Sample Design Issues in The National Children's Study

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Abstract
The National Children's Study will examine the effects of the environment, as broadly defined to include factors such as air, water, diet, sound, family dynamics, community and cultural influences, and genetics on the growth, development, and health of children across the United States, following them from before birth until the age of 21 years. This paper describes the national probability sample with counties at the first stage of sampling and two methods for the second stage of sampling, geographical segments and providers. Initial promising results testing an alternate provider-based recruitment strategy within the geographical segment method have led to recent explorations of designing a provider-based sampling method at the second stage in three study locations. We discuss the statistical, sampling, operational, and recruiting issues and implications of these alternative second stage sampling methods. While this paper is focused on these design and operational experiences, the NCS continues to explore additional design options.

Key Words: Sampling, provider-base, children, women

1. Introduction

The National Children's study was congressionally mandated by the Children's Health Act of 2000. The Children's Health Act states that that the study's planners shall "plan, develop, and implement a prospective cohort study, from birth to adulthood, to evaluate the effects of both chronic and intermittent exposures on child health and human development" and that the study shall "investigate basic mechanisms of developmental disorders and environmental factors, both risk and protective, that influence health and developmental processes." It goes on state that 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."

One of the key early decisions for the NCS was to determine the study's sampling design. In 2004, after much debate, and based on the advice of an expert panel, which was later endorsed by a Federal Advisory Committee, a decision was made to utilize a national probability sample as the main sampling design for the NCS (Section 2).

In the first stage of sampling, Study Locations (generally corresponding to single counties) were selected from the full complement of counties. Later that same year, eight of the Study Locations in that sample were selected as potential locations for conduct of a pilot study, termed the Vanguard Study. The counties included two densely populated "certainty" locations, four metropolitan locations, and two relatively rural non-metropolitan locations. There were two locations in each of the four U.S. Census regions. Seven contracts were ultimately awarded for recruitment and data collection is seven of the Study Locations. Many strategies were considered for the second stage of sampling. The goal of obtaining a nationally representative sample of births, with enrollment of the mothers during pregnancy and, for a subset of women, before pregnancy ultimately guided the planners to choose a geographic based approach. In this approach each study location was divided into segments and a sample of segments were selected. Women residing in households within the sampled segments were potentially eligible for the study and a door to door household approach was used to enumerate household members and identify, screen, and recruit eligible women. Preliminary analyses indicated that this approach was too costly for expansion to all counties for the main study (Section 3).

Thus, three modified approaches to recruitment were tested, each in 10 of the originally selected study locations. The three approaches included an enhanced household approach, an approach that utilized direct outreach to potential participants and a third approach that recruited women through their prenatal care providers. Early results of this pilot were encouraging, particularly the provider assisted recruitment approach which proved to be more efficient than the other two approaches. However, even with this recruitment approach, the second stage of sampling was based on geography such that a woman identified at a provider office was still required to live within a selected study segment to be eligible for inclusion in the study (Section 4).

To test a method that might yield even greater efficiencies and cost savings, a provider based sampling approach was proposed as the fourth and final arm in the sampling/recruitment substudy. In this approach locations at which women receive prenatal care (rather than geographic segments) are the units that comprise the second stage of sampling. All locations of prenatal care, within a selected county, are listed. A measure of size, based on the number of first prenatal care visits, is assigned to each provider location. Provider locations are selected with the probability of selection proportional to the measure of size. This approach is currently being tested in three Study Locations (Section 5).

2. Sample Design Options

Many sample design models were considered for the National Children's Study. Two large scale reports were prepared documenting alternative sample design options and their associated merits and implications (Westat, 2002 and Strauss et al. 2004). Several meetings were organized to review and discuss these reports and other sample design materials. The upshot of these efforts was that two main models emerged as potentially viable for the NCS: Household-based and Center-based.

