



**GUIDANCE, EXAMPLES AND
TOOLS FOR PROBABILITY
SAMPLING WHEN
DESIGNING
A POPULATION-BASED
BIOMONITORING STUDY**

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention

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PREFACE

This document provides guidance, tools and examples to help select an appropriate probability sampling design for a population-based biomonitoring study or survey within a state. The intended audiences of this document include the following:

- State health departments and their biomonitoring study collaborators
- Centers for Disease Control and Prevention (CDC) programs that provide resources to their recipients
- CDC programs and other programs that present surveillance data, including data from biomonitoring studies and surveys

The guidance will be useful for developing measures to be displayed on the National Environmental Public Health Tracking Network (Tracking Network), and can be used when:

- Designing biomonitoring studies, with the aim of making data from these studies useful for public health surveillance
- Evaluating existing biomonitoring data from Tracking Program state/local recipients
- Evaluating existing biomonitoring data from non-Tracking Program state/local recipients and other agencies or programs

This document only focuses on biomonitoring studies for population health surveillance and on examples of population-based or probability sampling. This guidance complements information from other guidance documents developed by the Association of Public Health Laboratories (APHL) and the Council of State and Territorial Epidemiologists (CSTE):

- APHL's Guidance for Laboratory Biomonitoring Programs: Developing Biomonitoring Capabilities: <https://www.aphl.org/aboutAPHL/publications/Documents/EH-Oct2019-Biomonitoring-Guidance.pdf>
- CSTE's Biomonitoring in Public Health: Epidemiologic Guidance for State, Local, and Tribal Public Health Agencies: <http://www.cste2.org/webpdfs/BioMonISFINAL.pdf>

The guidance does not replicate topics already addressed in these documents, such as communicating biomonitoring results, types of specimens, or laboratory protocols for collecting and storing specimens.



DEFINITIONS

Target population: The complete collection of observations we want to study

Sample: a sub-set of a population

Sampling frame: a list or map of sampling units in the population from which a sample may be selected

Sampling unit: a unit that can be selected for a sample. In studying human populations, observation units are often individuals.

Observation unit: an object on which a measurement is taken

Public health surveillance: the ongoing, systematic collection, analysis, and interpretation of health-related data essential to planning, implementation, and evaluation of public health practice



INTRODUCTION

Biomonitoring

Biomonitoring assesses human exposure to an environmental chemical by measuring that chemical, its metabolite(s), or reaction product(s) in human blood, urine, milk, saliva, adipose, or other tissue [1]. In the environmental public health field, measurements in individuals are generally taken together to constitute a population [1]. Biomonitoring helps us determine the environmental chemicals to which people have been exposed [2]. Biomonitoring can reveal spatial, temporal, and socio-demographic trends of body burdens of these chemicals in populations for public health surveillance. We can use these data to identify populations at risk for environmental exposures or to determine the effectiveness of interventions, laws, and regulations [1].

In exposure studies or surveys, detecting an environmental chemical in human tissue is not enough to say that the chemical is causing disease [2]. Other research studies and additional information on health outcomes are needed to determine whether the chemical level measured is associated with disease [2]. However, results from exposure studies can help inform and prioritize research on health effects from exposure to environmental chemicals [2].

The Centers for Disease Control and Prevention's (CDC) National Environmental Public Health Tracking Program (Tracking Program) maintains the Environmental Public Health Tracking Network (Tracking Network) (<https://ephtracking.cdc.gov/>). The Tracking Network displays standardized environment and health surveillance data and measures from national, state, and local partners. This information can be used to show trends over time and make comparisons among states. These data can also be used to identify common issues among states and support regional responses.

The Tracking Network currently displays the 50th and 95th percentile and geometric mean concentration levels of analytes from the following chemical groups:

- metals
- perfluoroalkyl and polyfluoroalkyl substances
- personal care and consumer products metabolites
- pesticide metabolites
- polycyclic aromatic hydrocarbon metabolites
- phthalate metabolites
- disinfection by-products
- volatile organic compounds
- tobacco metabolite

The analytes are measured in urine or blood in the U.S. population, collected as part of CDC's National Health and Nutrition Examination Survey (NHANES). The results are presented in the National Report on Human Exposure to Environmental Chemicals (<https://www.cdc.gov/exposurereport/index.html>). These data are national in scope, and a goal of the Tracking Program is to add state-level biomonitoring data to the Tracking Network.



In 2012, a review of biomonitoring data available to state tracking programs revealed that several of the same chemicals were measured in state biomonitoring studies [3]. The review also revealed some disparities in study populations, laboratory methods, and population sampling methods used in studies that produced these data [3]. These differences, particularly the use of non-probability or convenience sampling instead of probability population sampling, precluded the development of standard data that could be representative of a population and displayed on the Tracking Network for public health surveillance. Unlike probability sampling, convenience sampling does not allow generalization of the findings to the entire population from which the sample is drawn [4]. However, convenience sampling can be useful in pilot or exploratory studies, or if limited resources do not allow selecting a representative sample [4].

Biomonitoring studies

For our review of state biomonitoring data, we broadly classified the biomonitoring studies into the following categories:

- **Mandatory reporting:** Passive collection of data from mandatory reporting of chemical exposures or body burden levels to a public health agency (e.g., childhood blood lead testing).
- **Population-based study or surveillance:** Conducted to detect and measure exposure in a population (e.g., pregnant women or children). Such studies can be used to study and monitor spatial, temporal, or demographic differences, or to evaluate the efficacy of public health actions.
- **Targeted public health investigation:** Conducted in response to health concerns in a community resulting from the discovery of environmental contamination or a cluster of disease from a possible chemical exposure (e.g., targeting residents using well water, or those near a hazardous waste site). (Note: some studies target a community or geographic area because of a health or exposure concern but use a probability sampling design to allow the results to be representative of that population.)
- **Disease investigation or rapid response:** Conducted in response to an exposure event to evaluate clinical measures in individuals and support diagnosis of poisonings and assessment of need for medical treatment (e.g., investigating extremely elevated blood lead levels).
- **Research project:** Done independently or in collaboration with an existing research effort (e.g., Markers of Autism Risk in Babies - Learning Early Signs [MARBLES]).

