



National Children's Study Update

NCS Advisory Committee
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National Children's Study



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

What the Law Says



- “ (1) 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;*
- (2) investigate basic mechanisms of developmental disorders and environmental factors, both risk and protective, that influence health and developmental processes.”*

The Study is required to:

- “(1) incorporate behavioral, emotional, educational, and contextual consequences to enable a complete assessment of the physical, chemical, biological, and psychosocial environmental influences on children’s well-being;*
- (2) Gather data on environmental influences and outcomes on diverse populations of children, which may include the consideration of prenatal exposures; and*
- (3) Consider health disparities among children, which may include the consideration of prenatal exposures.”*

NCS Principles



- Data driven
- Evidence based
- Community and participant informed

Examples of Exposure Areas of Interest



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

Examples of Exposure Areas of Interest



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

Examples of Outcome Areas of Interest



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

Prevalence of Conditions of Potential Interest



- Of 100,000 children, an estimated
 - 30,000 will be overweight; 17,000 with obesity
 - 5,000 with learning disorders
 - 5,000 with asthma
 - 1,000 – 3,000 with autism spectrum disorders
 - 1000 with schizophrenia
 - 750 with congenital heart disease
 - 320 with childhood cancers
 - 125 with Down syndrome
 - ~ 65 = *Federal threshold for rare disease*
 - 50 with Fragile X syndrome

Many conditions of potential interest are along a biological and clinical continuum with the most affected people generally diagnosed but others in the general population also affected

NCS Structure



- The NCS is an integrated system of activities
- All components and phases together form the NCS
- Current major components are the
 - NCS Vanguard Study- pilot phase for methods-runs for 21 years-started in 2009 expanded in 2010 and 2011 with additional locations
 - NCS Main Study-exposure response phase- runs for 21 years about 3 years time shifted from Vanguard Study-planned start in 2012
 - NCS Substudies- studies within studies
 - Formative Research-short term limited studies, often methods development, to support and inform the Vanguard and Main Studies

Where are the hypotheses?



- The NCS is a platform for constructing a resource and is not a study in the conventional sense
- While there are and will continue to evolve domains of interest, the NCS is not constructed to address a limited number of specific hypotheses, but rather to allow other scientists to use the data, samples and specimens to test hypotheses and perform multiple analyses with an emphasis on exposure-response relationships and mechanisms

The NCS as a platform



- The NCS as a data acquisition platform invites collaboration for both the Vanguard and the Main Study
- The NCS is designed to be interoperable because future opportunities cannot be anticipated with precision and some not at all.
- *“As [the progress of the human mind] becomes more developed, more enlightened, as new discoveries are made, new truths discovered and manners and opinions change, with the change of circumstances, institutions must advance also to keep pace with the times.”*

Thomas Jefferson to H. Tompkinson (AKA Samuel Kercheval), July 12, 1816 and adapted for the Jefferson Memorial

Attrition and Retention



- Attrition-anticipate differential attrition for various subpopulations
- Item and Visit Completion rates will vary per participant and over time
- Modeling using 3 different methods indicates potential attrition over 21 years to yield a population of about 40% of initial enrolled population
- Vanguard Study will systematically address retention globally and in specific subpopulations

Proposed strategy to leverage data



- Harmonize with other studies, general birth cohort and condition specific, domestic and international, regarding data collection and data elements
- Share data and perform pooled analyses on uncommon conditions of interest
- Requires ongoing discussion and cooperation with assurances for quality and consistency of data

Costs



- Major Drivers
 - Recruitment
 - Data Acquisition
- Potential Approaches to be cost effective
 - Consolidation of redundant operations
 - Currently consolidating informatics
 - Use data standards and non-proprietary instruments and methods
 - Modular operations to allow swapping out of components

Summary



- NCS is Congressionally mandated longitudinal activity beginning prior to or during pregnancy.
- Complex system to function as an integrated data collection platform
- Use of standards and harmonization efforts to leverage data collection and analyses
- For further information
 - <http://www.nationalchildrensstudy.gov>
 - ContactNCS@mail.nih.gov



Preliminary Recruitment Analysis from the NCS Vanguard Study Alternate Recruitment Substudy

Recruitment method appears to influence recruitment efficiency and profile of the enrolled population

NCS Vanguard Study Goals



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

Vanguard Study Current Sampling Frame (simplified)



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

Recruitment Strategies



- The goal is cost-effective recruitment for the Main Study, employing direct data analysis and predictive modeling
 - Household based - participants learn about the study through field workers going door-to-door
 - Provider based - participants learn about the study through trusted health care providers (broad definition of provider, including pediatricians, obstetricians, public health nurses, midwives, etc.)
 - Direct outreach- participants learn about the study through media and community outreach