2.1 Household-Based Model

This model employs an area sampling frame, as is generally used for household surveys that involve face-to-face interviewing. The model employs home-based screening, in which a large national probability sample of households is contacted and screened to locate pregnant women. Additionally, non-pregnant women (not surgically sterile) of

childbearing years (18-49) are followed during the recruitment period and enrolled if they become pregnant. Multiple stages of probability sampling are employed:

- Selected Primary Sampling Units (PSUs): metropolitan areas or counties)
- Selected Segments (groups of Census blocks and housing units within)
- Eligible women within listed housing units

2.2 Center-Based Model

This model employs a nonprobability approach. It involves the selections of a number of health care institutions (centers). The purposefully selected (though not probabilistically) set of centers would be throughout the nation. Each center is responsible for recruiting a number of women and/or pregnancies over the entire recruitment period. In some respects, this could be thought of as a two-stage selection process:

- Purposely selected centers
- Women and/or pregnant women within selected centers and likely expanded to recruit others through various community and other outreach mechanisms

2.3 Model Selection

Ultimately, the concurrence from the Sample Selection Workshop panel was that the probability–based household sampling model was preferable in its ability to support key objectives, including:

- Greater coverage of women, particularly those outside the traditional medical system
- Greater clustering of sample into neighborhoods – potential linkage advantages
- Potential to recruit sample women early - prior to conception or soon after conception

Both models have histories of successful implementation, but just not with the combined scope, size, and detail of the planned NCS Main Study. So, feasibility was still in question.

3. NCS Vanguard Study Sample Design

3.1 Multiple Stage Design Features

3.1.1 PSU Selection

For the first stage of sample selection, a wide range in the number of sample PSUs was under consideration; from as few as 30 to as many as 800. The end points in the range were supported by the more extreme positions of minimization of costs (30) and of coverage of rare environmental exposures (800). It was difficult to be able to definitely determine the optimal number of PSUs. With several different study objectives, an optimal solution that counterbalanced relative costs and between-PSU sampling variance was not easily discernible. However, some operational cost modeling indicated certain substantial inefficiencies below 1,000 births per PSU. This argued for an initial target of about 100 PSUs. After addressing concerns with the smallest PSUs being able to support potential increased sample size requirements, the final PSU design resulted in the selection of 110 sample PSUs including 18 large certainty PSUs, 66 non-certainty metropolitan PSUs, and 26 non-certainty non-metropolitan PSUs.

3.1.2 Segment Formation and Selection

The second stage of selection was the selection of area segments with the sampled PSUs. The area segments were formed by combining contiguous census blocks. A range of about 10 to 20 sample segments were selected in each PSU. The four basic steps in the process included:

- Segment stratification
- Measure of size determination
- Finalizing segment sampling frame
- Sample segment selection: single-stage or two-stage in large PSUs

3.1.3 Listing

All dwelling units (DU) with the geographic boundaries of the sampled segments were listed. In a few segments deemed to be too large the segments were divided into smaller 'chunks' with one chunk randomly selected prior to listing.

3.1.4 Enumeration

A household interview was attempted to be conducted at each listed DU to enumerate all eligible women. All eligible women were asked to complete a pregnancy screener.

3.1.5 Enrollment

Pregnant eligible women were recruited to enroll in the NCS and non-pregnant eligible women (the preconception cohort) were asked to participate in followup interviews to ask about pregnancy status.

The rough design goals across all the stages of sample selection were 250 births per year for four years per PSU (~100) for a total of about 100,000 births nationally.

3.2 Initial Vanguard Implementation

Seven PSUs were identified to implement the initial Vanguard Study sample design as part of feasibility testing. All stages were conducted in these seven PSUs starting in early 2009, recruiting through the summer of 2010. Again, the sample design goal was for about 250 births per PSU per year (~1,000 per PSU over 4 years). Thus, a one-year yield of about 1,750 would have been expected across these seven PSUs.

3.3 Results

After a year in the field only about 800 pregnant women had been enrolled. The lack of effectiveness of initial household-based recruitment methodology motivated the exploration of other potential alternate recruitment methods.

4. Alternate Recruitment Substudy

4.1 Alternate Recruitment Strategies

To explore ways to possibly improve the rates at which women would enroll into the NCS, three alternate recruitment strategies were attempted. The underlying geographic-based segment sample design was unchanged. The operation steps outlined in Section 3.a through the listing of DUs apply to each of the three alternate recruitment strategies. Ten additional PSUs were assigned to each of the three alternate recruitment strategies.

4.1.1 Enhanced Household Recruitment (EHR)

This recruitment strategy was built off of experiences from the initial household recruitment efforts. Besides bringing best Initial Vanguard Study practices of enumeration, screening, and enrollment to bear, a greater effort was made to engage the community as a whole.