These categories show that biomonitoring studies are conducted for various uses. The purpose and objectives of the project will determine the type of biomonitoring study selected, the target population, sampling frame, and the study design. The study design includes selecting the appropriate population sampling design. Using the classifications above, this guidance focuses on population-based studies and surveys or targeted studies within a state. The biomonitoring studies in the categories listed above could use probability or non-probability sampling methods. However, the focus of this document is on population-based studies or targeted studies that use a probability sampling design. Such studies produce findings that can be generalizable to the target population and can be used for population health surveillance. The study can be a state-level study or community-level within the state.



Probability sampling designs

Overview: In a probability sample, each unit in the population has a known non-zero probability of selection, and units are randomly selected to be included in the sample. This sample can be used to make inferences about the larger target population [5]. Probability sampling designs all begin by identifying a sampling frame, which reflects all the persons in the target population of interest. The individuals or elements of the sampling frame could be aggregated to become primary sampling units (PSUs) for multi-stage or cluster sampling. A cluster or PSU consists of a group of elements (e.g., census tracts, ZIP codes, or households). After selecting the PSUs, you can use various approaches to randomly select study participants within selected PSUs. Some methods for probability sampling include the following:

1. Simple random sampling of all elements within the sampling frame [6, 7, 8, 9]
Every eligible person within the population of interest has the same chance or probability of being selected for the study. Using random selection, a sample of persons from this population is selected for the study or survey. Other types of random sampling include systematic, stratified and cluster sampling.

Pros and cons: Simple random sampling is the simplest form of probability sampling. However, you need a complete list of all eligible persons before sampling which might not be available, especially for large populations. Because simple random sampling gives each eligible person an equal chance of being selected, it may result in samples spread out over a large geographic area. The logistics of contacting people over a wide geographic area can be challenging [8, 9]. For these reasons, simple random sampling is rarely used.

2. One-stage sampling [6, 7, 10]
One-stage sampling requires a list of primary clusters. In a cluster sample, observation units in the population are aggregated into larger sampling units called clusters. When applying this method, you first identify the primary clusters (e.g., households) for the study area. The households are randomly selected from the study area, and all persons in each selected cluster (household) are then included in the study sample. [Example 1A](#) below provides insights on applications of one-stage sampling.

Pros and cons: One stage sampling is simpler to implement than multistage sampling. A complete list of units within each sampled primary cluster is needed but is rarely available for large populations and is difficult to assemble. Because of this, studies often use multistage sampling.

For one stage sampling to be beneficial, any given cluster should reflect the variation in the overall target population. One stage sampling can introduce cluster effects (i.e., concentration of people based on similar factors) for population estimates when all persons in selected clusters are included [9].

3. Multistage sampling [6, 7, 11, 12]
 - a. Two-stage sampling



Two-stage sampling includes a primary and a secondary cluster. The study area population is divided into groups (primary cluster), then households from these groups (secondary cluster). Groups are randomly selected, then households within these groups are randomly selected. All persons within selected households are then included in the study (See [examples 2A-F](#) below.)

b. Three-stage sampling

Three-stage sampling has 3 levels of clusters. The population in the study area is divided into primary, secondary, and tertiary sampling units. First, a sample of primary units is randomly selected. A sample of secondary units is then randomly selected from the selected primary units. Finally, a sample of tertiary units is randomly selected from the selected secondary units. (See [Example 3A](#) below.)

Examples of geographic units of primary, secondary and tertiary clusters

One-stage	Two-stage	Three-stage
<ul style="list-style-type: none"> Primary – Households 	<ul style="list-style-type: none"> Primary – Census Blocks Secondary – Households 	<ul style="list-style-type: none"> Primary – Boroughs Secondary – Census Blocks Tertiary – Households

Pros and cons: Multistage sampling is cost effective and practical, especially for large populations [9]. For example, it is not possible to list all households in a state for a sample. However, with two-stage sampling, you could use a county as the primary cluster and census blocks as the secondary cluster. Then you would only have to identify households in the census blocks that have been randomly selected for your sample. This makes this method feasible for large populations. However, multi-stage sampling can produce more sampling errors than other probabilistic methods [9]. If the members of the different clusters are different from one another, this reduces the efficiency, i.e., the precision, of the estimates.

4. Using an existing population-based study or survey

Some programs may wish to recruit from existing population-based surveys by asking to add interest-gauging questions for participation in a biomonitoring study. Information on persons who agree to participate would then be transferred to the biomonitoring study team, and separately followed-up on for participation. (See [Example 4A](#) below.)

Pros and cons: This method may be less resource intensive as there is an existing infrastructure to recruit participants. However, the biomonitoring study would inherit any limitations of the existing study, for example some existing studies only focus on school-aged children, therefore, limiting the biomonitoring study to this population.

Sources and types of sampling biases

Under coverage is failing to include all of the target population in the sampling frame [5]. Therefore, some members of the population are inadequately represented in the sample. This may make it difficult to provide estimates for hard-to-reach or marginalized populations (e.g., certain race/ethnic minorities) [13].



Voluntary response bias occurs when the sample consists only of those who volunteered to participate in the survey. That is, the sample members are self-selected volunteers. The respondents may not be representative of the whole population. This could lead to biased estimates therefore, affecting the validity of the estimates.

Non-response occurs when only a fraction of the sampled population responds to a survey such that they are no longer representative of the whole population. That is, the respondents differ meaningfully from the non-respondents. Low response rates could lead to underestimating certain populations (e.g., younger populations) [13]. This could lead to biased estimates, thereby affecting the validity of the estimates.

In general, participation rates in epidemiological studies have been declining over the past 30 years [14]. Some reasons for this include the increasing burden for participants from survey assessments, biologic sampling, and requests for follow-ups [14]. For biological sampling, biomonitoring studies may use invasively collected matrices such as blood and adipose tissue or non-invasively collected matrices such as urine and saliva. Non-invasively collected matrices result in increased participation rates [15].

It has also been increasingly difficult to find and talk to potential study participants. Some reasons for this include the increasing number of unlisted telephone numbers; use of cell phones; telephone screening; and unsolicited mail and phone calls [14].

Improving participation rates may require evaluating recruitment methods. Face-to-face recruitment usually has higher participation rates than telephone or less personal methods [14]. Using mixed methods for data collection, such as an alternative data collection method for non-respondents might help increase participation. An example is using telephone interviews for persons who did not respond to a mail survey that is recruiting study participants [14].

Oversampling methods can also be used to sample larger numbers of subpopulations of interest, thereby increasing their coverage. These methods can be used to improve the reliability and precision of estimates from subgroups [16]. (See [Examples 5A-C](#) below.)

