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Featured Article

Importance of home study visit capacity in dementia studies

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Abstract

Introduction: The importance of home research study visit capacity in Alzheimer's disease (AD) studies is unknown.
Methods: All evaluations are from the prospective Adult Changes in Thought study. Based on analyses of factors associated with volunteering for a new in-clinic initiative, we analyzed AD risk factors and the relevance of neuropathologic findings for dementia comparing all data including home visits, and in-clinic data only. We performed bootstrapping to determine whether differences were greater than expected by chance.
Results: Of the 1781 people enrolled during 1994–1996 with ≥1 follow-up, 1369 (77%) had in-clinic data, covering 61% of follow-up time. In-clinic data resulted in excluding 76% of incident dementia and AD cases. AD risk factors and the relevance of neuropathologic findings for dementia were both different with in-clinic data.
Discussion: Limiting data collection in AD studies to research clinics alone likely reduces power and also can lead to erroneous inferences.

Keywords: Home research study visits; Research clinic study visits; Missing data; Bias; Prospective studies; Cohort studies; Longitudinal studies; Inference; Dementia; Neuropathology

1. Introduction

Many studies do not include capacity for home study visits. Home visits add staff travel time, expense, and complexity to study administration. Despite these burdens, there is a modest literature encouraging home visit capacity for studies of older people [1–5]. These articles emphasize benefits of increasing underrepresented ethnic diversity [2] or larger samples [6]. One article suggests home visit capacity may improve generalizability [1]. To our knowledge, the relevance of home visit capacity for validity of findings in dementia studies has not been addressed.

We recently invited active study participants who had agreed to brain autopsy and were thus especially prone to volunteer to consider a new initiative that included data collection in a research clinic—but not at home—and a magnetic resonance imaging (MRI) scan. Our study participants are particularly interested in research [7]. We analyzed factors associated with volunteering. As we will show, whether the previous study visit was at home or at the research clinic was the most important factor associated with volunteering.

These findings led us to consider the importance of home study visit capacity. We analyzed data from the Adult Changes in Thought (ACT) study original cohort, for whom we have 20 years of follow-up. We considered the data we would observe if we lacked home visit capacity. We focused on risk factors for Alzheimer's disease (AD)

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and associations between autopsy neuropathologic findings and dementia during life.

2. Methods

2.1. Parent study description, ethical considerations, and funding

Detailed methods for ACT have been published [8–10]. The Original Cohort enrolled during 1994–1996 included 2581 randomly selected dementia-free people aged ≥65 who were members of Group Health, a Washington State health care system. An additional 811 participants were enrolled during 2000–2003, and in 2005 we began continuous enrollment. Participants are evaluated at 2-year intervals at a research clinic or in their home at the participant's choice to identify incident dementia cases. Other than location (i.e., home vs. clinic), study visits are identical.

All active participants with autopsy consent—regardless of enrollment cohort—were eligible to be invited to consider a new initiative, as detailed in the following. Subsequent risk factor and neuropathologic analyses reported here are from the Original Cohort enrolled during 1994–1996.

Study procedures were approved by Institutional Review Boards of Group Health and the University of Washington. Participants provided written informed consent.

ACT is supported by the National Institute on Aging, which had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

2.2. Dementia identification

Participants were assessed at home or in clinic for dementia every 2 years with the Cognitive Abilities Screening Instrument, for which scores range from 0 to 100 and higher scores indicate better cognitive functioning [11]. Participants with scores ≤85 underwent further evaluations, including a clinical examination and a battery of neuropsychological tests; dementia evaluations are in the participant's home regardless of the location of the triggering visit. Results of these evaluations, laboratory testing, and imaging records were reviewed in a consensus conference, where research criteria were used to identify cases of dementia [12] and probable or possible AD [13]. Dementia-free participants continued with scheduled follow-up visits.

2.3. Autopsy consent

Information about postmortem brain examination procedures is made available at study visits; participants are invited to provide consent for brain autopsy. Between 25% and 30% of ACT participants have consented to autopsy.

2.4. Section 1: Factors associated with volunteering for an ancillary study that involved an in-clinic visit and MRI

We asked 145 active ACT participants with current autopsy consent to consider a new initiative that included in-clinic data collection and an MRI. We analyzed associations between volunteering and a variety of factors as listed in Table 1. Medical comorbidity was estimated using RxRisk [14] and Charlson [14] scores. We used Fisher's exact test, *t* tests, or Wilcoxon's rank-sum tests, as appropriate. All variables with a univariate $P < .20$ were candidates for a multivariate logistic regression model, where volunteer status was the dependent variable. We controlled multivariate models for age and sex.

2.5. Section 2: Importance of home visits for analyses of AD risk factors

We constructed two data sets from the original cohort: one with all data (the "all data" data set), and the second excluding home visit data (the "clinic-only" data set). We modeled probable or possible AD [13]. We used Cox models with age as the time axis [15] and included age at baseline as a covariate. We evaluated the factors listed in Table 2. We compared hazard ratios (HRs) from the "all data" and "clinic-only" data sets using a bootstrapping procedure. The "clinic-only" data are a subset of the "all data" data set, so different findings could be due to the smaller sample. We, therefore, drew (with replacement) random subsets of the "all data" data set that were the same size as the "clinic-only" data set. Each randomly drawn data set has the same size as the "clinic-only" data set, so different sample sizes do not drive results. In each drawn data set, we performed the same risk factor analyses. We determined the proportion of drawn data sets with HRs more extreme than those of the "clinic-only" data set. The bootstrap *P* values indicate the proportion of drawn data sets with more extreme findings than the "clinic-only" data set, which enables us to determine whether "clinic-only" and "all data" HRs differ more than expected by chance alone.

2.6. Section 3: Importance of home visits for analyses neuropathologic findings and dementia

We considered the 347 members of the Original Cohort who died and came to autopsy as of November 2014. We required the most recent study visit to be within 2 years of death for people who died without a diagnosis of dementia to minimize dementia misclassification. Again we constructed two data sets, one in which people with dementia could have that diagnosis on the basis of either a home or research clinic study visit, and people who died without dementia had a home or research clinic study visit within 2 years of death (the "all data" data set), and a second data set limited to those who died without a diagnosis of dementia and had a research clinic visit within 2 years of death, and those who died with dementia had that diagnosis made at a research clinic visit (the "clinic-only" data set).

Details of the neuropathology protocols have been published [16,17]; microscopic evaluations are performed blinded to clinical information. We considered neuritic