disparities in specific health outcomes (for example, diabetes, obesity, and asthma) are very limited. The National Health and Nutrition Examination Survey cannot provide adequate measures because it does not represent the rural population well enough. She added that it is important for the Study to address health disparities.

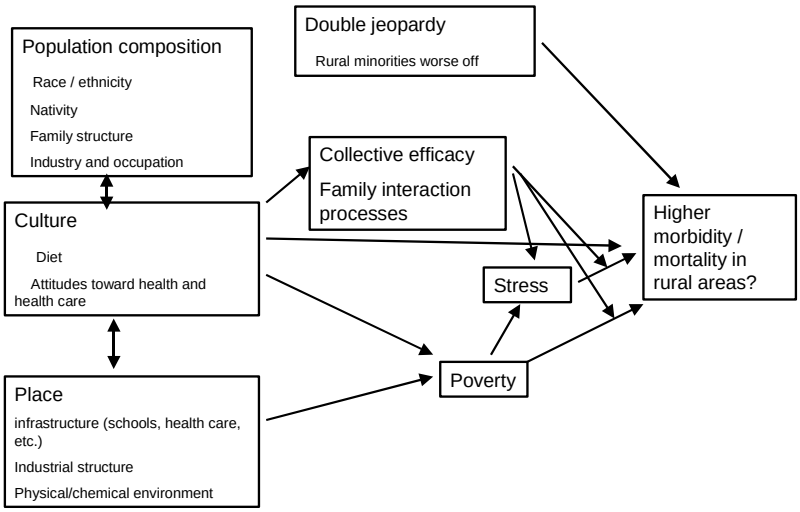
The group felt that the Study is a unique opportunity to evaluate how rural children's health and development are influenced by the distinctive characteristics of rural areas, including characteristics of the people who live in rural areas (population composition), cultural characteristics, and characteristics related to rural place (infrastructure and types of industry). The group developed a model to summarize the pathways hypothesized to be relevant to rural children's outcomes (see Figure).

Cultural aspects of rural life relevant to children's health include diet and attitudes towards health and health care. The group discussed diets of rural children and countered the myth that rural populations grow and consume their own food. Diets of rural children may be affected because it is expensive to transport fresh fruits and vegetables to rural areas. Parents may be suspicious of health care providers and reluctant to bring children to a doctor.

A major feature of rural environments is the lack of infrastructure, including health, social, and educational services. Hospitals are poorly funded, struggle to remain open, and in some cases are dilapidated. Health care is provided mostly by family practitioners, and few specialists are available. There may be poor continuity of care, and many physicians are on J-1 visas, have poor command of English, or are from a different culture. Many rural families must travel great distances to obtain health care or dental care, and families often lack health insurance.

Figure

A model of childhood morbidity and mortality



Infrastructure for education is also often substandard in rural areas. Concerns include dilapidated school buildings, distance to schools, lower quality of teachers, and the need to change schools often because of school consolidation.

The group identified a number of factors and processes that are likely to mediate the effects of rural residence on health outcomes, but noted that very little research has studied these mediating processes. Mediating pathways include poverty, increased stress, and patterns of family and social interactions. Poverty is both a function of diminished opportunities in rural areas and, in addition to increasing family stress, reduces families' abilities to invest in their children's health and development as well as protect them from health threats.

The social worlds of rural children may be different in ways that can affect health both positively and negatively. In many rural communities, communities and families may be highly cohesive. On the other hand, in widely dispersed communities the family may be the entire social world for children, and children in dysfunctional families may have few other resources to turn to for support.

The group discussed several health outcomes that might emerge from these characteristics of rural environments, including:

- Stress and alcohol leading to obesity and diabetes
- Poor nutrition as a function of poverty
- Asthma (wood or coal used for heating, mold and mildew, or mushroom farms)
- Injury due to child labor on farms.

Lynne Vernon-Feagans, Ph.D., University of North Carolina, presented a summary of the Mental Health and Development Breakout Session. This group addressed the question, "What are unique characteristics of rural environments that affect children's mental health and health outcomes?" After much discussion, participants concluded that there are real differences in opportunity structures and resources available in rural areas, and that these have significant effects on mental health and developmental outcomes.

Many rural areas are resource-poor. Compared to non-rural areas, they have:

- Higher rates of poverty
- Lower availability of mental health services
- Lack of specialized programs in schools
- Less access to childcare (especially licensed childcare)
- Less access to support services for disabled parents
- Less access to advanced media and technology.

This lack of resources is complemented by social and cultural differences that moderate rural children's outcomes. For example, poverty is likely to compromise rural children's development less in communities with strong and cohesive social structures. Such communities certainly exist in rural areas, but they are not universal. The physical isolation of rural settings can adversely affect social networks and support structures. Shared concepts of safety and what is defined as a threat to safety differ in rural areas, and these can influence how resources are deployed to protect children.

Thus, the processes contributing to positive or negative outcomes may be different in rural areas. Parenting processes are different in rural areas because the rural environment allows types of parental monitoring not feasible in cities. With respect to developmental outcomes, people in a rural setting might characterize a condition differently than people in an urban area. One example is the diagnosis of Attention Deficit/Hyperactivity Disorder, which may be overdiagnosed and overmedicated in children from urban areas. In a rural area, a child might be viewed as simply rambunctious, and that might be advantageous for the child.

In rural areas, the mentally ill may never be defined or diagnosed. Perception, treatment, and care of the mentally ill may differ dramatically from that in urban areas. Rural areas have fewer resources for early intervention and, often, stigma is attached to mental health services. One-stop shopping for health services (including mental health services) sometimes prevents stigma in rural settings. The role of faith-based institutions in dealing with mental health problems was discussed.

The group stressed the need for sufficient variation in rural communities' circumstances to permit the rigorous testing of hypotheses related to size of place and children's outcomes. It also stressed the need for the designers of the Study to be sensitive to differences in interpretation of health-related issues across rural and urban areas, differences that need to be considered in the design of Study materials.

Current Sampling Design Options Under Consideration

James J. Quackenboss, M.S., EPA

In the afternoon, discussion at the workshop shifted to methodological challenges in designing the Study to address outcomes for rural children. Mr. Quackenboss provided an initial presentation on sample design options currently under consideration for the Study. He explained that decisions about the Study design will be based on a set of "givens," including:

- The Study will be national in scope, but not necessarily nationally representative.
- A large sample is required to allow for evaluation of infrequent outcomes.
- Recruitment needs to occur as early in pregnancy as possible.
- Access to and collection of biological samples at birth is needed.
- Stratification is needed to obtain adequate ranges of exposures.
- Recruitment/retention, efficient collection of measures, access to infrastructure, community engagement, and flexibility to conduct special studies are additional considerations.
- Organizational structure(s) necessary to operationalize the design will also be considered.

He said that a decision has not yet been made on the sampling design for the Study, and a Sampling Design Workshop later in the month would examine a variety of potential options. These options are based on two basic sampling strategies:

- National household probability sampling
- Recruitment through medical centers of excellence, which could include a probability sample of center patients, or the area surrounding the center.

Probability-based sampling can use stratification and oversampling (sampling at higher rates than other populations), and can generalize to a broader population in a straightforward manner. Nonprobability-based sampling selects participants from the population in a nonrandom manner. It may involve the use of quotas and purposive selection of certain types of participants. With nonprobability sampling, generalization to a broader population depends on model-based analysis and additional assumptions. Most of the options under consideration are hybrids involving combinations of these strategies. The options are being evaluated for cost, statistical power, recruitment and retention, and other criteria.

The Sampling Design Workshop will have an expert panel to review the options and develop a report. In addition to this report, Study decision-making will be informed by input from the National Children's Study Advisory Committee, the Study Design Working Group, the Interagency Coordinating Committee, and the Study Program Office. Duane Alexander, M.D., NICHD Director, NIH, DHHS, will be responsible for the ultimate decision.

Mr. Quackenboss next discussed the designs currently under consideration and showed a slide representing groupings of designs. Mr. Quackenboss was asked if center-based designs would

have no representation of rural areas. It is undecided, but he added that one of the issues to consider was how to incorporate rural children in a center-based design.

Mr. Quackenboss concluded by identifying issues for participants of the Rural Workshop to consider:

- Center-Metropolitan Statistical Area and patient frames may exclude rural areas and populations.
  - Should centers be required to provide some rural coverage?
  - Should centers be established in rural areas?
- National probability frame
  - Use household or physician office frame?
  - Oversample rural PSUs so that they are proportionally represented in the Study?
- Combine PSUs to screen an adequate number of households?

Considerations in Designing the Study to Address Rural Children

William Kalsbeek, Ph.D., Ohio University, and *Ann Tickamyer, Ph.D., Ohio University*

The final hours of the workshop were devoted to discussion of design and logistical issues relevant to ensuring that the Study will be able to answer important questions about rural children. Drs. Tickamyer and Kalsbeek began the discussion with some initial comments.

Dr. Tickamyer noted that the morning's discussion indicated consensus that there are reasons to study rural children because processes, outcomes, and exposures differ between rural and urban children. She said that existing national studies do not adequately represent rural populations. Other research that has been conducted has been limited to case studies or studies of small communities in particular contexts. The research is often excellent, but it is not generalizable to a larger population. It is important to deal seriously with the issue of how to include rural children in the Study because it is a study of importance and magnitude. Dr. Yeargin-Allsopp agreed on the importance of including rural children the Study.

Dr. Kalsbeek noted two key issues in sampling children who live in rural areas. These were the need to:

- Ensure an adequate sample size of rural children
- Encompass adequate diversity (including race/ethnicity, poverty, and geographic region).

He said that planners must consider if the sample size will be adequate. Specifically, if 20 percent of the 100,000 children come from rural areas, is this an adequate number to answer relevant questions? If not, oversampling may be needed to obtain adequate numbers.

Dr. Kalsbeek said that, given a defined population, random selection in probability samples achieves diversity naturally and more effectively than non-probability samples. However, probability sampling cannot reflect diversity in the population as a whole if only a portion of the population is sampled. For example, a probability sample of urban communities only will not capture variation that exists in urban and rural areas together.

Dr. Ozkaynak reminded participants that the Study is not a surveillance survey but a testing of specific hypotheses. Thus, appropriate sample size and diversity in independent variables are the key factors needed in order to obtain answers.

Participants considered the potential of a Study design based on competitive recruitment of medical centers of excellence, and the steps that could be taken to include rural populations in such a design. Such designs could include probability samples of local residents or center patients, but the areas to be studied would be selected on the basis of proximity to medical centers rather than probability sampling methods.

Mr. Quackenboss responded to a question about the advantages of a nonprobability sample by suggesting that such a sample has many strengths, including:

- Retention (self-selected volunteers have more motivation to remain in the Study)
- Potential to collect more frequent measures
- Ability to collect more technically advanced measures in medical settings
- Potential lower cost of recruiting and keeping a sample.

Joseph Waksberg, M.S., Westat, agreed that medical centers are advantageous because they are able to do the measurements in a standardized way, and they have the intellectual capacity to analyze data. However, he suggested that there is confusion about two issues: how a sample is obtained versus who carries out the measurement. He said that one could select areas on a probability basis and then recruit centers to do the measurement work. He argued that there is no way to assure adequate diversity without using a probability sample. A nonprobability sample requires assumptions, brings up issues of credibility, and creates uncertainties.

Dr. Kalsbeek pointed out that if a center model were used, there would be a limited number of rural respondents because most of the centers are in urban areas. If hospitals are used as the centers, there are also the issues of reaching the people who do not go to hospitals and whether the rural people who go to the hospital represent the needed diversity. One way to address this would be to expand the definition of center to include larger community hospitals. Dr. Bokemeier agreed that relying on medical centers for data collection would introduce bias because people living in rural areas often do not have access to that care. Eileen M. Holloran, Office of Rural Health Policy, HRSA, DHHS, noted also that the Study would be missing rural areas if it only includes counties that have major medical centers. Rand Conger, Ph.D., University of California, Davis, said that medical centers and physician's offices may improve efficiency, but may so bias the results that they aren't useful.

Mr. Quackenboss reminded participants that the Study was trying to get away from the idea of probability sampling versus a center model. Instead, the current direction considers options that combine center-based samples with a national household probability sample or combine center-based samples with household probability samples drawn from the center's metropolitan area. He also noted that location and population coverage could be made a requirement in the Study. Centers could be required to serve other areas (including rural areas). He pointed out that large medical schools are usually located in inner city areas, and that children in these areas are also at risk.

Dr. Bachrach suggested two models that would enable a center-based design to include rural populations:

- Major medical centers would be given responsibility for probability sampling and measurement in rural as well as urban areas in a geographic region.
- Coordinating bodies or partnerships involving medical centers and survey units would share responsibility for the probability sampling and measurement for a geographic region.

Participants considered the challenges associated with designs that use probability sampling of households. Mr. Waksberg explained how multi-stage probability sampling could be used to get the diversity needed in a rural sample as well as a sample of women who were not yet pregnant:

- Select the areas (usually counties)
  - Use stratification based on area characteristics such as geography, mean income, and race distribution
  - Stratification might be limited by Study resources.
- Select blocks, then households, within the selected areas
  - From census information, stratify blocks on relevant characteristics
  - Select a sample of blocks and then select a sample of houses within selected blocks
- Interview each household
  - Conduct a 10-minute interview
  - Recruit women of childbearing age and contact them on a quarterly basis for 3 years to build up a sample of pregnant women.

Appropriate stratification is important in order to capture adequate diversity within the rural population. Dr. Bokemeier said that there are significant regional differences that need to be considered. Stratification on either race/ethnicity or region would suffice to ensure including distinct areas of persistent rural poverty such as the Ozarks and Appalachia. Stratification should be based on measures of exposures, not outcomes. Measures of rurality used in stratification should be fine-grained, like those developed by the U.S. Department of Agriculture.

Several participants discussed the possibility of oversampling rural populations. Oversampling increases sample size for oversampled groups, but reduces the relative representation of—and ability to answer questions about—other groups, raising questions of equity. If oversampling is used, Dr. Kalsbeek suggested that planners should carefully consider how to define “rural,” since various definitions of this concept exist. For example, rural has been defined at the county level or at finer levels of aggregation, such as the population density of block groups. Finer levels of aggregation in combination with disproportionate stratified sampling at those same levels leads to greater statistical and cost efficiency in the oversampling process.

Rural areas pose special challenges for the Study because of their population dispersion and lack of infrastructure. Mr. Quackenboss suggested that household sampling might not work well in rural settings, because of the distance between households. Dr. Bachrach replied that many ongoing studies that use household probability sampling are successfully conducted in rural areas. Others suggested that, rather than sending people to a central location for the Study to collect data, data collectors should be sent to the people in rural areas. It was pointed out that other agencies already visit households in rural areas, including the U.S. Department of Agriculture, which goes out to farms on a yearly basis. Rogelio Saenz, Ph.D., Texas A&M

University, agreed and said that relying on physicians or centers excludes people who do not have access to health care, including the very poor or immigrants. Patterns may be missed unless an effort is made to access hard-to-reach populations. Others also stressed the importance of including hard-to-reach populations such as migrant workers and noncitizens, but noted this would be challenging.

Dr. Bachrach asked how the Study could overcome barriers to obtaining advanced medical measures and tests in rural settings. Ann Bullock, M.D., Eastern Band of Cherokee Indians, suggested that physician's offices would be a good place to collect data because the staff already has excellent relations with their patients, which will help to increase retention. Using physician's offices allows data to be collected at the local level, and in order to accomplish this, doctors and patients can be given incentives. Data could be collected at the local level and then sent elsewhere for analysis. Dr. Bachrach asked if collection of placentas at local hospitals would be a problem and she was told that many hospitals sell placentas for a profit and might be reluctant to provide them to the Study without appropriate incentives.

Arthur M. Bennett, M.E.A., B.E.E., NICHD, NIH, DHHS, noted that without collecting information at medical centers, some data would be missed. For instance, data collectors cannot obtain a three-dimensional (3-D) ultrasound in rural areas. Dr. Bullock responded that instead of using 3-D, they could do two-dimensional ultrasound, allowing the Study to include a large high-risk rural population.

To address the challenges in rural areas, the Study will need to use creativity in building on the existing structures, such as the Critical Access Hospitals Program (a federal government program that supports small rural hospitals), community health services, rural utility services, nutrition education programs through the Cooperative Extension Service, churches, and other faith communities. Gladys H. Reynolds, Ph.D., CDC, DHHS, recommended hiring people who are known and trusted in the community to help with recruitment and retention.

Concluding Thoughts

The group was asked to share any concluding thoughts. Remarks included general comments about the Study:

- The Study has a huge potential to identify mediators between risks and outcomes that are not currently known and that cannot be obtained other than from a study of this type and magnitude.
- The Study provides an opportunity to examine the childhood roots of adult health (for example, obesity and diabetes in American Indians).
- Plan the Study to have broad objectives and build in flexibility to respond to new issues and questions that will arise over the next 20 years.