Studies or surveys using a probability sample design can improve the representation of population subgroups in their sample by using features such as stratification [17]. This involves dividing the population into smaller, mutually exclusive groups called strata [17]. The strata are formed on population members shared attributes or characteristics, e.g., income, race/ethnicity and population density in geographic area. Each stratum is sampled separately using probability sampling methods, and then the results are combined across strata to provide estimates for the target population [17]. See examples [2A](#), [3A](#) and [5B](#) below for examples of applying stratification.

Sample weights

The weighting of sample data permits researchers to produce estimates of the statistics that would have been obtained if the entire eligible population had been surveyed [18]. Sample weights can be considered measures of the number of persons in the target population represented by the particular sampled participant [18]. Weighting takes into account the different probabilities of selection or inclusion, survey nonresponse, and differences between the distribution of the target population and



the final sampled population [18]. For data analysis, only one final weight per sampled participant is used which adjusts for all these factors.

Weighting is used for valid statistical inference, to reduce bias, and to keep the weighted sample distribution close to the distribution of the target population, especially when oversampling is used for specific subpopulations [19]. Weighting reduces bias, e.g., nonresponse bias, but does not remove all nonresponse bias.

No one protocol exists for computing weights; rather, computing weights varies among studies depending on study design, including sample selection and recruitment, and availability of information on the target population and nonresponse [20]. When computing a weight for each sampled individual, a combination of the following steps is usually used [20]:

1. Determine the base weight to account for sample selection
2. Adjust for nonresponse
3. Adjust further for undercoverage, i.e., incomplete sampling frame coverage
4. Adjust further to account for distribution in the target population by key characteristics

The final weight for the sampled individual is the product of the value generated in each step above. This final weight should appear on each respondent data record as a variable to be used in data analysis. Some datasets could include the individual component weights as well as the final weight.

STUDY DESIGN GUIDANCE, EXAMPLES AND TOOLS

Some considerations and questions to ask when designing a biomonitoring study are listed below. These also indicate stages at which guidance can be targeted:

- What is the aim of the study?
- What is the target population?
- What probability sampling design will be used?
- Who will be measured (*randomly selected persons or everyone in household*)?
- What is an appropriate sample size for the study?
- Do I need to oversample certain populations?
- How do I compute weights for study participants?
- What demographic information will be collected and how will it be formatted?

The flowchart, frequently asked questions (FAQ) section with more detailed responses, and examples that follow provide guidance, examples and tools to help answer these questions. The guidance assumes that the study aim is population health surveillance, and only focuses on examples of probability sampling.



Flow-chart

What is the aim of the study?

What is the target population?

What probability sampling design will be used?

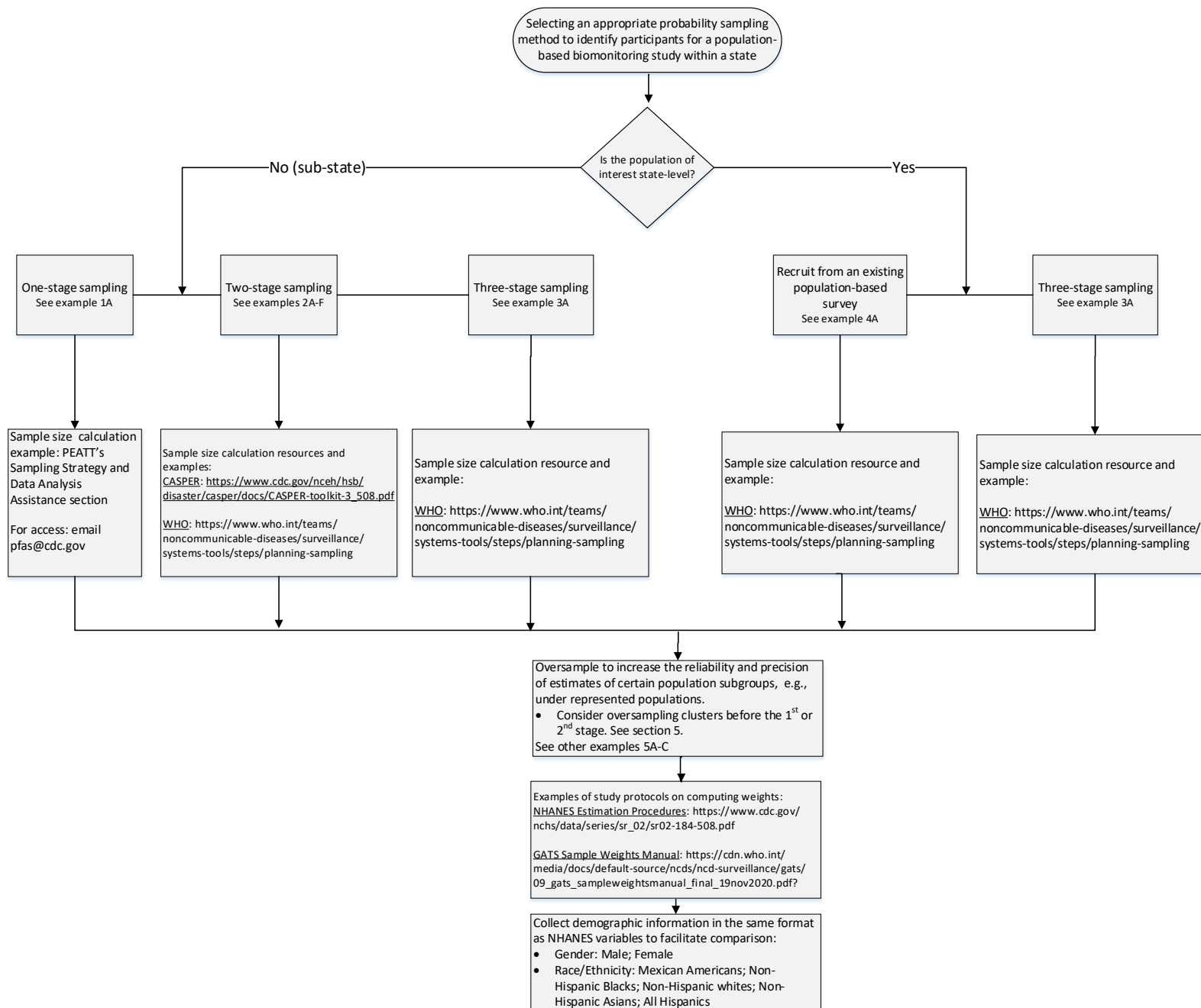
Who will be measured (randomly selected persons or everyone in household)?

