

Predictors of attrition in a longitudinal cognitive aging study: Results from the Maastricht Aging Study (MAAS).

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Predictors of attrition in a longitudinal cognitive aging study: The Maastricht Aging Study (MAAS)

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Abstract

A large sample of older participants of the Maastricht Aging Study (MAAS) were compared to drop-outs at the 3-year follow-up with respect to socio-demographic, health, and cognitive characteristics. In addition, the impact of selective drop-out on measures of cognitive change was examined. To this end, hypothetical scores were estimated for drop-outs by using single and multiple imputation methods. Of the initial sample of 539 subjects, aged 49 years and older at baseline, 116 (22 %) did not return for the follow-up ($n = 32$ had died, $n = 84$ refused participation). Drop-outs who refused to participate in the follow-up were more often women, had lower educational levels, and had lower baseline scores on neurocognitive tests. Follow-up drop-outs who had died were more often men, older, and had a poorer performance on cognitive tests than the follow-up participants. Although follow-up participants and drop-outs differed in terms of socio-demographic and cognitive characteristics, attrition appeared to have little effect on the estimates of cognitive change. © 2002 Elsevier Science Inc. All rights reserved.

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1. Introduction

The main focus of longitudinal cognitive aging studies is on intraindividual changes in cognitive functioning with age. Why do some individuals show cognitive impairment while others remain healthy until advanced old age? Although a longitudinal design is the only way to study these changes, it has some methodological drawbacks, some of which may affect the accuracy of the estimates of cognitive change. One such potential drawback is the occurrence of selective attrition [1–3], which may bias estimates of cognitive change over time. For example, in a longitudinal study by Siegler and Botwinick [3], elderly participants showed almost no intellectual decline; however, close inspection of the data revealed that the subjects who remained in the study at follow-up were characterized by higher levels of general intelligence. In yet another 7-year longitudinal study, subjects who were lost due to illness or death had a lower intellectual level at baseline [2]. Thus, it seems that estimates of cognitive change may be distorted by higher functioning individuals who continue to take part in longitudinal studies. However, such bias may occur only if the

rates of change vary as function of health, education, or intelligence.

A general finding of longitudinal studies is that participants tend to differ from drop-outs in their socio-demographic and health characteristics. The latter are more likely to be older, lower educated, in poorer health [4–6], and to perform poorer on neuropsychological tests at baseline [2,3,7]. Lower educated individuals and individuals who are less healthy also show a greater cognitive decline with age [8,9]. Both observations tend to suggest that estimates of changes in cognitive functioning with increasing age may be underestimated. For this reason, we examined differences between subjects who returned for follow-up (referred to as participants) and those who did not (referred to as drop-outs). Because previous research suggested that predictors of attrition are different for those who dropped out because of death (referred to as “deceased” drop-outs) or refusal to participate (referred to as “refusal” drop-outs) [2,7], we analyzed these two main reasons for nonparticipation separately.

The second aim of this study was to determine whether differences between participants and drop-outs affect estimates of cognitive change. Analysis of follow-up data will only yield unbiased results when the follow-up participants are a random subsample of the original sample. If this is not the case, a hypothetical test score can be calculated for the

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follow-up drop-outs to correct for attrition bias. This hypothetical test score can be calculated in several ways, but it should be remembered that the method chosen has implications for the accuracy of the estimated test scores. As described by Little and Rubin [10–12], the most simple way is to impute the missing data with the unconditional mean. However, they argued that imputation of missing data in this way gives rise to standard errors that are far too low, because the variability of the imputed values is underestimated. In addition to this, the sample size is overestimated. They suggested that it is better to impute a conditional mean, which incorporates the differences between participants and drop-outs. However, the overestimation of precision remains a problem because the imputed data are treated as if they are real data. One way to solve this problem is to generate more than one value for the missing data, and thus producing more than one complete data set (multiple imputation [11]). These complete data sets can be analyzed by complete data methods. To produce overall estimates and standard errors that reflect missing data uncertainty the complete data sets can be used by rules according Little and Rubin [11].

To estimate the impact of potential selective attrition on cognitive change, we estimated hypothetical test scores for the follow-up drop-outs, using both single and multiple imputation procedures. We then determined which variables predicted cognitive change. This was done for the sample without imputation, with single imputation, and with multiple imputation.