4.1.2 Direct Outreach Recruitment (DOR)

The Direct Outreach recruitment strategy is also known as the Two-tiered High-Low Intensity recruitment strategy. During recruitment, this strategy used marketing, direct mail, and other referral techniques to enroll a broad based population in larger geographic areas beyond the originally selected sample segments into a Low Intensity NCS. After a period of time, during which participants were periodically provided with web-based, mail-in, or telephone-based brief questionnaires to complete, those participants within the original sampled segments are invited to engage in a higher intensity data collection effort. The high intensity data collection used the same instruments and protocols as used in EHR and PBR strategies.

4.1.3 Provider-Based Recruitment (PBR)

With provider-based recruitment (PBR), women were approached to participate in the NCS through the health care system. Study Center staff identified and engaged health care providers that provided services to the sample county. Specifically, by secure and HIPPA-compliant means, the Study Center staff processed lists of women addresses to identify those who lived within the selected sample segment boundaries. Enrollment could have occurred at the provider location or through referral off-site. Regardless, informed consent was administered by Study Center staff not provider staff.

4.2 Results

4.2.1 Enhanced Household Recruitment (EHR)

Overall, EHR results were fairly consistent with some limited improvement relative to what had been observed in the seven initial Vanguard Study PSUs. Of women approached, the EHR recruitment rate through Pregnancy Screener, Consent and finally Enrollment was about 50%. Yields of enrolled pregnant women were still below expectations.

4.2.2 Direct Outreach Recruitment (DOR)

Overall, the DOR results were about the same as those observed for the EHR strategy. However, when yields of enrolled pregnant women were properly restricted to those residing in the original set of sample segments (excluding women in supplementary adjacent segments and beyond), they fell well below expectations.

4.2.3 Provider-Based Recruitment (PBR)

When yields of enrolled pregnant women were restricted to the original set of sample segments, they were on par with the EH results. However, the recruitment of a preconception cohort within PBR was extremely limited relative to both EHR and DOR.
Overall, the PBR recruitment rates (Pregnancy Screener, Consent & Enrollment) were the highest among the three strategies at about 60%. However, this result was likely influenced by the fact that women being recruited were more likely to be pregnant under PBR than either EHR or DOR. Of operational note, the need to recruit all provider locations was time consuming and resource intensive.

4.2.4 Summary

Overall, no "magic bullet" was found to identify an alternate recruitment strategy that was cost effective in establishing both a sample of pregnant women and a preconception cohort. However, PBR did exhibit some potential operational efficiency for recruiting a sample of pregnant women.

5. Provider-Based Sampling (PBS) Pilot Study

Despite the promise of PBR, some operation limitations have been identified with overlaying provider-based recruitment on top of the geographic-based sample. In particular, virtually all providers must be approached to seek their cooperation in allowing their patients addresses to be screened as to whether they live in any of the sample segments throughout the PSU. Additionally, some providers will only have a handful or fewer of their patients that actually live within one of the sample segments.

A different approach to recruitment is to select eligible women through providers but without the restriction to sampled segments, using a strategy termed Provider-Based Sampling (PBS). It has been suggested that a provider-based sample underlying a provider-based recruitment approach would address the above operational concerns. In response to this suggestion, the NCS has entered into agreements with three additional SCs to participate in the PBS Pilot study.

Below we provide a discussion of PBS guiding principles, general sample design parameters, and the application of the Eligibility Screener followed by a high-level overview of the various operational components under discussion and development: List and Frame Creation, Provider Location Sample Selection, Provider Location Recruitment, and Sampling of Women.

5.1 PBS Guiding Principles

A goal of the NCS PBS Pilot study is to sample women in the PSU as early in their pregnancy as possible via their prenatal care providers. The aim is to have an equal probability sample of the eligible women over the two stages of sampling within the PSU (i.e., the selection of sample provider locations and the sampling of women within the sampled provider locations). For statistical and operational efficiency, the design calls for sampling provider locations with probabilities proportional to their estimated numbers of eligible women (MOS's) in the study enrollment period.

To illustrate the probability proportional to estimated size (PPES) selection process, consider the selection probability of woman β in provider office α. This probability is given by:

$$P(\alpha\beta) = P(\alpha)P(\beta \mid \alpha)$$
$$= \frac{aMOS_\alpha}{\Sigma MOS_\alpha}\frac{b}{MOS_\alpha} = \frac{ab}{\Sigma MOS_\alpha} = f$$

where $P(\alpha)$ is the PPES (probability proportionate to size) selection probability for location α and $P(\beta \mid \alpha)$ is the rate for sampling women at that office, *a* is the number of provider offices sampled, *b* is the desired number of women sampled at each sampled provider location, and *f* is the constant overall selection probability for every eligible

woman. The sampling rate applied within provider location α is then $k = b / MOS_\alpha$. The sample size will be *b* if the measure of size is the actual size, but otherwise it will depart from *b*. Small departures from *b* are inevitable and not serious, but large departures are problematic. Thus good measures of size should be sought.