What is an appropriate sample size for the study?

Do I need to oversample certain populations?

How do I compute weights for study participants?

What demographic information will be collected and how will it be formatted?



The flow-chart above guides the selecting of an appropriate probability sampling method to identify participants for a population-based biomonitoring study within a state.

If the population of interest is sub state-level, select from the following probability sampling designs and resources:

- One-stage sampling. See example 1A. Sample size calculation example: PEATT's Sampling Strategy and Data Analysis Assistance section. For access: email pfas@cdc.gov.
- Two-stage sampling. See example 2A-F. Sample size calculation resources and examples: CASPER: https://www.cdc.gov/nceh/hsb/disaster/casper/docs/CASPER-toolkit-3_508.pdf; and World Health Organization (WHO): <https://www.who.int/teams/noncommunicable-diseases/surveillance/systems-tools/steps/planning-sampling>
- Three-stage sampling. See example 3A. Sample size calculation resource and example: WHO: <https://www.who.int/teams/noncommunicable-diseases/surveillance/systems-tools/steps/planning-sampling>

If the population of interest is state-level, select from the following probability sampling designs:

- Recruit from an existing population-based survey. See example 4A. Sample size calculation resource and example: WHO: <https://www.who.int/teams/noncommunicable-diseases/surveillance/systems-tools/steps/planning-sampling>
- Three-stage sampling. See example 3A. Sample size calculation resource and example: WHO: <https://www.who.int/teams/noncommunicable-diseases/surveillance/systems-tools/steps/planning-sampling>

For all probability sampling designs, consider oversampling to increase the reliability and precision of estimates of certain population subgroups, e.g., under-represented populations. Consider oversampling clusters before the 1st or 2nd stage. See section 5. See other examples 5A-C

For all probability sampling designs use the following resources for computing weights for study participants: NHANES Estimation Procedures: https://www.cdc.gov/nchs/data/series/sr_02/sr02-184-508.pdf; and GATS Sample Weights Manual: https://cdn.who.int/media/docs/default-source/ncds/ncd-surveillance/gats/09_gats_sampleweightsmanual_final_19nov2020.pdf?

For all probability sampling designs, consider collecting demographic information in the same format as NHANES variables to facilitate comparison:

- Gender: Male; Female
- Race/Ethnicity: Mexican Americans; Non-Hispanic Blacks; Non-Hispanic whites; Non-Hispanic Asians; All Hispanics



Frequently asked questions when designing a biomonitoring study

- *What is the aim of the study?*
The focus is on population-based studies or surveys, or targeted studies within a state, which produce findings that can be generalizable to the target population, and that can be used for population surveillance.
- *What is the target population?*
State- or community-level studies
- *What probability sampling design will be used?*
You will find guidance and examples of some probability sampling designs in the “[Examples](#)” section below. These include guidance on using one-stage, two-stage and three-stage designs and existing population-based surveys or programs.
- *Who will be measured (randomly selected persons or everyone in household)?*
The goals of the study and resources will determine if the biomonitoring data will be collected on individuals or the entire household.
- *What is an appropriate sample size for the study?*
Two resources offer examples of sample size calculation:
 - **Per- and Polyfluoroalkyl Substances (PFAS) Exposure Assessment Technical Tools (PEATT)**
This resource provides information on how to conduct a one-stage cluster sampling approach and estimate sample size at the household level. For a copy of this guidance, email the Centers for Disease Control and Prevention at pfas@cdc.gov.
 - **Community Assessment for Public Health Emergency Response (CASPER)**
This resource provides information on two-stage cluster sampling in which 30 clusters are selected, and then seven households in each cluster are interviewed. It also provides methods for how to modify this 30 × 7 design. The sampling methodology is available from the Centers for Disease Control and Prevention at: <https://www.cdc.gov/nceh/casper/sampling-methodology.htm>.

A publicly available resource that can help you calculate an appropriate sample size for any study:

 - **STEPwise approach to surveillance (STEPS) Sample Size Calculator and Sampling Spreadsheet**
This resource from the World Health Organization (WHO), available at <https://www.who.int/teams/noncommunicable-diseases/surveillance/systems-tools/steps/planning-sampling>, provides a spreadsheet with a sample size calculator. It also provides a sampling spreadsheet with worksheets for:
 - Probability proportional to size (PPS) sampling
 - Simple random sampling, and
 - Weighting your data
- *Do I need to oversample certain populations?*
We oversample to increase the reliability and precision of estimates of certain population subgroups.



For example, the National Health and Nutrition Examination Survey (NHANES) used oversampling to sample larger numbers of subgroups of interest, such as minorities, adolescents, and older adults [16]. This increases reliability and precision of estimates in these population subgroups [16]. Rural populations might be another subgroup of interest when considering oversampling to help ensure that you achieve a large enough N value for appropriate statistical power.

For sub-populations that are at least 10% of the total population, a general sample will usually produce reliable estimates [21]. For subpopulations between 1% and 10% of the total population, the oversampling methods described in the [Examples 5A-C](#) below are needed [21].

By considering oversampling clusters before the first or second stage, you have a better opportunity to net a desired sample size.

- Possible oversampling methods include increasing the number of units (e.g., census blocks) in your first stage [22]. You could also increase the number of units (e.g. households) in the second stage [22].
- An example of oversampling to increase cluster selection is a modified application of the CASPER study design whereby the 30 × 7 design is modified to a 35 × 7 therefore increasing the N value by 16.6% [23].

The NHANES study design, as another example, draws its sample in the following stratified, four stages [24]:

- Stage 1: PSUs are first stratified according to population size, and then PSUs are selected from each stratum. These are mostly single counties or, in a few cases, groups of contiguous counties with probability proportional to a measure of size (PPS).
- Stage 2: The PSUs are divided up into segments (generally city blocks or their equivalent). As with each PSU, sample segments are selected with PPS.
- Stage 3: Households within each segment are listed, and a sample is randomly drawn. In geographic areas where the proportion of age, ethnic, or income groups selected for oversampling is high, the probability of selection for those groups is greater than in other areas.
- Stage 4: Individuals are chosen to participate in NHANES from a list of all persons in selected households. Individuals are drawn at random within designated age-sex-race/ethnicity screening subdomains. On average, 1.6 persons are selected per household.

