

NCS Advisory Committee Draft Questions

Draft NCS Main Study Protocol

1. Various models of retention and attrition at different stages of the proposed NCS Study schedule indicate a plausible but optimistic projection of 1 to 2% attrition per year. Additionally, models and projections of compliance (or alternatively item completion and unit completion) for responding to the array of questions, observations, biological specimen and environmental sample collections yield plausible estimates of between 55 to 70% of all potential data points may be collected. In order to examine conditions or exposures that have a 5% or lesser prevalence in the general population, the NCS has targeted a study population of 100 000 remaining after 21 years. Given attrition between women enrolling into the study and giving birth into the study and an estimated 1.5% annual attrition, the target number of women to enroll is on the order of magnitude of 250 000. Do you have suggestions or comments on the target enrollment population?
2. In order to enroll 250 000 women in a reasonable time frame such as about 2 years per study location, the NCS needs to make adjustments to the sampling frame. The NCS is also committed to a probability sample to minimize bias meaning that any eligible woman has an equal chance of being enrolled as any other eligible woman. Adjustments to the current sampling frame that are under consideration are increasing the size of secondary sampling units, consolidating locations into new primary sampling units such that the expected yield of live births per year is increased, adding additional locations and primary sampling units, and pooling less dense locations into larger primary sampling units. Do you have comments or additional suggestions on adjustments to the sampling frame?
3. The Main Study will incorporate the collection of operational data elements to inform the ongoing recruitment and data collection process. The NCS plans interim analyses on some of the operational data elements in combination with an adaptive design to allow adjustments in recruitment strategies and tactics. For example, an interim analysis at landmarks such as one to follow the first 5000 women enrolled, then 10 000, 20 000, 50 000, 100 000, 150 000 and 200 000 could allow ongoing adjustments to recruitment strategies. All adjustments would be prospectively defined and described in the protocol and activated based on objective trigger conditions. Please comment on the general concept of using an adaptive approach to monitor and adjust recruitment.
4. The Main Study will utilize recruitment approaches informed by NCS Vanguard Study data and attempt to align particular recruitment strategies based on projections about the local environment. For example, in some localities a house to house recruitment approach may be efficient and cost effective while in others a provider based recruitment approach may be the more advantageous approach. Particular populations may be more responsive to one approach over another and the NCS would like to maintain flexibility to assure as complete and unbiased a sample as feasible. Please comment on using a flexible approach to recruitment.

5. The Main Study protocol emphasizes early data collection with a target of two visits during the first 20 weeks of pregnancy with the first as early as pregnancy is detectable and the second no less than 4 weeks and no more than 8 weeks after the first visit. A third pregnancy visit is targeted during the second half of pregnancy. Do you have additional comments or suggestions on the timing of visits during pregnancy?
6. The Vanguard Study currently has about 20% of enrolled women identified prior to conception and completion of a preconception visit. The efficiency of women contacted and enrolled in a preconception pool to those from that pool who become pregnant and give birth in the study is less than expected. Do you have any comments or suggestions on approaches to enrich the pool of all eligible women for efficient identification of women likely to become pregnant?
7. Continuing the theme of early data collection, the Main Study protocol is targeting data collection at birth, 2 months, 4 months, 6 months, 9 months and 12 months and then every 6 months until 60 months. Do you have any suggestions of comments on the proposed visit schedule?
8. Some child visits are scheduled as face to face visits and others as remote follow up using telephone, e-mail or web based modalities. The strengths of face to face visits are ability to collect specimens and samples by trained personnel and direct observation. The challenges of face to face visits are the resources and need to schedule. Please comment on the proposed balance between face to face and remote visits. What factors should we consider if we substitute any face to face visits with a remote visit or the reverse?
9. The proposed visit schedule targets landmark dates in the life course of each participant. If meeting a schedule is logistically and socially challenging, an alternative is a flexible visit schedule where, for example 3 visits should be scheduled in the first 6 months with a minimum of 4 weeks between visits? Similarly, subsequent visit schedules could be twice a year with a minimum of 5 months between visits. Potential advantages of a flexible visit schedule would be logistical options to cluster visits with NCS teams in selected geographic areas several times a year and analytic options to collect data on children at various ages. Please comment or provide suggestions on a flexible approach to the timing of data collection.

Provider Based Sampling

10. If the location within a Primary Sampling Unit of a provider service facility is the primary determinant of geographic eligibility, one option is that all women who visit the provider be eligible, no matter where they live. An alternative is that both the provider service facility address and the woman's residence address are within the Primary Sampling Unit. Please comment on both options.

11. An early step in developing a provider based sample is characterization of the provider practice with regard to the demographics and distribution of the women who seek care at the provider facility. Please comment on potential approaches when a provider practice has a unique demographic profile and the provider is not responsive or declines to work with the National Children's Study.
12. Recruitment into the Main Study is currently targeted for 2 year duration at any location. Please comment on potential approaches if a provider withdraws involvement with the study after several months.
13. Although most women seek prenatal care, not all do. Please comment on potential approaches to enroll women who do not seek prenatal care.
14. Some Primary Sampling Units may have fewer than 5 provider facilities and some may have more than 100. Please comment on approaches to provider selection and potential substitution in areas with few or many providers.