5.2 General PBS Pilot Study Sample Design Parameters

The goal is to understand the process and feasibility of Provider Based Sampling. For planning purposes the target is 250 births in each PSU. We are currently assuming that 80% of consented/enrolled women will be retained through to the birth and that 80% of sampled eligible women will agree to consent/enroll into the NCS. So, this means about 315 (250/0.8) women will need to be consented/enrolled in each PSU and that about 400 (315/0.8) eligible women will need to be identified through the application of the eligibility screening process in each PSU. The last figure of 400 eligible women is used in the calculation to determine the overall sampling rate needed in each PSU.

In each PSU, it is estimated that between 15 and 25 provider offices will be selected. The actual number sampled in each PSU will be dependent on the distribution of the provider location Measure of Size (MOS) in each PSU's frame. And in a complementary sense, the average number of eligible women sampled from each of the selected provider offices will roughly be between 25 and 15.

For example, if 20 provider offices are randomly sampled, then the aim would be to sample about 20 eligible women from each office (in practice, the number selected from an office will differ from 20 because of inaccuracy in the MOS). In reality, some very large provider locations may be included with certainty and more than 20 eligible women would be expected to be selected from these locations; also very small provider locations may also require special procedures.

Current plans are to enroll the sample of women over a four month period. The sampling rates for sampling women within the selected provider locations will be computed based on this assumption.

5.3 Application of Eligibility Screener

The screening criteria in the Eligibility Screener are:

- Pregnant
- Age (18-49)
- First health care provider visit for this pregnancy (to one of the provider locations on the frame)
- Resides in the sample PSU

5.4 Provider Location List/Frame Creation

Conceptually, there are two valid approaches to sampling women through a provider-based sampling method. One is based on sampling women from a frame of provider locations with addresses within the sample PSU; in this case, all women receiving services are eligible irrespective of the locations of their residences. The other is based on sampling women from a frame of provider locations that serve women who reside in the sample PSU; in this case some provider locations may be outside the sample PSU but only women who reside in the PSU are eligible. Both are statistically valid if applied consistently across all PSUs. However, the second method has the advantages that it is more attuned to PSU geographic boundaries and it would provide for a more statistically

consistent design if some PSUs were given the option of employing a geographic-based within-PSU sampling scheme. With these advantages in mind, the NCS Provider-Based Sample pilot study adopted the second approach for all three SCs.

The first step in the sampling process is to create a list frame of provider locations. Since the aim of the NCS recruitment is to enroll women in the study as early as possible in their pregnancies, the aim is to construct a complete list of such provider locations for women who reside in the sample PSU. To avoid multiple chances of selection, the women are then sampled only for their first prenatal visit. For statistical efficiency, the provider locations should be sampled with probabilities proportional to size (PPS), using measures of size (MOSs) that approximate their numbers of first prenatal visits for women living in the sample PSU.

The four key elements of the frame creation process will consist of:

- Generate a list of all provider locations that provide prenatal services to women who reside in the sample PSU;
- Collect information about the characteristics of each provider location guided by the use of the Provider-Based Sampling (PBS) Frame Creation Questionnaire and/or other data sources;
- Compute the MOS based on data from the PBS Frame Creation Questionnaire and/or other data sources;
- Supplement the frame file with additional provider location characteristics from auxiliary data sources, including geocoding. The aim is to add characteristics that may serve as useful stratification or sorting variables during provider location sample selection.

Birth certificate data is one of the potential other data sources to inform the list and frame building operation. If available in full detail, the information on attendant name and address can be used to identify provider locations that provider birth delivery services to women. Additionally, by linking to the address of the mother, these data can be used to inform the MOS for each provider location that corresponds to women who reside in the sample PSU. This has a potential advantage over the use of the PBS Frame Questionnaire which requires the provider location to distinguish there count of women receiving first prenatal care by whether the women reside in the sample PSU or not. For some provider locations, especially those near the sample PSU border, this accuracy of this delineation could have a sizeable impact on the MOS determination. So, to the extent that the births correspond to providing first prenatal care services, the processing of birth certificate data could provide real advantages.

