Published in final edited form as:

J Int Neuropsychol Soc. 2015 January ; 21(1): 85–90. doi:10.1017/S1355617714000952.

Correcting bias caused by missing data in the estimate of the effect of apolipoprotein $\epsilon 4$ on cognitive decline

Charles B. Hall, PhD^{1,2}, Richard B. Lipton, MD^{1,2}, Mindy J. Katz, MPH², and Cuiling Wang, PhD^{1,2}

¹Department of Epidemiology and Population Health, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY

²Saul B. Korey Department of Neurology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY

Abstract

Objective—Longitudinal administration of neuropsychological instruments are often used to assess age-related changes in cognition. Informative loss to follow-up may bias the results of these studies. Herein, we use auxiliary data to adjust for informative loss to follow-up.

Method—In the Einstein Aging Study, memory was assessed annually in a community sample of adults age 70+, free of dementia at baseline, using the free recall from the Free and Cued Selective Reminding Test, and via telephone using the Memory Impairment Screen for Telephone (the auxiliary data). Joint linear mixed models were used to assess how the effect of the APOE $\epsilon 4$ genotype may be affected by informative missingness in the in-person data.

Results—620 EAS participants contributed 2085 person years of follow-up to the analyses. Memory decline rates estimated in joint models were 19% greater in $\epsilon 4$ negative participants and 27% greater in $\epsilon 4$ positive participants compared to traditional approaches; the effect of APOE $\epsilon 4$ on memory decline was 37% greater.

Conclusions—Joint modelling methods can help address bias caused by informative missing data in the estimation of the effect of risk factors on cognitive change, and may be applicable to a broader range of outcomes in longitudinal aging studies.

Keywords

Memory; Longitudinal Studies; Bias (Epidemiology); Risk Factors; Apolipoprotein E4; Models, Statistical

Introduction

Aging research often focuses on rates of decline in cognitive performance as assessed by neuropsychological instruments, and on the influence of risk factors on these rates of

Corresponding Author: Charles B. Hall, Department of Epidemiology and Population Health, Block 312, Albert Einstein College of Medicine, Bronx NY 10463; phone 1-718-430-3724; charles.hall@einstein.yu.edu.

All authors report no financial or personal conflicts of interest.

decline. Assessing decline in longitudinal studies is complicated by informative loss to follow-up; that is, study participants who miss scheduled evaluations often perform more poorly than those who complete their visits (Wang & Hall 2010; Sliwinski *et al.* 2006; Rubin 1976; Little & Rubin 2002). This problem is well exemplified by cognitive decline.

Cognitive decline in elderly populations may be underestimated by prospective observational studies because the individuals with the greatest change are lost to follow-up. This informative loss to follow-up may bias estimates of the effects of risk factors on cognitive performance. This well-recognized problem in longitudinal aging studies may make it more difficult to discover genetic and environmental risk factors for cognitive decline and may lead to underestimates of the effects of risk factors.

Using “auxiliary” information that is correlated with the missing outcome is an emerging approach to help correct this bias (Ibrahim, Lipsitz & Horton 2001; Daniels & Hogan 2008). When cognitive test data is missing, auxiliary information might include a clinical assessment, an informant interview, or a telephone interview with a participant unable to complete a clinic visit. We have previously shown that auxiliary data from an in-person clinical assessment based on the Clinical Dementia Rating (CDR; Morris 1993) can be used to refine estimates of memory decline based on the free and cued selective reminding test (FCSRT) (Grober & Buschke 1987) in the context of a dementia screening study. The results suggested that memory decline in the clinic-based cohort with over a one year follow-up was underestimated by approximately ten percent (Wang & Hall 2010). We have not yet examined the use of auxiliary data to estimate the influence of genetic risk factors on cognitive decline.

Herein, we use data from the Einstein Aging Study (EAS) (Katz *et al.* 2012) to assess the rates of memory decline associated with carrying an APOE $\epsilon 4$ allele. APOE $\epsilon 4$ is the major genetic variant that influences rates of memory decline and the incidence of late onset Alzheimer’s disease. We then corrected for informative loss to follow-up using auxiliary telephone cognitive assessments. These approaches may increase our ability to find genetic variants associated with cognitive decline and prove useful in neurologic research and clinical practice. Our *a priori* hypothesis was that methods that take into account the effect of missing data would show a larger estimated difference in the rate of memory decline between persons with at least one $\epsilon 4$ allele ($\epsilon 4+$), and persons without an APOE $\epsilon 4$ allele ($\epsilon 4-$) than the more commonly used methods that ignore the effect of missing data.

