



NACC Data: Who is Represented Over Time and Across Centers, and Implications for Generalizability



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51,984

Participants analyzed from the September 2024 NACC Data Freeze.

42 ADRCs

Included across past and present Alzheimer's Disease Research Centers (ADRCs).

2005-2024

Recruitment window used to access temporal shifts and center heterogeneity.

BACKGROUND

The NACC Uniform Data Set has supported Alzheimer's disease and related dementia research since 2005, but the composition of recruited participants has evolved over time and differs across centers. Those differences matter because NACC is a volunteer cohort rather than a probability sample of the U.S. older population.

OBJECTIVE

This study asked who is represented in NACC over time and across ADRCs, and what those recruitment patterns imply for generalizability of findings derived from NACC-based research.

METHODS

We used the September 2024 NACC data freeze and summarized characteristics at the initial UDS visit. Variables included age, sex, race, education, clinical diagnosis, provider referral, family history of cognitive impairment, and co-participant relationship.

Temporal changes were evaluated with the multinomial Cochran–Armitage trend test, and between-center differences were assessed using chi-square tests of homogeneity.

STUDY POPULATION

Among 42 ADRCs, 23 had contributed recruitment data since the start of UDS, whereas others entered later. Site sample sizes ranged from 96 to 3,249 participants, with a median of 1,188.

KEY FINDINGS

1. RECRUITMENT OVER TIME

- Nearly all baseline characteristics except sex and family history shifted over the two-decade recruitment period.
- Recent enrollees were more likely to be:
 - Younger than earlier recruits.
 - More racially diverse.
 - More highly educated.
 - More often cognitively normal at baseline.
 - More likely to enter through provider referral.

2. CENTER HETEROGENEITY

- Between-center variation was substantial for every characteristic examined.
 - The proportion of participants younger than 70 years ranged from 19% to 78% across centers.
 - The proportion of White participants ranged from 12% to 95%
 - The proportion with normal cognition at baseline ranged from 18% to 76%.
 - Provider referral also varied markedly, from approximately 20% to 90% across ADRCs, indicating important differences in how participants enter studies.

INTERPRETATION

The cohort is not static. Recruitment has shifted alongside evolving scientific priorities, including increasing emphasis on early detection, prevention, and preclinical stages of Alzheimer's disease, as well as broader outreach to historically underrepresented groups.

IMPLICATIONS FOR GENERALIZABILITY

- The absence of uniform recruitment criteria across ADRCs creates a patchwork of population samples, which complicates efforts to derive generalizable conclusions.
- The central question is whether the exposure–outcome association of interest can be transported beyond the recruited sample despite selection processes that vary across centers and time.
- Selection bias depends on specific scientific questions and need to be studied case by case.
- Advanced statistical methods recommended:
 - Sensitivity analysis for assessing how results are sensitive to unmeasured bias.
 - Hierarchical model or meta analysis to address center-level effect heterogeneity.

CONCLUSION

NACC should be understood as an evolving multi-center volunteer cohort. While center-level heterogeneity and change in recruitment over time creates challenges for simple population-level claims (e.g. prevalence), its diversity allow a wide variety of scientific questions to be addressed.

REFERENCE

Chan KCG, Xia F, Kukull WA. (2025) NACC data: Who is represented over time and across centers, and implications for generalizability. *Alzheimer's & Dementia*; 21(9):e70657.
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