2. Methods

2.1. Sample

Subjects in this study were participants of the Maastricht Aging Study (MAAS), a longitudinal study into determinants of cognitive aging. The study started in 1993, and included 1869 subjects aged 24 to 81 years. Individuals were randomly drawn from a patient database of general practices connected to the University of Maastricht, The Netherlands [13]. The patient database contains all relevant past and current medical morbidity of the patients. Subjects were not included in the MAAS study if they had brain-related morbidity. The sample was stratified for age (12 classes, ranging from 25 ± 1 years, 30 ± 1 years, up to 80 ± 1 years), sex, and occupational achievement (in two levels), the latter being used as an indicator of general ability. Participants were tested in four independent panel studies that were comparable with respect to inclusion and stratification criteria. An extensive description of the subject recruitment and stratification procedures is provided elsewhere [14,15].

Information from the patient database enabled comparison of several important background characteristics of the participants and drop-outs at baseline, such as age, sex, educational level, and general health status. Participation rate at baseline was found to be slightly affected by age, sex, and

education. It was lowest in the oldest age group (70 years and older). Sex affected participation in both the youngest and the oldest age groups: more younger women (participation rate was 59 and 48% for women and men, respectively), and fewer older women were willing to participate. Across all ages, individuals with a lower education were less willing to participate.

The interval between the baseline and follow-up investigations was 3 years. Only subjects aged 50 years and older were included (divided over four age classes: 50–53, 54–63, 64–73, 75+ years). At the time of analysis, information about participation status was available for two completed panel studies, including 539 individuals.

3. Measures

3.1. Predictor variables

3.1.1. Demographic variables

Information on marital status and educational level was obtained by questionnaire. The latter was measured on an eight-point scale, ranging from primary education only to higher vocational training or university degree [16]. Educational level was classified into a low and high level based on a median split procedure.

3.1.2. Health measures

Three health measures were used. First, the subject was asked to rate his/her health on a five-point scale (range: “very bad” to “very good”). Because only a few persons rated their behavior as “very bad” or as “very good,” a median split was applied to collapse the outcome in two categories. Subjective health also was measured by means of an inventory of subjective health (VOEG-21) [17]. The number of physician-prescribed medications currently taken was used as an objective index of health status [18].

3.1.3. Cognitive measures

The Mini-Mental State Examination (MMSE) was used to assess general cognitive functioning [19]. Because most persons had a MMSE-score of 27 or higher, the distribution of this variable was very skewed. Therefore, the score was dichotomised by using a median split procedure. Subjects with a score of 27 or lower were categorised as having poor cognitive functioning.

Memory was assessed with the Verbal Learning Test [20], which probes the capacity to store and retrieve newly learned verbal material. Briefly, 15 monosyllabic words were presented on a computer screen in a fixed order, one by one at a rate of one word every 2 sec. Then the subject was asked to recall as many words as possible, in his or her own order. This procedure was repeated five times. The number of correctly reproduced words after 20 min was used as the delayed recall score.

The Letter Digit Substitution Test (LDST) was used to measure the speed of processing of general information. This paper-and-pencil task is a modification of the procedurally identical Symbol-Digit-Modalities Test (see [21] and [22]).

The subject was instructed to copy numbers in cells indexed by a letter. The letter referred to nine letter/number combinations at the top of the form. The number of correctly copied numbers in 90 sec was recorded.

3.2. Statistical analyses

3.2.1. Predictors of attrition

To determine potential predictors of attrition, demographic, health, and cognitive characteristics (measured at baseline) were compared between follow-up participants and drop-outs. χ^2 statistics were used to test for differences in categorical variables. For continuous variables, such as the cognitive measures, ANOVAs were performed. To correct for possible confounding of the predictor variables, multivariate logistic regression with stepwise forward selection was used. Two multivariate analyses were performed. In the first analysis refusal status at follow-up was used as the dependent variable, and in the second one death was used as the dependent variable. In both analyses the significance of the following variables were tested: sex, educational level, marital status, health (self-rating of health, dichotomized), subjective health (VOEG), dichotomized MMSE score, delayed recall, and processing speed.

3.2.2. Estimation of test scores for follow-up drop-outs

To examine the impact of attrition on the estimated change in cognitive functioning, we computed hypothetical follow-up test scores for the drop-outs, using two methods. The first method, single based-model regression [11,12], estimated a multiple regression model from data for the follow-up participants. In the model, the test performance at follow-up was the dependent variable and the following covariates were included: age, education, sex, health (self-rating of health, dichotomized), subjective health, MMSE, and cognitive test performance at baseline. The resulting regression model was then used to compute predicted test scores for the drop-outs. The baseline values of the covariates for the drop-outs were coupled to the regression coefficients that predicted test performance at follow-up. These estimated test scores were imputed for the missing follow-up test scores of the drop-outs.