To the extent possible, the study centers will attempt to employ both frame building processes and use the information to evaluate the merits of the alternative methods. Potential evaluation analyses are presented in Appendix B, Section 1.

5.5 Provider Location Sample Selection

Once the frame has been constructed and checked, the sample of provider locations will be selected. The sample will be selected using a stratified PPS sample design. The variables used for stratifying and sorting the provider locations will come from the PBS Frame Creation Questionnaire, birth certificate data, geocode information and any other auxiliary characteristics added to the frame file by each Study Center. Provider locations will be selected with probability proportionate to size where the MOS is intended to be

the number of first prenatal care visits from women who reside in the sample PSU. Where the number of first prenatal care visits are not available, consideration will be given to use of proxy measures, e.g. the number of deliveries from birth certificate data files.

In some cases, location level information for a multiple location practice may be unavailable and only practice level information is reflected on a single record on the frame. If such a practice is selected, then an additional stage of sample selection may be employed to randomly select one (or more) of the practice locations.

The number of sample provider locations to be selected will depend on several factors and parameters. Most critically, it will depend on the total required sample size, the expected number of women to be selected from each sample provider location, the number of locations on the frame and the distribution of the MOS across all the locations on the frame. Since the last two factors will likely vary among the SCs, the number of sampled provider locations may vary, as well.

To avoid highly inefficient operational situations, a lower bound threshold for the MOS for a provider location will likely need to be determined, below which the location would not be eligible for selection.

5.6 Provider Location Recruitment

The SCs will contact each provider location to gain their cooperation in participating in the PBS pilot study. In order to maintain the desired sample size yield, substitute provider locations will also be identified and associated with each selected original sample location. Substitute provider location recruitment will be activated if the original location refuses to participate. As an additional step to ensure sufficient sample yield for the PBS Pilot study, substitutes will also be activated for out-of-scope original provider locations. The corresponding response and yield rates will be computed to evaluate the provider location recruitment processes. The rate definitions are presented in more detail in Appendix B, Section 2.

5.7 Sampling of Eligible Women

More than one statistically valid method can be employed in selecting the sample of eligible women within each sample provider practice location. (A woman's eligibility is defined by those women who reside in the sample PSU and are coming in for their first prenatal care visit.) Possible methods could be a systematic sample taking every n^{th} eligible woman or a time-based sample, taking say every n^{th} day and all (or a sample of) eligible women seen on the sampled days. The value of n will vary by sampled provider location, depending on the measure of size used in selecting the provider location. A more detailed discussion of the various methods are discussed in Appendix A. Operational considerations at the provider location level and by the SC staff will need to be taken into account in determining plausible procedures. One of these operational considerations relates to the use of "prescreening".

5.8 Use of Prescreening

To compute the sampling rates, the number of eligible women is used. However, the number of women that will be selected to actually go through the screening process to determine eligibility is dependent on the degree of prescreening that takes place in each sampled provider location. Recall, the screening criteria in the Eligibility Screener are

based on pregnancy, age, first health care provider visit for this pregnancy (to one of the providers on the frame), and resides in the sample PSU.

If the list of women visiting a provider office during the selected sampling period (say, a random week) has no prescreening applied, then the number of women that will need to be contacted and screened for eligibility would be very large relative to the number of eligible women. A 10 to 1 ratio at a minimum might be expected. The SC staff time and costs to carry out this large-scale screening could be very large. However, this effort would be substantially reduced if the provider location office staffs could apply some prescreening criteria. Logical choices of criteria would include: pregnant (yes), age (18-49), and first visit to this office. Possibly, residency could be explored, as well, but care would need to be taken to avoid making incorrect county of residence classifications. There would still need to be further screening by SC staff to determine whether the woman had a prior visit associated with this pregnancy to another provider office on the sampling frame.

The Eligibility Screener instrument would then be applied by the SC staff to the reduced list of prescreened women to fully assess a sampled women's eligibility. In deciding on the use of prescreening, consideration will need to be given to how to balance the effort between the provider location office staff and the SC staff. A key issue is how reliably the provider location office staff would carry out their component of this work. The particular concern is that the provider location office staff may erroneously screen out some of the eligible women. A failure to screen out some ineligible women is not serious since these women will be identified by the SC staff using the Eligibility Screener.

Appendix B, Sections 3 - 4, presents the various women level response, eligibility, consent, and yield rates that could potentially be used to evaluate the performance of the PBS methods and operations for sampling women.