Method

Study Population

The Einstein Aging Study (EAS) is an ongoing longitudinal prospective study of cognitive aging and dementia started in 1993. The sample includes older adults drawn from a multi-ethnic, community-dwelling population in Bronx County, NY, USA, and recruited using Medicare eligibility and voter registration lists. Eligible participants were at least 70 years old, resided in the Bronx, were not living in institutions, and spoke English. Exclusion criteria included visual or auditory impairments that preclude neuropsychological testing, active psychiatric symptomatology that interfered with the ability to complete assessments,

and non-ambulatory status. Participants receive comprehensive annual medical and neuropsychological evaluations at approximately 12 month intervals (Katz *et al.* 2012). Oral consent was obtained on first telephone contact and written informed consent was obtained at the initial clinic visit. The local institutional review board approved the study protocol.

Outcome Measure

All EAS participants are administered the Free and Cued Selective Reminding Test (FCSRT) (Grober & Buschke 1987), a test of episodic memory that has been shown to be sensitive and specific for dementia, and are periodically evaluated for dementia and mild cognitive impairment (MCI). The FCSRT includes presentation and learning of 16 pictures by having subjects identify each of the 16 pictures. It also consists of three trials of immediate free recall, each of which is followed by cued recall in which a category cue is presented to the subjects to facilitate recall of the items not freely recalled. Total recall is the sum of free and cued recall; free recall (range 0–48) was used in analyses.

APOE $\epsilon 4$ Status

Most participants also agree to submit blood for genotyping. APOE genotyping was performed using methods previously described (Sanders *et al.* 2010; Derby *et al.* 2012). Individuals were classified as APOE $\epsilon 4$ carriers if they had at least one $\epsilon 4$ allele ($\epsilon 4+$), and non-carriers otherwise ($\epsilon 4-$).

Auxiliary Data

The administration of the Memory Impairment Screen for Telephone (MIS-T) (Lipton *et al.* 2003) began in March, 2003 regardless of whether the study participant was able to make a clinic visit for in-person cognitive assessment. MIS-T is a brief test of episodic memory that uses procedures similar to the FCSRT. Specifically, the telephone interviewer presents 2 (of 4) target words and asks the subject to repeat the words to ensure that they heard correctly. The interviewer then presents a category cue associate with one of the target words. The subject is asked to select the word that corresponds to the category cue. The interviewer then presents a second category cue that corresponds to the other target word. This procedure is repeated for the next two target items. After an interference task lasting 2–3 minutes, the subject is then asked to recall as many target items as possible (free recall). For each word not recalled, the interviewer presents a cue category and asks the subject to recall the word (cued recall). The scoring of the MIS-T is calculated as: total MIS-T = ((2*free) + cued). The application of the MIS-T is used as auxiliary data for the FCSRT using methods described below. For all analyses in this report, follow-up began with the first administration of the MIS-T and continued through July 2011.

Additional data collected to characterize the cohort

Demographic information including self-reported race/ethnicity as defined by the U.S. Census Bureau in 1994 and education (in years) were obtained during in-person evaluations at baseline and at subsequent 12-month intervals. Global cognition was measured at baseline and annually by the Blessed Information Memory Concentration test (BIMC; Blessed, Tomlinson, & Roth 1968). BIMC scores range from 0 to 33; higher scores reflect greater

cognitive impairment. A diagnosis of dementia was based on standardized clinical criteria and required impairment in memory plus at least one additional cognitive domain, accompanied by evidence of functional decline. A diagnosis of amnesic Mild Cognitive Impairment required objective memory impairment as stated above, subjective memory impairment indicated by responses to self or informant reports, absence of functional decline, and absence of dementia. Details are in Katz *et al.* 2012.

Statistical methods

Non-random missingness is likely to be common in longitudinal aging studies. A subset of such situations, called auxiliary variable missing at random (A-MAR) (Ibrahim *et al.* 2001; Daniels & Hogan 2008), occurs when the missing data process depends on the unobserved data through the auxiliary data. Here, the free recall score from the FCSRT (Grober & Buschke 1987) is the outcome of interest, and the MIS-T (Lipton *et al.* 2003) is used as auxiliary data. We compared three linear mixed effects models (Laird & Ware 1982) that modeled cognitive change over time as a function of chronological age: (1) A “traditional” model, ignoring non-random missingness, with random effects used to take into account heterogeneity across study participants and the lack of independence of repeated measurements on those individuals. This is the most common approach used in longitudinal studies of aging, and implicitly assumes that data are missing at random. (2) A correlated random effects model (previously called simply a “random effects model”) (Wang & Hall 2010), in which separate random effects are used to model the FCSRT and MIS-T, with the correlation between the random effects estimated from the data. (3) A shared random effects model in which the FCSRT and MIS-T are assumed to vary together through a common random effect.