The second method, the multiple model-based imputation, also started with the estimation of a multiple regression model based on data for the follow-up participants. To introduce uncertainty in the imputed data random components were added (for the formula that were used see Crawford et al. [23] in the appendix of their paper). First, random components were added to the estimated regression variance and coefficients of the regression model based on data for the follow-up participants. At the next step, the resulting values of the regression variance and coefficients were used to predict the test scores for the drop-outs. The baseline values of the covariates for the drop-outs were coupled to these drawn regression coefficients. To account for uncertainty in predicting the outcome, a random component was added to this predicted test score, based on the estimated variance.

This procedure was repeated five times, and at the end five complete data sets were available. Following the rules of Little and Rubin [11,12] the data sets were then combined to create estimates of the overall means and regression coefficients. The variability associated with these estimates has two components (the averaged within- and between-imputation components) that were computed according to the formulas given by Little and Rubin [11,12].

4. Results

4.1. Description of participation status

The number of subjects who were lost to follow-up is presented by age group and sex in Table 1. Of the 539 subjects at baseline, 116 subjects were lost to follow-up for two main reasons: death (32 subjects, 28%) and refusal (84 subjects, 72%). The most frequently mentioned reasons for refusal to participate were “being too occupied,” “feeling too ill,” or “participation is too time-consuming.” The refusal group included one person who could not be traced after 3 years.

The proportion of drop-outs increased as a function of age. In the oldest age group (75+ at baseline) 62% returned for the follow-up, but relatively more people had died in this group. When participation was corrected for the subjects who had died, the proportion of participants was comparable across the age groups (84%).

Overall, more women than men dropped out (20 vs. 12%), but more men died. Slightly more men in the older age groups refused to participate ($\chi^2(3) = 17.24$; $P < .01$): 94% of men in the youngest group (50–55 year at baseline) participated versus 79% of men in the oldest age group. Age did not affect participation among the women ($\chi^2(3) = 2.05$; ns).

Measures taken to improve participation, such as transport to the laboratory or testing at home, increased the participation rate. In total 46 subjects, particularly older individuals, agreed to participate when they were offered transportation to the laboratory or testing at home. This resulted in an increase of 8% in the overall participation rate.

4.2. Univariate comparison of characteristics between follow-up participants and drop-outs

In Table 2 demographic, health, and cognitive characteristics are presented for the participants and drop-outs. The “refusal” drop-outs, but not the “deceased” drop-outs, had a lower educational level than the participants. Moreover, more women than men refused to participate in the follow-up, and more men than women died in the interval between baseline and follow-up. The proportion of subjects with a lower MMSE score was higher among the drop-outs (both groups) than among the participants. No differences in age, marital status, prescribed medications, or subjective health were found between the participants and the “refusal” drop-outs. In contrast, the “deceased” drop-outs were older and had a poorer subjective health than the participants.

Table 1
Participation status in MAAS by age and sex at baseline and the 3-year follow-up by age group and sex

Age	Participants (n)	Drop-outs (n)		Preserved ^a (n)		Participation rate	
	Baseline	deceased	refusal	taxi	home	%	% ^b
Men							
50–53	80	2	5	0	0	91	94
54–63	81	3	9	1	1	85	89
64–73	80	12	11	3	4	71	86
75+	34	6	7	6	4	62	79
Total	275	23	32	10	9	80	88
Women							
50–53	82	0	18	1	0	78	78
54–63	81	1	15	1	1	80	81
64–73	80	2	17	8	10	76	79
75+	21	6	2	3	3	62	90
Total	264	9	52	13	14	77	80
All	539	32	84	23	23	78	84

Note. ^anumber of subjects who made use of transport or testing at home.
^bParticipation rate corrected for the number of deceased subjects.

The scores for delayed recall and processing speed of the drop-outs differed significantly from those of the participants (processing speed: $F(2,520) = 7.544, P < .01$; delayed recall: $F(2,517) = 10.325, P < .01$). Post hoc comparisons showed that differences in processing speed were not significant between the “refusal” drop-outs and the par-

ticipants or between the “refusal” drop-outs and the “deceased” drop-outs. The baseline processing speed of the “deceased” drop-outs was slower than that of the participants, and the baseline memory scores for the drop-outs (both groups) were lower than those for the participants. Memory performance was the same in the two groups of drop-outs.