References

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Appendix A: PBS Within-Provider Sampling Protocol Development Material

The eligibility criteria for screening are pregnant, age (18-49), first prenatal care visit for this pregnancy, and resident of sample county.

Our general goal is to identify about 20 eligible women over a four-month recruitment period. Note that the active recruitment period may be more or less than 4 months.

There are different ways to select the random sample of women. Discussions need to be held with each sampled provider location to determine a method that is best suited to the location's operations, logistics, and availability of information.
Responses to general questions along with an assessment of the various criteria associated with each of the four methods for sampling women outlined below will be

used to determine which method is most appropriate for each provider location. The chart following Appendix B illustrates the application of the alternate methods for various sampling rates in charts A through F.

Method 1
A sample from a listing of all women would be systematically selected and screened for eligibility through the Eligibility Screener.

Method 2
A 1 in every x (2 or more) weeks skip interval is applied to randomly select a subset of weeks and each day of the selected week is in sample. *X* is selected such that systematic subsampling of women from the list is not needed; the list is the sample.

Method 3
A 1 in every x (2 or more) weeks skip interval is applied to randomly selected subset of weeks and each day of the selected week is in sample. *X* is selected to include more sample weeks than under the Method 2, but in doing so now requires that systematic subsampling of women from the list be implemented.

Method 4
A 1 in every x week(s) skip interval is applied to randomly selected subset of weeks and a rotating string (<5) of s day(s) of the week for each sampled week is in sample. The combination of x and s are selected such that systematic subsampling of women from the list is not needed; the list is the sample.

Appendix B: Potential Evaluation Analyses

1. Provider Location List and Frame Building

1.1 Coverage Assessment
A critical component in evaluating the PBS substudy is to assess the completeness of the list of provider locations. Undercoverage of provider locations, especially if it is differential by certain critical subpopulations, can introduce additional biases. There are a few ways to assess the coverage of the list/frame of provider locations that provide "first prenatal care" to women. These may include:

- Compare the total MOS across all provider locations on the list to historically known number of births in the sample PSU.
- Where possible, compare a historic birth certificate attendant-based list of provider locations to the list built from administrative records identified as "first prenatal care" provider locations from the Frame Questionnaire.
- Review birth records from all or a subset of birthing hospitals/centers from the recruitment period to determine if attendant name and address identify provider locations not on the provider location list. This can also be used to assess the degree to which no prenatal care births could be covered through the sampling of birth records from birthing hospitals/centers.

1.2 Provider Location Measure of Size (MOS) Accuracy
The MOS for the PBS substudy is the number of "first prenatal care" visits to a "doctor" of women who reside in the sample PSU. The efficiency of the PBS probability based sampling relies on an accurate MOS, both in terms of determining the provider location

selection probability and the within provider location sampling rate of women. The accuracy of the MOS can be assessed in a couple ways:

- Comparisons of MOS as derived from processing birth certificate based information versus MOS as reported by provider locations. This is of particular interest in providers located outside or near sample PSU boundaries as it may be difficult for provider locations to provide an MOS properly restricted to only those patients who reside in the sample PSU.
- For sampled provider locations (originals and recruited substitutes), the actual sample yields of eligible women will be compared to the MOS from the frame.

1.3 Provider Location Characteristics Comparisons

The provider location characteristics are used to stratify the provider locations into homogenous groups from which one or more provider locations are selected from each stratum. The efficiency in this process to reduce variances in the sample is impacted by the accuracy of the measures of these characteristics. To the extent possible, comparisons will be made between birth certificate based information and similar dimensions collected in the Frame Questionnaire completed by provider locations.

2. Sampled Provider Location Recruitment

One of the key measures in evaluating the operational feasibility of PBS is whether sampled provider locations are willing to participate or not. And for those not willing to participate, assess the ability to recruit substitute provider locations. Relevant measures are outlined below:

2.1 Provider Location Recruitment Response Rate

$$\frac{Total\ No.of\ Recruited\ Original\ Provider\ Locations}{Total\ No.of\ Inscope\ Original\ Provider\ Locations}$$

Response rates need to remove the out-of-scope units from the denominator, in this case, the out-of-scope original provider locations. This rate is used when "officially" reporting on the PBS Provider Location Recruitment Response Rate.

