



National Children's Study

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National Children's Study Description



- The National Children's Study (NCS) is a Congressionally mandated activity coordinated among Federal agencies including the Environmental Protection Agency, the Centers for Disease Control and Prevention, and the National Institutes of Health with the National Institute of Environmental Health Sciences contributing and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development serving as the program lead.
- The NCS is a large multicomponent multiyear longitudinal study that is unprecedented in scope and complexity and therefore necessitates a planning process that is systematic, dynamic, flexible, and evidence based.

National Children's Study Goal



- The NCS will examine the multiple effects of environmental influences on the health and development of 100,000 children across the United States, following them from before birth until age 21, by providing high quality data to analyze scientific hypotheses.
- The overall goal of the National Children's Study is to improve the health and well-being of children.

National Children's Study Structure



- The NCS is being implemented in several phases
- All components and phases together form the NCS
- Current major components are the
 - NCS Vanguard Study
 - NCS Main Study
 - NCS Substudies and Supplemental Methodological Studies

NCS Vanguard Study Goals



- The Vanguard Study is designed to evaluate the
 - Feasibility (technical performance)
 - Acceptability (the impact on participants, study personnel, and infrastructure)
 - Cost (personnel, time, level of effort and money)
- of
 - Study recruitment
 - Logistics and operations
 - Study visits and study visit assessments

NCS Vanguard Study Outcomes



- The outcomes of the Vanguard Study will have a continual and major impact on how the Main Study will be executed; thus, it is imperative that the Vanguard Study be planned, implemented, and monitored to a level of precision that enables it to serve as a reliable and valid platform to evaluate recruitment, study procedures, visits, scale up potential, resource requirements and other aspects for the Main Study.

National Children's Study Main Study



- The Main Study will focus on data acquisition related to the interaction of genetics and environment as they impact the growth, development and health of children and the analyses of those data for multiple scientific hypotheses.
- The Vanguard Study and the Main Study have different goals and the assessment types and assessment techniques used in each of the NCS components may be different. Thus there is no intent to categorically merge data among NCS components.
- The Vanguard and Main Study will run in parallel, and together with additional NCS funded substudies, supplemental methodological studies and adjunct studies will form the composite National Children's Study.

Relationship of Vanguard Study to Main Study



Vanguard Study
N = estimated 2000

NCS Main Study
N = 100 000

National Children's Study Terminology



- Studies that integrate with the Vanguard Study, are funded by the NCS and focus on a limited question with limited duration will be known as substudies
- Studies that integrate with the Vanguard Study and have independent funding will be known as Supplemental Methodological studies
- Studies that integrate with the Main Study and have independent funding will be known as Adjunct Studies

National Children's Study Activity



- The Vanguard Study began in January 2009 with 2 sites; then an additional 5 sites began enrollment in April 2009
- The Main Study will begin when there are enough data from the Vanguard Study to responsibly construct the Main Study design
- The Main Study start date will be data based and evidence driven rather than calendar driven