Table 2
Sociodemographic, health, and cognitive characteristics at the baseline

	Score at baseline, reassessed cases only	Score at baseline, refusals	Score at baseline, deceased
N	423	84	32
Sociodemographic variables			
Sex			
Men (n)	220 (52%)	32 (38%)	23 (72%)
Women (n)	203 (48%)	52 (62%)*	9 (28%)*
Educational level			
Low (n)	293 (69%)	70 (83%)	24 (75%)
High (n)	130 (31%)	13 (17%)**	8 (25%)
Marital status			
Not married (n)	94 (22%)	23 (28%)	9 (28%)
Married (n)	327 (78%)	60 (72%)	23 (72%)
Mean age (years) at baseline			
Health variables	63.73 (9.4)	65.83(9.2)	73.28 (8.2)**
Subjective health ^a	5.66 (4.6)	6.05 (4.1)	7.13 (5.5)
Subjective health^b			
Poor ≤ 3 (n)	157 (37%)	37 (44%)	19 (59%)
Good > 3 (n)	265 (63%)	44 (56%)	13 (41%)*
Medication			
yes (n)	221 (52%)	46 (59%)	22 (69%)
no (n)	202 (48%)	38 (41%)	10 (31%)
Cognitive variables			
MMSE			
Low ≤ 27 (n)	145 (35%)	42 (50%)	24 (75%)
High > 27 (n)	266 (65%)	41 (50%)*	8 (25%)**
Delayed recall	8.6 (3.0)	7.7 (3.0)*	6.3 (3.4)**
Processing speed	51.4 (10.2)	48.7 (11.5)	44.5 (9.6)**

Note. Subjective health^a = VOEG; Subjective health^b = self-rating of health on a five-point scale; Medication = yes/no prescribed medications; Delayed recall (# words reproduced after 20 min); Processing speed = copying task (# items correctly copied).

Univariate tests were used to compare the baseline characteristics between reassessed cases, drop-outs and deceased persons. An asterisk indicates for differences (*P < .05; **P < .01) between the reassessed group and the drop-outs.

4.3. Multivariate comparison of characteristics of follow-up participants and drop-outs

A multivariate analysis, with stepwise forward method, was performed to determine which factors contributed to attrition after controlling for other variables (see Table 3). When we compared the “refusal” drop-outs and the participants, sex and memory function were significant predictors of attrition. A higher attrition rate was predicted for women and for individuals with a lower memory performance at baseline. The second model indicated that male sex, older age, and lower MMSE score at baseline were associated with death at follow-up. In the multivariate models the variables educational level, marital status, self-rated and subjective health, medication use, and processing speed were not significant predictors of attrition.

4.4. Estimation of change scores for follow-up drop-outs and the impact of imputation on cognitive test scores

To estimate hypothetical test scores for the drop-outs, we first estimated a multiple regression model from the data of the follow-up participants. For the single imputation method, the regression coefficients of this model were used to estimate a follow-up test score for the refusal drop-outs. The multiple imputation method started by using the same regression coefficients but added random components to the regression equation. The procedure was repeated five times, and resulted in five new complete data sets. The resulting statistics were computed according the formulas of Little and Rubin [11,12]. In the upper part of Table 4, the means and standard errors are given for the memory score at baseline and for the mean score at follow-up, based on the data for the follow-up participants and on single and multiple imputation methods. Performance on the memory task seemed to be better at follow-up, which in part may be due to procedural learning. As can be seen from Table 4, the mean memory score was somewhat lower when hypothetical data were imputed. These predicted means did not differ between the two imputation methods. As expected, the standard error was larger when the multiple imputation methods was used. Next, we tested which variables predicted the follow-up memory score for the following data samples: one without imputation data, one with imputed data from the single method, and one with imputed data from the multiple

method. With all methods, a higher memory score at baseline, female sex, and a better MMSE score predicted a higher memory score, in this case more effect of procedural learning, at follow-up. Older age predicted a lower memory score at follow-up. Thus, it seems that older individuals benefit less from procedural learning. Health was not a significant predictor of memory function when only the data for the participants were used, but became significant when imputed data for the drop-outs were used. In the lower part of Table 4, the same information is given for processing speed. A lower score indicates a deterioration of the processing speed. The differences in speed scores at follow-up were minimal between the observed scores and the imputed scores. Also, the predictors of processing speed at follow-up were the same for the imputation methods used. Baseline performance explained most of the variance in processing speed at follow-up. Also, older people performed worse (had a slower processing speed) and individuals with poorer health showed a larger deterioration at follow-up. The impact of predictors on cognitive performance measures did not, however, differ between the imputation methods used.