Vanguard Study Progress



- 2009-Began field activities using household based (door to door contacts in designated neighborhoods) at 7 locations
- 2010- expanded from 7 initial locations to an additional 30 locations for a total of 37 using additional recruitment strategies
- 2011- completed initial recruitment phase with about 6750 families

NCS Recruitment Status

-based on data as of 12/15/2011



| | Initial Household (2009 cohort) | Alternate Recruitment (2010 cohort) | All Vanguard to date |
|--|------------------------------------|---|----------------------|
| Locations | 7 | 30 | 37 |
| Recruitment Duration, months | 18 active+ 14 follow up | 12 | |
| A. Women eligible for contact | 35000 | 45600 | 80550 |
| B. Contacted for Pregnancy Screen (% of eligible) | 34350 (98%) | 40000 (88%) | 74350 (92%) |
| C. Completed Screen (% of contacted) | 30900 (90%) | 34850 (87%) | 65730 (88%) |
| D. Pregnant or Trying (% of screened) | 3100 (10%) | 6550 (19%) | 9650 (15%) |
| E. Enrolled (% of pregnant or trying) | 2000 (64%) | 4800 (73%) | 6750 (70%) |
| F. Babies Enrolled | 1050 | 1150 | 2200 |

Alternate Recruitment Substudy Recruitment Summary

- as of 12/15/2011



| | Provider Based | Enhanced Household | Direct Outreach |
|---|----------------|--------------------|-----------------|
| A. Women eligible for contact | 3350 | 26000 | 16250 |
| B. Contacted for Pregnancy Screen (% of eligible) | 3000 (89%) | 20800 (80%) | 16200 (99%) |
| C. Completed Screen (% of contacted) | 2050 (69%) | 19450 (93%) | 13350 (82%) |
| D. Pregnant or Trying (% of screened) | 1750 (84%) | 2500 (13%) | 2300 (14%) |
| E. Enrolled (% of pregnant or trying) | 1400 (81%) | 1500 (60%) | 1850 (81%) |
| F. Babies Enrolled | 500 | 400 | 250 |

Pregnancy Screen Completion by Recruitment Strategy

- as of 12/15/2011



| | Provider Based | Enhanced Household | Direct Outreach |
|--|----------------|--------------------|-----------------|
| A. Women eligible for contact | 3350 | 26000 | 16250 |
| B. Contacted for pregnancy screen (% of identified) | 3000 (89%) | 20800 (80%) | 16200 (99%) |
| a. Final ineligible | 550 | 100 | 1250 |
| b. Refused | - | 750 | 450 |
| c. Other non-response | 50 | 500 | 1200 |
| d. Incomplete information, unable to classify | 350 | 50 | - |
| C. Completed screen (% of contacted) | 2050 (69%) | 19450 (93%) | 13350 (82%) |