NCS Vanguard Study Enrollment Target



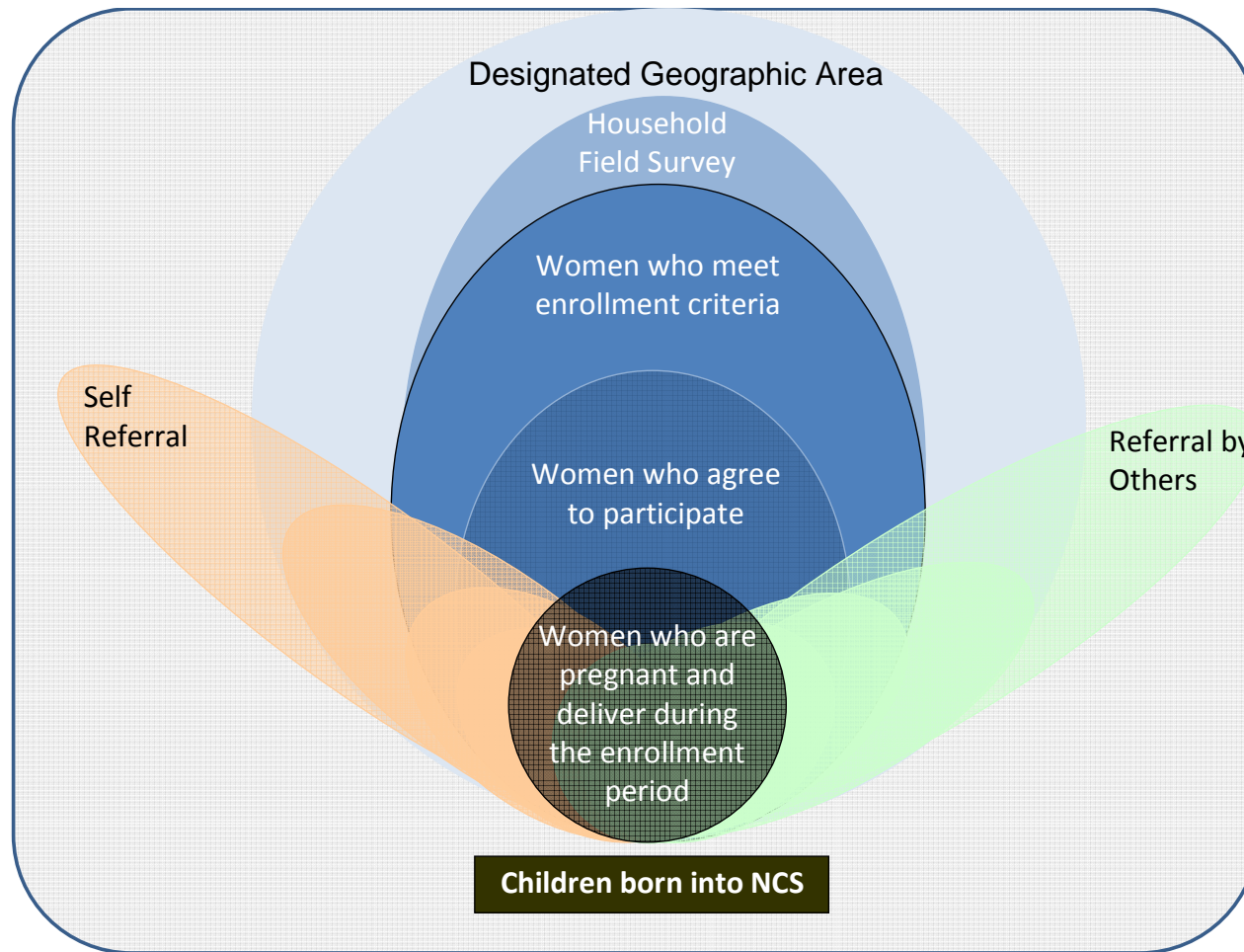
- The enrollment target for the Vanguard Study will be determined empirically by two factors
 - Recruitment data indicate a sufficient number of informative events to assess different strategies for scale up to the Main Study
 - An adequate cohort size to evaluate the study visit assessments for the duration of the study

NCS Current Recruitment Strategy



- Goal is a representative sample
- Representative sample achieved through demographics of predetermined geographic areas that are divided into segments
- All households within a geographic segment are eligible
- All women that meet enrollment criteria and live in the household are potentially eligible to enroll into the study
- When a woman becomes pregnant she is formally enrolled into the NCS
- The woman must live at an address in an eligible geographic segment when her child is born for the child to be enrolled into the NCS

NCS Current Recruitment Strategy



NCS Recruitment Status (as of November 2009)



- Households with women that meet enrollment criteria- 50%
- Proportion of eligible women that are pregnant – 3%
- Proportion of eligible pregnant women that agree to enter the study and consent- 60%
- Expected is average 250 births/center/year
- Observed would have a maximum average of about 100 births/center/year
- $83000 * 0.5 * 0.03 * 0.6 = 750$ births on first pass enumeration that takes about 12 months. If new pregnancies continue at the same rate, which may be optimistic, then each 12 month period would have about the same number of 750 births.

NCS Recruitment Challenges



- Variation among sites-
 - Proportion of completed enumeration ranges from 59 to 93%
 - Pregnancy screening varies from 76 to 91%
 - Pregnant women enrolled varies from 41 to 71%
- Need to improve efficiency of enrolling and retaining pregnant women and their children

Recruitment Next Steps



- Recanvassing after initial pass in the 7 Vanguard Centers
- Explore alternate strategies using additional sites based on
 - Provider based recruitment
 - Improve household recruitment methodology
 - HiLo recruitment
- Each approach is 4 to 6 months from concept to field implementation and then 4 to 6 months to acquire sufficient data for preliminary analysis

Provider-based recruitment



- Preliminary survey of NCS contract sites showed 2/3 of those surveyed respond provider-based recruitment is potentially feasible
- Estimated 10% conversion of women contacted to enrolled children at birth- need to empirically verify
- Field plan under preparation with deployment target of first quarter calendar 2010
- To be conducted in 10 sites using pre-existing geographic based sampling frame

Enhanced household recruitment method



- Assign enumeration to professional research organization with enumerators drawn from professional field staff with experience in population-based study recruitment methods.
- Methodologies would incorporate best practices of first Vanguard Center experience with best practices from other studies
- Targeted outreach efforts to accompany enumeration
- Deployment planned for second half FY 2010 in 10 sites using pre-existing geographic based sampling frame

HiLo



- Modeled after U.S. Census with short form and long form
- High intensity participation with visits
- Low intensity participation with survey instruments
 - Improves community tolerance for study
 - Decreases immediate privacy issues associated with enumeration and enrollment
 - Facilitates random assignment into high intensity group with participant's permission
 - Allows increased opportunity for testing items
- Deployment planned for first quarter FY 2010 in 10 sites
- May expand or adjust pre-existing geographic based sampling frame