All three models can be described using the following model equations:

$$y_{ik} = b_{0i} + \beta_1 * age_{ik} + \varepsilon_{ik}$$

$$z_{ik} = c_{0i} + \gamma_1 * age_{ik} + \delta_{ik}$$

$$(b_{0i}, c_{0i}) \sim BVN \left((\beta_0, \gamma_1), \begin{pmatrix} \sigma_b^2 & \rho\sigma_b\sigma_c \\ \rho\sigma_b\sigma_c & \sigma_c^2 \end{pmatrix} \right) \text{ (bivariate normal distribution)}$$

$$\varepsilon_{ik} \sim N(0, \sigma_e^2) \text{ (normal distribution)}$$

$$\delta_{ik} \sim N(0, \sigma_d^2) \text{ (normal distribution)}$$

Here, y_{ik} is the value of the outcome of interest for study participant i at assessment k , z_{ik} is the value of the auxiliary variable for study participant i at assessment k , ε_{ik} and δ_{ik} are the residual terms that are assumed to be uncorrelated with each other and with the random effects, β_1 is the effect of age on the outcome of interest – the parameter we are most interested in estimating – and γ_1 is the effect of age on the auxiliary variable. b_{0i} is the random intercept for the subject i for the outcome of interest, and c_{0i} is the random intercept for subject i for the auxiliary variable. The random effects are allowed to be correlated with each other with correlation ρ . For model 1 (traditional), $\rho = 0$; for model 3 (shared random effects) $\rho = 1$; for model 2 (correlated random effects) $0 < \rho < 1$.

The models are fit separately for $\epsilon 4+$ and $\epsilon 4-$ study participants and we compare age-associated rates of decline between the two groups. Akaike's information criterion (AIC, Akaike 1974), an information-theory-based measure that takes into account model complexity, was used to compare fit between models. The models were fit via maximum likelihood using SAS version 9.3's NLMIXED and MIXED procedures (SAS Institute, Cary, NC, USA; <http://www.sas.com>).

Results

The analysis cohort included 620 EAS participants active since March 1, 2003 who had at least one administration of the MIS-T along with the FCSRT and were genotyped for APOE. 147 of the 620 study participants (24%) were $\epsilon 4+$, a lower prevalence than reported in other studies (Ward *et al.* 2011). Ten study participants had dementia and 77 had amnesic mild cognitive impairment (aMCI) at the time of the first telephone assessment. The sample included 2085 person years of follow-up. During the follow-up period (March, 2003 to July, 2011) there were 48 incident cases of dementia and 52 incident cases of aMCI based on in-person evaluations.

Table 1 shows the baseline demographic and cognitive characteristics by APOE $\epsilon 4$ status separately for participants with and without missing in person assessments. Significant baseline differences between those who missed an in person assessment and those who did not were few. $\epsilon 4+$ participants were a year younger on average, and were more likely to be non-Hispanic Black, but were otherwise similar to $\epsilon 4-$ participants. 177 $\epsilon 4+$ participants (37.4%) and 51 $\epsilon 4-$ participants (34.7%) had one or more missing in person assessments. For both $\epsilon 4+$ and $\epsilon 4-$ participants, 88% of telephone assessments were followed by an in person assessment. FCSRT scores were positively correlated with MIS-T scores (Pearson correlation 0.52 for first assessment, $p < 0.001$). Rates of age-related decline on the FCSRT were lower in those missing at least one evaluation (0.354 vs. 0.301 points/year) but differences were not significant.