In stage 3, households from each segment are randomly drawn. For geographic areas where the proportion of age, ethnic, or income groups selected for oversampling is high, the probability of selection for those groups is greater than in other areas [16]. This can be replicated in other biomonitoring studies that apply probability sampling to oversample populations of interest.

- *How do I compute weights for study participants?*

Two examples of study protocols that can serve as resources for computing weights are listed below:

- NHANES provides information on the health and nutritional status of the noninstitutionalized civilian resident population of the United States. The sample for NHANES is selected using a complex, four-stage sample design. NHANES carries out sample weighting in three steps. The first step computes base weights to compensate for unequal probabilities of selection. The second step adjusts for nonresponse to reduce bias. In the third step, sample weights are post stratified to the reference (target) population. The procedures for computing these weights are detailed in the [National Health and Nutrition Examination Survey, 2015 – 2018: Sample Design and Estimation Procedures](#) document (https://www.cdc.gov/nchs/data/series/sr_02/sr02-184-508.pdf).



- The Global Adult Tobacco Survey (GATS) is a nationally representative household survey of adults 15 years of age or older, and its used to enhance the capacity of countries to design, implement and evaluate tobacco control interventions. GATS uses a geographically clustered multistage sampling methodology to identify households to be included in the study. GATS recommends a three-step approach in computing sample weights: compute a base weight for each sample respondent, adjust the base weights for nonresponse, calibrate the adjusted weights to known population totals. **Their Sample Weights Manual** (https://www.who.int/tobacco/surveillance/en_tfi_gats_sampleweightsmanual_v2_final_15dec2010.pdf) details requirements and recommendations on how to approach computing sample weights for a country GATS. The step-by-step manual can be modified to country-specific sample design and analysis needs.

- *What demographic information will be collected and how will it be formatted?*
Consider collecting demographic information in the same format as NHANES so that you can compare local estimates with national estimates.



Examples

1. One-stage sampling

Identify the primary cluster unit (e.g., households). Households are randomly selected from the study area. All individuals in each selected cluster/household are included in the sample.

Example 1A: Per- and Polyfluoroalkyl Substances (PFAS) Exposure Assessment Technical Tools (PEATT) — One-stage cluster sample enrolling entire households within a PFAS-affected community

Program: Centers for Disease Control and Prevention (CDC)

Access: To request PEATT documentation, email CDC at pfas@cdc.gov

Methods:

- The sampling frame is a list of households in a community of interest
- A complete listing of all households within the sampling frame is obtained
- A sample size for the study is determined
- Households from the list are randomly selected to fit the selected sample size
- All household members are recruited to participate in the study

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Statistically based. Information learned can be applied to others in the targeted population (those not tested). • Presents formulas to be used to determine the sample size with step-by-step example of how to apply it. • Mentions Census.gov as backup resource if municipal water/well sampling frame information are unavailable. 	<ul style="list-style-type: none"> • Information learned can only be applied to others within the sampling frame. • Need to have some level of statistical experience to understand the formulas. Most significantly, applying the formulas requires a sampling frame which requires a complete list of all households in the area and the total population of the geographic area of interest. For water contamination issues, a list of those on public water or on private well water is needed, 	<ul style="list-style-type: none"> • Can modify to select sampling frame based on geographic area (i.e., not an exposed community). • Can only use this strategy if you know the number of households within the geographic area being assessed (or census data), total population of the area, and analyte data (either from preliminary testing in that area or from NHANES).



<ul style="list-style-type: none"> • Gives two options for calculating sample size based on whether local preliminary biomonitoring results from the exposed community are available and if not, then states to use NHANES data for the analyte of interest. • Gives formula for adjustment of household sample size based on an estimate of non-response. 	<p>depending on the exposure; the latter may be hard to come by.</p> <ul style="list-style-type: none"> • Census.gov information on housing units is only available at the state and county level and for towns and cities with populations greater than 5,000. That means one can't use the calculations in the PEATT for communities lacking addresses of households on municipal water supply or private wells (if exposure applies to analyte[s] of interest) or those with <5,000 people. • The formulas can't be used if neither preliminary nor NHANES data are available (e.g., for emerging contaminants). • Need to have an idea of non-response rate to use the formula. 	
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2. Two-stage sampling

The state population is divided into groups (primary cluster). Groups are randomly selected, then persons within these groups are randomly selected and included in the study.

Example 2A: Survey of the Health of Wisconsin — Two-stage cluster sampling

Reference: Nieto FJ, Peppard PE, Engleman CD, McElroy JA, Galvao LW, Friedman EM, et al. The Survey of the Health of Wisconsin (SHOW), a novel infrastructure for population health research: rational and methods. BMC Public Health 2010; 10:785. doi: [10.1186/1471-2458-10-785](https://doi.org/10.1186/1471-2458-10-785)

Link: <https://www.med.wisc.edu/show/>

Methods:

- The target population at initial selection is Wisconsin non-institutionalized/non-active duty adult residents aged 21 – 74 years
- The sampling frame is a list of census block groups or clusters of census block groups in Wisconsin state
- The initial sampling frame is constructed using Census 2000 data to generate 4,388 census blocks groups (CBG) or clusters of CBGs as the primary sampling units (PSUs)



<ul style="list-style-type: none"> • CBGs with <40 households are merged with a neighboring CBG to form a cluster • CBGs that fall in sovereign native American nation territories with no authorization to be included in survey are excluded • PSUs are stratified according to 1) congressional district and 2) percentage of population living below 100% poverty level • CBGs are randomly selected within each stratum using the Sampford explicit probabilities proportional to size without replacement method (36-72 CBGs usually are selected) • A list of households addresses by CBG is generated using U.S. Postal Service sequence delivery files • From the household sampling frame, 12-38 addresses are randomly selected using simple random sampling 		
Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Provides a mechanism to collect subjective (self-reported) and objective (physical exam and biospecimen) individual data. 	<ul style="list-style-type: none"> • Results are limited to those from the same communities. • Requires many resources. • Household canvassing requires significant staff numbers to accomplish in timely manner. 	<ul style="list-style-type: none"> • SHOW infrastructure can be used to do specific biomonitoring studies. • To increase participation, a public relations campaign is launched in communities 6-8 weeks before recruitment in that location. • The selected households are mailed an information package 1-3 weeks before the team arrives in the selected block group. The package includes a description of the project, how households were selected, and benefits of participation.