Enrollment Rates by Recruitment Strategy

- as of 12/15/11



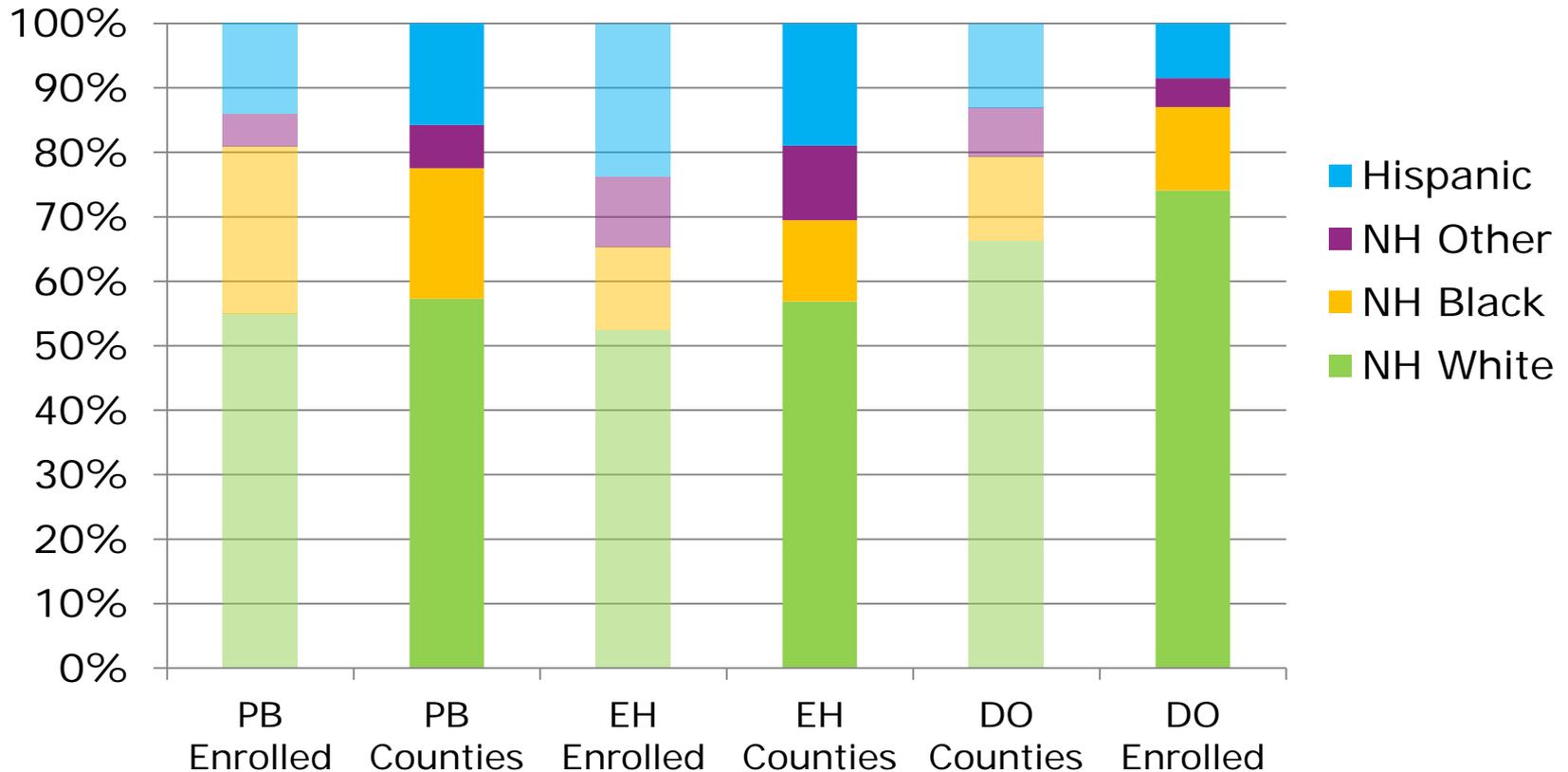
| | Provider Based | Enhanced Household | Direct Outreach |
|--|----------------|--------------------|-----------------|
| C. Completed screen (from prior table) | 2050 | 19450 | 13350 |
| D. Pregnant or trying (% of completed screening) | 1750 (84%) | 2500 (13%) | 2300 (17%) |
| a. Refused | 50 | 150 | 50 |
| b. Other non-response | 50 | 50 | 100 |
| c. Incomplete information, unable to classify | 250 | 800 | 250 |
| E. Enrolled (% of pregnant or trying) | 1400 (81%) | 1500 (60%) | 1850 (81%) |
| Proportion of enrolled who are pregnant / trying | 87%/ 13% | 52%/ 48% | 54%/ 46% |