Participants also stressed the need for obtaining a diverse sample:

- Rural areas are diverse, so sampling design is very important.
- In designing the sample, distinguish rural from suburban areas and be sure to represent both adequately.

- The Study should ensure that a sufficient sample is obtained in different populations, for example, by race and ethnicity.
- In 20 years the racial mix will be different than it is today, and families that are currently in rural areas may no longer be in rural America in the future. This argues for oversampling racial and ethnic minorities in rural areas.
- Keep sampling and measurements planning separate and coordinate them later.

Others made suggestions and observations about measurements:

- If measures are selected that cannot be obtained in rural areas, then an opportunity to learn will be lost. It is necessary to balance getting the best biological measures with the newest technology against what is practical in rural areas.
- An effort to include multiple methods and measurements (for example, measurement of cultural and social environment) would be helpful.
- Measure the level of difficulty for obtaining services in rural areas ("opportunity structure").
- Consider the family's health as a unit, not just the child's health, in order to determine how family health may affect outcomes.
- It is important to look at risks to populations from common exposures (for example, family dysfunction, abuse, and neglect), not just rare exposures.
- Family interactions can be risk factors as well as protective factors for rural children.
- The manner in which questions are asked in rural areas will have to be carefully crafted in order for the answers to be comparable to those from other areas.

Other suggestions included:

- It would help to develop a white paper or literature review identifying key issues unique to rural areas.
- In order to make the results of the Study publicly available, many confidentiality issues need to be addressed.

Dr. Tickamyer and others ended the workshop by saying that this has been a stimulating, thoughtful discussion that showed the complexities of the task ahead. These are things that should be done and can be done. She thanked participants for giving rural children the attention that they need and deserve.

Participants

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Built Environment and Physical Activity in Children

Resubmitted June 23, 2004

I. Hypothesis

Increasingly the achievement of an active lifestyle in childhood is seen as one manifestation of positive health. Newly recognized biochemical pathways may explain the linkages between obesity and asthma as well as other immunologically or metabolically related health outcomes to an inactive life style in childhood. In adults the built environment is increasingly being recognized as a key determinant of physical activity in that stage of life. However, full understanding of how the various parameters of the built environment interact to affect physical activity has not been achieved. Far less is known about the relationship of the built environment and childhood physical activity as a child matures.

We hypothesize that various aspects of the built environment are related to the development of an active childhood and that the relative importance as well as even direction of the relationships may vary among children of varying demographic and age groups. Furthermore, we postulate that the built environment may also influence a child's diet and thus both directly and indirectly affect a child's probability of becoming obese.

Below are subhypotheses that identify specific aspects of the built environment that are high priority targets for assessment of their influence on childhood physical activity. For each subhypothesis, it is important to establish their relationship to childhood physical activity within the major demographic subpopulations as well as across children of various ages.

1. Time spent out-of-doors, overall physical activity levels, and likelihood of walking to school is likely to be higher for children who live in pedestrian-friendly environments. Such environments feature continuous wide sidewalks, low traffic volume/speed, safe crosswalks, access to public transit, attractive surroundings, convenient destinations, and a perceived low risk of crime.

2. Physical activity overall will be more prevalent among children who walk or bicycle to school; walking and bicycling to school will be more common among children who live close to school (i.e. <1 mile) and have walking and bicycling routes that are safe and well maintained. While varying by age, the amount of walking and bicycling for transportation will be higher for children living in neighborhoods that have a mix of desirable destinations, access to public transit, and high connectivity. Connectivity is the extent to which the sidewalks and trails in a neighborhood connect to each other and to desirable destinations such as schools, stores, other neighborhoods, parks, playgrounds, trails, etc. at convenient distances; typically streets with short block lengths connected in a grid pattern have higher connectivity than areas with cul-de-sacs and long block lengths.

3. The amount of walking for transportation will be higher for children living in neighborhoods that are perceived to have low rates of unintentional injury and of crimes against persons and property. (Perceived and actual safety data should be compared).

4. Physical activity overall will be more prevalent in children who walk and bicycle to destinations other than school, which is more common in children who live close to stores, parks, playgrounds, neighborhood friends, gyms, dance studios, YMCAs, and entertainment venues. After controlling for other factors, the level of total physical activity for children (and their parents) will be higher in localities that offer more acres of parkland and greenspace per capita if those places are maintained to be clean, safe, and attractive (no litter or graffiti, etc).

5. Children's level of physical activity in school will be higher if there are more square feet of athletic field and gymnasium space per student available for informal play and team sports and if the recreational areas are maintained to be clean, safe, and attractive.

6. Children's level of physical activity will be synergistically higher due to the combined effects of a pedestrian-friendly environment and a social environment that supports activity (e.g., parents who encourage and peers who participate in physical activity), than from either favorable environment alone.

The following 3 hypotheses are considered to be of lower priority than those above:

7. Consumption of food of low nutritional value (junk food) will be more frequent in children and adolescents who live and/or attend school near stores that sell such food, and in those who attend schools with vending machines that sell sodas and other junk food.

8. Consumption of fruits and vegetables will be more frequent in children and adolescents who live and/or attend school near stores that sell such food, and in those who attend schools with vending machines that sell fruits and vegetables.

9. Smoking cigarettes and consuming alcohol will be more frequent in adolescents (and their parents) who live and/or attend schools near stores that sell cigarettes and alcohol.

II. Workgroup(s) – Physical Exposures

III. Contact Person for Proposed Core Hypothesis\Question: Andrew Dannenberg, MD, MPH email: acd7@cdc.gov phone 770-488-7103

IV. Public Health Significance

Increasing levels of obesity in children and adolescents and the long term adverse health consequences of obesity and physical inactivity are well documented [Ogden 2002, DHHS 1996, National Task Force 2000]. The major contributors to obesity are inadequate physical activity, excessive caloric intake relative to physical activity, and genetic predisposition. The level of physical activity in children (and adults) is directly influenced by the design of the built environment, which includes community design, land use, and transportation systems [Handy 2002]. Physical activity decreases when children lack adequate opportunity to exercise during or after school and when they rely on private automobile transportation rather than walking, biking, or mass transit [Cummins 2001]. Increased access to and promotion of safe routes to

school leads to increased walking and biking by children [Staunton 2003]. Boys who walk to school have higher overall daily physical activity levels that those who are driven to school [Cooper 2003]. Children who participate in organized school sports are more likely to be physically active as adults [Kraut 2003].

CDC recommends providing physical and social environments that encourage and enable safe and enjoyable physical activity for children [CDC, 1997]. By examining child health and development in relation to the built environment, the National Children's Study will better document the importance of well designed communities to promote healthy child development.

V. Justification for a large, prospective, longitudinal study

The data to examine the hypotheses above can only be derived from a prospective cohort study such as being proposed for the NCS. Multiple reviews have called for confirmation of associations observed in cross-sectional studies through well-designed prospective studies that will in turn form the basis for intervention studies. The number of important subgroups and the presence of limited but extant evidence of differential effects of the built environment on health and physical activity call for a large prospective study so that all the suspected key variables can be simultaneously investigated and appropriate confounders be controlled for in the analysis.

Sample size issues:
To examine the relationship between the built environment (such as presence of sidewalks) and obesity/physical activity by gender, race-ethnicity, urban/rural, SES, and other factors, a large sample is required. Taking into account the desired level of stratification, if we want to detect a 5% difference in obesity, a cohort size of approximately 35,000 is needed. That sample size requires 20 annual measures of obesity in the children throughout the study. If the number of measures is reduced to 10, the required sample size increases to 40,000. Also, the sample size calculation does not account for attrition which would further increase the sample size required at the beginning

Assumptions:

Using the repeated measure formula by Leon (Sample-Size Requirements for Comparisons of Two Groups on Repeated Observations of Binary Outcome) the following assumptions were made:

Prevalence Obesity 15% Exposed Group (sidewalk present)
Prevalance Obesity 10% in Unexposed Group (sidewalk absent)
Alpha=0.05
Power=80%
Intraclass Correlation Coefficient=0.2
Two-tailed Test
Number of Repeated Measures=20
Difference between proportions 5%
Adjustment factor for multiple covariates: 1.1
Number of Cells(gender x urban/rural x SES x race ethnicity): 48

VI. Scientific Merit

Humpel et al. reviewed the literature surrounding the relationship of environmental factors and adults' participation in physical activity (Humpel et al., 2002). They observed that physical environment factors show consistent associations with physical activity behavior in these studies. They also noted the studies using composite measures of the physical environment (built environment is part) show weaker associations than those using more specific measures. Specifically, they found the following aspects of the neighborhood environment to be associated with physical activity in adults. These aspects included availability of and access to, cycleways, footpaths, health clubs, and swimming pools. They also noted that favorable aesthetics (e.g., indicating that a neighborhood is friendly or it is pleasant near the home) are associated positively with physical activity.

They specifically call for prospective studies of environmental factors as predictors of physical activity change. They noted only one such study. An accompanying editorial (Sallis et al., 2002) echoed Humpel et al.'s findings but noted that another literature in the transportation and urban planning areas has demonstrated that people walk and cycle more for transportation when they live in traditional communities where they can walk and cycle to shops than when they live in more modern auto-dependent communities. Handy et al. have summarized the urban planning literature linking the built environment and physical activity (Handy et al. 2002).

Sallis et al. summarized the literature on the correlates of children's physical activity in a comprehensive manner in 2000 (Sallis et al., 2000). They report that youth physical activity is a complex behavior determined by many factors. Nineteen categories of correlates were found to be related. One of which is the physical environment. However, the review showed that the influence of the built environment on children's physical activity was largely unexplored at that time. Overall, they call for prospective studies to confirm the associations they noted. About 75% of the extant literature was cross-sectional in nature. Cooper et al. in a very recent review state that there is mounting evidence that physical activity in childhood plays its most substantial role in diseases that have in common altered stress, inflammation, and leukocyte function such as asthma and arthritis (Cooper et al., 2004). They point out that the impact of physical activity on critical periods of development in children need not be limited to the walking child. They noted a number of studies that demonstrate that assisted exercise in preterm infants can increase body weight and improve bone strength.

VII. Feasibility - please address the following issues to the extent possible:

In addition to the measures directly relating to the built environment listed below, to address this hypothesis we are relying on the collection of data on obesity, physical activity, diet, and smoking that are described in the obesity hypothesis.

Proposed measures of built environment in priority order

1. GPS coordinates. This is the most important measure for the built environment. Measure coordinates on handheld GPS device of each child's house/apartment/living space. Results can be linked to existing and future databases containing geospatially coded data including locations of schools, parks, trails, transit stops, and stores and other measures such as crime, lead, air pollution, traffic volume, density of fast food restaurants, neighborhood connectivity, etc.

2. Distances to common destinations. Ask distance or walking time to school, parks, trails, stores, churches, nearest playmates. Ask distance to nearest store that sells junk food, that sells fruits and vegetables, and that sells cigarettes and alcohol. Validate some of these distances on a map using street addresses of friends, stores, and other destinations.

3. Ask how many children of similar age live on same block or in same neighborhood (need to define), and with how many of these children the study participant interacts.

4. Physical characteristics of neighborhood. For a subset of study participants, conduct an audit of the child's neighborhood: observe traffic volume and speed, street width, presence and quality of sidewalks, crosswalks, presence/absence of trails, parks, play areas, backyards, pools, gated community, types and density of houses, etc. Also observe quality of neighborhood parks and other recreational areas such as presence or absence of landscaping, trash, graffiti, broken windows, etc.

5. Measures at child's school of square feet of athletic field and gymnasium space per child, and types of play and sports equipment available (swings, basketball courts, ball fields, etc), for a subset of study participants.

6. Parental characteristics. Ask about parental attitude toward and participation in physical activity, amount of driving, time spent commuting, parental occupation and hours worked per week, smoking/drinking habits, gym use, number of cars and number of drivers in household, body mass index, socioeconomic measures, and reasons for moving if new home during study.

Ideally the following will be asked by other subcommittees and then can be used for analyses relevant to built environment:

7. Child's physical fitness/activity measures, such as a motion sensor (e.g. accelerometer) and an activity log.

8. Body mass index.

9. Child's 3 day diet history

10. Child's physical and mental health history including asthma, other respiratory illnesses, motor vehicle/pedestrian/bike-related injuries, disabilities, ADHD, school performance, etc.

Comment on overall study design
It will be very important to have clusters of children within a limited number of geographic areas to be able to collect enough neighborhood and community data to study the impact of the built environment on children's health. For example, if there are 1000 children being studied in each of several metropolitan areas, then substudies comparing children in each of those areas will be practical.

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I. Child Maltreatment Hypotheses (21 May 2004)

The child maltreatment hypotheses are designed to address two overarching aims: (1) to identify the predictors of childhood physical abuse (CPA) that occur to the child in the first three years of life and (2) to identify the consequences of childhood physical and sexual abuse (CSA).

Hypothesis 1: Marital and/or relationship violence during pregnancy or in the 1st year of the child's life will lead to increased incidence of CPA of the child by age 3.

Sub-hypothesis: Parent psychopathology [(depression, anxiety, and post-traumatic stress disorder (PTSD)] and neighborhood factors (high rates of crime, violence, joblessness, poverty, and high family mobility) will further increase the likelihood of CPA.

Hypothesis 2A: Chronic physical abuse will result in altered cortisol levels, increased likelihood of PTSD, Conduct Disorder (CD), and Oppositional Defiant Disorder (ODD), and impaired developmental functioning (including cognitive, social, and emotional development).

Sub-hypotheses:

- Chronic CPA will result in more severe outcomes (listed above) than single incidents of CPA.
- The relationship between CPA and it's adverse consequences are exacerbated by environmental (e.g., household lead and pesticides) and community (high rates of poverty, exposure/witnessing violence, unemployment, family mobility, and chld care burden) factors.
- Of those children who experience CPA, those with genetic vulnerabilities will develop CD or ODD.
- The quality and duration of intervention programs will decrease the likelihood of adverse outcomes for children who experience CPA.

Hypothesis 2B: Chronic sexual abuse will result in altered cortisol levels, increased likelihood of PTSD and impaired developmental functioning (including cognitive, social, and emotional development).

Sub-Hypotheses:

- Consequences of CSA will be modified by the developmental age of the child at the start of the abuse and the duration of the abuse.
- The relationship between CSA and its adverse consequences will be exacerbated by community factors including high rates of poverty, exposure/witnessing violence, and the child care burden in the home.
- The quality and duration of intervention programs will decrease the likelihood of adverse outcomes for victims of CSA.

II. Workgroup(s) - Injuries

III. Contact Person for Proposed Core Hypothesis/Question:

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IV. Public Health Significance

Approximately three children die each day from child maltreatment. Each year, over 800,000 children experience child maltreatment severe enough to be substantiated by child protective services (U.S. Department of Health and Human Services, Administration on Children, Youth, and Families, 2002).

Sequelae of child maltreatment include cognitive deficits, particularly in verbal abilities (Walsh, 1990), internalizing problems such as anxiety, depression, withdrawal, and posttraumatic stress disorder (e.g., Cerezo & Frias, 1994; Mannarino & Cohen, 1996; Widom, 1999), low self-esteem, social competency deficits, problems in interpersonal relationships (Bolger, Patterson, & Kupersmidt, 1998; Mannarino & Cohen, 1996), substance abuse (e.g., Kang, Magura, Laudet, & Whitney, 1999), and risk for suicide (Plunkett et al., 2001). Children who have been maltreated also appear to be at greater risk for revictimization (Roodman & Clum, 2001; Wekerle & Wolfe, 1998) or for perpetration of violence in later life (Hawkins et al., 1998; Maxfield & Widom, 1996).Long-term sequelae have linked child maltreatment to many of the leading causes of death in adults in the U.S. (Felitti et al., 1998).

Child maltreatment has been conservatively estimated to cost $24 billion annually in direct costs for health care services, child welfare, law enforcement, and the judicial system. When indirect costs associated with the long-term consequences of child maltreatment are included, such as special education and mental health services, lost productivity, and juvenile delinquency and adult criminality, the annual cost of child maltreatment has been estimated at $94 billion (Fromm, 2001).

The linkages between environmental factors, exposure to child maltreatment and other violence, and children's development are not yet clear. The NCS can improve our understanding of the relationships between different types of violence, the contributions of multiple environmental factors to the occurrence of violence, and children's developmental outcomes. With improved understanding of causal factors and mediators and moderators of these relationships, more effective prevention and intervention programs can be designed. For example, the comparative efficacy of some of the naturally occurring interventions may be suggested by their association with reduced child maltreatment or improved parenting environments, and this could have very important implications for public policy development.

V. Justification for a large, prospective, longitudinal study

The large sample of approximately 100,000 is necessary to determine predictors and consequences of child maltreatment. Official reports underestimate actual occurrences of maltreatment because only the most severe cases generally come to the attention of authorities. However, official reports suggest that the incidence of different types of child maltreatment vary widely. In 2001, 2.3 per 1000 children were substantiated victims of child physical abuse and 1.2 per 1,000 children were substantiated victims of sexual abuse (U.S. Department of Health and Human Services, Administration on Children, Youth and Families, 2003).