2.2 Provider Location Recruitment Response Rate with Substitution

$$\frac{\begin{array}{c}Total\ No.of\ Recruited\ Original\ Provider\ Locations\\ +Total\ No.of\ Recruited\ Substitute\ Provider\ Locations\\ linked\ to\ Inscope\ Original\ Provider\ Locations\end{array}}{Total\ No.of\ Inscope\ Original\ Provider\ Locations}$$

As above, the out-of-scope original provider locations are removed from the denominator. Participating substitutes "linked" to in-scope non-participating original provider locations are included in the numerator. Note that this rate should not be thought of as a representation of the PBS's provider location recruitment response rate, instead to the degree that substitute provider locations are like the original provider locations they are replacing; it provides some indication of the degree to which non-response bias at the provider location level may be mitigated.

2.3 Provider Location Recruitment Yield Rate

$$\frac{\begin{array}{c}\textit{Total No.of Recruited Original Provider Locations}\\ +\textit{Total No.of Recruited Substitute Provider Locations}\\ \textit{linked to Inscope Original Provider Locations}\end{array}}{\textit{Total No.of Original Provider Locations}}$$

3. Operational Evaluations of Methods for Sampling Women

There is a very wide range of operational characteristics associated with the sampled provider locations. These differences in provider location characteristics can very across several dimensions, including size; willingness to allowing eligibility screening to take place in the office, to maintain a list of patients, or to prescreen patients on eligibility; and the method for identifying and contacting sampled patients (i.e., release of PII information and possible HIPPA requirements).

In order to support the process of selecting a sample of women from provider locations with varied characteristics and operational constraints, alternative sampling methods with corresponding sets of protocols were developed. Guidance materials and training were provided to assist in the determination and use of an appropriate sampling method.

An evaluation of the operational aspects of the sampling methods may include a review of the following dimensions:

3.1 Sampling Method Selection Process

- What methods chosen?

3.2 Women Listing Procedures

- Provider location staff or field staff

3.3 Prescreening Procedures

- Frequency and pattern of use
- Prescreened ineligibles listed with reason, listed only, only counts, or no information on number?
- Proportion of women prescreened as ineligible

3.4 Contacting Sampled Women

- Real-time or retrospectively
- HIPPA requirements

4. Recruitment, Use of Eligibility Screener, and Enrolling Women

4.1 Eligibility Screener Response Rate (ESRR)

$$\frac{\sum \textit{No.of Sampled Women with Completed Eligibility Screener}_{ij} * w_{ij}}{\sum \textit{No.of Sampled Women}_{ij} * w_{ij}}$$

where w_{ij} = (No. of women listed and eligible for sampling$_{ij}$ + No. of women prescreened as ineligible$_{ij}$ (Pre_Screened_Status = 2))/No. of women listed and eligible for sampling$_{ij}$ for each provider location$_i$ and sampling visit$_j$. The weighting factor w_{ij} is needed in

order to compute the Eligibility Screener Response Rate properly. There needs to be an accounting of the women who are prescreened as ineligible and not even asked to complete the Eligibility Screener. If no eligibility prescreening of women was conducted at a particular sampling visit, then $w_{ij} = 1$. This response rate is a weighted proportion across all provider location visits of all the women approached to complete the Eligibility Screener that are willing to do so.

4.2 Eligibility Rate (ER)

$$\frac{\sum No.of\ Eligible Women_{ij}}{\sum No.of\ Sampled Women with Completed\ Eligibility\ Screener_{ij} * w_{ij}}$$

As above, in order to compute the Eligibility Rate properly, there needs to be an accounting of the women who are prescreened as ineligible and not asked to complete the Eligibility Screener, otherwise the computed rate will overstated the true Eligibility Rate. In particular, the estimated number of women who would have been asked to complete the Eligibility Screener but didn't due being prescreened as ineligible need to be accounted for in the denominator.

4.3 Eligible Women Consent/Enrollment Rate (EWCR)

$$\frac{\sum No.of\ Women who Consent to Participate_{ij}}{\sum No.of\ Eligible Women_{ij}}$$

From the completed Eligibility Screener, this rate is the proportion of all the women eligible for enrollment into the NCS that consent to do so.

4.4 Overall Yield Rate

$$\frac{\sum No.of\ Women who Consent to Participate_{ij}}{\sum No.of\ Sampled Women_{ij} * w_{ij}}$$

In other words, the overall yield rate is the product the three individual rates above: Overall Yield Rate = Eligibility Screener Response Rate (ESRR) * Eligibility Rate (ER) * Eligible Women Consent Rate (EWCR).