Table 2 shows the results for the three approaches to modeling rates of decline in free recall in APOE $\epsilon 4$ allele carriers and non-carriers. Using the traditional model, the decline in free recall from the FCSRT was 0.284 points per year for $\epsilon 4-$ participants and 0.500 points per year for $\epsilon 4+$ participants. In the correlated random effects models rates of decline were 0.337 for APOE $\epsilon 4$ negative individuals and 0.632 for APOE $\epsilon 4+$ individuals, representing 19% and 27% increases in the rates of decline, compared to the traditional model. In the shared random effects models the corresponding rates of decline were 0.349 and 0.638, representing 23% and 28% increases in the rate of decline compared to the traditional model. The differences in the rate of memory decline (as measured by FCSRT) between $\epsilon 4+$ and $\epsilon 4-$ participants were 0.295 and 0.292 for the correlated and shared random effects models, 37% and 35% greater than the 0.216 difference seen in the traditional model. Corresponding changes in the rates of decline in the MIS-T were small. AIC indicated that the correlated random effects model fit best for both groups. High correlations between the random effects in the correlated random effects models indicated a strong association between the FCSRT and MIS-T measures. Sensitivity analyses (not shown) using the ranks of the FCSRT and MIS-T values rather than the actual measurements showed similar results.

We were concerned that the heterogeneous population that included persons with dementia or mild cognitive impairment at the beginning of the analysis period, might not be typical of all longitudinal cohort studies of cognition, so we repeated the analyses excluding the individuals with dementia or amnesic mild cognitive impairment at the first telephone assessment. The differences in the rate of memory decline (as measured by FCSRT) between 462 ϵ 4+ and 140 ϵ 4- participants were 0.315 and 0.313 for the correlated and shared random effects models, 27% and 26% greater than the 0.248 difference seen in the traditional model, showing robustness of this methodology.

Discussion

We have shown that a telephone assessment of memory that is modestly correlated with a sensitive and specific in-person assessment instrument can be used to address the informative nature of the missing data process in the in-person assessments. Numerous methods now exist for addressing potentially informative missingness situations where the missingness is associated only with the observed data, the “missing at random” (Rubin 1976) case. When missingness is associated with unobserved outcomes, the “missing not at random” case, sensitivity analyses are sometimes used to estimate the potential for bias, but this approach is of severely limited utility. The framework we present here allows the use of auxiliary data to inform investigators of the magnitude of the missingness biases.

This demonstration is limited to modeling linear decline in cognition as a function of age; more work, with larger samples, is needed to evaluate more complex trajectories. The higher the correlation of the auxiliary data with the missing outcome data of interest, the more accurate the correction should be. In addition, death itself is a cause of non-random missingness, and these analyses did not control for the well-known phenomenon of terminal decline (Sliwinski *et al.* 2006; Wilson, Beckett, Bienias, Evans & Bennett 2003; Wilson, Beck, Bienias & Bennett 2007; Thorvaldsson *et al.* 2008; Dodge, Wang, Chang & Ganguli 2011). Additional theoretical and empirical work is needed to address these concerns, and more research is needed to identify brief assessment instruments that can be used as auxiliary data for other cognitive domains as well as other outcomes of interest in longitudinal aging studies such as mobility and frailty.

Despite these limitations, this work may be significant for research in settings where informative loss to follow up is likely. In aging research, there is much interest in identifying genetic and environmental factors that are associated with increased or decreased rates of cognitive decline. Taking missingness into account may provide more robust estimates of decline and increase power for detecting the effects of genetic or environmental risk factors on cognitive trajectories, and this approach would be equally applicable to randomized trials if drop out is associated with unobserved outcomes.

Acknowledgements

Funding was provided by the National Institute of Aging, Grant # P01 AG03949, the Einstein Aging Study (PI: Richard B. Lipton), which provided partial salary support to all authors. Funding for the APOE genotyping was provided by the National Center for Research Resources, Grant # UL1 RR025750, Clinical and Translational Science Award (PI: Harry Shamoon).

