



National Children's Study Update

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National Children's Study



- **Congressionally mandated by Children's Health Act of 2000**
- An integrated system of activities to examine the relationships between environmental exposures and genetics on growth, development and health
- Environment is broadly defined to include factors such as air, water, soil, dust, noise, diet, social and cultural setting, access to health care, socio-economic status and learning.

What the law says



The Study is required to:

(1) incorporate behavioral, emotional, educational, and contextual consequences to enable a complete assessment of the physical, chemical, biological, and psychosocial environmental influences on children's well-being;

(2) Gather data on environmental influences and outcomes on diverse populations of children, which may include the consideration of prenatal exposures; and

(3) Consider health disparities among children, which may include the consideration of prenatal exposures."

NCS Principles



- Data driven
- Evidence based
- Community and participant informed

Examples of Exposure Areas of Interest



- Exposure to industrial chemicals and byproducts in the air, water, soil and commercial products
- Exposure to natural products in the air, water, soil and commercial products
- Exposure to pharmaceuticals used for therapy and in the environment
- Radiation exposure
- Effects of proximity to manufacturing, transportation and processing facilities

Examples of Exposure Areas of Interest



- Living with animals, insects and plants
- Media and electronic device exposure, noise
- Access to routine and specialty healthcare
- Learning opportunities that are structured and unstructured
- Diet and exercise
- Family and social network dynamics in cultural and geographic context

Examples of Outcome Areas of Interest



- Interpersonal relationships and bonding
- Inflammatory processes including allergies, asthma and infections
- Genetic and epigenetic status
- Epilepsy and other neurologic disorders
- Cardiovascular screening and function
- Childhood cancer
- Multidisciplinary multidimensional aspects of sensory input, learning and behavior
- Precursors and early signs of chronic diseases such as obesity, asthma, hypertension and diabetes

Prevalence of Conditions of Potential Interest



- Of 100,000 children, an estimated
 - 30,000 will be overweight; 17,000 with obesity
 - 5,000 with learning disorders
 - 5,000 with asthma
 - 1,000 with autism spectrum disorders
 - 750 with congenital heart disease
 - 320 with childhood cancers
 - 125 with Down syndrome
 - 50 with Fragile X syndrome

NCS Structure



- The NCS is an integrated system of activities
- All components and phases together form the NCS
- Current major components are the
 - NCS Vanguard Study- pilot phase for methods-runs for 21 years-started in 2009 with 7 centers- expanded in 2010 with 30 additional centers
 - NCS Main Study-exposure response phase- runs for 21 years about 3 years time shifted from Vanguard Study-planned start in 2012
 - NCS Substudies- studies within studies
 - Formative Research-short term limited studies, often methods development, to support and inform the Vanguard and Main Studies

NCS Activities



Administration

Communications

Dissemination

Planning

Operations

Analysis

Instrument
Development

Protocol
Development

Main Study

**Vanguard
Study**

Data
Repository

**Formative
Research**

Case
Management

Central
Informatics

Data
Acquisition

Sample &
Specimen
Repository



NCS Vanguard Study Goals



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

Current Sampling Frame (simplified)



- Random selection of about 100 of ~ 3000 counties in the United States
 - Counties = Primary Sampling Unit
- Counties divided into segments that are normalized to have ~ 250 live births per year. Some sparsely populated areas involves merging counties
 - Segments = Secondary Sampling Unit
- Recruitment is restricted to the Secondary Sampling Units

Alternate Recruitment Substudy



- NCS Vanguard is now at 37 locations across the country with 30 engaged in new recruitment using one of three different strategies
 - Household based- participants learn about the study through field workers walking through neighborhoods
 - Provider based- participants learn about the study through trusted health care providers with a broad definition of provider including physicians, public health nurses, midwives, etc.
 - Direct to the public- participants learn about the study directly through media and community outreach
- The goal is compare strategies to assemble a toolkit for cost effective directed recruitment for the Main Study launch
- Both direct data analysis and predictive modeling employed

NCS Recruitment Status

-based on data as of 10/06/11



	Provider	Enhanced Household	Direct Outreach	All Alt. Recruitment	Initial Household‡	All Vanguard
Locations	10	10	10	30	7	37
Recruitment Duration, months	10	10	10		18 full + 12 monitoring	
Women eligible for contact	2350	22700	12550	37550	34900	72450
Pregnancy Screened	1600	15050	10750	27400	30900	58350
Pregnant or Trying	1450	2100	1850	5400	3450	8850
Women Enrolled	1150	1300	1500	3950	2000	5950
Babies Enrolled	350	300	150 [^]	800	1000	1800

Person and participant numbers above have been rounded to the nearest 50, following the NCS Rounding policy.