Alternate Recruitment Substudy Screening Efficiency



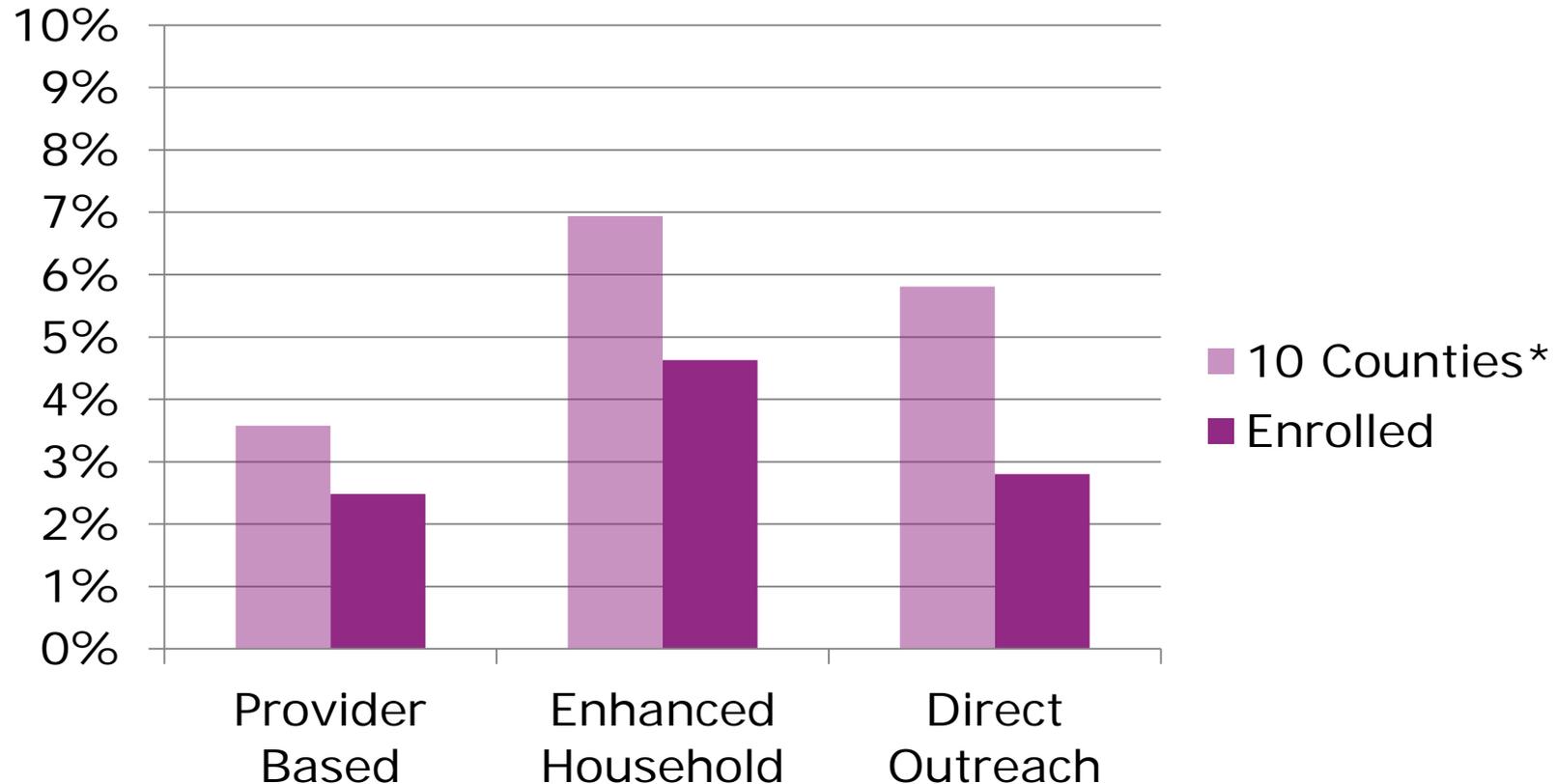
| | Provider Based | Enhanced Household | Direct Outreach |
|--|-----------------------|---------------------------|------------------------|
| Number of Locations x Weeks in field | 403 | 479 | 471 |
| Mean number of women enrolled per week | 3.5 | 3.2 | 3.9 |
| Mean number of women screened per woman enrolled | 2.1 | 13.7 | 8.7 |

Percent Distribution of Enrolled Women by Race/Ethnicity According to Recruitment Strategy