Within the NCS sample of 100,000 children, we conservatively estimate that between 3-4% of children (N = 300-400) may experience CPA or CSA (rates for neglect are higher). Power calculations underestimate actual power, because incidence rates are used. It is likely that more cases would be identified in a longitudinal study that involves direct assessment of child experiences resulting in greater power. However, existing data that suggest a large sample size is needed to adequately examine the predictors and consequences of these types of child maltreatment.

VI. Responses to ICC questions regarding the measurement of child maltreatment. How can the various aspects of child maltreatment be measured in the NCS and maintain subject participation, confidentiality, and the necessary protection of the child?

A. Confidentiality and Protection of Participants

In a large-scale, multi-dimensional, and prospective longitudinal study, such as the proposed National Children's Study (NCS), many possible situations may occur which would require both an ethical obligation to report to a medical or other authority and human subjects' issues regarding the protection of the individual and preservation of the confidentiality of the data. For example, during the course of a routine NCS medical exam, it is likely that children with active tuberculosis will be discovered. This disease requires reporting to public health authorities as well as to the child's primary care physician. How will issues of confidentiality and protection of the participant be balanced? The issues raised here transcend the child maltreatment hypotheses and need to be addressed by the larger NCS community. It is the understanding of the Injury Working Group that NCS has formed an Ethics Working Group to address these issues for the study as a whole (including the child maltreatment hypotheses).

Fortunately, other longitudinal studies (e.g., LONGSCAN – Longitudinal Studies of Child Abuse and Neglect) have worked through many of these same issues and have established procedures for consent, assent, and confidentiality techniques that can be adapted for the NCS. Thus, if, during the course of the NCS data collection efforts, there is evidence that child maltreatment is occurring or suspected to be occurring, procedures will be followed to deal responsibly and ethically with the situation.

In addition, the Journal of Interpersonal Violence dedicated a special issue (2000, vol. 15, no.7), edited by Dr. Desmond Runyan, to the ethical, legal, and methodological implications of asking children about abuse and neglect. Papers cover a range of important issues:

- discussions of the ethical issues in longitudinal child maltreatment research and balancing reporting of suspected maltreatment while maintaining confidentiality (J. K. Kotch);

- ethical principles guiding research on child and adolescent subjects regardless of the content area (N. M. P. King & L. R. Chruchill);

- solutions to methodological and ethical challenges associated with asking children for self-reported discipline and maltreatment experiences (E. D. Knight et al.);

- a review of survey measures used to ask children and adolescents about maltreatment (L. Amaya-Jackson et al.); and

- the use of computer administered interviews in interviews with children about maltreatment (M. M. Black & A. Ponirakis).

B Procedures to Protect the Child

We have reviewed several papers concerning the ethical, practical and legal issues on questioning parent and child respondents about abuse and neglect (Amaya-Jackson et al., 2000; Knight et al., 2000; Kotch, 2000; Runyan, 2000; Steinberg et al., 1999) and recognize the complexities and sensitive nature of such research. We have also corresponded with project study teams from the Great Smoky Mountain Study (GSMS: Costello et al., 1996), National Youth Victimization Prevention Survey (Finkelhor & Dziuba-Leatherman, 1994), and National Survey on Child and Adolescent Well-Being (NSCAW, personal communication with Kathryn Dowd, 2003) to discuss issues regarding consent and reporting procedures as well as consequences, if any, of reporting incidents or imminent harm towards self or others and suspected maltreatment.

Based on this reading and discussions, parent informants and official Child Protection Agency records should be used for information about physical and sexual abuse and neglect for children who are under the age of 10. Children ages 11 and older will be asked to self-report in response to questions regarding abuse and neglect. Both LONGSCAN and NSCAW developed techniques and procedures to determine whether there was sufficient evidence or justification to invoke mandatory reporting laws, including key questions to illicit necessary information and additional probes to further explore the details of the situation. Consent and assent forms will guarantee the adult and child participants confidentiality except under circumstances in which either the adult or child or the child is in danger.

In the event that the interviewer learns that the respondent, child, or someone else is in serious danger, the interviewer needs to notify his/her supervisor. If required by law, the case needs to be reported to the appropriate county or state agency. As reporting guidelines, requirements, and procedures vary by state, we will follow state-by-state guidelines (updated yearly by the National Clearing House on Child Abuse and Neglect). Precedent for this procedure was established in the context of the NSCAW (2002), a national longitudinal study of children in the welfare system, and has been successfully implemented.

In general, consent and assent forms need to inform parents and children that confidentiality will be broken should threat of imminent harm be disclosed. New incidents of maltreatment are reported to CPS, as necessary (Knight et al., 2000). Consent/assent forms also inform participants that participation is voluntary and participants may skip any question or stop the interview at any time for any reason.

Numerous specific procedures have been developed and used by existing longitudinal studies (e.g., LONGSCAN and the Great Smoky Mountain Study of Youth (Costello et al., 1996) to minimize or protect participants from possible risks:

1. Pilot and study data, while in active use, is kept in password protected computer files or locked file cabinets.

2. All child maltreatment data is stripped of all identifiers at the data collection site and electronic data is encrypted prior to being sent anywhere.

3. Pilot data related to child maltreatment is destroyed after review by project staff who are blind to the identity of the respondent.

4. Computer administered interviews and audio-assisted computer administered interviews (A-CASI) have been found to be an extremely useful tool for collecting data which could be embarrassing or distressing to the participant. LONGSCAN has successfully used A-CASI methods to collect self-report of maltreatment from children and adolescents. The A-CASI interview process is entirely private and may thus minimize any embarrassment associated with the interview questions. It also increases the likelihood that participants will candidly acknowledge behavior that they may deem unacceptable. Finally, this technique minimizes the likelihood of interviewer effect on a respondent's answers. (See Black & Ponirakis, 2000 for details on computer administered interviews with children.)

5. The ordering of items on questionnaires is manipulated in order to increase the likelihood that a sense of safety is established. This is done by beginning with less sensitive questions, then moving gradually into the more sensitive, then moving back into less sensitive and more positive questions toward the end of the interview. This approach allows children/participants to have a chance to rebound from any

embarrassment or distress occasioned by the research questions.

6. Interviewers are carefully trained to detect signs of distress or upset during the interview. In the experience of the LONGSCAN project and pilot work it has been found that even when asking for extensive self-report of trauma and maltreatment very few children became upset, needed to terminate the interview, or required significant debriefing following the interview.

7. Sites have clinical back-up available as necessary to handle incidents on a case-specific basis.

8. Project staff, interviewers, and clinical and data management staff are trained in the importance of confidentiality and general research procedures to assure confidentiality.

9. Any data that is sent to a central data archive is stripped of potentially identifying information and study investigators work directly with data archive staff to develop 'user agreements' that demand agreement to protect the identity of participants and prohibit reconstructing participant identity through efforts to combine variables such as family structure, age, gender, race, and socio-economic information.

C. Subject Recruitment

Longitudinal studies have successfully asked caregivers and children about maltreatment without resulting in a substantial loss of participants. Only one LONGSCAN site (Seattle) informed parents upon their entry into the study that they would be asked about maltreatment. Unfortunately, there is no systematic evidence that the recruitment process suffered. Pilot studies should be conducted to determine whether different strategies would facilitate participation of parents.

All participants in LONGSCAN, however, were informed in the initial and all subsequent consent processes (as per local IRB requirement) that if they disclosed information indicating they had harmed their child the interviewer would be required to report this information to the appropriate authority. This did not impair recruitment efforts.

D. Subject Retention

Analyses of LONGSCAN data from pre-Age 12 (i.e., pre- child self-report) interview points demonstrate that caregivers/families who were reported to CPS by LONGSCAN as a result of information that came out during an interview were no more likely to drop out/withdraw from the study than those caregivers/families who did not disclose information that required mandatory reporting (L. Knight, personal communication, Oct. 20, 2002).

With respect to child self-report of maltreatment, anecdotal evidence from the North Carolina site (statistical analyses pending) indicate that there was no significant drop out post-self report at the Age 12 interview. Preliminary analyses are underway.

Similar experiences have been reported by the Principal Investigators of at least two other major longitudinal studies (i.e., Costello of the GSMS and Rolf Loeber of the Pittsburgh Youth Study). For most of the cases identified or suspected, children and families were already known to CPS.

An important factor in the retention rate post-child LONGSCAN self-report is the use of the computer assisted interview protocol (A-CASI). A pilot study by Knight and Everson (personal

communication, Oct. 20, 2002) found that children reported they were more comfortable disclosing sensitive information in the context of a structured computer assisted interview than in a face-to-face interview. In addition, children reported maltreatment incidents above and beyond those known to authorities in the computer assisted interview.

VII. Conclusion

Although child maltreatment has been the focus of recent research in the context of a few small scale prospective longitudinal studies, the NCS is particularly well suited to address key questions and policy issues related to child abuse and neglect with the scientific rigor only available in a large-scale prospective longitudinal research. The collective experiences of the various existing longitudinal studies of child maltreatment suggest that interviews related to experiences of abuse and neglect are feasible and confer only minimal risk upon participants and their families. Overall, the clear benefits of research on child maltreatment and the knowledge gained from this research far outweigh the possible social, legal, ethical, and psychological risks posed by study participation.

I. Unintentional Injury Hypothesis (25 May 2004)

While data regarding the extent and type of injuries sustained by children is collected through hospital reports in the U.S., what has been neglected has been the circumstances and context of injuries as well as biological reactivity of individuals.

Hypothesis 1: The relationship between risk taking behaviors of children and parental supervision of children is meditated by environmental (e.g., household hazards) and community (e.g., hazards, park access) factors.

1A: Children living in households with fewer hazards and high levels of parental supervision will experience less severe injuries, regardless of risk behaviors.

1B: Children who attend schools that provide safety education will experience less severe injuries, regardless of risk behaviors and context.

Hypothesis 2: Frequency and severity of injuries sustained early in childhood can be used to predict subsequent injuries.

1A: Children who experience frequent minor injuries are more likely to experience severe, disabling injuries prior to adulthood.

Hypothesis 3: Risk taking behavior in children and adolescents is related to the biological reactivity of the individual in infancy.

3A: This reactivity is modified during development by parent rearing styles and the physical context in which the child is raised.

Hypothesis 4: Individuals with increased risk of injury are also at increased risk of other high-risk behaviors such as substance abuse, early initiation of sexual activity, and delinquency.

II. Workgroup(s) – Injuries

III. Contact Person for Proposed Core Hypothesis\Question

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IV. Public Health Significance

Injuries are the most common cause of death for children and adolescents beyond the first six months of life, the most common cause of serious acquired disability, one of the most common reasons for acute medical care. In the year 2000, 17370 children and adolescents under the age of 20 died from injuries, for a rate of 21.54 fatalities per 100,000 population. Of these 12, 172 were unintentional injuries. Injuries cause 45% of the deaths among 1- to 4-yr-old children and three times more deaths than the next leading cause, congenital anomalies. For the rest of childhood and adolescence up to the age of 19 yr, nearly 70% of deaths are due to injuries, more than all other causes combined. Injuries result in more years of potential life lost than any other cause.

Mortality statistics reflect only a small part of the effects of childhood injuries. Approximately 15-20% of children and adolescents receive medical care for an injury each year in hospital emergency departments, and at least an equal number are treated in physician offices. Of these, 2.5% require inpatient care and 55% have at least short-term temporary disability from their injuries. The overall rate of injury hospitalization is 374 per 100,000 per year. The most common injuries resulting in hospitalizations are fractures followed by traumatic brain injury.

The injury attributable medical expenditures alone for children and adolescents were $10.5 billion in the US in 2000, and account for 14% of all medical costs for children and adolescence.

As many as one-third of injury fatalities in this age group could be prevented through the full implementation of available prevention strategies: motor vehicle occupant protection, traffic calming to prevent pedestrian injuries, use of bicycle helmets, safe storage of guns, adequate pool fencing and use of personal flotation devices, use of smoke detectors, and adoption of self-extinguishing cigarettes. Some of these intervention strategies require behavior change on the part of the individual, while others require behavior change at the level of communities and legislatures. In injuries, as in many other parts of medicine, a critical need is for the fruits of the last few decades of research to be translated into actual improved health of the population. Other nations have much more fully implemented these strategies throughout their society.

Nevertheless, two-thirds of the injuries are not "preventable" with the current information we have. This is an enormous cost to our society and the families of these children.

V. Justification for a large, prospective, longitudinal study

The data to examine the hypotheses above can only be derived from a prospective cohort study such as being proposed for the NCS. Retrospective studies will simply not have the information needed. We will need to collect information on children *as they age.* Measures of infant reactivity to stress, on parenting styles and styles of child rearing in child care centers, on other aspects of the environmental context of the infant and child, and on the circumstances and context of minor and severe injuries are critically important for developing prevention strategies. These must be collected in the context of the developing child, and their physical and social environment to determine their impact of the child's behavior. This type of data is not currently available in the context of large scale longitudinal studies.

<u>Sample size issues</u>: While injuries are very common events, they are a heterogeneous group. The sample will need to be stratified by gender, injury type, and other factors, which will affect power and require a large sample. For example, if we stratify by gender and by type of injury, and want to study a mechanism of injury that accounts for 10% of all medically treated injuries, we would need a cohort of 93,000 individuals to detect a relative risk of injury = 1.3 due to a risk factor present in 10% of the group.

Further information on sample size is included in our February 2001 report.

VI. Scientific Merit

It is clear from the last three decades of research that injuries are not randomly distributed in the population, and that the presence or absence of risk in the immediate environment is not enough to explain the occurrence of injury. As a result, many injuries cannot be prevented through simple environmental or product changes. In addition, children and adolescents who are injured are also more likely to engage in other high-risk behaviors that have a major impact on the prevalence of adult disease. To understand the underlying causes of injuries, and to develop more effective interventions, at a minimum, we need to understand: (1) the parenting practices to which these children are exposed and study how these affect risk taking behavior and exposure to risky environments, (2) the nature of the physical environment at home and in the community and understand why some children exposed to risks are injured while most are not, and (3) the bio/psycho/social environment of the child and examine how the norms to which children and families are exposed modify risk taking or risk adverse actions. *None of these types of interactions has ever been examined on a large scale in a representative sample of children and families because the data to do such analyses have not been available.*

In addition, over the last few decades, there has been work on infants' biologically based reactivity, and its interaction with context and development. This has great promise for better understanding why some individuals have high-risk behavior, and others do not. It has important implications for determining points for intervention. It also may have important implications for understanding the reaction to injury as well, i.e. who will develop symptoms of PTSD and who won't. There are relevant non-human primate data. For example, Suomi has shown that about 15% to 20% of rhesus monkeys, whether reared in the wild or in captivity, seem "excessively fearful." Any sort of challenging situations elicit a pronounced physiological arousal. While these monkeys can be identified in early infancy, the manifestations of this reactivity are contextually related: in familiar settings, they are not distinguishable from other monkeys (ref). In contrast, another 5% to 10% of monkeys appear be more aggressive than the norm. They are more impulsive and aggressive in their interactions with peers, and more risk taking (ref). Impulsive juvenile males are more likely to make dangerous leaps, and be injured. In addition, these two types of monkeys have different levels of 5-HIAA in the CSF, and these differences appear early in life (ref).

There are a number of enticing human analogs of some of these primate findings. The work of Thomas and Chess (ref), Strelau (ref), Fox (ref) and others indicate that individuals differ in the arousal levels of their nervous systems. Infants with a high threshold for sensory arousal (i.e. those with low resting heart rates and low reactivity) would be risk-takers in order to raise their arousal level to the threshold needed for positive affect (Fox). In contrast, recent studies suggest that individuals who have more tachycardia after a traumatic incident are at higher risk of developing later PTSD symptoms than those who do not exhibit this autonomic reactivity (ref). In sum, other than cross-sectional studies, little solid prospective evidence exists for the role of biological reactivity and risk-taking behavior leading to injuries.

January 25, 2004

I. New Unintentional Injury Hypothesis

It is known that risk of injury during childhood and adolescence is associated with risk-taking behavior. We hypothesize that risk taking behavior in children and adolescents is related to the biological reactivity of the individual in infancy, and that this reactivity is modified during development by parent rearing styles and the physical context in which the child is raised. Moreover, we postulate that the biological reactivity related to risk taking is affected by polymorphisms in genes controlling serotonin metabolism.

II. Workgroup(s) – Injuries

III. Contact Person for Proposed Core Hypothesis\Question

Contact Person for Proposed Core Hypothesis\Question: Frederick P. Rivara, MD, MPH email: fpr@u.washington.edu; phone 206 521 1530

IV. Public Health Significance

Injuries are the most common cause of death for children and adolescents beyond the first six months of life, the most common cause of serious acquired disability, one of the most common reasons for acute medical care. In the year 2000, 17370 children and adolescents under the age of 20 died from injuries, for a rate of 21.54 fatalities per 100,000 population. Of these 12, 172 were unintentional injuries. Injuries cause 45% of the deaths among 1- to 4-yr-old children and three times more deaths than the next leading cause, congenital anomalies. For the rest of childhood and adolescence up to the age of 19 yr, nearly 70% of deaths are due to injuries, more than all other causes combined. Injuries result in more years of potential life lost than any other cause. Mortality statistics reflect only a small part of the effects of childhood injuries. Approximately 15-20% of children and adolescents receive medical care for an injury each year in hospital emergency departments, and at least an equal number are treated in physician offices. Of these, 2.5% require inpatient care and 55% have at least short-term temporary disability from their injuries. The overall rate of injury hospitalization is 374 per 100,000 per year. The most common injuries resulting in hospitalizations are fractures followed by TBI.