[^] - Implementation of Birth Visit data collection for Low-Intensity women was delayed due to logistical reasons.

‡ - Initial Household includes participants from the initial protocol and the minimal visit protocol

Alternate Recruitment Substudy Recruitment Summary

- as of 10/06/11



	Provider Based	Enhanced Household	Direct Outreach
Women Identified to be age- and geographically eligible	2350	22700	12550
Pregnancy Screened	1600	15050	10750
Pregnant or Trying	1450	2100	1850
Enrolled (% pregnant)	1150 (91%)	1300 (58%)	1500 (56%)
Babies Enrolled	350	300	150*
Number of Locations x Weeks in field	313	379	355
Mean number of women enrolled per week	3.7	3.5	4.2
Mean number of women identified per woman enrolled	2.0	17.3	8.4

NOTE: Estimates are based on preliminary data that are not yet complete and are rounded to the nearest 50, following the NCS Public Presentation Policy.

*Implementation of Birth Visit data collection for Low-Intensity women was delayed due to logistical reasons.

Pregnancy Screening Completion by Recruitment Strategy

- as of 10/06/11



	Provider Based	Enhanced Household	Direct Outreach
A. Number of women identified to be age- and geographically eligible	2350	22700	12550
B. Number of women contacted for pregnancy screening	2050	17400	12500
a. Final ineligible	150	100	50
b. Refused	-	650	200
c. Other non-response	50	400	1550
d. Incomplete information, unable to classify	250	1200	-
e. Completed screening	1600	15050	10750
Pregnancy screening complete rate (=e/(A-a))	74%	67%	86%

NOTE: Estimates are based on preliminary data that are not yet complete and are rounded to the nearest 50, following the NCS Public Presentation Policy. '-' means number is too small to present.