5. Discussion

The purpose of the present study was twofold. First, we studied the extent of attrition and whether the characteristics of follow-up participants and drop-outs differ. Second, we examined whether the attrition of a select group affects the cognitive change score. Twenty-two percent of the subjects did not return for follow-up assessment. This percentage decreased to 16% when a correction was made for the subjects who had died. If additional measures had not been taken to reduce attrition, the participation rate would have been considerably lower. In total, 8% of the participants made use of the transport service or the possibility to be tested at home. We found that drop-out was not random—older people and individuals with a lower MMSE score at baseline were less likely to return for follow-up when drop-outs were analyzed as a single group. When we distinguished between those drop-outs who refused to participate (“refusal” drop-outs) and those who had died (“deceased” drop-outs), other predictors became significant. Women were more likely than men to refuse follow-up participation, irrespective of their age, as were individuals with a poor memory performance

Table 3
Summary of the logistic regression analysis on attrition for people who refused to participate and for people who had died

	Model for “refusal” drop-outs		Model for “deceased” drop-outs	
	B (SE)	Odds ratio (95% C.I.)	B (SE)	Odds ratio (95% C.I.)
Sex	.89 (.28)**	2.45 (1.42–4.20)	–1.06 (.44)*	.34 (.15–.81)
Age (in 10 years)	—	—	1.00 (.26)**	2.72 (1.62–4.57)
MMSE score	—	—	—	.28 (.12–.67)
Delayed recall	–.11 (.05)*	.89 (.82–.97)	–1.26 (.44)**	—

Note. *P < .005; **P < .01; B = regression coefficient; SE = standard error; C.I. = confidence interval

Sex: 0 = male, 1 = female; MMSE score: 0 = lower, 1 = high. Delayed recall = # words reproduced after 20 min.

Table 4

True and estimated means and standard errors of memory and speed scores at follow-up: estimated means and regression coefficients were derived by means of two different imputation methods (in the lower part: the estimated standardized regression coefficients and their standard error for the predictors)

	Score at baseline	Score at follow-up (reassessed cases only)	Score at follow-up (single imputation method)	Score at follow-up (multiple imputation method)
Memory score				
Means	8.35	9.41	9.29	9.16
SE	.13	.15	.13	.15
Speed score				
Means	50.35	50.28	49.89	49.79
SE	.46	.53	.48	.53
Predictors memory				
Baseline score		.510 (.042)**	.521 (.034)**	.526 (.045)**
Education		.043 (.329)	.045 (.204)	.048 (.256)
Sex		.080 (.226)*	.087 (.186)**	.065 (.216)*
Age		-.248 (.013)**	-.266 (.011)**	-.259 (.045)**
Self-rated health		.070 (.223)	.075 (.182)*	.083 (.242)*
MMSE		.098 (.067)*	.100 (.054)**	.103 (.070)*
	% variance	52	57	57
Predictors speed				
Baseline score		.753 (.032)**	.776 (.026)**	.771 (.033)**
Education		.013 (.644)	.011 (.546)	.019 (.616)
Sex		.037 (.573)	.037 (.473)	.035 (.525)
Age		-.154 (.035)**	-.155 (.028)**	-.152 (.036)**
Self-rated health		.062 (.589)*	.063 (.482)**	.063 (.552)**
MMSE		.023 (.176)	0.24 (.146)	.024 (.167)
	% variance	73	77	76

Note. MMSE = Mini-Mental State Examination. % variance = proportion explained variance.

at baseline. Male sex, older age, and lower MMSE score at baseline increased the likelihood of a person dying during the follow-up interval. Thus, after other socio-demographic factors were controlled for, cognitive performance seemed to be an important factor that affected the return of individuals for follow-up assessments. With respect to those individuals who died during the follow-up period, this is consistent with the terminal drop theory [24], which predicts an abrupt decline in cognitive functioning just before death. Why a lower memory performance affected participation among the “refusal” drop-outs is less obvious but seems consistent with the results of Levin et al. [25], who showed that cognitive impairment contributes to attrition bias. They gave several explanations for why this may happen. First, the tasks used in the assessment may rely on executive functions. Subjects with lower performance on such tasks may have difficulties with planning and organizational skills, which in turn, may interfere with making appointments. Another explanation that was discussed was that subjects try to avoid being confronted with possible cognitive decline and may be concerned about the possibility of developing dementia. However, it is unlikely that this reason can be applied to our individuals. First, individuals in their study were older than in this study. Second, in our study drop-out at follow-up was not restricted to older individuals only. One can only speculate about the reasons why younger participants withdrew from the study, but anticipated low performance on cognitive (particularly memory) tests may play a role.