The injury attributable medical expenditures alone for children and adolescents were $10.5 billion in the US in 2000, and account for 14% of all medical costs for children and adolescence.

As many as one-third of injury fatalities in this age group could be prevented through the full implementation of available prevention strategies: motor vehicle occupant protection, traffic calming to prevent pedestrian injuries, use of bicycle helmets, safe storage of guns, adequate pool fencing and use of personal flotation devices, use of smoke detectors, and adoption of self-extinguishing cigarettes. Some of these intervention strategies require behavior change on the part of the individual, while others require behavior change at the level of communities and legislatures. In injuries, as in many other parts of medicine, a critical need is for the fruits of the last few decades of

research to be translated into actual improved health of the population. Other nations have much more fully implemented these strategies throughout their society.

Nevertheless, two-thirds of the injuries are not "preventable" with the current information we have. This is an enormous cost to our society and the families of these children.

V. Justification for a large, prospective, longitudinal study

The data to examine the hypotheses above can only be derived from a prospective cohort study such as being proposed for the NCS. Retrospective studies will simply not have the information needed. We will need to collect information on infant reactivity to stress, on parenting styles and styles of child rearing in child care centers, and on other aspects of the environmental context of the infant and child. These must be collected in the context of the developing child, to determine their impact of the child's behavior. In addition, the data will be most useful if it can be examined in conjunction with search for specific gene polymorphisms such as those related to serotonin metabolism and monoamine oxidase activity.

Sample size issues: While injuries are very common events, they are a heterogeneous group. The sample will need to be stratified by gender, injury type, and other factors, affecting power and thus requiring a large sample. For example, if we stratify by gender and by type of injury, and want to study a mechanism of injury that accounts for 10% of all medically treated injuries, we would need a cohort of 93,000 individuals to detect a relative risk of injury = 1.3 due to a risk factor present in 10% of the group.

Further information on sample size is included in our February 2001 report, included as an appendix.

VI. Scientific Merit

It is clear from the last 3 decades of research that injuries are not randomly distributed in the population, and that the presence or absence of risk in the immediate environment is not enough to explain the occurrence of injury. As a result, many injuries cannot be prevented through simple environmental or product changes. In addition, children and adolescents who are injured are also more likely to engage in other high-risk behaviors that have a major impact on the prevalence of adult disease.

Over the last few decades, there has been work on infants' biologically based reactivity, and its interaction with context and development. This has great promise for better understanding why some individuals have high-risk behavior, and others don't. It has important implications for determining points for intervention. It also may have important implications for understanding the reaction to injury as well, i.e. who will develop symptoms of PTSD and who won't.

There are non-human primate data on the interaction of genes and environment to shape the emotional regulation of the individual. For example, Suomi has shown that about 15% to 20% of rhesus monkeys, whether reared in the wild or in captivity, seem "excessively fearful." Any sort of challenging situations elicit a pronounced physiological arousal. While these monkeys can be identified in early infancy, the manifestations of this reactivity are contextually related: in familiar settings, they are not distinguishable from other monkeys (ref).

In contrast, another 5% to 10% of monkeys appear be more aggressive than the norm. They are more impulsive and aggressive in their interactions with peers, and more risk taking (ref). Impulsive juvenile males are more likely to make dangerous leaps, and be injured. These two types of monkeys have different levels of 5-HIAA in the CSF, and these differences appear early in life (ref).

There are a number of enticing human analogs of some of these primate findings. For example, it has long been known that adult criminals have lower resting heart rates than non-adult criminals, and that this is true in childhood as well (ref). These may be the opposite of the fearful monkeys who have higher resting heart rates. The work of Thomas and Chess (ref), Strelau (ref), Fox (ref) and others indicate that individuals differ in the arousal levels of their nervous systems. Infants with a high threshold for sensory arousal (i.e. those with low resting heart rates and low reactivity) would be risk-takers in order to raise their arousal level to the threshold needed for positive affect (Fox).

In contrast, recent studies suggest that individuals who have more tachycardia after a traumatic incident are at higher risk of developing later PTSD symptoms than those who do not exhibit this autonomic reactivity (ref).

Tremblay and colleagues in Montreal have shown that aggression is the norm in infancy, and that babies learn to control their aggressive behavior as they develop. This learning is contextually based, in interactions with peers and by parenting. However, about 5% of infants do not learn to control their aggression, and they continue to have developmental trajectories exhibiting aggressive, externalizing behavior (ref). These infants may be biologically the same as the 5% of the primates described above who are impulsive and aggressive. The origins of this behavior are likely to lie in the interaction of gene polymorphisms and the parenting and peer environment.

Caspi describes three different kinds of interactions with the environment that affect how this innate reactivity is manifested at later ages. These include different reactions among individuals in the same environment (reactive transactions), the effects of the individual on the response of the environment (evocative transactions), and selection of environments by the individual (proactive transactions). These kind of interactions can only be determined through longitudinal studies.

VII. Feasibility - please address the following issues to the extent possible:

- Critical period for exposure and outcomes
- Sampling needs: targeted groups or settings, special strategies, sample size (provide power calculations if possible), special subgroups of interest, etc
- Contact – if more than one contact is needed, frequency and timing of the recontact
- Measurement tools for assessing exposures or outcomes: questionnaires, educational or psychological testing, medical diagnosis or clinical assessments, biological specimens, interviews.
- For each measurement tool:
- Have the measurement tools been demonstrated to be valid and reliable in the population in which NCS will use them?
- Is specialized expertise and equipment needed?
- Is there sufficient capacity to measure these factors on a large scale?
- What are the estimated costs of the measurements?
- What are the risks associated with these measurements?
- Are there other ethical considerations associated with these measurements, e.g. reporting issues, etc.?
- What are the burden to the participant and family associated with these measurements?
- Community Involvement
- Other burden to the participant and family associated with this hypothesis not covered in the measurement tool section.

APPENDIX 1

Report

Longitudinal Studies of Injuries on Children

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February 9, 2001

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Charge from Peter Scheidt, MD:

- Identify existing longitudinal cohort studies (LCS) which have examined risk factors for injuries in children and adolescents.
- Identify existing LCS which have examined outcomes of injuries in children and adolescents
- Summarize data on the incidence of injuries in children and adolescents resulting in death, hospitalization, or emergency department visits.
- Suggest possible hypotheses related to injury research for a potential new large LCS

A. Identify existing longitudinal cohort studies (LCS) which have examined risk factors for injuries in children and adolescents.

We conducted a search of Medline and Embase, checked reference lists in articles, searched the HIPRC procite database, and used the Lewin group report to identify LCS related to etiologic risk factors for injury. We did not include other LCS studies which have been done but do not include injury data. Nor did we include studies in which the primary outcomes were delinquency or criminal activity.

We identified 40 articles which report on LCS involving injury (Table 1). Nine of thee studies provided data on intentional injuries, 13 provided data on unintentional injuries and 18 provided data on both (Table 3).

Of these studies, 17 provided data on all types of injuries, 7 only on MV injuries, 1 was limited to pedestrian injuries, 8 provided information on risk factors for interpersonal violence, one provided data on risk factors for suicide, and a number provided data on specific types of unintentional injuries (Table 4).

The sample size of these studies were highly variable. Some population based studies (eg. Scholer 1997) provided data on 1.5 million infants. The Dunedin Multidisciplinary Child Development Study analyzed extensively by Langley had approximately 1000 subjects. The British Birth Cohort Study had approximately 20,000 subjects.

There were a wide variety of risk factors examined and those which were shown to be significantly associated with injury are shown in Table 5. None collected data on genotype, and only limited data were collected on the environment. None collected complete hierarchical environmental data (e.g. family, neighborhood, community).

Twenty-five studies were conducted in the US and 15 abroad (Table 6). The duration of follow-up also varied widely. Nineteen studies had only 1-3 years of longitudinal follow-up (Table 7) 15 studies had follow-up as long as 10 years, and 6 studies –all done abroad—had follow-up for more than 10 years. The longest has been the Dunedin cohort, in which the subjects are now in their mid-twenties.

Table 1. List of Cohort Studies Examining Etiologic Risk factors for Injury

Study Name or Authors	Year	Country	Study Population	Sample Size	Follow-up Period	Types of Injuries	Types of Risk Factors Found
Powell, JW[1]	2000	U.S.A.	High school players	39,032 player seasons	2 years	Sport injuries	Female gender
Woodward, LJ[2]	2000	New Zealand	Selected birth cohort	1,265 children	8 years	MV injury	Adolescent attentional difficulties (A.D.D.)
Loeber, R[3]	1999	U.S.A.	Inner-city boys	506 participants	5 years	Gun injuries	Previous delinquency, gang fights, selling drugs, gun carrying, poor academic performance, poor parental supervision, poor parental communication, behavior problems
Kozik, CA[4]	1999	Thailand	Rural schoolchildren	40,119 children	2 years	MV injuries, drowning, animal bites, penetrating injuries, burns, falls, near drowning	Male gender
Sege, Rx[5]	1999	U.S.A.	Adolescents seen at the east Boston Health Center	438 subjects	Median 5 years	Violence-related injuries	Male gender, cigarette smoking, alcohol & drug use, poor relationships with parents, no school, failing school, history of fighting
Scholer, SJ[6]	1999	U.S.A.	US infants born from 1985 to 1991	18.6 million infant years	1 year	Overall injuries	Birth to mothers younger than 20 years, < than high school, > than 2 children

Begg, DJ[7]	1999	New Zealand	Young people born in Dunedin b/w 4/1/72 and 3/31/73	1,037 people	Birth to 21 years	Crashes, injury crash, non-injury crashes, serious non-MV injury	Lifestyle factors, low involvement with family, prior crash, high ADD scores, conduct disorder
Martin, J[8]	1998	New Zealand	Males and females from the Dunedin cohort	944 subjects	Birth to 21 years	Assault injuries	Gender, Perpetrator characteristics
Kennedy, CM[9]	1998	U.S.A.	Pre-school age children	230 children	Birth to 54 months	Overall injuries	Risk-taking behaviors
Scholer, SJ[10]	1998	U.S.A	Children <5 y/o in TN b/w 1980 and 1995	1,428,694 children	Birth to 5 years	Fatal fire injuries	Mothers high school education, mother with more than 2 other children, children of mothers < 20 y/o, male gender, unmarried mothers, delayed prenatal care
Rasanen, P[11]	1998	Finland	North Finnish birth cohort	12,058 children	Birth to 27 years	Suicides, Injuries	Schizophrenia, other psychoses, personality disorders, criminality
Russell, KM[12]	1998	U.S.A.	National probability sample of African-American and White mothers	4,287 mothers	6 years	Repeat injuries in the home	Poor maternal health status, unmarried mother, male child, difficulty managing child, maternal depression
Murray, A[13]	1998	Sweden	Swedish young drivers born in 1972	4,034 subjects	16-22 years	Traffic injuries	School marks and educational achievement and attainment
Scholer, SJ[14]	1997	U.S.A.	Tennessee children 0 to 4 y/o	1.5 million children	Birth to 4 years	Overall injuries	Maternal education, age, parity

Scholer, SJ[15]	1997	U.S.A.	Tennessee children 0 to 4 y/o	1.5 million children	Birth to 4 years	Overall injuries	Young children, maternal education, age, parity
Dufort, VM[16]	1997	New Zealand	Dunedin cohort subjects who visited hospital ER	1,361 subjects	4 years	Injuries to upper extremities, eyes, And lower extremities, Lacerations, sprain/strain, foreign body, struck by or against an object	Construction risks, transportation, manufacturing (including meat and fish processing), business and repairs services
Kotch, JB[17]	1997	U.S.A.	Children receiving care in out-of-home settings in Piedmont region of NC	656 families	1 year	Minor and severe injuries	Center based care highest risk, home care, out-of-home care
Nada-Raja, S[18]	1997	New Zealand	Birth cohort of New Zealand adolescents	916 adolescents	Birth to 15 years	Traffic crashes/offenses	History of ADHD and conduct disorder predominantly in females
Begg, DJ[19]	1996	New Zealand	Birth cohort of New Zealand adolescents	916 adolescents	Birth to 15 years	Participation in delinquency and aggressive behavior	High sporting activity was associated with increased delinquency but not team sports
Cummings, P[20]	1996	U.S.A.	Children in a sample of licensed day care facilities	255 day care centers (2,738,279 hrs of day care attendance)	1 year	Medically attended injuries	Physical hazards at day care locations
Dowd, MD[21]	1996	U.S.A.	New Zealand hospitalized for injuries	16,892 children and adolescents	1 year	Assault injuries	Prior injury, prior assault
Stuart, MJ[22]	1995	U.S.A.	Ice-Hockey players	120 subjects	3 years	Strains, lacerations,	Playing Hockey Practice

			17-20 years			contusions, sprains	vs. game, time of game
Phillips, K[23]	1995	U.S.A.	Infant and toddler twins	100 subjects	Birth to 36 months	Overall injuries	Activity and impulsivity
Skuse, DH[24]	1995	U.K.	Whole pop birth cohort, 1986 inner city London	2,609 births	4 years	Child abuse or neglect	Early postnatal non-organic failure to thrive, poor parenting, neglect
Kogan MD[25]	1995	U.S.A.	**Children followed by the National Maternal and Infant Health Survey in the U.S.A.**	8,145 children	Birth to 3 years	Medically attended non-fatal injuries, falls, burns, striking or cutting injuries, poisonings	Male gender and upper SES
Maio, RF[26]	1994	U.S.A.	Adolescents 13-18 years Admitted to hospital ER	176 Injured adolescents	5 years	Overall injuries	Prior injury or psychiatric history
Harris, MJ[27]	1994	U.S.A.	Newborn infants	367 mothers of infants	1 year	Unintentional injuries in the home, burns, poisonings, falls, airway problems	Family conflict, <2 siblings, maternal unemployment. Social support reduced stress
Anderson, R[28]	1994	U.S.A.	Adolescents 12-16 years School District Allegheny Co.	1,245 students	2 years	Overall injuries	SES
McMahon, KA[29]	1993	Australia	Children & adolescents football players	1,253 players	1 year	Sprains, hematomas, lower limb injuries	Field size, decreased contact player numbers, age, game rule modifications
Stier, DM[30]	1993	U.S.A.	Consecutive index children born to inner-city women	219 children of <18 y/o mothers & 219 children of >19	5 years	Maltreatment (abuse, neglect or sexual abuse)	Maternal age

				y/o mothers			
Kowal-Vern, A[31]	1992	U.S.A.	Urban children under 3 y/o admitted for fractures	124 urban children	Birth to age 3	Fractures due to MVA, pedestrian, other, or child abuse	Caretaker ignorance, carelessness
Alexander, CS[32]	1992	U.S.A.	Rural Maryland 12-14 y/o students	758 students	3 years	Overall injuries	Behavioral risk factors; previous injuries, risk-taking behaviors, delinquency, alcohol/ drug use, exercise, parental supervision, work experience
Bijur, PE[33]	1991	U.S.A.	British adolescents born one week in 1958	8,231 adolescents	15-17 years	Overall injuries	Prevalent stressors in adolescence, conflict b/w parents and adolescents (frequency of arguments)
Pless, IB[34]	1989	Canada	1958 British cohort of children	>16,000 children	<18 years	Traffic injuries	Age, gender, “fidgeting”, abnormal behavior, family crowding, family problems, removal from family
Bijur, PE[35]	1988	U.S.A.	1970 British birth cohort	10,394 children	Birth to 5 years and 5 to 10 years	Overall injuries	Previous injuries, male sex, aggressive child behavior, young maternal age, many older siblings, few younger siblings
Larson, CP[36]	1988	Canada	Children of a selected cohort	918 children	Birth to 3 years	Overall injuries	Single, unemployed smoking mothers, absence of younger siblings

Davidson, LL[37]	1988	U.S.A.	Selected cohort of children	951 children	3 years after 5th b/day	Overall injuries	Male gender, discipline problems, maternal characteristics, behavior problems, encopresis and marked fears
Garrard, J[38]	1988	U.S.A.	Children of a day-care center	224 children	1 year	Human bites	Male gender, toddlers, number of days of enrollment
Beautrais, AL[39]	1982	New Zealand	Selected birth cohort	1,082	3 years	Injuries, burns, scalds, poisonings	Number of Family life events
Langley, J[40]	1980	New Zealand	New Zealand Birth cohort	991	Birth to 5 years	Overall injuries	Developmental, behavioral and medical factors