Consent Rates by Recruitment Strategy

- as of 10/06/11

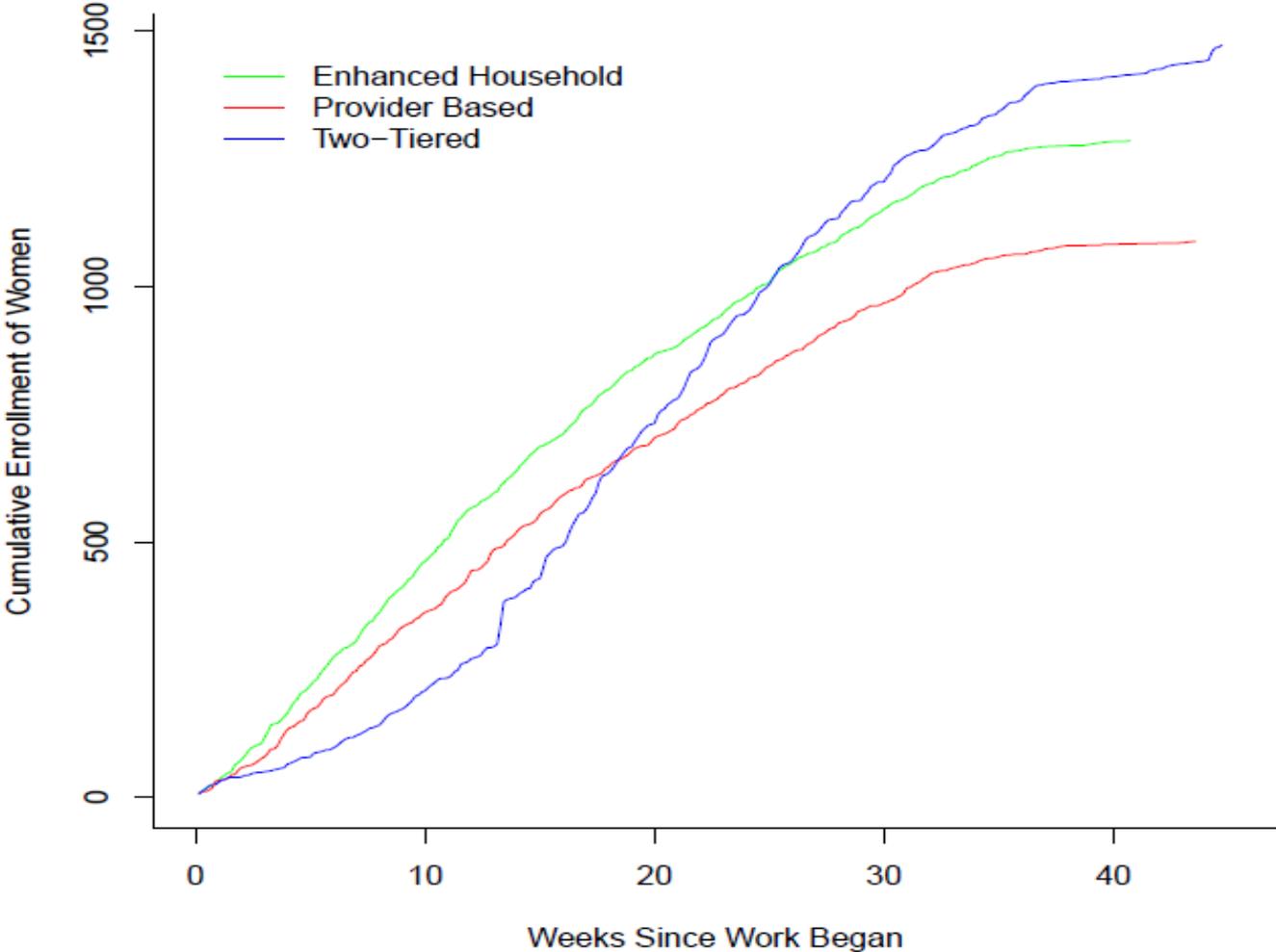


	Provider Based	Enhanced Household	Direct Outreach
A. Number of women pregnant or trying to become pregnant	1450	2100	1850
a. Final Ineligible	-	-	-
b. Refusal	50	150	50
c. Other non-response	50	50	100
d. Incomplete information, unable to classify	200	600	200
e. Enrolled	1150	1300	1500
Consent rate (=e/(A-a))	81%	62%	82%