Recruitment Plans-Three comparators with current method



- Current: Continue re-enumeration in current 7 Vanguard Centers
- New Strategy 1: Provider based strategy in 10 additional sites
- New Strategy 2: Enhanced household survey enumeration in 10 additional sites
- New Strategy 3: HiLo strategy in 10 additional sites
- Total of 37 sites with up to 37 Study Centers in Vanguard Study
- Parallel activity for improved efficiency in evaluation of recruitment numbers, community tolerance and cost to inform methods appropriate for Main Study

Potential Advantages of Expansion of Vanguard Study



- Greater precision in selecting recruitment strategies for Main Study
- Increased flexibility in allowing for multiple recruitment strategies for Main Study
- Parallel activities can increase rate of data accumulation
- More sites with NCS experience when Main Study launch begins

Schedule of Visits (Vanguard Study)



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

Other data collections

- Diary
- Phone
- Mail in samples
- Observational data
- Settings outside the home
- Community samples

 Clinical Setting

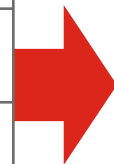
 Home

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

Priority Exposures and Health Outcomes



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



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

NCS Visit Assessments



- Visit assessments (those tests and assays administered to study participants at a visit) can be tested in all current contract sites
- Currently developing a series of analytic criteria
- About 250 different visit assessments (environmental samples, biospecimens, measurements, questionnaires, etc.) currently in NCS catalog to evaluate

Vanguard Study Candidate Visit Assessment Types



Assessment Type	Number of Assessments	Distribution by Person		
		Mother	Father	Child
Anthropometric Measures	5	N/A		
Biospecimens	95	67	26	2
Environmental Measures	99	N/A		
Physical Measures	31	10	10	11
Questionnaire	16	6	5	5
Total Number of Visit Assessment Types	246			

Evaluating Visit Assessments for Feasibility



- Each visit has a schedule that may contain questionnaires, physical and laboratory measurements, biological samples, environmental sample collections, or other assessments
- For each outcome assessment for each visit an *a priori* analysis is underway to determine the estimated count of informative events to provide 95% confidence limits around the reproducibility of the assessment that will allow an evaluation of whether to
 - scale up with an acceptable standard deviation
 - modify the outcome assessment and retest empirically
 - eliminate the outcome assessment from consideration for the Main Study

Evaluating Study Visit Assessments for Inclusion into Main Study



- Feasible, reliable, reproducible
- Informative
- Value
- Lack of redundancy
- Able to address a question that
 - has potentially important public health impact
 - requires a study of NCS size and robustness to answer
 - unlikely to be answered in another context

NCS Hypothesis Selection



- The selection of scientific hypotheses for the Main Study will be guided by
 - the empiric data of the Vanguard Study and other NCS funded substudies
 - by the efforts of the various workgroups and interested parties that proposed and vetted candidate hypotheses
 - potential scientific and public health impact
 - a perceived requirement to use the NCS and not another alternative as the data acquisition platform

NCS Target: Main Study



- All current NCS efforts are directed to inform Main Study with regard to design and elements
- Main Study design dependent upon results of recruitment evaluations
- All components for Main Study must have relative value and be scalable

Constructing the Main Study Process Considerations



- Main Study recruitment rate estimates based on Vanguard Study empiric data will determine the duration of enrollment to reach the accrual target of 100,000
- Main Study cost estimates will be based on study design factors such as;
 - **duration, effort and costs for recruitment**
 - **geographic location and resource footprint for each visit. For example, home based visits will have different requirements than clinic based visits**
 - **scale up costs of data processing, quality assurance, data archiving and data analysis**
 - **number, complexity and costs for outcome assessments**
- Additional secular factors such as health care, transportation, data security and other costs will also impact the Main Study cost estimates

Evaluating NCS Cost Drivers



- In general major cost drivers are:
 - recruitment strategy
 - number of visits
 - complexity of each visit
- The resource footprint for each visit as well as study operations is largely a function of the number of personnel involved and the level of effort required for data collection

National Children's Study Data Sharing



- Data from the NCS is intended to be shared and will be made accessible through the policies outlined in the Data Access Manual
- Everyone will have equal access opportunity to the data.
 - No priority or preference for participating NCS investigators
- Data from Supplemental Methodological Studies (integrated with the Vanguard Study) and from Adjunct Studies (integrated with the Main Study) will be governed by the policies relevant to the funding source and policies of the NCS

National Children's Study Program Office



- The NCS Program Office is committed to
 - Compliance with the highest ethical and scientific standards
 - Complete fiscal responsibility, accountability and transparency
 - Respect for all involved
 - Listen to and work with NCS partners including the Interagency Coordinating Committee, the NCS Advisory Committee, the NCS Steering Committee and all the NCS investigators
 - Engage subject matter experts and other advisors when needed to provide guidance on specific scientific and operational activities
 - Strive that adequate resources are in place in advance for operations
 - Establish performance metrics monitoring and reporting progress Identify potential risks and address them proactively
 - Actively monitor and make adjustments based on empiric evidence and study needs

National Children's Study



- For further information, please inquire at ncs@mail.nih.gov