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Table 3. Cohort Studies of Risks of Injury on Children by Intent

Author	Intentional	Unintentional	Both
Loeber, R[3]	X		
Sege, Rx[5]	X		
Martin, J[8]	X		
Rasanen, P[11]	X		
Begg, DJ[19]	X		
Dowd, MD[21]	X		
Skuse, DH[24]	X		
Stier, DM[30]	X		
Garrard, J[38]	X		
Powell, JW[1]		X	
Woodward, LJ[2]		X	
Kozik, CA[4]		X	
Begg, DJ[7]		X	
Scholer, SJ[10]		X	
Russell, KM[12]		X	
Murray, A[13]		X	
Nada-Raja, S[18]		X	
Stuart, MJ[22]		X	
Harris, MJ[27]		X	
McMahon, KA[29]		X	
Pless, IB[34]		X	
Beautrais, AL[39]		X	
Scholer, SJ[6]			X
Kennedy, CM[9]			X
Scholer, SJ[14]			X
Scholer, SJ[15]			X
Dufort, VM[16]			X
Kotch, JB[17]			X
Cummings, P[20]			X
Phillips, K[23]			X
Kogan MD[25]			X
Maio, RF[26]			X
Anderson, R[28]			X
Kowal-Vern, A[31]			X
Alexander, CS[32]			X
Bijur, PE[33]			X
Bijur, PE[35]			X
Larson, CP[36]			X
Davidson, LL[37]			X
Langley, J[40]			X
Total Number	9	13	18

Table 4. Cohort Studies of Risks of Injury on Children by Type of Injury

Author	Type of Injury
	Overall Injuries
Scholer, SJ[6]	X
Kennedy, CM[9]	X
Russell, KM[12]	X
Scholer, SJ[14]	X
Scholer, SJ[15]	X
Dufort, VM[16]	X
Kotch, JB[17]	X
Cummings, P[20]	X
Phillips, K[23]	X
Maio, RF[26]	X
Anderson, R[28]	X
Alexander, CS[32]	X
Bijur, PE[33]	X
Bijur, PE[35]	X
Larson, CP[36]	X
Davidson, LL[37]	X
Langley, J[40]	X
Total	**17**
	Motor Vehicle Injuries
Woodward, LJ[2]	X
Kozik, CA[4]	X
Begg, DJ[7]	X
Murray, A[13]	X
Nada-Raja, S[18]	X
Kowal-Vern, A[31]	X
Pless, IB[34]	X
Total	**7**
V. Pedestrian injuries	
Kowal-Vern, A[31]	X
Total	**1**
	Violence-related injuries, guns, child abuse
Loeber, R[3]	X
Sege, Rx[5]	X
Martin, J[8]	X
Begg, DJ[19]	X
Dowd, MD[21]	X
Skuse, DH[24]	X
Stier, DM[30]	X
Kowal-Vern, A[31]	X

Total			**8**
			Suicides
Rasanen, P[11]			X
Total			**1**
			Cutting/piercing injuries
Dufort, VM[16]			X
Stuart, MJ[22]			X
Kogan MD[25]			X
Total			**3**
			Sport injuries
Powell, JW[1]			X
Stuart, MJ[22]			X
McMahon, KA[29]			X
Total			**3**
			Falls
Kozik, CA[4]			X
Kogan MD[25]			X
Harris, MJ[27]			X
Total			**3**
			Burns
Kozik, CA[4]			X
Scholer, SJ[10]			X
Kogan MD[25]	**VI.**	**X**	
Harris, MJ[27]			X
Beautrais, AL[39]			X
Total			**5**
			Drownings
Kozik, CA[4]			X
Total			**1**
			Bites (human and animal)
Kozik, CA[4]			X
Garrard, J[38]	**VII.**	**X**	
Total			**2**
			Poisonings
Kogan MD[25]			X
Harris, MJ[27]			X
Beautrais, AL[39]			X
Total			**3**

Table 5. Cohort Studies of Risks of Injury on Children by Type of Risk Factors Found to be Significant

Author	Significant Risk factors
	Female gender
Powell, JW[1]	X
Total	**1**
	Socio-economic Strata (SES)
Kogan MD[25]	X
Anderson, R[28]	X
Total	1
	Male gender
Kozik, CA[4]	X
Sege, Rx[5]	X
Martin, J[8]	X
Scholer, SJ[10]	X
Russell, KM[12]	X
Kogan MD[25]	X
Pless, IB[34]	X
Bijur, PE[35]	X
Davidson, LL[37]	X
Garrard, J[38]	X
Total	10
	Physical (environmental) or occupational hazards
Dufort, VM[16]	X
Kotch, JB[17]	X
Cummings, P[20]	X
Total	3
	Sports activities
Begg, DJ[19]	X
Stuart, MJ[22]	X
McMahon, KA[29]	X
Total	3
	Stress, behavioral factors
Loeber, R[3]	X
Begg, DJ[7]	X
Phillips, K[23]	X
Skuse, DH[24]	X
Harris, MJ[27]	X
Kowal-Vern, A[31]	X
Alexander, CS[32]	X
Bijur, PE[33]	X
Pless, IB[34]	X
Bijur, PE[35]	X
Davidson, LL[37]	X

Beautrais, AL[39]	X
Langley, J[40]	X
Total	13
	Unemployment
Harris, MJ[27]	X
Larson, CP[36]	X
Total	
	A.D.D.
Woodward, LJ[2]	X
Nada-Raja, S[18]	X
Total	
	Age
Scholer, SJ[14]	X
Scholer, SJ[15]	X
Pless, IB[34]	X
Bijur, PE[35]	X
Total	4
	Young mother
Scholer, SJ[6]	X
Scholer, SJ[10]	X
Stier, DM[30]	X
Bijur, PE[35]	X
Total	4
	Mental disorders
Rasanen, P[11]	X
Russell, KM[12]	X
Nada-Raja, S[18]	X
Maio, RF[26]	X
Total	4
	Mother < high school
Scholer, SJ[6]	X
Scholer, SJ[10]	X
Scholer, SJ[14]	X
Scholer, SJ[15]	X
Total	4
	Academic performance
Loeber, R[3]	X
Sege, Rx[5]	X
Murray, A[13]	X
Langley, J[40]	X
Total	4
	Number of children
Scholer, SJ[6]	X
Scholer, SJ[10]	X
Scholer, SJ[14]	X

Scholer, SJ[15]	X
Harris, MJ[27]	X
Pless, IB[34]	X
Bijur, PE[35]	X
Larson, CP[36]	X
Total	8
	Risk-taking behaviors
Loeber, R[3]	X
Kennedy, CM[9]	X
Phillips, K[23]	X
Alexander, CS[32]	X
Bijur, PE[35]	X
Total	5
	Previous injuries/delinquency
Loeber, R[3]	X
Dowd, MD[21]	X
Maio, RF[26]	X
Alexander, CS[32]	X
Total	4
	Poor family relationships
Loeber, R[3]	X
Sege, Rx[5]	X
Russell, KM[12]	X
Kowal-Vern, A[31]	X
Alexander, CS[32]	X
Bijur, PE[33]	X
Davidson, LL[37]	X
Total	7
	Substance abuse
Sege, Rx[5]	X
Alexander, CS[32]	X
Total	2

Table 6. Cohort Studies of Risks of Injury on Children by Country of Origin (U.S. versus Non-U.S.)

Author	U.S.A. Study	Non-U.S.A. Study
Powell, JW[1]	X	
Loeber, R[3]	X	
Sege, Rx[5]	X	
Scholer, SJ[6]	X	
Kennedy, CM[9]	X	
Scholer, SJ[10]	X	
Russell, KM[12]	X	
Scholer, SJ[14]	X	
Scholer, SJ[15]	X	
Kotch, JB[17]	X	
Cummings, P[20]	X	
Dowd, MD[21]	X	
Stuart, MJ[22]	X	
Phillips, K[23]	X	
Kogan MD[25]	X	
Maio, RF[26]	X	
Harris, MJ[27]	X	
Anderson, R[28]	X	
Stier, DM[30]	X	
Kowal-Vern, A[31]	X	
Alexander, CS[32]	X	
Bijur, PE[33]	X	
Bijur, PE[35]	X	
Davidson, LL[37]	X	
Garrard, J[38]	X	
Total	**25**	
Woodward, LJ[2]		X
Kozik, CA[4]		X
Begg, DJ[7]		X
Martin, J[8]		X
Rasanen, P[11]		X
Murray, A[13]		X
Dufort, VM[16]		X
Nada-Raja, S[18]		X
Begg, DJ[19]		X
Skuse, DH[24]		X
McMahon, KA[29]		X
Pless, IB[34]	**VIII. X**	
Larson, CP[36]		X
Beautrais, AL[39]		X
Langley, J[40]		X
Total Number		**15**

Table 7. Cohort Studies of Risks of Injury on Children by Duration of Follow-up

Author	Duration of Follow-up
	1 to 3 years
Powell, JW[1]	X
Kozik, CA[4]	X
Kennedy, CM[9]	X
Kotch, JB[17]	X
Cummings, P[20]	X
Dowd, MD[21]	X
Stuart, MJ[22]	X
Phillips, K[23]	X
Kogan MD[25]	X
Harris, MJ[27]	X
Anderson, R[28]	X
McMahon, KA[29]	X
Kowal-Vern, A[31]	X
Alexander, CS[32]	X
Bijur, PE[33]	X
Larson, CP[36]	X
Davidson, LL[37]	X
Garrard, J[38]	X
Beautrais, AL[39]	X
Total	**19**
	4 to 10 years
Woodward, LJ[2]	X
Loeber, R[3]	X
Sege, Rx[5]	X
Scholer, SJ[6]	X
Scholer, SJ[10]	X
Russell, KM[12]	X
Murray, A[13]	X
Scholer, SJ[14]	X
Scholer, SJ[15]	X
Dufort, VM[16]	X
Skuse, DH[24]	X
Maio, RF[26]	X
Stier, DM[30]	X
Bijur, PE[35]	X
Langley, J[40]	X
Total	**15**
	> 10 years
Begg, DJ[7]	X
Martin, J[8]	X
Rasanen, P[11]	X
Nada-Raja, S[18]	X

Begg, DJ[19]	X
Pless, IB[34]	X
Total	**6**

B. Identify existing LCS which have examined outcomes of injuries in children and adolescents

We identified 32 reports of studies which have examined injury outcomes (Table 2). The sample size in nearly all of these was very small, with the exception of the Aitken paper which reports on data from the National Pediatric Trauma Registry. However, this study reports only on status of children at the time of discharge from the hospital.

Of these studies, most (26) report on the outcome only of traumatic brain injury (TBI) (Table 8). Twenty-four of the studies were done in the US and 8 abroad (Table 9). A variety of outcomes were reported (Table 10), including functional disability (n=15), developmental or neurobehavioral disability (n=13), physical or neurological disability (n=10). Only 2 reported on quality of life, 1 on family functioning, 3 on PTSD and 1 on return to work or school.

The duration of follow-up was very varied, ranging form just assessment at hospital discharge to follow-up 23 years post-injury. However, the majority followed patients for 3 years or less.

Table 2. List of Cohort Studies Examining Consequences of Injuries in Children

Primary author	Year	Country	Sample size	Age at Injury	Injury Type(s)	Follow-up Duration	Outcome(s)
Thornhill, S[1]	2000	Scotland	549	14 years or more	Head injury	1 year	Disability
Brookshire, BL[2]	2000	U.S.A.	91	6-10 years	Severe and mild head injury	3 years	Cognitive abilities, discourse production and groups' performance on measures of language, executive function, memory, and processing speed.
Aitken, ME[3]	1999	U.S.A.	13,649	7-18 years	Trauma without significant head injury	Hospital discharge	Functional Independence Measure (FIM)
Prassad, MR[4]	1999	U.S.A.	8	13-32 months	Crush head injury	1 year	IQ, motor functioning (motor scores, cognitive scores)
De Vries, AP[5]	1999	Netherlan ds	102	3-18 years	Traffic crash injuries	7-12 months	Post-traumatic stress disorder
Taylor, HG[6]	1999	U.S.A.	94	6-12 years	Traumatic brain injury	1 year	Cognitive, achievement, and behavioral sequelae
Carrillo, EH[7]	1998	U.S.A.	19	Adolescents	Spinal cord injury after gunshot wounds	1 year	Medical care related to the injury, work and

							scholastic status, satisfaction with rehabilitation
Ewing-Cobbs, L[8]	1998	U.S.A.	61	children	Traumatic brain injury	2 years	Computational arithmetic and reading comprehension sub-tests
Colantonio, A[9]	1998	Canada	62	15-19 years	Head injuries	5 years	Quality of life, impairment, disability, and handicap
Levi, L[10]	1998	Israel	Cohort 1: 117; Cohort 2: 152	0-14 years	Severe head injury	1 year	Mortality and neurological status
Max, JE[11]	1998	U.S.A.	50	6-14 years	Traumatic brain injury	2 years	Post-traumatic stress symptomatology
Stallard, P[12]	1998	U.K.	119	5-18 years	Traffic crash injuries	12 months	Post-traumatic stress disorder
Anderson, VA[13]	1997	Australia	73	5-10 years	Severe and mild head injuries	12 months	Poorer intellectual, language and memory abilities worst with severe injuries
Ewing-Cobbs, L[14]	1997	U.S.A.	79	4 months to 7 years	Traumatic brain injury	2 years	Deficits and lack of catch-up over time of (1) Composite IQ and motor, (2) Receptive and expressive

							language, and (3) Verbal and Perceptual-Performance IQ scores
Max, JE [15]	1997	U.S.A.	50	5-10 years	Traumatic brain injury	3 years	Psychiatric disorders
Thakker, JC[16]	1997	U.S.A.	105	1 month-14 years	Traumatic brain injury requiring endotracheal intubation	8-70 months	Functional outcome
Barker, M[17]	1996	England, Scotland, Wales	12,537	16 years	Unintential injuries requiring hospitalization	7 years	Permanent disability
Massagli, TL[18]	1996	U.S.A.	30	6-15 years	Severe traumatic brain injury	1 year	Neurobehavioral deficits
Rivara, JM[19]	1996	U.S.A.	81 families	6-15 years	Closed head injury	3 years	Family functioning
Levin, HS[20]	1996	U.S.A.	181	5-16 years	Closed head injury	12 months	Semantic and episodic memory
Graf, WD[21]	1995	U.S.A.	194	5 months-18 years	Submersion	Hospital discharge	Vegetative state or death
Jaffe, KM[22]	1995	U.S.A.	72	6-15 years	Mild, moderate, and severe traumatic brain injury (TBI)	3 years	Neurobehavioral, academic, and “real world” deficits
Fay, GC[23]	1994	U.S.A.	72	Children 6 to 15 years	Mild, moderate, and severe traumatic brain injury	3 years	Neurobehavioral, academic and “real world” consequences of

							injury
Polissar, NL[24]	1994	U.S.A.	53	Children 6 to 15 years	Mild traumatic brain injury	3 years	Neurobehavioral skills affected
Greenspan, AI[25]	1994	U.S.A.	95	Children 5 to 15 years	Head injury	1 year	Functional limitations
Norholt, SE[26]	1993	U.S.A.	55	Children 5 to 20 years	Pediatric condylar fractures	Mean 10.1 years	Radiologic abnormalities, >age associated to more functional limitations
Ruff, RM[27]	1993	U.S.A.	242	12-65 years	Severe head trauma	1 year	Return to school or work after coma. (Age, length of coma, speed for both attending and motor movements, spatial integration, and intact vocabulary were analyzed). Most important factors: Intactness of the patient's verbal intellectual power, speed of information processing and age.
Fay, GC[28]	1993	U.S.A.	53	Children 6 to 15 years	Mild traumatic brain injuries	3 years	Shows no clinically significant neuropsychological, academic or “real world functioning deficits

Jaffe, KM[29]	1993	U.S.A.	94	Children 6 to 15 years	Traumatic brain injury	1 year	Neurobehavioral functioning (intelligence, adaptive problem solving, memory, academic performance, motor performance, psychomotor problem solving)
Klonoff, H[30]	1993	Canada	159	Childhood through age 30	Mild head injury	23 years	Severity of injury associated to subjective sequelae (physical, intellectual and emotional), IQ, educational lag, unemployment, psychologic/psychiatric problems, relationship with family members
Levin, HS[31]	1992	U.S.A.	82	Children 0-15 years	Severe head injury	1 year	Glasgow Outcome Scale (GOS) assessment
Klonoff, H[32]	1977	U.S.A.	231	Children	Head injuries	5 years	Neuropsychological function, neurological status, EEG status, and school progress

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Table 8. Cohort Studies of Consequences of Injuries on Children by Type of Injury

Author	Type of Injury
	Head/Brain injury
Thornhill, S[1]	X
Brookshire, BL[2]	X
Aitken, ME[3]	X
Prassad, MR[4]	X
Taylor, HG[6]	X
Ewing-Cobbs, L[8]	X
Colantonio, A[9]	X
Levi, L[10]	X
Max, JE[11]	X
Anderson, VA[13]	X
Ewing-Cobbs, L[14]	X
Max, JE [15]	X
Thakker, JC[16]	X
Massagli, TL[18]	X
Rivara, JM[19]	X
Levin, HS[20]	X
Jaffe, KM[22]	X
Fay, GC[23]	X
Polissar, NL[24]	X
Greenspan, AI[25]	X
Ruff, RM[27]	X
Fay, GC[28]	X
Jaffe, KM[29]	X
Klonoff, H[30]	X
Levin, HS[31]	X
Klonoff, H[32]	X
Total	26
	Spinal cord injury
Carrillo, EH[7]	X
Total	1
	Traffic injury
De Vries, AP[5]	X
Stallard, P[12]	X
Total	2
	Submersion
Graf, WD[21]	X
Total	1
	Fractures
Norholt, SE[26]	X
Total	1
	Unintentional injuries
Barker, M[17]	X
Total	

Table 9. Cohort Studies of Consequences of Injuries on Children by Country of Origin (U.S. versus Non-U.S.)