Example 2B: Minnesota East Metro PFAS Biomonitoring Projects —Two-stage cluster sample enrolling randomly-selected adults likely to be exposed to PFAS and from a PFAS-affected community

Program: Minnesota Biomonitoring: Chemicals in People, Minnesota Department of Health.

Reference: Landsteiner A, Huset C, Johnson J, Williams A. Biomonitoring for perfluorochemicals in a Minnesota community with known drinking water contamination. J Environ Health. 2014 Dec;77(5):14-9

Link: <https://www.health.state.mn.us/communities/environment/biomonitoring/projects/pfas.html>

Methods:

- The study location was a community with known PFAS exposures
- The sampling frame is a list of households from two groups in the community:



- People using community water— billing addresses of all households receiving municipal water service from city of Oakdale before January 1, 2005 (before the remediation)
- People using private wells— private well sampling results were used to identify all households with PFOS or PFOA above trace levels
- A household survey was sent to a random sample of people on water billing records, and to all homes with contaminated private wells
- The households were asked to enumerate all eligible adults who lived there. Eligibility was restricted to those who lived in Oakdale before January 1, 2005
- A sample size, determined by state legislature, was identified for the study
- Eligible adults were randomly selected from the list to fit the selected sample size. For anyone who declined, replacements were selected

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> ● Population-based sample. ● Results can be applied to others from the same communities (those not tested). ● Using an existing list as sampling frame was an economically efficient means of recruitment. ● With extensive prior agency outreach and community interest, participation rates can be high. ● These sampling frames work especially well when water is the source of exposure. ● Able to assess some differences between participants and refusals. 	<ul style="list-style-type: none"> ● Results are limited to those from the same communities and not the general population. ● Renters and non-homeowners are underrepresented on water billing lists, so may be missing important, possibly vulnerable sub-populations. (This was addressed in the third study by including a group of renters, but it was difficult to find a sampling frame and participation rates were lower.) 	<ul style="list-style-type: none"> ● Community outreach key to make residents familiar with issue/study and likely to participate. ● Important to consider health equity issues and alternate ways to include renters and non-homeowners. ● Don't have to restrict residence length.

Example 2C: Washington Environmental Biomonitoring Survey (WEBS) — Two-stage sampling to measure exposure in the general population of WA state

Program: Washington State Department of Health



Links: <https://www.doh.wa.gov/Portals/1/Documents/1500/WEBSOverview2013.pdf>

<https://www.doh.wa.gov/Portals/1/Documents/1500/WEBSFactSheet.pdf>

Methods:

- The study area is Washington State
- The sampling frame is a list of census block groups in Washington state
- 70 census block groups were randomly selected from the state
- 27 housing units were randomly selected from each census block group
- All household residents aged 6 years and older were invited to participate in the survey
- 1422 participants from 666 households were included in the survey

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Population-based sample. • Results can be applied to others from the same communities (those not tested). • Measured analytes also measured by NHANES: speciated arsenic, 12 metals (antimony, barium, beryllium, cadmium, cesium, cobalt, lead, molybdenum, platinum, thallium, tungsten and uranium), pesticide metabolites (chlorpyrifos, and four pyrethroids), bifenthrin metabolites, BPA and phthalates. 	<ul style="list-style-type: none"> • Children <6 years were not included in the sample. 	<ul style="list-style-type: none"> • Online publication of the results by population characteristics, which the local health departments and community can access to understand the chemicals populations are being exposed to.

Example 2D: Community Assessment for Public Health Emergency Response (CASPER) — Two-stage cluster sampling design in which 30 clusters are selected and then seven interviews are completed in each of the 30 clusters

Program: Centers for Disease Control and Prevention (CDC)



Link: <https://www.cdc.gov/nceh/hsb/disaster/casper/overview.htm>

Methods:

- A sampling frame boundary is defined and includes a list of census blocks in that boundary
- A sample of 30 census blocks, weighted by household numbers (using information from the U.S census), is selected from within the sampling frame. Use sampling with replacement
- Census blocks are visited by on-the ground teams over 3 days to gather seven interviews per census block
- Each interview asks about everyone within the entire household
- Residential units are selected systematically by dividing total units (using census information) by 7 and visiting each nth residence. Units are replaced by adjacent units after three failed attempts at contact
- Results are weighted based on census block size and completion rate (if unable to achieve seven interviews in each block)

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Some states/counties/localities already have experience in using CASPER for post-disaster health surveillance and disaster preparation. • A national disaster epidemiology coalition is available for support. 	<ul style="list-style-type: none"> • A list of all clusters within the sampling frame is required. • Household canvassing requires significant staff numbers to accomplish in timely manner. 	<ul style="list-style-type: none"> • CASPER sampling methodology can be used to identify potential study participants. However, other appropriate and more feasible methods must be used to contact those persons and to collect their samples for the study (e.g., via mail). • In rural areas, clusters might have fewer than seven households which might require modifying the traditional 30 (clusters) x 7 (households) design of CASPER. Rural area clusters (census blocks) with fewer than seven households might make it hard for sampling teams to interview the needed number from that cluster.



Example 2E: Optimizing cluster survey design for planning schistosomiasis preventive chemotherapy — School-based two-stage cluster sampling implementation

Reference: Knowles SCL, Sturrock HJW, Turner H, Whitton JM, Gower CM, Jemu S, et al. Optimising cluster survey design for planning schistosomiasis preventive chemotherapy. *PLoS Negl Trop Dis* 2017; 11(5): e0005599.

Link: <https://doi.org/10.1371/journal.pntd.0005599>

Methods:

- The sampling frame was a list of primary schools in a health or educational school district
- 15-20 primary schools were randomly selected, and then 30 children were randomly selected per school
- Children aged 10 - 14 years were eligible for participation
- Eligible children were line up and a sampling interval was used to select the required 15 participants of each sex
- The sample size was determined based on precision-based sample size calculations that took into account spatial heterogeneity in prevalence of schistosomiasis using methods from Lohr, S. *Sampling: design and analysis*. Boston , MA: Cengage Learning; 2010

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Could use schools as distribution points for recruitment material and collection points for samples. 	<ul style="list-style-type: none"> • Designed to sample school age children. Would need to send information home with children to families to recruit for sampling. Would be biased toward people with school-age children. Therefore, this structure might not be suitable for other biomonitoring studies. • Home-schooled children are left out of sampling frame. • Study was based on detection of schistosomiasis endemicity. The number needed to sample will likely not translate exactly for biomonitoring. 	<ul style="list-style-type: none"> • Could be modified at the levels of sampling such that schools are randomly selected from within a county or a primary care area. • Could also do probability-based sampling for the first stage instead of simple random sampling to oversample more populated areas or certain populations of interest.