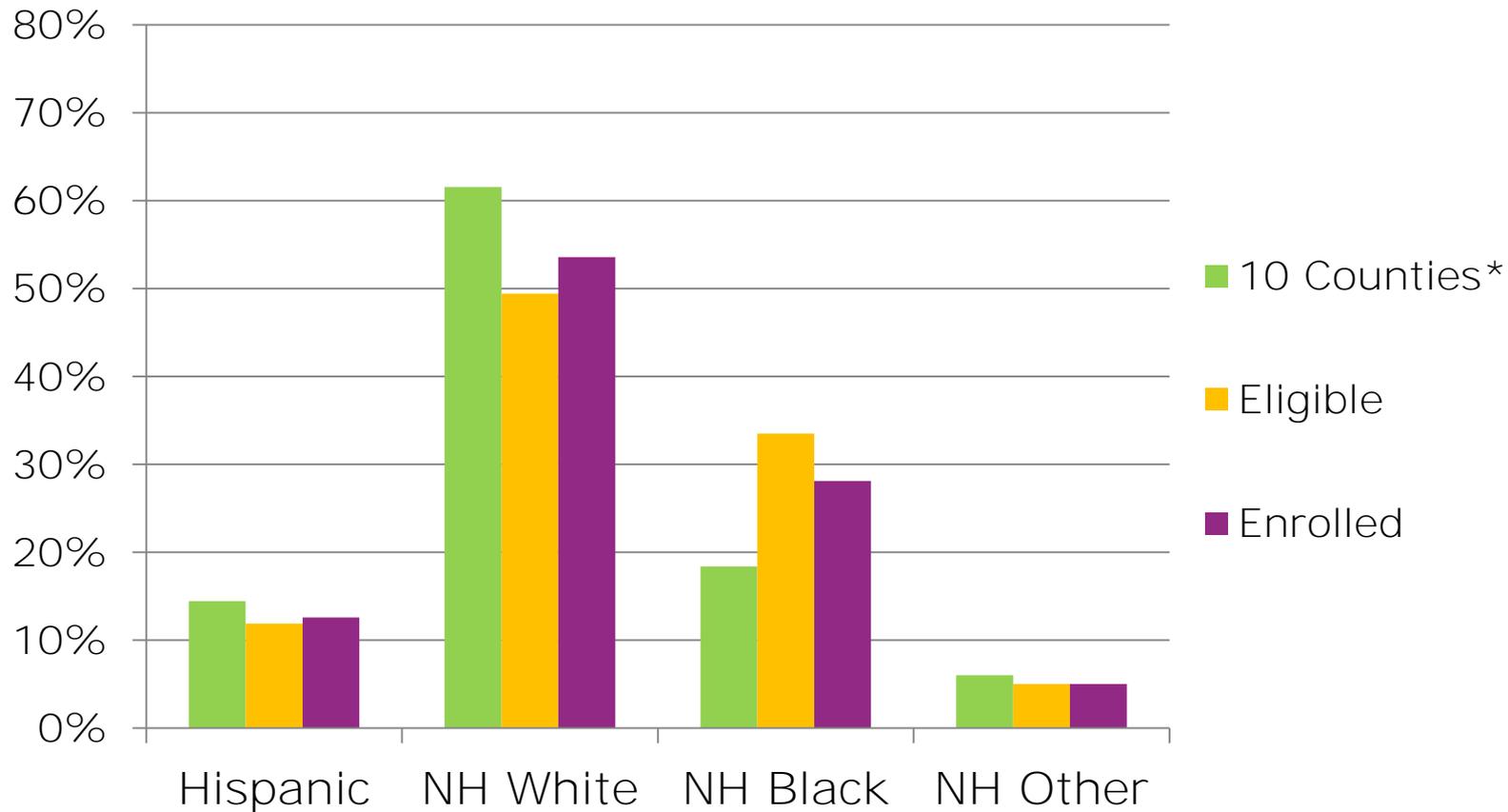
NOTE: Estimates are based on preliminary data that are not yet complete and are rounded to the nearest 50, following the NCS Public Presentation Policy. '-' means number is too small to present.