References

- Akaike H. A new look at the statistical model identification. *IEEE Transactions on Automatic Control*. 1974; 19(6):716–723.
- Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Br J Psychiatry*. 1968; 114:797–811. [PubMed: 5662937]
- Daniels, MJ.; Hogan, JW. *Missing Data in Longitudinal Studies: Strategies for Bayesian Modeling and Sensitivity Analysis*. New York: Chapman & Hall; 2008.
- Derby CA, Burns LC, Wang C, Katz MJ, Zimmerman ME, L'Italiend G, Lipton RB. Screening for Predementia AD: Time dependent operating characteristics of episodic memory tests. *Neurology*. 2013; 80:1307–1314. [PubMed: 23468542]
- Dodge HH, Wang CN, Chang CC, Ganguli M. Terminal decline and practice effects in non-demented older adults: the MoVIES project. *Neurology*. 2011; 77:722–730. [PubMed: 21832224]
- Grober E, Buschke H. Genuine memory deficits in dementia. *Developmental Neuropsychology*. 1987; 3:13–36.
- Ibrahim JG, Lipsitz SR, Horton N. Using auxiliary data for parameter estimation with non-ignorably missing outcomes. *Appl. Statist*. 2001; 50:361–373.
- Katz MJ, Lipton RB, Hall CB, Zimmerman ME, Sanders AE, Verghese J, Derby CA. Age-specific and Sex-specific Prevalence and Incidence of Mild Cognitive Impairment, Dementia, and Alzheimer Dementia in Blacks and Whites: A Report From the Einstein Aging Study. *Alzheimer Dis Assoc Disord*. 2012; 26:335–343. [PubMed: 22156756]
- Lipton RB, Katz MJ, Kuslansky G, Sliwinski MJ, Stewart WF, Verghese J, Buschke H. Screening for dementia by telephone using the memory impairment screen. *J Am Geriatr Soc*. 2003; 51:1382–1390. [PubMed: 14511157]
- Laird NM, Ware JH. *Biometrics*. 1982; 38:963–974.
- Little, RJA.; Rubin, DB. *Statistical Analysis with Missing Data*. 2nd ed.. New York: Wiley; 2002.
- Morris JC. The clinical dementia rating (CDR): current version and scoring rules. *Neurology*. 1993; 43:2412–2414. [PubMed: 8232972]
- Rubin DB. Inference and missing data. *Biometrika*. 1976; 63:581–592.
- Sanders AE, Wang C, Katz M, Derby CA, Barzilai N, Ozelius L, Lipton RB. Association of a Functional Polymorphism in the Cholesteryl Ester Transfer Protein (CETP) Gene with Memory Decline and Incidence of Dementia. *J Amer Med Assn*. 2010; 303:150–158.
- Sliwinski MJ, Stawski RS, Hall CB, Katz M, Verghese J, Lipton R. Distinguishing Preterminal and Terminal Cognitive Decline. *European Psychologist*. 2006; 11:172–181.
- Thorvaldsson V, Hofer SM, Berg S, Skoog I, Sacuiu S, Johansson B. Onset of terminal decline in cognitive abilities in individuals without dementia. *Neurology*. 2008; 71:882–887. [PubMed: 18753475]
- Wang C, Hall CB. Correction of Bias from Non-random Missing Longitudinal Data Using Auxiliary Information. *Statistics in Medicine*. 2010; 29:671–679. [PubMed: 20029935]
- Ward A, Crean S, Mercaldi CJ, Collins JM, Boyd D, Cook MN, Arrighi HM. Prevalence of apolipoprotein E4 genotype and homozygotes (APOE e4/4) among patients diagnosed with Alzheimer's disease: a systematic review and meta-analysis. *Neuroepidemiology*. 2012; 38(1):1–17. [PubMed: 22179327]
- Wilson RS, Beckett LA, Bienias JL, Evans DA, Bennett DA. Terminal decline in cognitive function. *Neurology*. 2003; 60:1782–1787. [PubMed: 12796531]
- Wilson RS, Beck TL, Bienias JL, Bennett DA. Terminal Cognitive Decline: Accelerated Loss of Cognition in the Last Years of Life. *Psychosomatic Medicine*. 2007; 69:131–137. [PubMed: 17327212]

Table 1

Cohort characteristics by presence/absence of an APOE $\epsilon 4$ allele, and whether the study participant missed at least one in-person memory assessment.