Author	U.S.A. Study	Non-U.S.A. Study
Brookshire, BL[2]	X	
Aitken, ME[3]	X	
Prassad, MR[4]	X	
Taylor, HG[6]	X	
Carrillo, EH[7]	X	
Ewing-Cobbs, L[8]	X	
Max, JE[11]	X	
Ewing-Cobbs, L[14]	X	
Max, JE [15]	X	
Thakker, JC[16]	X	
Massagli, TL[18]	X	
Rivara, JM[19]	X	
Levin, HS[20]	X	
Graf, WD[21]	X	
Jaffe, KM[22]	X	
Fay, GC[23]	X	
Polissar, NL[24]	X	
Greenspan, AI[25]	X	
Norholt, SE[26]	X	
Ruff, RM[27]	X	
Fay, GC[28]	X	
Jaffe, KM[29]	X	
Levin, HS[31]	X	
Klonoff, H[32]	X	
Total	24	
Thornhill, S[1]		X
De Vries, AP[5]		X
Colantonio, A[9]		X
Levi, L[10]		X
Stallard, P[12]		X
Anderson, VA[13]		X
Barker, M[17]		X
Klonoff, H[30]		X
Total		8

Table 10. Cohort Studies of Consequences of Injuries on Children by Type of Outcomes Studied

Author	Type of Outcome Studied
	Functional disability
Thornhill, S[1]	X
Brookshire, BL[2]	X
Aitken, ME[3]	X
Prassad, MR[4]	X
Colantonio, A[9]	X
Levi, L[10]	X
Ewing-Cobbs, L[14]	X
Thakker, JC[16]	X
Barker, M[17]	X
Graf, WD[21]	X
Greenspan, AI[25]	X
Norholt, SE[26]	X
Ruff, RM[27]	X
Fay, GC[28]	X
Levin, HS[31]	X
Total	15
	Developmental/neurobehavioral disability
Brookshire, BL[2]	X
Taylor, HG[6]	X
Ewing-Cobbs, L[8]	X
Ewing-Cobbs, L[14]	X
Massagli, TL[18]	X
Jaffe, KM[22]	X
Fay, GC[23]	X
Polissar, NL[24]	X
Ruff, RM[27]	X
Fay, GC[28]	X
Jaffe, KM[29]	X
Klonoff, H[30]	X
Klonoff, H[32]	X
Total	13
	Physical/neurological disability
Brookshire, BL[2]	X
Prassad, MR[4]	X
Colantonio, A[9]	X
Levi, L[10]	X
Anderson, VA[13]	X
Ewing-Cobbs, L[14]	X
Levin, HS[20]	X
Graf, WD[21]	X
Ruff, RM[27]	X

Klonoff, H[30]	X
Total	10
	Quality of life
Carrillo, EH[7]	X
Colantonio, A[9]	X
Total	2
	Family functioning
Rivara, JM[19]	X
Total	1
	PTSD
De Vries, AP[5]	X
Max, JE[11]	X
Stallard, P[12]	X
Total	3
	Psychiatric disorders
Max, JE [15]	X
Klonoff, H[30]	X
Total	2
	Return to school/work
Ruff, RM[27]	X
Total	1

C. Incidence data

C.1. Hospitalization:

The annual rates of hospitalization for an injury are shown in Table 11. The overall rate is 374 per 100,000 per year. The most common injuries resulting in hospitalizations are fractures followed by TBI.

Because not all states surveyed in the HCUP data set have E-codes, these data could not be used to generate rates of injury by mechanism. Therefore, we instead used data form the state of California, which has approximately 10 million individuals under the age of 21 in the state. California has mandatory E coding of injury discharges.

The rates of hospitalization for injury in California are virtually identical to that for the US as a whole as shown in Table 12: 370 vs 374 per 100,000 annually. The highest hospitalization rate is in the 16-20 year age group and the lowest in the 5-12 year olds. Overall, unintentional injuries account for approximately three-fourths of the hospitalizations, although the proportion is lowest in the oldest age group. Falls were the single most common reason for hospitalization overall, as well in all age groups except the oldest in which MV injuries and assaults were more common.

AIS data were not available to categorize the severity of these injuries. However, injuries resulting in hospitalization appeared to be mostly moderate in severity with a median length of stay of 2 days (Table 13). However, there was clearly a skewed distribution with a much longer mean LOS. The overall case-fatality rate was 2.0% (Table 14).

Table 15 displays the number of injury hospitalizations each year as well as the cumulative number of injury hospitalizations in the cohort. This assumes 1997 rates apply throughout. By age 5 there would be over 2000 injury hospitalizations in the cohort, by age 10 there would be 3100 and by age 21 there would be over 8000.

Table 16 displays the number of MV related injury hospitalizations expected, based on 1997 rates. There would be 232 by age 5, 462 by age 10, and 1721 by age 21. Similar data are shown in Table 17 for Suicide attempts and Table 18 for assaults.

Table 11. HCUPnet data: Nationwide inpatient sample

Hospital discharge rates per 100,000 persons 0-17 years for injuries and poisoning
United States, 1997. Principal Diagnosis

Diagnosis	Number of injuries	Rate
All	260 359	374
Dislocations and joint trauma	6 030	8.7
Fractures	76 957	110.59
Spinal cord injury	1 248	1.79
All Intracranial injury (incl. Concussion)	32 087	46.11
Concussion	7 047	10.13
Crush or internal injury	13 951	20.05
Open wounds	17 791	25.57
Sprains and strains	3 927	5.64
Superficial injury	5 166	7.42
Burns	10 197	14.65

Table 12. California, 1997, annual rates of hospitalization for injuries per 100,000

Cause	**Total**	**<1**	**1-4**	**5-12**	**13-15**	**16-20**
B. All injuries	370.08	322.31	343.0	235.85	421.46	622.1
C. Unintentional	288.86	267.90	330.0	223.76	290.05	372.95
Cutting	10.7	1.83	9.27	8.62	11.34	17.43
Drowning	4.72	8.80	14.25	2.0	2.0	1.3
Fall	85.69	90.80	107.49	87.12	81.41	63.55
Fire and burn	10.49	26.03	26.25	4.93	3.13	6.46
Firearms	2.45	0	1	1.0	4..40	6.91
Motor vehicle	71.5	13.89	43.14	46.12	67.01	161.30
Occupant	42.67	12.52	19.00	17.39	35.37	123.13
Pedestrian	17.28	1.17	22.86	19.14	15.6	13.37
Bicycle	13.27	0	4.75	18.50	22.68	9.25
Other Transport	8.18	1	2.54	5.94	16.42	14.50
Environment	10.82	13.11	17.35	11.0	5.90	6.70
Overexertion	5.56	1	1.60	2.61	10.82	12.64
Poisoning	20.1	32.28	45.68	5.44	16.49	21.86
Struck by object	19.23	10.	13.0	15.47	31.94	26.56
Suffocation	3.0	18.40	7.48	1.0	<1	<1
Other unintent.	19.57	50.50	31.38	12.34	14.62	17.34
Intentional –self inflicted	31.34	0	0	2.64	76.41	83.86
Cutting	4.05	0	0	<1	9.50	12.70
Guns	0.3	0	0	<1	<1	1.26
Poisoning	25.76	0	0	2.17	64.25	76.29
Intentional-assault	37.89	45.40	7.24	3.79	40.30	126.65
Guns	14.8	1.17	1.0	1.0	16.20	56.05

Table 13. HCUPnet Query - Nationwide Inpatient Sample, US 1997

Outcomes by Patient and Hospital Characteristics for Expanded CCS Diagnosis Category 16 Injury and poisoning

		Total Number of Discharges	LOS, days (mean)	LOS, days (median)
Total Number of Discharges		2,684,017 (100.0%)	5.4	3.0
Age Group	<1	18,012 (0.7%)	5.7	2.0
	1-17	242,347 (9.0%)	3.8	2.0
	18-44	766,362 (28.6%)	4.4	2.0
	45-64	542,751 (20.2%)	5.4	3.0
	65-84	836,150 (31.2%)	6.3	4.0
	85+	277,708 (10.3%)	6.6	5.0
	Missing	687 (0.0%)	6.8	4.0

Table 14. HCUPnet Query - Nationwide Inpatient Sample, US 1997 Principal Diagnoses - Fatality rates, Individuals 0-17 years

Outcomes for 16 Injury and poisoning

	16 Injury and poisoning
Total Number of Discharges	2,684,017
In-hospital Deaths	52,851 (2.0%)

Weighted national estimates from HCUP Nationwide Inpatient Sample (NIS), 1997, Agency for Healthcare Research and Quality (AHRQ), based on data collected by individual states and provided to AHRQ by the states. Total number of weighted discharges in the U.S. based on HCUP NIS = 35,406,187. Note that no significance testing for differences is provided. Values based on 70 or fewer unweighted cases are not reliable and have been suppressed (designated with an asterisk*).

Table 15. Number and cumulative number of hospitalizations for injuries in the cohort of 100,000

Age	Number of injury hospitalizations	Cumulative number
<1	**322**	**322**
1	**343**	**665**
2	**343**	**1008**
3	**343**	**1351**
4	**343**	**1694**
5	**235**	**1929**
6	**235**	**2164**
7	**235**	**2399**
8	**235**	**2634**
9	**235**	**2869**
10	**235**	**3104**
11	**235**	**3339**
12	**235**	**3574**
13	**421**	**3995**
14	**421**	**4416**
15	**421**	**4837**
16	**622**	**5459**
17	**622**	**6081**
18	**622**	**6703**
19	**622**	**7325**
20	**622**	**7947**
21	**622**	**8569**

Table 16. Number and cumulative number of hospitalizations for motor vehicle injuries in the cohort of 100,000

Age	Number of injury hospitalizations	Cumulative number
<1	**14**	**14**
1	**43**	**57**
2	**43**	**100**
3	**43**	**143**
4	**43**	**186**
5	**46**	**232**
6	**46**	**278**
7	**46**	**324**
8	**46**	**370**
9	**46**	**416**
10	**46**	**462**
11	**46**	**508**
12	**46**	**554**
13	**67**	**621**
14	**67**	**688**
15	**67**	**755**
16	**161**	**916**
17	**161**	**1077**
18	**161**	**1238**
19	**161**	**1399**
20	**161**	**1560**
21	**161**	**1721**

Table 17. Number and cumulative number of hospitalizations for self inflicted injuries in the cohort of 100,000

Age	Number of injury hospitalizations	Cumulative number
<1	**0**	**0**
1	**0**	**0**
2	**0**	**0**
3	**0**	**0**
4	**0**	**0**
5	**3**	**3**
6	**3**	**6**
7	**3**	**9**
8	**3**	**12**
9	**3**	**15**
10	**3**	**18**
11	**3**	**21**
12	**3**	**24**
13	**76**	**100**
14	**76**	**176**
15	**76**	**252**
16	**84**	**336**
17	**84**	**420**
18	**84**	**504**
19	**84**	**588**
20	**84**	**672**
21	**84**	**756**

Table 18. Number and cumulative number of hospitalizations for assault related injuries in the cohort of 100,000

Age	Number of injury hospitalizations	Cumulative number
<1	**45**	**45**
1	**7**	**52**
2	**7**	**59**
3	**7**	**66**
4	**7**	**73**
5	**4**	**77**
6	**4**	**781**
7	**4**	**85**
8	**4**	**89**
9	**4**	**93**
10	**4**	**97**
11	**4**	**101**
12	**4**	**105**
13	**40**	**145**
14	**40**	**185**
15	**40**	**225**
16	**127**	**352**
17	**127**	**479**
18	**127**	**606**
19	**127**	**733**
20	**127**	**860**
21	**127**	**987**
	127	**1114**

IX. C.2. Emergency Department Visits

There are approximately 15-21 emergency department visits for injury annually per 100 children, adolescents and young adults (Table 19). Most commonly these are due to falls or being struck (Table 20). ED visits for MV crashes are much less common. Lacerations and superficial injuries predominant in the younger age groups, well sprains are more common in the older individuals (Table 21). Firearm injuries are as common in the 5-14 year age group as in the 15-24 year olds (Table 22).

Table 19. Emergency department visit rates for injury per 100 persons

by age and sex: United States, 1993-1994

Age	Male	Female	Both
<5 years	**19.6**	**16.5**	**18.1**
5-14 years	**17.8**	**12.4**	**15.2**
15-24 years	**24.7**	**17.4**	**21.1**

Source: Health United States 1996-1997 and Injury Chartbook, U.S. Dept of Health and Human Services

Table 20. Emergency department visit rates for leading first-listed causes of injury per 100,000 persons by sex and age: United states, 1993-1994

Males				
Age	Fall	Struck	Motor vehicle	Cut or Pierce
< 5 years	**6482**	**2398**	**864**	**819**
5-14	**4376**	**3243**	**115**	**1571**
15-24	**2971**	**3769**	**243**	**2985**
Females				
Age	Fall	Struck	Motor vehicle	Cut or Pierce
< 5 years	**5146**	**1545**	**128**	**440**
5-14	**3350**	**1646**	**120**	**966**
15-24	**2443**	**1789**	**249**	**968**
Both				
Age	Fall	Struck	Motor vehicle	Cut or Pierce
< 5 years	**5830**	**1982**	**103**	**634**
5-14	**3875**	**2464**	**86**	**1276**
15-24	**2710**	**2788**	**183**	**1986**

Source: Health United States 1996-1997 and Injury Chartbook, U.S. Dept of Health and Human Services

Table 21. Emergency department visit rates for leading first-listed injury diagnoses per 100,000 persons by age and sex: United States, 1993-1994

Males				
Age	Open wounds	Superficial	Sprains & Strains	Fractures
< 5 years	**6593**	**2729**	**317**	**1119**
5-14	**5378**	**3586**	**1853**	**2747**
15-24	**6537**	**4414**	**4774**	**1929**
Females				
Age	Open wounds	Superficial	Sprains & Strains	Fractures
< 5 years	**3876**	**2907**	**306**	**921**
5-14	**2870**	**2748**	**1802**	**1750**
15-24	**2131**	**4038**	**3926**	**888**
Both				
Age	Open wounds	Superficial	Sprains & Strains	Fractures
< 5 years	**5266**	**2816**	**312**	**1022**
5-14	**4154**	**3177**	**1828**	**2260**
15-24	**4356**	**4228**	**4354**	**1414**

Source: Health United States 1996-1997 and Injury Chartbook, U.S. Dept of Health and Human Services

Table 22. Nonfatal firearm emergency department-treated injury rates per 100,000 population and firearm death rates per 100,000 population by age:

United States, 1992-1994

Age	Fatal	Non-fatal
< 5 years	**1.6**	**6.2**
5-14 years	**27.0**	**122.6**
15-24 years	**32.9**	**127.9**

Source: Health United States 1996-1997 and Injury Chartbook, U.S. Dept of Health and Human Services

C.3 Office visits

The number of office visits for injuries is very similar to the number of ED visits (Table 23) with one in 5 children under 15 having office care each year and 1 in 4 young adults 15-24 receiving care for an injury.

Table 23. Number and annual rate of injury related physician office visits, United States, 1998 National Health Interview Survey

Age	Number	Rate per 100 persons per year
< 15 years	11 672 000	19.5
15-24 years	9 418 000	25.2

C.4 Mortality

The fatality rates for injuries based on 1997 data are shown in Table 24. In any one year, the number of deaths will range from 9 to 74 depending on the age of the cohort. The number of deaths form MV crashes will range from 4 to 29, the number of deaths from homicide will range from 1 to 20 and the number of deaths from suicide will range form 0 to 14, again depending on the age of the cohort.

Data on cumulative number of deaths from injuries which would be expected based on 1997 national rates are shown in Table 25. By age 5 there would be 104 deaths from injuries, by age 10 there would be 153 deaths, by age 15 there would be 264 deaths, and by age 21 there would be 648 injury deaths in the cohort. By this age there would be an expected 1649 deaths in the cohort of 100,000 live births, of which 39% would be from injuries.