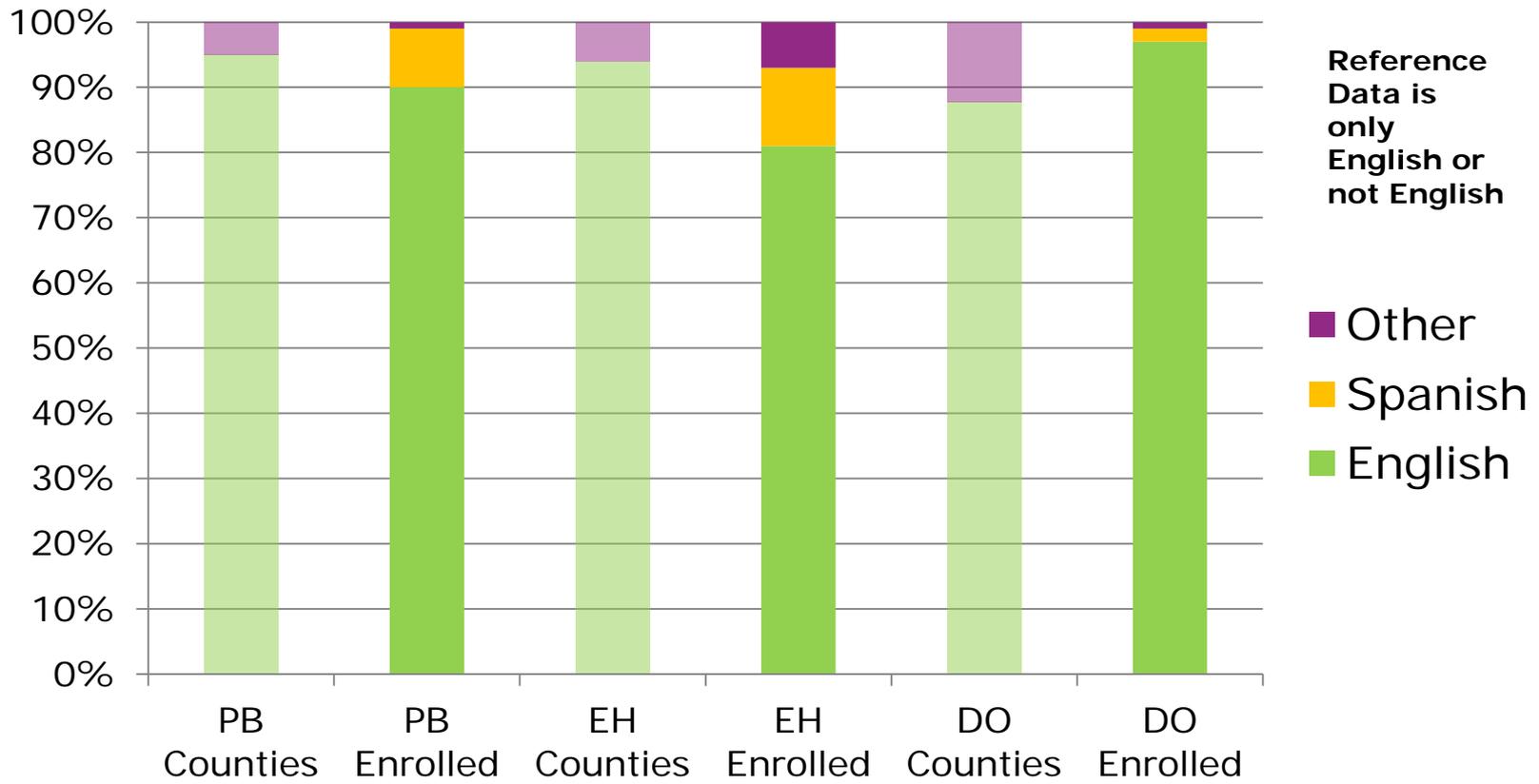
*Average race/ethnicity distribution in 10 counties from 2009 American Community Survey data.

Percent **Asian** Among Study Eligible and Enrolled Compared to County Population by Strategy