	$\epsilon 4-$ with no missing in-person assessments	$\epsilon 4-$ with 1 missing in-person assessments	$\epsilon 4+$ with no missing in-person assessments	$\epsilon 4+$ with 1 missing in-person assessments
N	296	177	96	51
# telephone assessments	1255	893	359	252
# in-person assessments	1255	643	359	177
Mean age at first telephone assessment (SD) [range]	79.9 (5.28) [70.3,92.2]	79.8 (5.16) [70.7,92.2]	78.5 (4.48) [71.7,89.5]	79.9 (5.34) [71.3,89.7]
Mean years formal education (SD) [range]	14.1 (3.46) [3,21]	13.6 (3.52) [4,21]	13.9 (3.24) [5,20]	13.6 (3.68) [6,22]
# by genotype	$\epsilon 2/\epsilon 2$ 5 $\epsilon 2/\epsilon 3$ 50 $\epsilon 3/\epsilon 3$ 241	$\epsilon 2/\epsilon 2$ 1 $\epsilon 2/\epsilon 3$ 29 $\epsilon 3/\epsilon 3$ 147	$\epsilon 2/\epsilon 4$ 11 $\epsilon 3/\epsilon 4$ 77 $\epsilon 4/\epsilon 4$ 8	$\epsilon 2/\epsilon 4$ 12 $\epsilon 3/\epsilon 4$ 37 $\epsilon 4/\epsilon 4$ 2
Ethnicity	Non-Hispanic White 194 Non-Hispanic Black 83 Hispanic 14 Other 5	Non-Hispanic White 139 Non-Hispanic Black 31 Hispanic 5 Other 2	Non-Hispanic White 57 Non-Hispanic Black 37 Hispanic 2 Other 0	Non-Hispanic White 28 Non-Hispanic Black 21 Hispanic 2 Other 0
# Male (%)	122 (41.2%)	56 (31.6%)	36 (37.5%)	16 (31.4%)
Mean free recall score from FCSRT (SD) [range]	30.6 (6.80) [1,48]	30.9 (6.33) [0,44]	29.0 (7.61) [2,42]	30.5 (7.18) [12,41]
Mean first MIS-T score (SD) [range]	7.12 (1.36) [1,8]	7.25 (1.25) [2,8]	6.81 (1.80) [0,8]	7.20 (1.36) [3,8]
Mean Blessed information Memory Concentration score at first MIS-T (SD) [range]	2.25 (2.22) [0,12]	2.13 (2.38) [0,10]	2.53 (2.75) [0,14]	2.22 (2.40) [0,10]

SD = standard deviation

Table 2

Results of linear mixed models estimating rates of memory decline in $\epsilon 4+$ and $\epsilon 4-$ participants.

	Model 1 (traditional)			Model 2 (correlated random effects)			Model 3 (shared random effects)		
	$\epsilon 4-$	$\epsilon 4+$	Difference	$\epsilon 4-$	$\epsilon 4+$	Difference	$\epsilon 4-$	$\epsilon 4+$	Difference
FCSRT change (std. err.) [95% CI]	-0.2841 (.03676) [-.3563, -.2119]	-0.5002 (.08503) [-0.6683, -.3322]	0.2161 (.09264) [.03453, .3977]	-0.3371 (0.03533) [-0.4066, -0.2677]	-0.6322 (0.08028) [-0.7909, -0.4736]	0.2951 (0.08771) [.1232, .4670]	-0.3467 (0.03548) [-0.4164, -0.2770]	-0.6383 (0.08084) [-0.7981, -0.4785]	0.2916 (0.08828) [.1186, .4646]
MIS-T change (std. err.) [95% CI]	-0.07181 (0.008093) [-0.08772, -0.05591]	-0.1324 (0.02063) [-0.1732, -0.09162]	0.0606 (0.02216) [0.01717, 0.09424]	-0.06426 (0.007512) [-0.07902, -0.04950]	-0.1245 (0.01821) [-0.1605, -0.08848]	0.0602 (0.01970) [0.02159, 0.1025]	-0.04970 (0.006720) [-0.06290, -0.03649]	-0.1130 (0.01710) [-0.1468, -0.07919]	0.0633 (0.01837) [-0.02729, -0.1168]
FCSRT random effect (std. err.)	5.7676 (0.2185)	6.9083 (0.4676)		5.7908 (0.2181)	7.0303 (0.4719)		5.6765 (0.2181)	6.9583 (0.4374)	
MIS-T random effect (std. err.)	1.0349 (0.04395)	1.4261 (0.1098)		1.0522 (0.04395)	1.4387 (0.1073)		0.8804 (0.0344)	1.3123 (0.0833)	
Correlation between random effects (std. err.)	0	0		0.7541 (0.02893)	0.8749 (0.03372)		1	1	
Akaike's Information Criterion (smaller is better)	18230	5596.4		17994	5479.7		18222	5511.0	

For all models, the in-person age effect is in units of change in the sum of three trials of free recall from the Free and Cued Selected Reminding Test (FCSRT), and the telephone age effect is in units of the core on the Memory Impairment Screen – Telephone (MIS-T). The Model 1, the naïve model ignores the potential impact of informative missing data. Model 2, the correlated random effects model, models the correlation between the FCSRT and MIS-T, allowing the more complete data from the telephone instrument to influence the rate of memory decline in the in-person instrument. Model 3, the shared random effects model, is a special case of model two with a stronger correlation assumption.