

Day 2 Roadmap

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Overall Roadmap

- **Day 1:** Focused on improving the use of existing data sources used in ADF evaluation
- **Day 2:** Focused on use and development of new sources and capabilities for ADF evaluation

Objectives

- **To determine whether** the marketing of a product with abuse-deterrent properties results in meaningful reductions in abuse, misuse, and related adverse clinical outcomes, including addiction, overdose, and death in the post-approval setting (*2015 Guidance*).
- **To determine whether** products discourage riskier forms of abuse and misuse

Populations

- At least one study should include a high-risk population, such as a population of known drug abusers, but formal studies should not be limited to only high-risk populations
(2015 Guidance)
 - Known drug abusers
 - Patients with new prescriptions
 - Patients on the verge of abuse

Requirements

- Identification of product-specific information, including brand and formulation
- Information on routes of abuse
- Ability to be rapidly modified, in response to changes in the prescription drug market
- Rigorous and valid outcome ascertainment
- Comparability over products
- Stability over time

Requirements (cont.)

- Well-defined populations, through probability sampling or otherwise
- Ability to measure in different populations (regions, at risk populations, demographic subgroups)
- Ability to handle drugs with small market share
- **To accomplish all this, we may need multiple data sources and studies.**

Data Sources: Examples

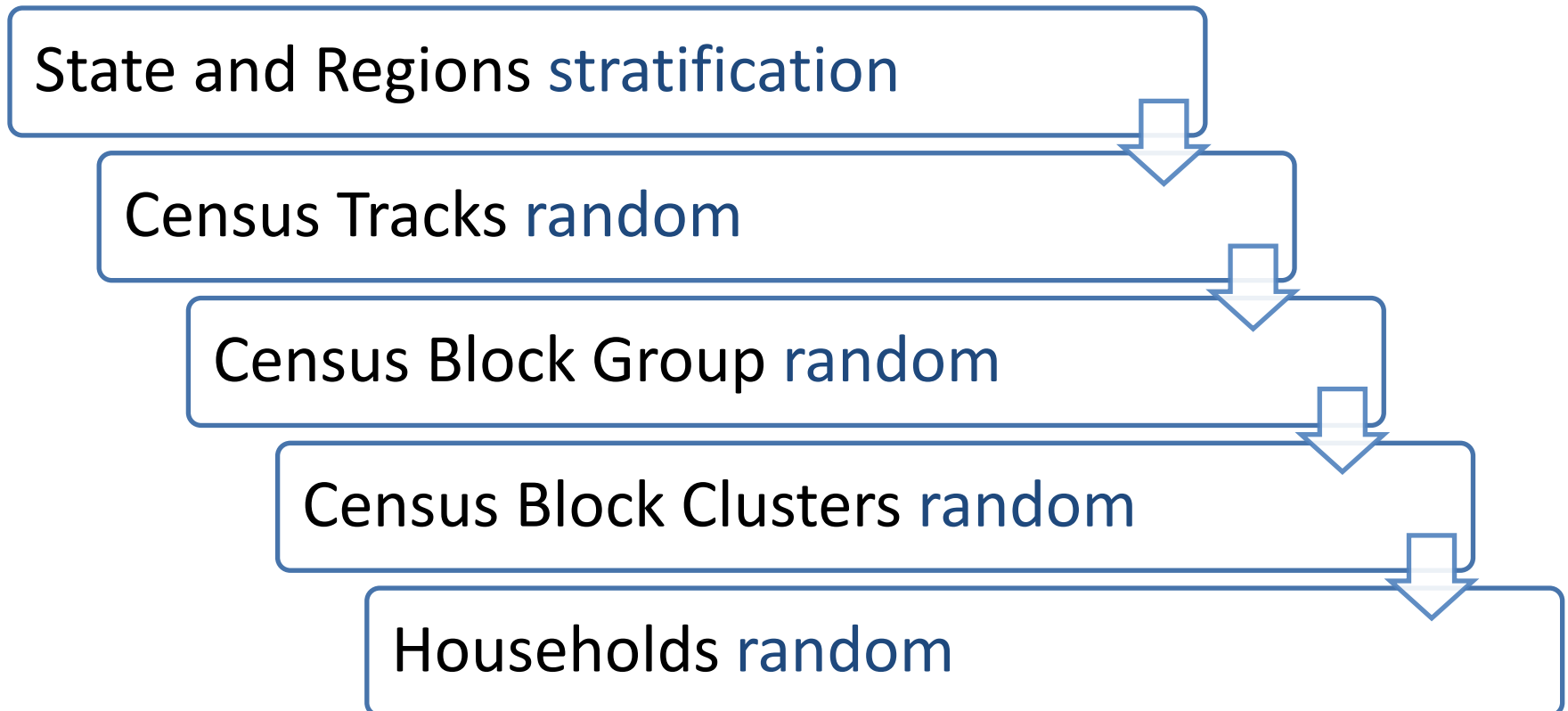


- **Probability sample:** NSDUH
- **Cohort:** FDA PMR 3033-2
- **Combination:** Hispanic Community Health Study

National Survey on Drug Use and Health



- Multistage area probability design



National Survey on Drug Use and Health



- Multistage area probability design
- Youths aged 12 to 17 and young adults aged 18 to 25 are oversampled
- Prescription drug use focus on 12 month period
- Questions on misuse
- Electronic images of pills used for identification