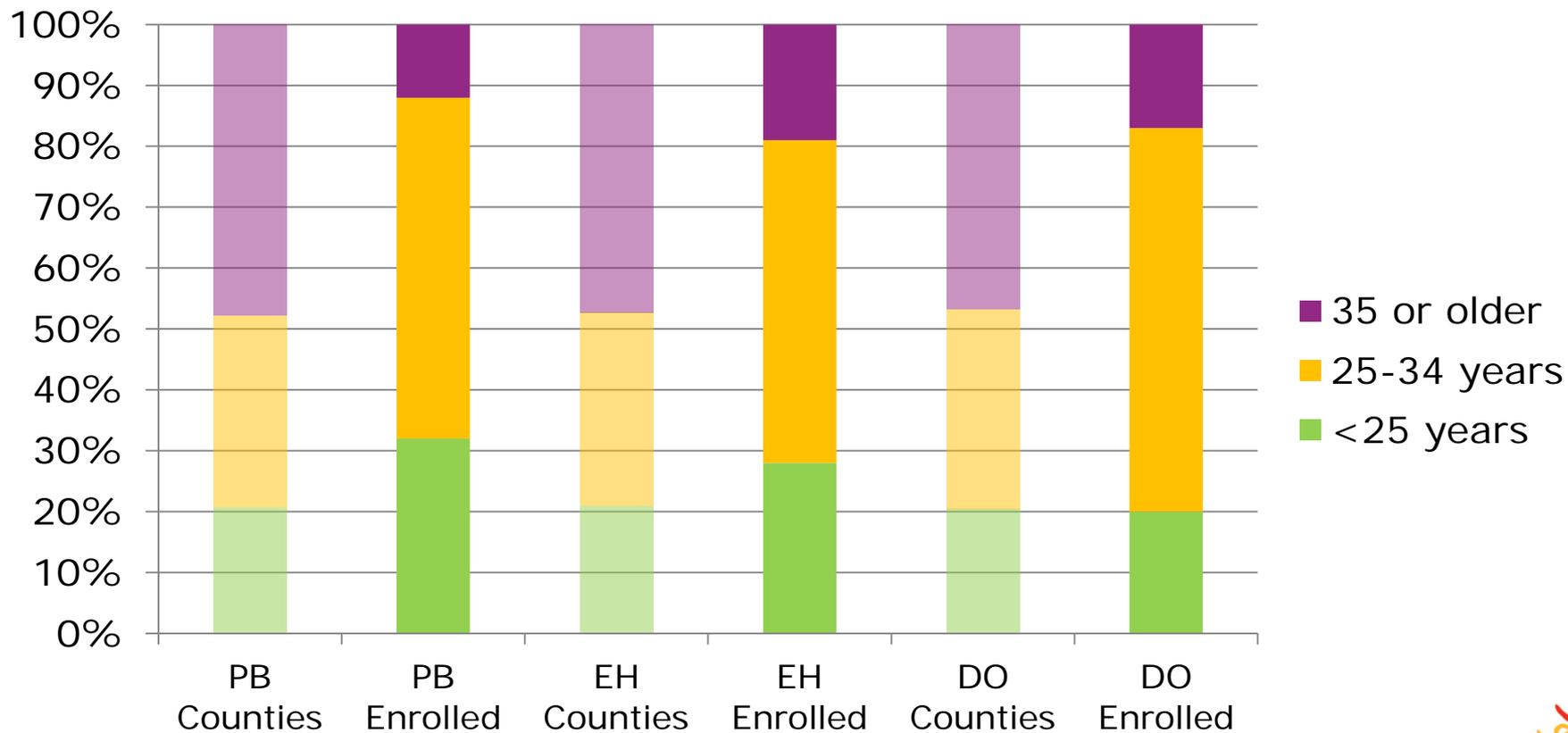


*Average percent Asian in 10 counties from 2010 Census data.

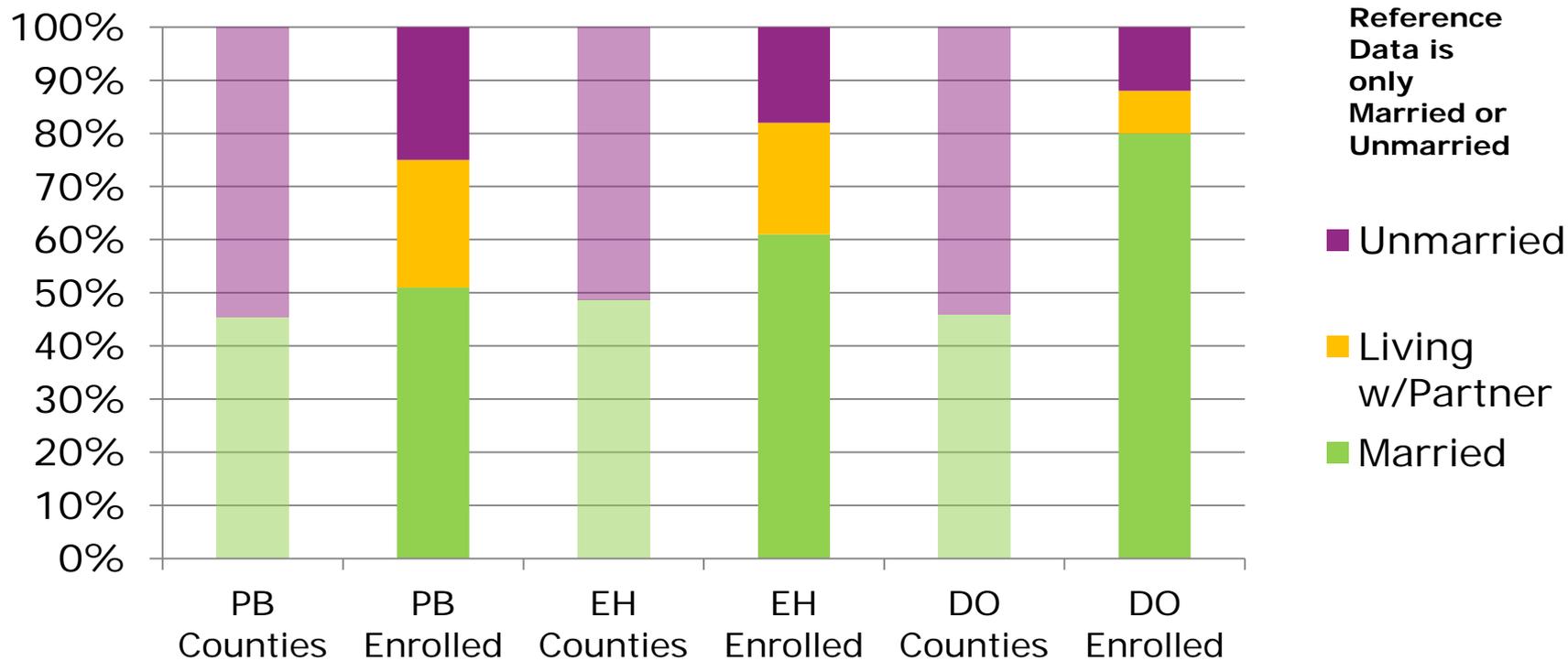
Percent Distribution of Enrolled Women by **Primary Language** According to Recruitment Strategy