Cumulative Enrollment of Women Since Work Began

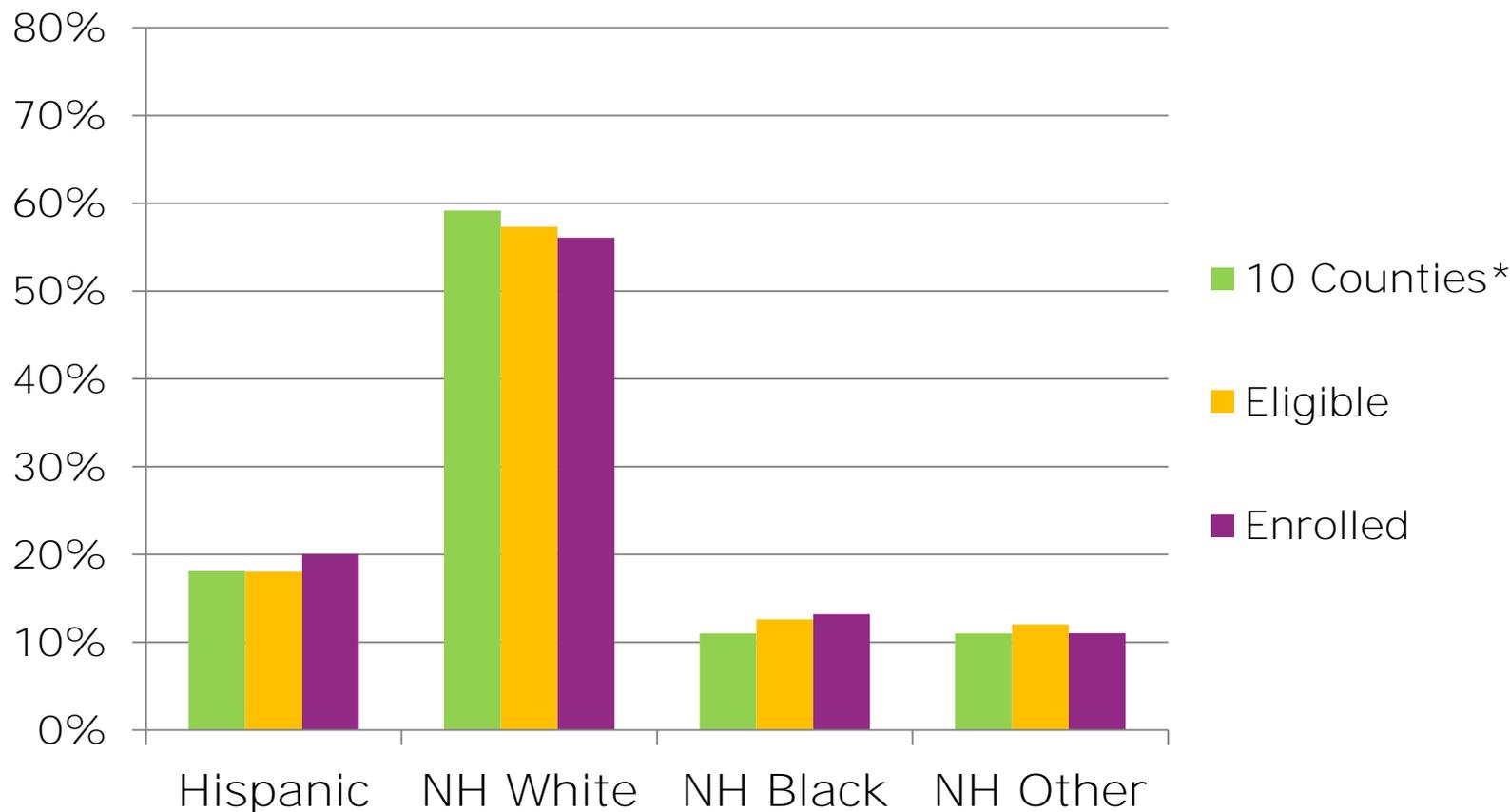


Race/ethnicity Distribution Among Study Eligible and Enrolled Compared to County Population – **Provider Based**