4.5 Distribution of Stage of Pregnancy (Gestational Age) at Time of Enrollment and First Study Visit

Enrolling women and beginning data collections as early as possible in the pregnancy is a major operation goal of the NCS to support efforts to understand the impact of environmental exposures on women and their children. Various measures can be considered:

- Proportion of women enrolled within two months of becoming pregnant (gestational age is <=2 months)
- Proportion of women enrolled in the first trimester, second trimester, third trimester, or at birth

Appendix A - Methods for Sampling Women within Selected Providers

Interpretation of Sampling Rate (1 in X week(s))

	Sampling rate = 1 in X week(s)					
	1	2	3	4	5	6
# of Sampled Periods	13	6 or 7	**4** or 5	**3** or 4	2 or 3	**2** or 3

A. Within-Provider Location Sampling Rate: 0.45

Within-List Skip Interval:

String of Consecutive Days (s)*	Sampling rate = 1 in X week(s)	
	1	2
5	**2.2**	**1.1**
4	**1.8**	
3	**1.3**	
2		
1		

B. Within-Provider Location Sampling Rate: 0.3

Within-List Skip Interval:

String of Consecutive Days (s)*	Sampling rate = 1 in X week(s)		
	1	2	3
5	**3.3**	**1.7**	**1.1**
4	**2.7**	**1.3**	
3	**2.0**	**1.0**	
2	**1.3**		
1			

C. Within-Provider Location Sampling Rate: 0.2

Within-List Skip Interval:

String of Consecutive Days (s)*	Sampling rate = 1 in X week(s)				
	1	2	3	4	5
5	5.0	**2.5**	**1.7**	**1.3**	**1.0**
4	4.0	**2.0**	**1.3**	**1.0**	
3	**3.0**	**1.5**	**1.0**		
2	**2.0**	**1.0**			
1	**1.0**				

D. Within-Provider Location Sampling Rate: 0.125

Within-List Skip Interval:

String of Consecutive Days (s)*	Sampling rate = 1 in X week(s)					
	1	2	3	4	5	6
5	8.0	4.0	**2.7**	**2.0**	**1.6**	**1.3**
4	6.4	**3.2**	**2.1**	**1.6**	**1.3**	**1.1**
3	4.8	**2.4**	**1.6**	**1.2**	**1.0**	
2	**3.2**	**1.6**	**1.1**			
1	**1.6**					

E. Within-Provider Location Sampling Rate: 0.06

Within-List Skip Interval:

String of Consecutive Days (s)*	Sampling rate = 1 in X week(s)					
	1	2	3	4	5	6
5	16.7	8.3	5.6	4.2	**3.3**	**2.8**
4	13.3	6.7	4.4	**3.3**	**2.7**	**2.2**
3	10.0	5.0	**3.3**	**2.5**	**2.0**	**1.7**
2	6.7	**3.3**	**2.2**	**1.7**	**1.3**	**1.1**
1	**3.3**	**1.7**	**1.1**			

F. Within-Provider Location Sampling Rate: 0.03

Within-List Skip Interval:

String of Consecutive Days (s)*	Sampling rate = 1 in X week(s)					
	1	2	3	4	5	6
5	33.3	16.7	11.1	8.3	6.7	5.6
4	26.7	13.3	8.9	6.7	5.3	4.4
3	20.0	10.0	6.7	5.0	4.0	**3.3**
2	13.3	6.7	4.4	**3.3**	**2.7**	**2.2**
1	6.7	**3.3**	**2.2**	**1.7**	**1.3**	**1.1**

NOTE: Within-list skip intervals that are less than 4 are in bold. Within-list skip intervals that are below 1 have been suppressed.

* Note that s = 5 corresponds to the entire week being in sample.

Method 1	List of women from each day is maintained. Periodically, the skip interval is systematically applied to cumulative list to select the sampled women for contact.
Method 2	Subsample of weeks (1 in x week(s)) are selected for listing women each day of each sampled week such that no further systematic selection of women is needed. Note that this solution is not viable for Tables D, E, and F.
Method 3	Subsample of weeks (1 in x week(s)) are selected for listing women each day of each sampled week with a systematic selection of sampled women needed, as well.
Method 4	Subsample of weeks (1 in x week(s)) are selected for listing women on a rotating subset of s days (s<5) each sampled week such that no further systematic selection of women is needed.