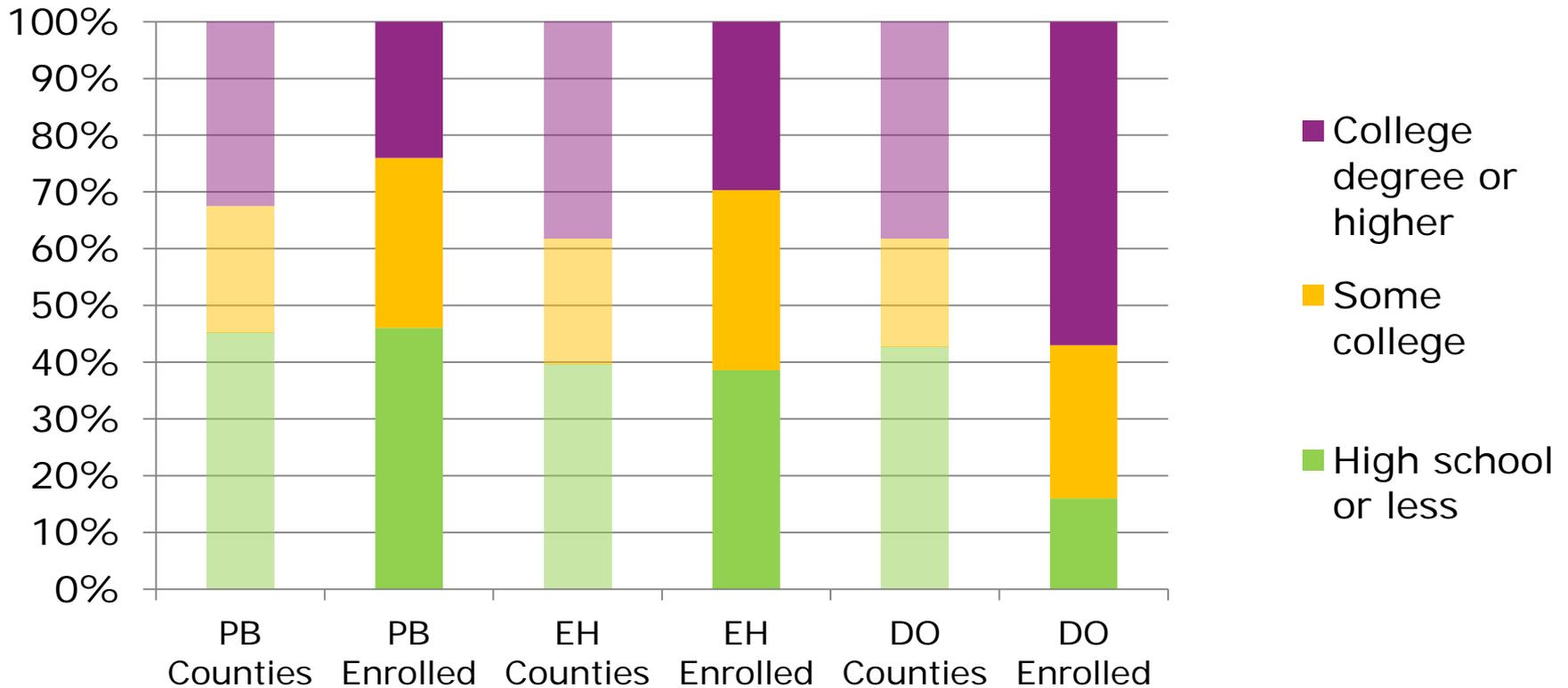
Percent Distribution of Enrolled Women by Age According to Recruitment Strategy