A second factor that influenced the participation rate was sex. Women were less likely than men to return for follow-

up. Findings of longitudinal studies have not been consistent on this point. In one study men were more likely to refuse [5], whereas another study found no effect of sex at all [26]. In the latter study, it was found that sex differences were mediated by living arrangements: women who lived alone were more likely to refuse. In older age categories more women than men live alone, and it is possible that they go out less. An alternative explanation for the sex difference may be related to health. The women in this study reported more somatic and psychosomatic health complaints than the men did, which may possibly have affected the motivation of the women, and especially those in the young age group (50–55 years at baseline), to participate.

In contrast to several studies [2,4,7,26], we did not find that older people were more likely to refuse participation. This discrepancy may be because our initial sample consisted of relatively healthy individuals, in whom health problems may not have been severe enough to hinder participation. In addition, the compliance-promoting measures, such as availability of transport to the assessment center and the option of home testing, may have overcome these drawbacks. Indeed, without such measures the problem of health selection bias would have been much greater.

The second part of the study suggested that attrition affected estimates of changes in memory and performance speed. Were the observed age-related changes in cognitive performance scores underestimated because individuals with a poor cognitive performance were less likely to come to the follow-up investigation? To analyze this, we estimated a cognitive test score for the drop-outs. Because the

accuracy of this estimate depends on the method used, we compared two different approaches. Both methods used baseline information for the follow-up drop-outs to predict hypothetical follow-up test scores for this group. This was necessary because the attrition was not random: participants and “refusal” drop-outs differed with respect to memory performance, age, and sex. With the single imputation method, we accounted for the differences between the participants and the drop-outs. However, with this method the variance was underestimated. In contrast, the multiple imputation method, which made use of more than one imputation, increased the standard error of the test scores. The impact of replacing the missing test scores of the drop-outs by hypothetical data was low—the mean scores for the memory and speed tasks at follow-up were reduced minimally compared to the real mean scores of the follow-up participants. In addition, we compared the regression coefficients of the predictors for the follow-up test scores. The regression coefficients did not differ substantially between both methods. However, when predicting cognitive change, similar variables were used to predict the change and to impute missing data resulting from attrition. One would, therefore, expect stronger effects of the predictors in the imputed data sets compared with the data-set with complete data only. Although this may underlie our finding that health became a significant predictor, when imputed data were used, increasing effect sizes were not consistently found (see Table 4). Using the conditional means as our best guess of missing data, our findings foremost show that substantial attrition does not seem to seriously affect estimates of cognitive change and its predictors.

The calculations were based on certain assumptions. First, the methods we used to estimate the hypothetical test scores for the drop-outs assume that the baseline variables affected cognitive functioning at follow-up in the same way for participants as for drop-outs. Thus, although the drop-outs differed from the participants with respect to some baseline characteristics, we assumed that the association between baseline characteristics and cognitive functioning at follow-up was the same for the participants and the drop-outs. Second, we assumed that all reasons for nonparticipation were included, but it is possible that the drop-outs and the participants differed in characteristics that were not measured. However, we examined a large number of possible variables that could be different in participants and the drop-outs. Third, it can be argued that the effect on change scores would become significant when the proportion of drop-outs increases. Indeed, in addition to the magnitude of differences between participants and drop-outs, bias in the estimates of cognitive change depends on the proportion of drop-outs [27]. Finally, similar variables were used for the prediction of cognitive change and the imputation, which potentially resulted in some circularity. Further research should employ more sophisticated techniques than we were able to use in this study to obtain more reliable estimates of attrition bias. For example, one may consider additional ef-

forts to obtain some cognitive outcome measures of (a part of) the nonparticipants at follow-up. These could then be used to compare the effect sizes of the predictors of cognitive change in a more reliable fashion.

In summary, we found that a select group of individuals returned for follow-up. Older persons and persons with a lower level of cognitive functioning were more likely to drop out. This information may be used to keep individuals with a high risk of dropping out in the study, for example, by taking additional measures to improve participation rates in these groups. Although the effect of attrition on cognitive change was small, there was some indication that cognitive change may be underestimated if a select group of people drops out of the study. To correct for this bias, multiple imputation methods may be helpful. However, it remains important to provide a detailed description of participants and drop-outs to allow a good interpretation of results.

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