Table 24. 1997 US Injury Death Rates per 100,000

Cause	0-4	5-9	10-14	15-19	20-24
All injury	**19**	**9**	**13**	**59**	**74**
Unintentional injury	**15**	**8**	**10**	**35**	**39**
MV	**4.9**	**4.3**	**5.9**	**27.4**	**28.6**
Fall	**.3**	**.1**	**.1**	**.5**	**.9**
Suffocation	**3**	**.4**	**1.4**	**3.1**	**3.9**
Drowning	**2.7**	**1.2**	**1.1**	**1.8**	**1.8**
Poisoning	**.2**	**.1**	**.1**	**1.3**	**2.8**
Fire/flame	**2.1**	**.9**	**.5**	**.4**	**.6**
Homicide	**3.6**	**0.9**	**1.5**	**13.6**	**20**
Firearm homicide	**.3**	**.4**	**1.1**	**11.7**	**16.8**
Suicide	**0**	**0**	**1.6**	**9.5**	**13.6**
Firearm suicide	**0**	**0**	**.7**	**6**	**8.3**

Source: WISQARS.

Table 25. Number of deaths from all causes, number of deaths from injury, and cumulative number of deaths in the cohort of 100,000 live births based on 1997 mortality rates.

Age	Deaths all causes	Cumulative deaths all	Injury deaths	Cumulative injury deaths
<1	**722**	**722**	**19**	**19**
1	**36**	**758**	**19**	**38**
2	**36**	**794**	**19**	**57**
3	**36**	**830**	**19**	**76**
4	**36**	**866**	**19**	**95**
5	**19**	**885**	**9**	**104**
6	**19**	**904**	**9**	**113**
7	**19**	**923**	**9**	**122**
8	**19**	**942**	**9**	**131**
9	**19**	**961**	**9**	**140**
10	**23**	**984**	**13**	**153**
11	**23**	**1007**	**13**	**166**
12	**23**	**1030**	**13**	**179**
13	**23**	**1053**	**13**	**192**
14	**23**	**1076**	**13**	**205**
15	**75**	**1151**	**59**	**264**
16	**75**	**1226**	**59**	**323**
17	**75**	**1301**	**59**	**382**
18	**75**	**1376**	**59**	**441**
19	**75**	**1451**	**59**	**500**
20	**99**	**1550**	**74**	**574**
21	**99**	**1649**	**74**	**648**

Initial Proposal for Core Hypothesis\Question
Gene-Environment Interactions

I. Proposed Core Hypothesis\Question:

Exposure to psychosocial stressors during vulnerable periods of pregnancy and early childhood can interact with genotype to permanently alter gene expression related to neurobehavioral outcomes.

- Children with one or two copies of the short allele of the 5-HTT promoter polymorphism will exhibit depressive symptoms when exposed to stressful life events, while those with the same genotypes but without serious negative life events, will not.

- Children homozygous for the long variation in the 5-HTTLPR Serotonin Transporter gene will be at greater risk for developing alcoholism in adolescence if they are also exposed to early life stress, than those who have this same allelic variant coupled with low stress and /or high nurturance.

- Children with the l/s form of the 5-HTT gene will exhibit abnormal impulsivity and aggression when their early rearing environment is stressful compared with children who have the same genotype but are reared in a nurturing environment.

- Maltreated children with low MAOA activity will be more likely to exhibit antisocial behavior than children with low MAOA who are not maltreated or maltreated children with high MAOA activity.

II. Workgroup(s):

Project Office

III. Contact Person for Proposed Core Hypothesis\Question:

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IV. Public Health Significance:

According to the Global Burden of Disease Study, depression is ranked as the fourth most important cause of death and disability (1-2). Not only is it a major cause of suicide and lost productivity, it is also associated with a worse prognosis for coronary heart disease patients, and predicts mortality in previously healthy individuals (3-11). Major depressive disorder affects up to 2.5% of children and 8.3% of adolescents, an age group where the female-to-male ratio of depression is 2:1 (12). The worst outcome of depression is suicide, which accounts for 6.8% of all deaths in 10-14 year olds and 11.9% of deaths in 15-19 year olds (13). However, depression is also significantly associated

with cigarette smoking (14-16) and drug abuse (1-19) in adolescents and has been associated with later obesity in girls (20). Despite its obvious public health significance, efforts to find a cure for depression have been confounded by lack of a clear understanding of its etiology. Part of the problem seems to be that the existing data indicate the involvement of complex gene/environment interactions. One prospective study in humans reported that individuals with one or two copies of the short allele of the 5-HT transporter promoter polymorphism reacted with more depression to stressful life events than those homozygous for the long allele (21). That study demonstrated that longitudinal population based studies are an important and useful tool in untangling complicated gene/environment interactions.

Results from another longitudinal study with important public health implications, further substantiate the benefits of the prospective approach to the study of gene/environment interactions. According to the Centers for Disease Control in Atlanta, 903,000 children in the United States experienced or were at risk for child abuse and/or neglect in 2003 (22). Child maltreatment has been significantly correlated with depression, substance abuse and antisocial behavior (23). A longitudinal cohort study of males from birth to adulthood found a significant association between child maltreatment and adult antisocial behavior, but reported significantly less antisocial behavior associated with child maltreatment among men with high MAOA activity than in those with low MAOA activity. However, there was no significant main effect of genotype (MAOA activity) on antisocial behavior. This means that although MAOA activity is not directly related to antisocial behavior, it does mediate the effects of maltreatment. The National Children's Study provides an unprecedented opportunity for the examination of gene/environment interactions and should be utilized to the fullest.

Justification for a Large, Prospective, Longitudinal Study

A *prospective* study is required because the exposures in question precede the outcomes by many years and because these exposures influence gene expression at different time points.

The *longitudinal* design is also required because it is important to trace the development of the cohort through childhood and adolescence, in order to measure the neurobehavioral outcomes of relevance. Several reports from smaller cohorts have indicated childhood antecedents (or perhaps risk factors) that can predate symptom development by long periods. In addition, the interactions under investigation require data on prenatal as well as early childhood exposures.

Gene expression is subject to multiple environmental influences: social connections, material resources (e.g., nutrition), and toxic exposures. A large cohort is needed to provide enough power for the candidate gene approach to studying these neurobehavioral outcomes, while accounting for multiple interactions. The use of a large cohort enables the examination of gene/environment interactions without the recruitment of additional family members.

Scientific Merit:

Animal research on genes associated with behavior and on the modification of gene expression

by psychosocial factors has been accumulating for a number of years. This research covers a fairly broad range of factors from physiological risk to behavioral traits, and has emphasized the extent to which the functional importance of a gene is determined by factors which influence expression (24). Intra- and extracellular environments play an important role not only in the magnitude of expression but in the direction of expression, i.e., whether it is up- or downregulated. The intracellular environment is a function not only of its genetic components, but of influences from the extracellular factors such as hormones, neurotransmitters, cytokines, and nutrients (24). Variation in these constituents can determine how and when a gene is functionally expressed. Psychosocial factors are involved in these interactions through their influence on hormones and neurotransmitters. This can be illustrated by the influence of stress on transcription factors. Glucocorticoids such as cortisol are part of the hormonal response to stress. The transcription factors cJun and cFos in the cell are sequence-specific DNA-binding proteins that bind to DNA in a multi-protein complex which controls cell proliferation and growth. These transcription factors are extremely responsive to extracellular stimuli (25) and it has been shown that they influence glucocorticoid receptor-induced transcription of proliferin, causing it to increase or decrease according to their presence together or alone in the surrounding environment (26). Research in rats has demonstrated that immobilization stress (physically restraining the animal) upregulates both of these transcription factors in endothelial, myocardial and smooth muscle cells of coronary vessels (27). Similarly, it has been demonstrated that immobilization stress influences gene expression in the hippocampus in rats, causing increased expression of corticotropin-releasing hormone mRNA (28) and a decrease in 5-HT1_a mRNA levels in the dentate gyrus (29-30). These latter data complement other research which has demonstrated that serotonin polymorphisms differentially influence heart rate and blood pressure responsivity to stress (31), by showing that stress also influences the functional expression of serotonin polymorphisms. Similar interactions have been demonstrated for the á $_2$-adrenoceptor variants which influence the magnitude of stress responsivity. Animal research shows that the functional expression of this gene is itself influenced by stress (32). In addition, stress induced expression of corticosteroid receptors has been demonstrated to vary by gender (33). Together, these data illustrate the complexity and ongoing nature of gene/environment interactions, emphasizing that “genes or environment?” is not a meaningful question. The presence of a linked allele at a locus is an indication of risk but it is not enough to predict functional expression. Understanding function requires knowledge of the factors that influence when and in what direction (e.g., up or down regulation) it is expressed.

One of the National Children’s Study core hypotheses states that excessive maternal psychosocial stress during pregnancy, in conjunction with maternal and fetal genetic susceptibilities, is reflected in specific measures of biologic function and results in an altered trajectory of fetal growth and development. At a recent workshop centered around this hypothesis, one of the mechanisms postulated for this influence was gene/environment interactions associated with gene expression.

Research on non-human primates has demonstrated the influence of mothering on gene expression. Research in Rhesus monkeys has demonstrated that a short form of the serotonin transporter (rh5- 5-HTTLPR) gene is associated with drinking alcohol to excess in monkeys reared in an environment with same age peers and no mother, indicating a genetic link to alcohol abuse. However, monkeys with this same genotype reared together with their mothers, actually

consume less alcohol (34), indicating that this same polymorphism under different circumstances, confers a protective effect. These data further illustrate that knowing the genotype is not sufficient for predicting phenotypic expression without additional knowledge of the psychosocial environment.

Many diseases that are of interest to the Study have complex etiologies and pathogenesis, involving multiple genes and environmental factors. They also often have low prevalence. Most studies of gene/environment interactions in humans use the *linkage approach*, which requires the recruitment of families but can be conducted on much smaller sample sizes. However, the linkage approach has limited power for identifying genes with low prevalence in the population. Association studies using the *candidate gene approach* require large sample sizes but have the power to investigate associations between a specific locus and a disease or trait even when the population prevalence is comparatively low. The Study provides a unique opportunity to study not only candidate genes for diseases such as autism and schizophrenia, but psychosocial and environmental influences that influence expression.

Potential for Innovative Research:

This hypothesis has the potential for some of the most innovative research in the Study. Complex behaviors such as aggression, substance abuse, depression, schizophrenia and autism have defied attempts at simple genetic or environmental explanations. Although there are a number of candidate genes in each area and a number of environmental factors that have been associated with these outcomes, none of them alone explain enough variance in the etiology to suffice as targets for intervention. The Study enables the measurement and timing of early stressors and the tracking of neurobehavioral outcomes throughout childhood and adolescence, thus providing an opportunity to investigate gene/environment interactions that is unprecedented.

Feasibility:

This study is highly feasible. The size of the study provides the power for genome scans of association to multiple traits and behaviors even without the use of family members for linkage. Because of the currently available molecular techniques and the number of environmental exposures to be measured in this study, investigation of gene/environment interactions is not only feasible, it can be done at reasonable cost with high benefit to the study.

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National Children's Study

Brief Working Paper
Submitted by the Health Disparities/Environmental Justice Working Group
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Introduction

Our intent is to briefly summarize some key principles to be taken into consideration in sampling, design and protocol development for the NCS. This thinking reflects the original mission of the workgroup: (1) to provide guidelines for conduct of the study that ensures fair treatment of all people, including minority and low-income populations; and (2) to inform the study protocol regarding health disparities and environmental justice issues. In addition to the October 2001, April 2002, and December 2002 Study Assembly Meeting Reports and the report from the December 2003 working group meeting, the workgroup sponsored the June 2004 workshop on Measuring Racial/Ethnic Disparities and Racism from a Developmental Perspective. To complete its task, the working group is providing this brief summary of recommendations to inform specific components of the protocol.

This summary provides a framework for environmental research, portions of which have been thoroughly reviewed elsewhere in the following reports: CDC (*Racial and Ethnic Approaches to Community Health (REACH) 2010: Addressing Disparities in Health, 2003*), EPA (*Framework for Cumulative Risk Assessment, May 2003*), Institute of Medicine (*From Neurons to Neighborhoods, 2003*), MacArthur Foundation Research Network on Socioeconomic Status and Health (*Socioeconomic Status and Health in Industrial Nations: Social, Psychological and Biological Pathways, 1999*), and Halfon and Hochstein's paper (*Life Course Health Development: An Integrated Framework for Developing Health, Policy and Research, 2002*). In addition, we direct attention to the upcoming reports from the National Scientific Council on the Developing Child (*Young Children Develop in an Environment of Relationships, 2004)* and the National Environmental Justice Advisory Council (*Ensuring Risk Reduction in Communities with Multiple Stressors: Environmental Justice and Cumulative Risks/Impact, 2004).* The framework provided here is not original, but combines current thinking about risk assessment and environmental justice with elements required for the design and implementation of a large cohort study—a study with the capacity to answer complex etiologic questions about individual child risk, while contributing to our understanding of population health disparities. We include three principles to guide the choice of populations to be studied, sample selection within those populations, and methods for analyzing risk comprehensively.

Principles for the NCS Protocol

1. Inclusion of populations and communities confronting environmental justice issues

At the risk of restating the obvious, populations and communities in the U.S. confronting environmental justice issues comprise low socioeconomic groups, race/ethnic minorities, and other marginalized groups such as immigrants. Such groups are the sources of numerous

persistent child health disparities. They are also the groups with disproportionate exposure to social and chemical stressors.

Background. The theoretical basis for most studies seeking to explain child health disparities rests heavily on a 'poverty paradigm', suggesting that impoverished groups are among the most vulnerable members of our society. Although children in poverty are disproportionately exposed to many environmental risks, not all poor children have adverse health outcomes. There are a number of systematic group differences in child health outcomes, including childhood asthma and developmental disorders, that are not explained by economic disadvantage. The poverty paradigm simply does not seem to explain many of the persistent and multiply-determined pregnancy and child health problems of African American and other minority communities (e.g., Rowley et al., 1993).

For example, regardless of income, African American infants are more than twice as likely as whites to experience fetal growth problems such as low birth weight and preterm delivery. Hispanic infants are one and a half times as likely as whites to experience these adverse birth outcomes. Although a number of risk factors for LBW have been identified (low pre-pregnancy weight or body mass index, inadequate gestational weight gain, pregnancy complications, smoking, low income, low educational achievement, sex of the infant, age of mother below 20 or over 34 years, alcohol consumption and late or no prenatal care), as much as half of LBW and more than half of preterm births in the U.S. are unexplained. Despite decades of research, we understand very little about these apparent ethnic disparities in fetal growth..

Social-structural inequality, a possible source of health disparities, includes the notion of relative deprivation, which may be at least as important an influence on child health outcomes as absolute deprivation (e.g., Wilkinson, 1997; Kennedy et al., 1998). One argument views relative poverty as a form of social exclusion, and suggests that the racial discrimination underlying this exclusion (including residential segregation) contributes directly to general health (Krieger and Sidney, 1996) as well as child health outcomes. Indeed, there is a substantial literature on the negative health effects of perceived discrimination (Williams et al., 1997), but it is not yet clear whether these risks operate primarily at the level of individual experiences, or whether additional risk is conferred by exposure to institutionalized racism (Stafford and Ladner, 1990; Krieger 1999). The presence of a large racial gap in rates of LBW and preterm delivery among college educated women further supports that idea that race-related factors or conditions leading to poor birth outcomes may be institutionalized in this country (Schoendorf et al., 1992; McGrady et al.,1992).

Closer inspection of population-based data suggests that there is tremendous variability in child health outcomes within race/ethnic groups. For example, birth weight appears to be more strongly affected by place of residence and social factors than by race or ethnicity. Specifically, African American women who reside in the U.S., but were born outside of the U.S., are less likely to have a low birthweight infant than their U.S.-born counterparts(Cabral et al., 1990; David and Collins Jr.,, 1997). Although much of the research on black Americans tends to treat them as a single undifferentiated group, these findings suggest that there is considerable heterogeneity within this population (Krieger, et al.,1993).

Similarly, analysis of Arizona state vital records showed that Mexico-born Mexican American women have lower rates of preterm and low weight births compared to U.S.-born Mexican American women (Balcazar et al., 1993). This reproductive advantage (termed the epidemiologic paradox) persists in spite of their limited use of prenatal care services, lower educational attainment and higher rates of poverty. Explanations for this phenomenon suggest that less acculturated women have better family support, better nutritional habits, higher regard for the parenting role, lower rates of substance abuse and less smoking (Alder, 1994). At least part of this buffering effect (which may protect some groups against the toxic effects of economic disadvantage) is due to specific behavioral and psychosocial characteristics, but a direct effect of identification with traditional culture is also operant and remains largely unexplained. A 1998 report from the National Research Council and the Institute of Medicine on the health of immigrant children called for increased funding for longitudinal studies on health and development among immigrant and native-born ethnic and racial groups to identify which, if any, of these factors influence birth outcomes (IOM, 1998).