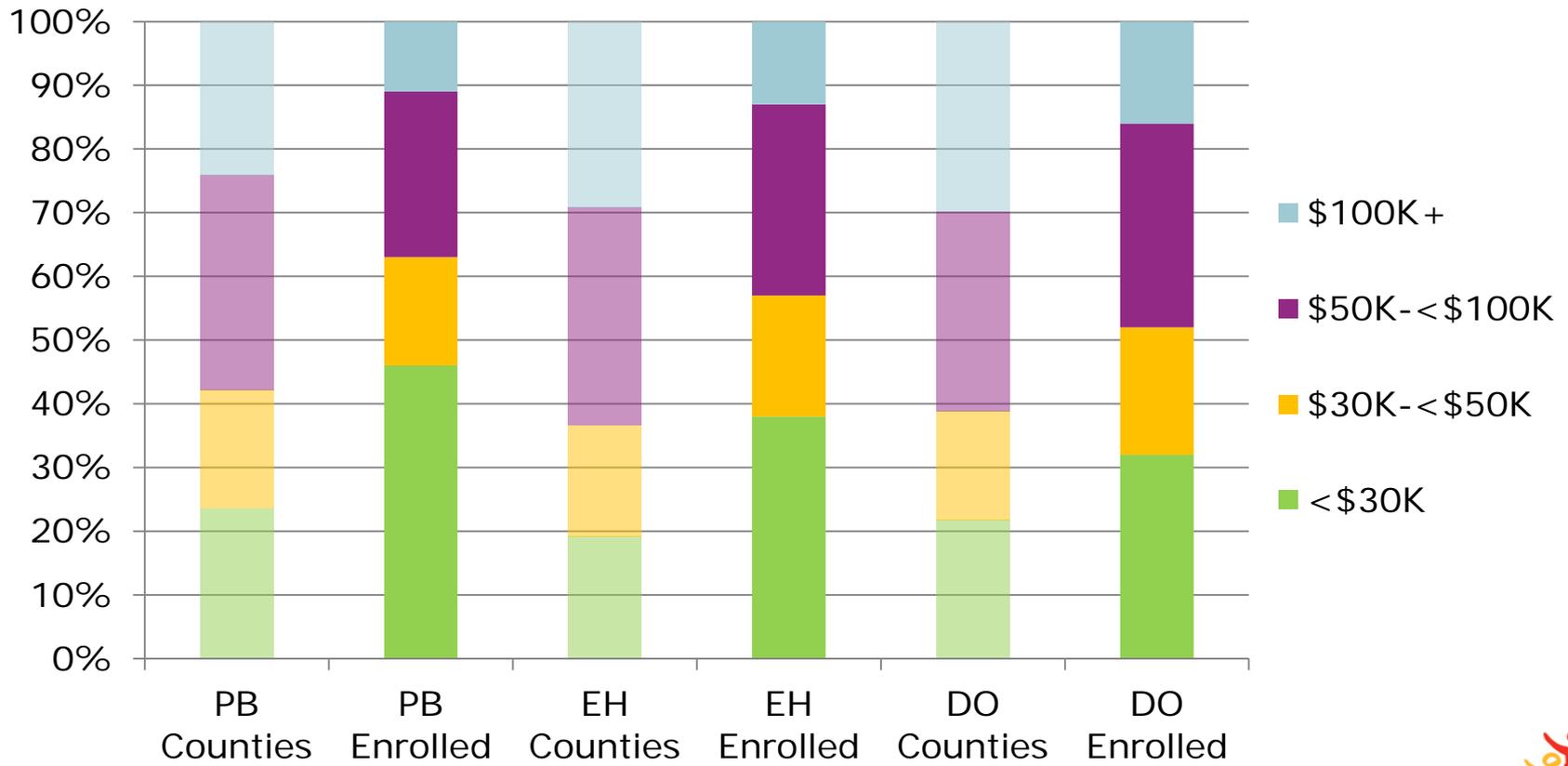
Percent Distribution of Enrolled Women by **Marital Status** According to Recruitment Strategy



Percent Distribution of Enrolled Women by Education According to Recruitment Strategy



Percent Distribution of Enrolled Women by **Family Income** According to Recruitment Strategy



Some Preliminary Findings



Each one of the three recruitment strategies was assigned to a group of 10 study locations

- Efficiency of enrollment differed among each recruitment strategy
- Baseline demographics for each recruitment strategy locations were generally similar
- Demographics of women enrolled for each recruitment strategy differed by varying degrees from baseline and from each other