FDA Post-Market Requirement 3033-2



- An observational study using patient health records, insurance claims, and death records
- Two companion studies to develop and validate algorithms using coded medical terminologies for opioid-related overdose, death, abuse, and misuse

Probability Sample Designs

- Subjects randomly selected from some well-defined population
- Longitudinal information may or may not be obtained
- Rigorous inference to population is possible

Eg. Incidence=

$$\frac{\text{pop. est. of subjects w/exposure and w/event}}{\text{pop. est. subjects w/exposure}}$$

Cohort Designs

- Subjects satisfying well-defined inclusion/exclusion criteria
- Subjects have longitudinal information on exposure, risk factors, and at risk for outcomes
- Incidences and relative risks based on aggregating subject level information

Eg. Incidence=

$$\frac{\textit{subjects in cohort with exposure and event}}{\textit{subjects in cohort with exposure}}$$

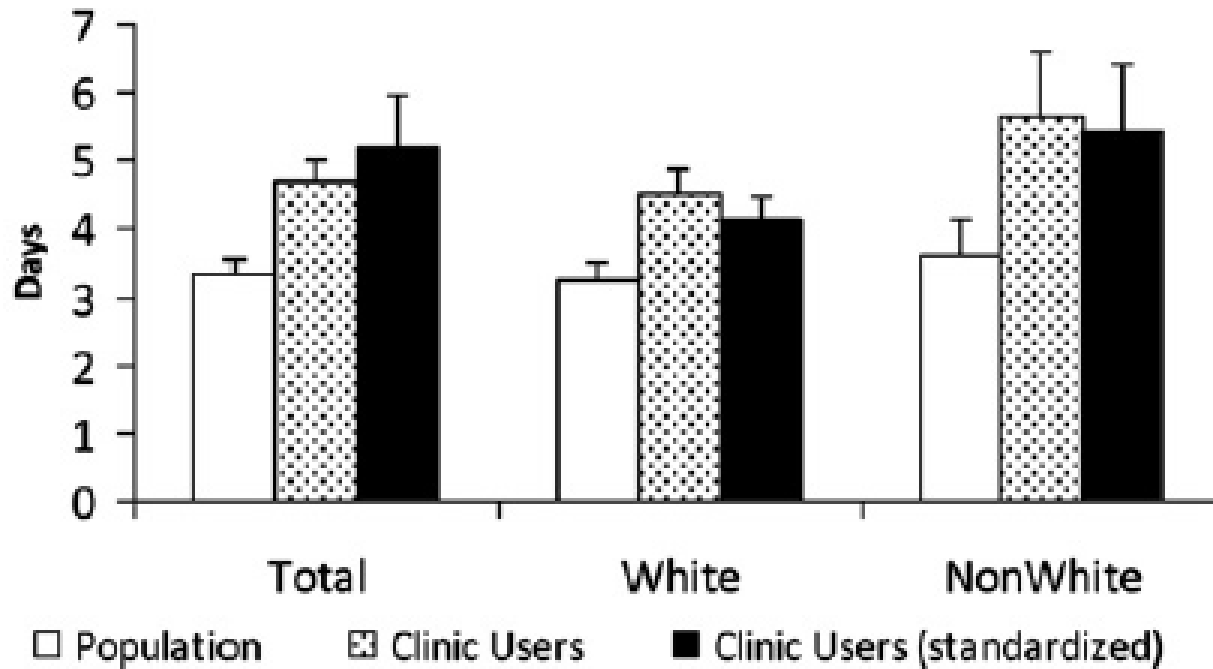
Cohort and Probability Sample Designs

| | Cohort Study | Probability Sample |
|--|--|---|
| Provides a direct denominator | ✓ | ✓ |
| Inferred population/representativeness | Cohort | Population |
| Allows valid estimates of incidence | ✓ | ✓ |
| Allows exploration of relationships (eg, exposure/outcome) | ✓ | ✓ |
| Challenges | Identifying appropriate cohort and obtaining information | Sampling or enriching for certain populations |

Simulated Comparison of Population and Cohort Estimates



Average number of work days missed per year due to illness or injury



Hispanic Community Health Study



- Objectives:
 - Estimate prevalences of baseline risk factors
 - Evaluate relationships between risk factors and health outcomes
- Design:
 - Probability sample embedded in multisite cohort study
 - Subjects 16,000 Hispanic/Latinos 18-74 y
 - Data collection: baseline and annual examinations

Hispanic Community Health Study: Subject Select



Communities **Non-Random**

Chosen to be enriched in Hispanics and provide breadth

Census Tracts **Non-Random**

Chosen for proximity to clinics and breadth

Census Blocks **Random**

Stratified random sampling

Households **Random**

Stratified random sampling

Day 2 Sessions

- **Session 5** National surveys: Opportunities for Evaluation of ADFs
- **Session 6** Designs That Assess Exposure and Outcome in the Same Individuals Over Time
- **Session 7** Leveraging other data: Linkages and Benchmarking
- **Session 8** Next steps

Discussion and Feedback



- Utility, strengths, and limitations of the existing national surveys
- Approaches and feasibility to modifying existing national surveys
- Development of new surveys, including internet panel surveys and other designs
- Novel study designs, including longitudinal cohort studies, and leveraging/linking multiple data sources
- Smaller local or regional studies and other types of information