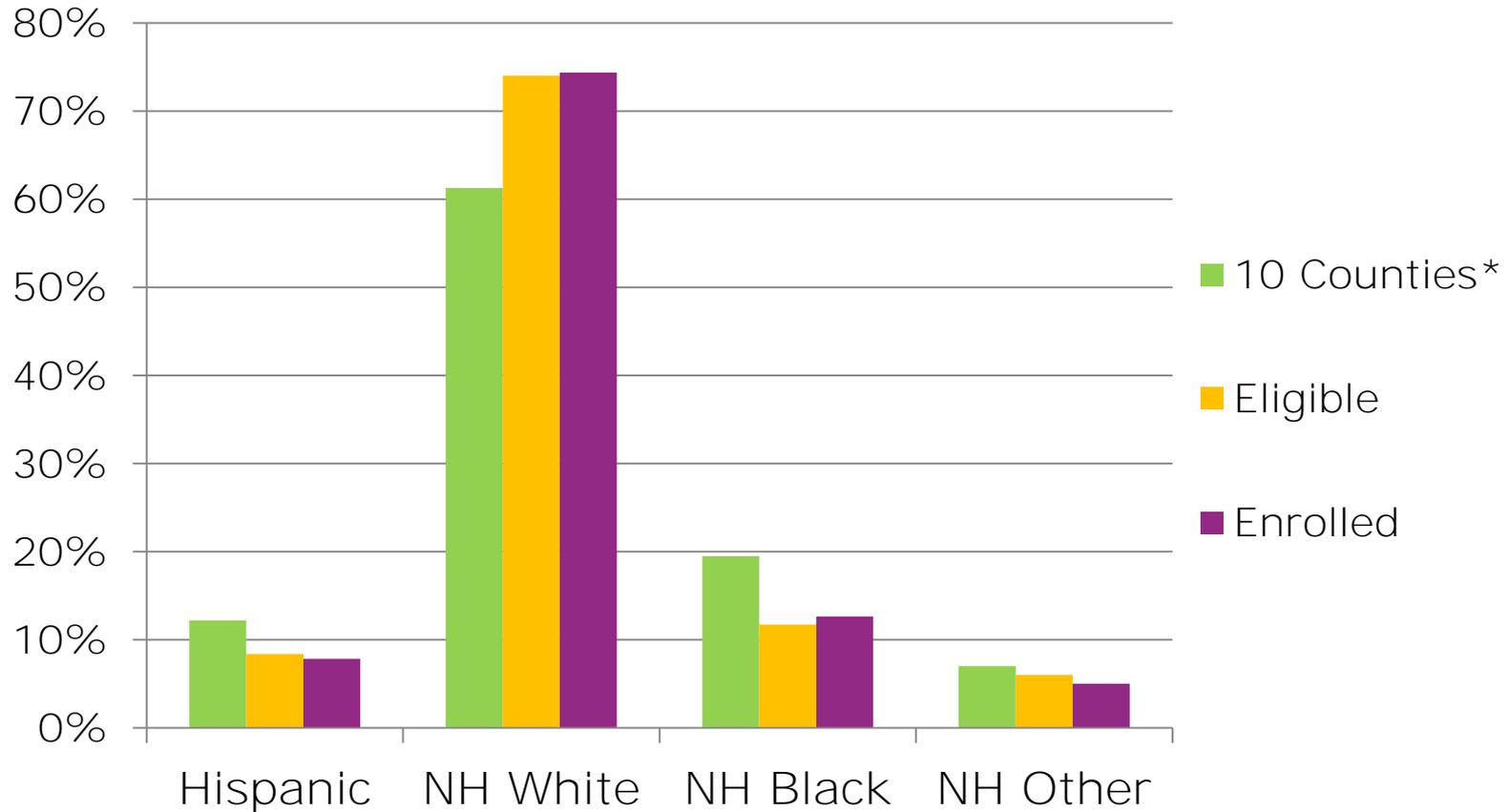
*Average race/ethnicity distribution in 10 counties from 2009 American Community Survey data.

Race/ethnicity Distribution Among Study Eligible and Enrolled Compared to County Population – **Enhanced Household**



*Average race/ethnicity distribution in 10 counties from 2009 American Community Survey data.

Race/ethnicity Distribution Among Study Eligible and Enrolled Compared to County Population – **Direct Outreach**



*Average race/ethnicity distribution in 10 counties from 2009 American Community Survey data.

Sample Size Considerations



- Attrition
 - Prior to birth- currently is at 20%
 - Following birth remains under study
 - Anticipate differential attrition for various subpopulations
- Item and Visit Completion rates
- Modeling using 3 different methods indicates potential attrition over 21 years to yield a population of about 40% of initial enrolled population

Sample Size Considerations



- Other national birth cohorts are sizing between 100 000 for countries the size of the UK or Japan to over 300 000 for China, which is planning 2 birth cohort studies.
- NCS not proposing threshold of rare disease-US has a legal definition of rare disease is a prevalence of about 0.06 % or 64 per 100 000 births
- Prevalence of 0.5 to 1 % for conditions of interest such as congenital heart disease, childhood cancer, and autism spectrum disorders because they are topics of separate NIH initiatives and Congressional mandates and supported by advocacy groups, and are expected to be addressed by the NCS. We have an implied, or in some cases, stated commitment to acquire data about these conditions.
- Boundary between normal variant and clinical condition is ever shifting. We should carefully consider what our rejection level should be because the sum of several uncommon but measurable conditions may be quite informative regarding whatever we may define as normal.

Cost drivers



- Recruitment
- Data Acquisition

Summary



- NCS is Congressionally mandated longitudinal birth cohort study beginning prior to or during pregnancy.
- Complex system of activities
- Vanguard recruitment is now in transition to retention
- For further information
 - <http://www.nationalchildrensstudy.gov>
 - ContactNCS@mail.nih.gov