In addition to better birth outcomes for foreign-born women, children of immigrants have fewer acute and chronic childhood diseases and fewer health-related school absences in adolescence (IOM, 1998). The social, economic, material, and cultural factors responsible for providing this protection are largely unexplored. Both ethnographic and epidemiologic approaches have been called for to identify not only individual but also social group and community factors associated with health outcomes among immigrants (Runyan et al., 1998; Rogers et al., 1996). Implicit in these findings is the view of race as a social rather than a biological construct, underscoring the need to consider the complex array of social conditions and physical exposures that accompany racial/ethnic identification.

Methodologic considerations. NCS decisions regarding inclusion of specific groups should take into consideration the magnitude of the health disparity, the overall burden of the health problem (the harm caused), and the socio-historical context of the environmental justice issue (e.g., rationale for inclusion of highly impacted communities and tribes). In selecting populations for study, we recommend that relative as well as absolute disparities in child health indicators and levels of exposure be considered. Significant differences in levels of exposure to certain pollutants by whole groups of children are an environmental justice issue, regardless of whether such exposures are (or were formerly) considered low-level or harmless, as has now been shown in the lead, ETS, pesticide, and pthlalate literatures (see reports by the Exposure workgroup).

With respect to inclusion, populations confronting environmental justice issues may be difficult to engage and difficult to assess. Participation of particular populations or communities may be maximized when the health outcome or disparity that is the focus of study is recognized by the community as a problem. Such recruitment and engagement issues have been addressed by the Community Participation and Communication Work Group; issues of assessment and the need for culturally sensitive measurement strategies have been addressed by the Social Environment Work Group. It is possible that the environmental burdens of some groups are not recognized by the regulatory or business communities, despite good intentions, and this is where the scientific community and the NCS can make an important contribution (see report by the National Environmental Justice Advisory Council, *Advancing Environmental Justice Through Pollution Prevention*, June, 2003).

2. Development of risk assessment models that accommodate multiple, cumulative and interactive risks

As advocated by the EPA's *Framework for Cumulative Risk Assessment*, predictive models must include multiple stressors, including not only chemicals but also a range of socioeconomic stressors. According to this model, risk assessment is done with the focus on a population or a community, rather than studying the risk of one exposure. The accumulation of toxic exposures has been shown to be a more powerful determinant of child health and development than any specific exposure (Weiss, 2000; Bellinger & Stiles, 1993; Needleman et al., 1996). Furthermore, as noted by the EPA's framework, a stressor may not cause harm directly, but may make the target more vulnerable to harm by other stressors.

Inclusion of social risk factors in environmental risk assessment models. The focus of most environmental science research is to identify and quantify associations between toxic physical or chemical exposures and disease outcomes. Consistent with a medical model, the introduction of biomarkers has moved this agenda forward by validating the degree of individual exposure and improving the precision of effect size estimates. This in turn has lead to increased technical and programmatic responses to the reduction of environmental pollution, including some positive changes in public health policy. However, little attention has been paid by environmental health scientists to the social conditions underlying gross inequities in the distribution of such toxic exposures in the first place, and even less attention to the processes whereby these social conditions may directly affect susceptibility to the toxic exposures themselves. It is quite likely that the systematic nature of these environmental injustices, and the resulting adverse living conditions that disproportionately affect whole groups of people, are directly responsible for specific health disparities. The continued reliance on a limited medical model, coupled with a focus on singular risk associations, may further refine our ability to identify factors that increase an individual child's chances of having a particular adverse health outcome in response to a toxic exposure, but will do nothing to reduce social and racial disparities in disease prevalence

The concept of vulnerability or susceptibility of certain groups underlies environmental justice and is implicit in the testing of interactions between risk factors, whether they be chemical or social. The idea is that exposure to one risk exacerbates the impact of exposure to another is complex because some risks may be pre-existing and/or chronic (as in the case where a prenatal exposure renders a child more susceptible to the harmful effects of other exposures later in childhood). The meaning of the interaction of social and physical environmental factors depends upon the level of analysis. At the individual biological level, interaction is perhaps more appropriately called synergism, and refers to verifiable biologic models describing mechanisms at the cellular level. Statistical interaction, observed as effect modification, does not refer to mechanisms of action at the biological level, but may be observed in populations. This use of the term refers to whether an effect measure varies in value over categories based on the level of some other factor. Regardless of biological synergism, this type of interaction can have important public health implications.

For example, the lead literature has demonstrated that adverse neurobehavioral effects of low-level exposures may appear at various ages as the child matures, develops capacities, or faces

challenges, with or without mediating effects on birth weight, length or head circumference (Wigg et al., 1988; Bellinger, Leviton et al., 1987; Needleman and Gatsonis, 1990). Furthermore, this literature has addressed the combined impact of lead exposure and social disadvantage, demonstrating that children with high lead exposure show particularly adverse cognitive effects under conditions of social disadvantage. Similarly, a recent report by Rauh et al. (2004) found that the adverse developmental effects of prenatal ETS exposure are heightened in families with high amounts of social adversity or hardships. Mechanisms by which other pollutants and social adversities render some children more vulnerable to the toxicant remain unclear. In addition, while identifying critical periods during which various ambient exposures are likely to be most toxic is key for risk assessment and management, the often chronic nature of exposures to both air pollutants and social adversities makes it difficult to determine windows of susceptibility and risk of combined exposures to the developing child.

Methodologic considerations. Large cohort studies that incorporate multiple exposures and multiple endpoints are not uncommon, and the analytic challenges facing such prospective designs have been well-reviewed elsewhere. The types of longitudinal questions being asked will require specific sampling and analytic strategies. The analytic challenge will involve quantification of cumulative risk as a result of repeated multiple exposures over time. This may require growth modeling and the building of trajectories to accommodate and assess change over time. Although not specifically designed for risk assessment, such approaches would seem to be workable for testing competing models of cumulative risk to better understand under what conditions selected populations are most likely to manifest health problems, and how social, chemical, and genetic conditions interact to exacerbate or ameliorate risk.

To specifically address health disparities, the NCS will need to determine whether children with different exposure patterns follow different growth and developmental trajectories. Further, the study will need to identify other conditions (social exposures, susceptibilities) that predict variations in trajectories. Finally, there is the question of how the manifestations of toxic exposures change as children mature. Growth modeling can accommodate any number of assessment waves, the occasions need not be equally spaced, and different participants may have different data collection schedules. Individual change can be represented by a variety of trajectory forms, including straight-line, curvilinear, or even discontinuous functions; simultaneous change across multiple domains can be investigated simultaneously; and the method can be used to fit curves for incomplete data (unlike traditional repeated measures methods).

The success of such analytic strategies, however, will depend entirely on the inclusion of groups of children with different exposure patterns, and this includes vulnerability factors such as genetic risk (see reports by the Genetics Work Group). As the NCS works to develop a sampling scheme, we recommend that whatever stratification method is employed, it be done with attention to the specific priority interactions that are of primary interest to the overall study or the individual sites. The HD/EJ Work Group has taken a great deal of time to work out some of the numbers that might be required to test specific toxic exposure/social condition interactions, including prevalence maps for selected cities to illustrate overlapping distributions of air pollution and social stressors, and we can provide the NCS with this material. Although it is not the mission of this group to develop complex interactive hypotheses, it is important to

understand that such interactions likely underlie and contribute to the most persistent child health disparities. From the perspective of the HD/EJ group, the challenge to the NCS is to determine the general classes of interactions to be tested (e.g., air pollutant/social deprivation, nutrient intake/genetic polymorphism, etc.) and to select a sampling scheme and study sites that can accomplish this goal. Most workgroups have proposed main effect hypotheses or interactive hypotheses within the same class of exposures. A final step prior to the completion of their work might be to select the workgroups representing the various exposures/vulnerabilities potentially involved in key interactions and commission them to develop several collaborative interactive hypotheses. To guide the selection of interactive hypotheses, we suggest a matrix approach, as described in the Council on Environmental Quality report, *Conducting Cumulative Effects Analysis under the National Environmental Policy Act.* We recognize that previous efforts to include social factors in cumulative risk models have relied on qualitative approaches, and that more progress is needed in this area to improve the quantitative models.

3. Inclusion of Multi-level Approaches

Background. The notion that community-level conditions can produce profound effects on host susceptibility to disease derives from the longstanding existence of strong social class gradients in health (Cassel, 1976). Recent studies have shown that women who live in violent, crime ridden, physically decayed neighborhoods are more likely to experience pregnancy complications and adverse birth outcomes, after adjusting for a range of individual level sociodemographic attributes and health behaviors (Zapata et al., 1992; Kleigman, 1992). Other studies have suggested that the stresses of racism and community segregation are associated with lower birth weights (David and Collins Jr., 1997). However, the question of whether community-level adversity has a deleterious impact on fetal and early childhood outcomes, independent of individual level risk factors, and whether the predictive power of these individual level factors depends upon community-level conditions, has only recently been put to empirical test. For example, O'Campo has found that the effects of individual poverty on birth outcomes are exacerbated by residence in a disadvantaged neighborhood (O'Campo et al., 1997). Rauh has shown that urban African American women were more likely to deliver low birth weight infants when they lived in socioeconomically disadvantaged areas, regardless of individual level poverty and other risk factors (Rauh et al., 2001).

Another example of community-level risk is the observation that diet may be determined by the availability of fresh produce in an area, independently of individual income. That is, if fresh produce is unavailable, there will be very little association between income and dietary deficiency. Although the dietary deficiency may be causal in the determination of disease, it is to some degree determined by the availability of fresh produce. The causal pathway is real, and income will permit higher consumption of fresh produce, but only if it is available. The availability of fresh produce is not captured by individual-level data because there is no analogue at the individual level. Degree of income inequality in a community is another example of a condition that can only be measured at the aggregate level. The mean income of a community may be a marker for housing conditions, traffic patterns, and other environmental conditions which affect everyone in the community regardless of individual income.

Methodologic considerations. Multi-level approaches integrate both contextual and individual-level determinants of health outcomes into a single analytic framework, making it possible to estimate simultaneously the effects of community context and individual attributes. These types of studies begin to answer the question of whether local area characteristics influence health and mortality over and above individual attributes, and whether the association documented between area-level aggregate measures and health outcomes simply reflects individual-level characteristics of area residents. If the characteristics of both the individual and residential context influence health outcomes, then models that exclude one or the other can be mis-specified and lead to misinterpretation of the effects of both individual and contextual-level factors on health.

Advances in statistical techniques that facilitate the modeling of multi-level influences and the growing interest in the use of geographic information systems have also made analyses of community-level variation and influences more feasible (Diez-Roux 1998; DiPrete and Forristal 1994; Goldstein 1995; Von Korff et al. 1992). However, multi-level studies are still relatively rare compared to individual-level and aggregate-level investigations of health and mortality. The results of these studies nevertheless point to the potential importance of residential context on health.

The addition of contextual level data to individual data requires accounting for the effects of clustering, as women who live in the same area will be similar since they share a number of unobserved characteristics defined at the community level. As a result, the usual assumptions of independence will be untenable. Previous work has shown that ignoring clustering with limited dependent variables may lead to over-optimistic estimates of standard errors and biased estimates of regression coefficients. To account for intra-cluster correlation, we suggest taking advantage of recent developments in multi-level modeling (Bryk and Raudenbush 1992; Rodriguez and Goldman 1995). This will also permits the testing of cross-level hypotheses, involving both individual- and aggregate-level variables. In addition, we suggest using spatial-effects models, where the random effects representing unobserved characteristics of a cluster are correlated with those of adjacent clusters. Such models have been applied in the context of disease mapping by Clayton and Kaldor (1987).

Communities will need to be characterized with respect to social conditions (i.e., violent crime rates, school drop-out rates, presence of local tenant organizations, social capital) and/or material conditions (i.e., overcrowding, location of diesel bus depots, waste transfer stations, transportation routes, sewage treatment plants, adequacy of garbage removal, abandoned buildings). Data sources will include U.S. Census and other administrative databases. These data will be linked to the macro social influences of the communities, including housing dimensions, to the individual-level findings generated by the intensive psychosocial, behavioral and biological study of the cohort, for the purpose of exploring the underpinnings of child health disparities. Because multi-level statistical techniques require sufficient variability of study factors within each of the target communities, cross-level effects can be explored (in which toxic exposure-disease relationships are conditioned by community context) only after careful scrutiny of the individual-level findings.

Selection of area-level boundaries. Most studies that examine area-level variation or the effects of community context on health outcomes have used administrative or political boundaries to

characterize neighborhoods and communities. In the United States, aggregate-level studies typically investigate area-level variation in health and mortality at the level of the state (Bird and Bauman 1995; Kaplan et al. 1996; refs), county (ref), or metropolitan areas and central cities (e.g., LaVeist 1992; Polednak 1991). Most studies that integrate both individual and community-level characteristics in the analysis use U.S. census tracts as the neighborhood unit (e.g., Anderson et al. 1996; Cubbin et al. 2000; Jackson et al. 2000; LeClere, Rogers, and Peters 1997, 1998; O'Campo et al. 1997; Rogers and Peters 1997, 1998; Robert 1998). Census block groups and alternative neighborhood boundaries are less frequently employed (e.g., Elo, Rodriquez and Lee 2001; Diez-Roux et al. 1997; Roberts 1997). Similarly in European studies political or administrative boundaries are typically used to define communities and neighborhoods (see Pickett and Pearl 2001 for a review). The choice of these areal units appears to be driven more by data availability and convenience than the fact that these areas are thought to represent neighborhoods as experienced by their residents. As noted by Pickett and Pearl (2001) "if they [geographic areas] do not correspond to the actual geographical distribution of the causal factors linking social environments to health" these neighborhood units provide only a rough ecological profile and may not adequately capture the potential effects of community context on outcomes of interest (see also Diez-Ruix, 1998).

To date, few studies have examined whether the way in which the neighborhood is defined matters. Elo, Rodriguez, and Lee (2001) show that whether the neighborhood is defined as a census block group, a tract, or a larger areal unit corresponding to two distinct Philadelphia neighborhood configurations, influences the extent to which racial differences in birth weight can be explained by neighborhood context. Using fixed effects estimates they explain more of the racial gap in birthweight using block groups than either census tracts or the alternative neighborhood configurations. Reijneveld et al. (2000) examined the same issue in Netherlands using three different neighborhood definitions (neighborhoods, postal service code areas, and boroughs) in Amsterdam to examine adult health outcomes. The authors conclude that although the clustering of poor health was most pronounced at the neighborhood level, the choice of geographic classification hardly mattered for the size of the effect of area-level deprivation. Soobader and LeClere (1999) investigated whether the effects of income inequality on self-perceived health status were stronger when income inequality was measured at the level of a county versus a census tract.

Protocol choices will have to be made to decide what are the most appropriate ways of conceptualizing and sampling neighborhoods and to what extent the effects of neighborhood characteristics vary depending on how boundaries are defined. Despite their convenience, political and administrative units may not be the most appropriate way to delineate neighborhood boundaries for a large, multi-site study. Furthermore, it may well be that contextual influences operate at various levels of aggregation. Larger catchment areas, for example, may be appropriate for measuring availability of goods and services, such as health care facilities, recreational opportunities and grocery stores, while smaller geographic units may be more appropriate for assessing the quality of housing stock, crime and social characteristics of neighborhoods. Thus, it may be important to incorporate multiple levels of influence simultaneously, depending on the question of interest and the theoretical framework guiding the analysis.

The NCS faces several additional challenges in modeling the effects of neighborhood context. The high correlation among various community-level characteristics poses problems in estimating the effects of distinct community characteristics. One way to get around this problem is to develop indices of related neighborhood level constructs, although indices may obscure the role of their distinct components. The key here is to link measures of neighborhood context to the pathways through which they are hypothesized to operate. At the same time, the ability to estimate the independent contribution of neighborhood context on health outcomes requires that adequate controls can be introduced at the individual-level. Otherwise contextual-level measures may reflect individual-level differences that are not adequately captured by the individual-level controls (Pickett and Pearl 2001).

Another problem with census tracts, or other administrative units, is that they impose a certain spatial scale on relationships. If nearby housing conditions affects a woman's likelihood of pre-term birth, how near or far does that housing conditions need to be? Do dangerous properties need to be within sight of a woman's house or within the larger area around her home where she spends most of her time? Census tracts assume a spatial scale, although because individuals do not live in the exact middle of the tract and because tracts vary in size and shape, they do not impose a consistent spatial scale.

Measures that use the study participant's address as the center of a specified neighborhood can avoid these aggregation/zone effects. These can simply include counts of the housing hazard or condition within a specified search radius of a woman's house or, more appropriately, the concentration of the hazard measured as a density. While simple counts can be calculated using vector GIS, which uses points, lines and polygons to represent map features, densities rely on raster GIS, which use grids made up of regular shaped cells to represent the change in values over space. In addition to overcoming issues with aggregation/zoning and scale effects, this approach to measuring neighborhood-level variables with raster densities at multiple scales also promises to increase the variance across the study sample. By using raster densities and testing the effects of different scales, this approach will help to distinguish the many different social and physical contexts from which the cohort families are drawn.