Example 2F: Two-stage cluster sampling based on census block and household units

Reference: Smith DA, Akira A, Hudson K, Hudson A, Hudson M, Mitchell M, Crook E. The effects of health insurance coverage and the doctor-patient relationship of health care utilization in high poverty neighborhoods. *Prev Med Rep* 2017; 7:158–61.

Link: <https://doi.org/10.1016/j.pmedr.2017.06.002>

Methods:

- The target population is defined based on census tract
- The primary sampling frame is a list of census blocks in a defined census tract, and the primary sampling unit is randomly selected census blocks from within the tract, where the number of census blocks selected is proportional to the number of blocks in the tract
- The secondary sampling unit is five randomly selected housing units from within each sampled census block
- The selected houses are contacted either by letter or a home visit

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • By randomly selecting houses from within a census block, eliminates the labor-intensive need to go door-to-door and could recruit by mailer. • Relatively simple strategy. 	<ul style="list-style-type: none"> • Recruitment of five selected households might be difficult if by mail (generally low response rate). • Five randomly selected houses might not be enough. 	<ul style="list-style-type: none"> • Could be modified to where sampling frame is county, primary sampling unit is census tract, and secondary unit is census block. Entire blocks could be contacted by overlaying blocks with a GIS layer with address and zip, and send mailers targeting census block.



3. **Three-stage cluster sampling**

The population is divided into primary, secondary and tertiary sampling units (e.g., counties, cities, households). First, a sample of primary units is randomly selected. A sample of secondary units is then randomly selected from the selected primary units, then a sample of tertiary units is randomly selected from the selected secondary units.

- a. Three-stage cluster sampling at the **city-level**

Example 3A: New York City Health and Nutrition Examination Survey (NYC-HANES)

Links: <https://www.nyc.gov/site/doh/data/data-sets/new-york-city-health-and-nutrition-examination-survey-how-to.page>

<https://www1.nyc.gov/assets/doh/downloads/pdf/hanes/hanes-manual.pdf>

<https://www.ncbi.nlm.nih.gov/pubmed/26844121>

<https://www.ncbi.nlm.nih.gov/pubmed/16776895>

Methods:

- New York City is divided into about 20,000 segments, then 144 segments are randomly selected; stratified by borough
- The primary sampling unit is segments which are an aggregation of census block groups (probability proportional to size)
- The secondary sampling unit is households within the primary sampling unit (simple random sample)
- The tertiary sampling unit is participants within households (simple random sample)

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Instruments and laboratory methods benchmarked against the national HANES. 	<ul style="list-style-type: none"> • Only city-wide estimates available. • Small sample sizes for some demographic subgroups. • Selection/non-response bias (partially corrected through non-response weighting adjustment). 	<ul style="list-style-type: none"> • Can be modified to where the sampling frame is the state.



4. **Recruit from an existing population-based survey or program**

Some programs may wish to recruit from existing population-based surveys by asking to add interest-gauging questions for participation in a biomonitoring study. Information on persons who agree to participate would be transferred to the biomonitoring study team, and separately followed-up on for participation.

- a. An example is the Minnesota Healthy Rural and Urban Kids Project. Minnesota Department of Health partnered with Minneapolis Public Schools, Becker County Public Health, Todd County Health & Human Services, and Wadena County Public Health to offer participation in the MN Healthy Rural and Urban Kids Project to kids coming in for their routine required Early Childhood Screening (ECS) visit before they enter kindergarten. Healthy Rural and Urban Kids is their first biomonitoring project focused on a broad range of chemicals in young children.

Example 4A: Minnesota Healthy Rural and Urban Kids Project — One-stage cluster sample enrolling preschool-aged children from selected communities in the state.

Program: Minnesota Biomonitoring: Chemicals in People, Minnesota Department of Health.

Link: <https://www.health.state.mn.us/communities/environment/biomonitoring/projects/ruralurbankids.html>

Methods:

- The study location is two geographically distinct communities in the state with different community exposure concerns: 1) group of rural counties in North-Central Minnesota, and 2) two ZIP codes in urban North Minneapolis.
- The sampling frame is preschool-age children who live in these areas and came in for their required pre-kindergarten early childhood screening visits during June – September 2018. Early childhood screening programs are administered by school districts (Minneapolis) or, in some cases, local public health agencies (rural counties in the study).
- Early childhood screening staff recruited children and conducted data collection:
 - Staff contacted parents with appointments scheduled and informed them about possibility to participate.
 - On the day of visit, staff introduced the study again to families, conducted informed consent, administered the survey while child was being screened, and collected the urine sample.
- Eligibility was restricted to children whose parents reported that their child could provide a urine sample (i.e., potty-trained and no health issues that would interfere), and to one child per family.
- A sample size for study was identified, and monthly target recruitment goals were set.



Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Children are required to complete Early Childhood Screening before entering kindergarten, so the sampling frame is based on an existing, universal program for preschool-aged children. • Contracting with local staff from existing programs was economically efficient and helped achieve high participation rates – people knew and trusted them. • Being able to complete all components of the study when families came in for their pre-scheduled screening visit increased retention, survey completion and sample collection. • Study embedded in existing public health programs that focus on children’s health and have strong interest in results. 	<ul style="list-style-type: none"> • Results are limited to children from the selected communities and not to the state-wide population. • Collecting a blood sample would be more complicated and resource-intensive with this design. • Lack of comparison data from NHANES and other sources for this age group. Note: NHANES samples children from ages 3 years and older for some analytes (not all). 	<ul style="list-style-type: none"> • Because program happens across the state, can tailor geography to meet study/community needs.

5. Over sampling populations

Oversampling is done to increase the reliability and precision of estimates of certain population subgroups. For example, studies such as the National Health and Nutrition Examination Survey (NHANES) used oversampling to sample larger numbers of subgroups of interest such as minorities, adolescents, and older adults [16]. This increases the reliability and precision of estimates in these population subgroups [16]. Rural populations may be another subgroup of interest when considering oversampling to help ensure that you achieve a large enough N value for appropriate statistical power.

Consideration of oversampling clusters before the first or second stage provides a benefit for netting a desired sample size:

- Possible oversampling methods could include increasing the number of units (e.g. census blocks) in your first stage [22]. In the second stage the number of units (e.g. households) also can be increased [22].
- An example of oversampling to increase cluster selection is a modified application of the CASPER study design whereby the 30 × 7 design is modified to a 35 × 7 therefore increasing the N value by 16.6% [23].



The NHANES study design, as another example, draws its sample in the following stratified, four stages [24]:

- Stage 1: PSUs are first stratified according to population size, and then PSUs are selected from each stratum. These are mostly single counties or, in a few cases, groups of contiguous counties with probability proportional to a measure of size (PPS).
- Stage 2: The PSUs are divided up into segments (generally city blocks or their equivalent). As with each PSU, sample segments are selected with PPS.
- Stage 3: Households within each segment are listed, and a sample is randomly drawn. In geographic areas where the proportion of age, ethnic, or income groups selected for oversampling is high, the probability of selection for those groups is greater than in other areas.
- Stage 4: Individuals are chosen to participate in NHANES from a list of all persons residing in selected households. Individuals are drawn at random within designated age-sex-race/ethnicity screening subdomains. On average, 1.6 persons are selected per household.

In stage 3, where households from each segment are randomly drawn, for geographic areas where the proportion of age, ethnic, or income groups selected for oversampling is high, the probability of selection for those groups is greater than in other areas [16]. This can be replicated in other biomonitoring studies that apply probability sampling to oversample populations of interest.

For sub-populations that are at least 10% of the total population, a general sample will usually produce reliable estimates [21]. For, subpopulations between 1% and 10% of the total population, the oversampling methods described in the tables below are needed [21].

Example 5A: Screening—Used when sampling frame does not have the subpopulation domain identifiers.

Reference: Kalton G. Methods for oversampling rare subpopulations in social surveys. Survey Methodol. 2009;35(2):125–41

Methods:

- Used if a sampled person’s membership in a rare population can be determined inexpensively, e.g., from responses to a few questions
- A large first phase sample size is identified from which to select members of subpopulation of interest
- This is the minimum sample size that will produce the required (or larger) sample sizes of subpopulations of interest
- All the members of the subpopulations of interest are then included in the second phase sample

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Uses probability sampling methods. 	<ul style="list-style-type: none"> • Large sample size required. • Requires expensive procedures. • With screening, the sample size for a rare population is a random variable and could be more or less than expected. 	<ul style="list-style-type: none"> • A large screening sample size is required to get an adequate sample size for the subpopulation(s) of interest, <ul style="list-style-type: none"> ○ Use an inexpensive mode of data collection (e.g., telephone surveys or mail questionnaire).



	<ul style="list-style-type: none"> • Noncoverage can be a significant problem when large-scale screening is used to identify rare populations. <ul style="list-style-type: none"> ○ Even though a frame has good overall coverage, its coverage of a rare domain might be inadequate 	<ul style="list-style-type: none"> ○ Share costs across surveys – e.g., partner with existing population-based surveys • When possible and useful, permit the collection of screening data from persons other than those sampled. For example, other household members may be able to accurately report the rare population status of the sampled member. • Use a sampling fraction to best ensure the sample size will meet the minimum needed for a rare population. Sample fractions can be in context of subdomain such as age, sex or income groups. • Consider non-response rates. • Allow for under-representation by taking into account issues such as noncoverage, non-response or misclassification of domain membership at the design stage to produce the required sample size.
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Example 5B: Disproportionate stratification—Identifying strata based on subgroups of interest

Reference: Kalton G. Methods for oversampling rare subpopulations in social surveys. *Survey Methodol.* 2009;35(2):125–41.

Methods:

- Used if the rare population is concentrated in certain identifiable parts of the sampling frame
- Make sure subpopulation is more prevalent in the strata
- Make sure the strata has a high proportion of subpopulation
- The cost of collecting data from the subpopulation should not be high

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> • Disproportionate stratification, with higher sampling fractions in the strata where the prevalence of the rare population is higher, can reduce the 	<ul style="list-style-type: none"> • Assumes the prevalence of the rare population in each stratum is known. • Assumes the identification of rare populations is relatively easy. • Errors in the prevalence estimates will reduce the precision gains achieved with disproportionate 	<ul style="list-style-type: none"> • This method will yield substantial gains in efficiency if the following conditions hold: <ul style="list-style-type: none"> ○ The rare population must be much more prevalent in the oversampled strata ○ The over-sampled strata must contain a high proportion of the rare population



<p>amount of screening needed.</p>	<p>stratification and could even result in a loss of precision for the survey estimates.</p>	<ul style="list-style-type: none"> ○ The cost of the main data collection per sampled unit must not be high ● If a list with names is accessible (e.g., telephone numbers merged with U.S. Postal Service delivery sequence file addresses), the names can be used to build strata of likely members of some racial/ethnic groups. Names can be effective for identifying certain ethnic groups. ● If area sampling is used, data from the last census and other sources can be used to allocate the area clusters to strata based on their prevalence estimates for the rare population.
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Example 5C: Two phase sampling—Used when accurate identification of subpopulation members is expensive

Reference: Kalton G. Methods for oversampling rare subpopulations in social surveys. *Survey Methodol.* 2009;35(2):125–41.

Methods:

- Used if a sampled person’s membership in a rare population can only be determined using expensive methods, e.g., medical examinations
- Start with an imperfect screening classification in the first phase e.g. screening questionnaires with high sensitivity to detect subpopulation of interest
- Follow with accurate identification for a disproportionate stratified subsample in second phase (e.g., assessment by medical personnel)

Pros	Cons	Recommendations for use and modifications to consider
<ul style="list-style-type: none"> ● Beneficial when first phase accurate identification is not known or expensive. 	<ul style="list-style-type: none"> ● A fairly common practice with two-phase designs is to take no second- (or third-) phase sample from the stratum of those classified as nonmembers of the rare domain, based on their responses at the previous stage. If the prevalence of the rare domain is more than minimal in this stratum, a substantial proportion of the domain may go unrepresented. 	<ul style="list-style-type: none"> ● The imperfect screening methods in the first phase should be less expensive than the accurate identification in the second phase. If area sampling is used, data from the last census and other sources can be used to allocate the area clusters to strata based on their prevalence estimates for the rare population.



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