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Enrollment in a Brain Magnetic Resonance Study: Results From the Women's Health Initiative Memory Study Magnetic Resonance Imaging Study (WHIMS-MRI)¹

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Abstract

Rationale and Objectives—The rates of enrollment of volunteers for brain magnetic resonance imaging (MRI) studies vary by demographic and clinical characteristics. We use data from a large MRI study to identify factors associated with differential enrollment and to examine potential biases this may produce in study results.

Materials and Methods—Results from recruitment of 1,431 women into the MRI substudy of the Women's Health Initiative Memory Study (WHIMS-MRI) are described. A sensitivity analysis was conducted to estimate the degree of bias associated with missing data on estimates of risk factor relationships.

Results—Of 2,345 women contacted from an established cohort of women older than 70 years of age, 72% consented to undergo screening for WHIMS-MRI. Scanning was ultimately completed on 61%. Completion rates varied according to a range of sociodemographic, lifestyle, and clinical characteristics that may be related to study outcomes. Plausible levels of selective enrollment in magnetic resonance imaging studies may produce moderate biases (< ±20%) in characterizations of risk factor relationships. Adverse events, such as claustrophobia, occurred during 1.7% of the attempted scans and, in 0.8% of instances, led to lost data.

Conclusions—Enrollment of older women into brain imaging studies is feasible, although selection biases may limit how well study cohorts reflect more general populations.

Keywords

Informed consent; magnetic resonance imaging; clinical trial

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Clinical trials and cohort studies increasingly are designed to include magnetic resonance imaging outcomes. Experiences with this new technology have provided successful protocols for standardized measurement, assessment, and safety (1-4). Brain magnetic resonance studies conducted in established cohorts have reported consent rates ranging from 71% to 90% and yields of completed imaging in 57%–72% of contacted individuals. However, these rates appear to vary markedly among subgroups based on important demographic and clinical factors (3,6-9). Thus, although it appears that recruitment into brain magnetic resonance imaging (MRI) studies is feasible, differential selection could have the potential to bias research findings.

We used data from the Women's Health Initiative Memory Study Magnetic Resonance Imaging Study (WHIMS-MRI) to explore potential biases. We report rates of women who consented to undergo screening for the study, as a whole and by various subgroups, to identify potential barriers to recruiting participants. We also report the rates that MRI images were obtained, which are jointly affected by consent, eligibility criteria, and factors that interfere with imaging, such as claustrophobia. A sensitivity analysis was then performed to understand how selection biases inherent in enrollment may ultimately influence estimates of relationships among study outcomes. Additionally, we also describe the rate and nature of serious adverse events that were reported during the scanning procedure, some of which resulted in interruption of scanning and loss of data.

METHODS

Study Design

The WHIMS program consisted of parallel placebo-controlled randomized clinical trials of postmenopausal estrogen therapy with and without progestin therapy. The WHIMS study designs, eligibility criteria, and recruitment procedures have been described previously (10). Participants were recruited from 38 of the 40 centers participating in the Women's Health Initiative (WHI) Estrogen-Alone and Estrogen Plus Progestin clinical trials (11,12). To be eligible, women were between 65 and 79 years of age and free of dementia according to standardized study protocols involving psychometric testing, clinical evaluation, and central adjudication (10). Written informed consent was obtained; the National Institutes of Health and Institutional Review Boards for all participating institutions approved the protocols and consent forms.

Following discovery of an unfavorable risk-to-benefit ratio of its noncognitive end points, administration of study drug in the WHI Estrogen Plus Progestin trial was stopped early (July 2002) (13). The WHI Estrogen-Alone trial was also stopped early for harm from an adverse risk profile with respect to stroke and a lack of benefit for cardiovascular disease (February 2004) (14). These decisions ended the two WHIMS trials, with average follow-up of 4.0 and 5.2 years, respectively (15-18). Women continued to be seen annually after the conclusion of the WHIMS trials, with the objective to understand whether the adverse consequences of hormone therapy on cognitive outcomes demonstrated by these two trials continued after cessation of study treatment.

WHIMS-MRI was designed to contrast neuroradiologic outcomes among women older than age 70 who had been assigned to active versus placebo therapy during the WHIMS trials. It was conducted in 14 of the original 38 WHIMS clinical centers, selected based on interest, experience in conducting multicenter MRI studies, participation in an ancillary study to WHIMS (the Women's Health Initiative Study of Cognitive Aging), and availability of necessary equipment. All participants in these centers were to be solicited for potential screening to join WHIMS-MRI, regardless of their prior adherence to the WHI study protocol, on-trial use of study medications, on-study measures of cognitive function, or their willingness

to continue posttrial follow-up. This contact was made by a variety of means, including telephone, mailings, and face-to-face meetings during scheduled study visits. The purposes of these contacts were to inform potential participants of the WHIMS-MRI study and to obtain informed consent for screening. A model consent form (<https://www.phsapps.wfubmc.edu/whims/index.cfm>) was circulated and clinical sites tailored this according to local practices and institutional review board guidance. Trained WHI clinic staff described the purpose of obtaining MRI images, steps taken to protect the participant's confidentiality and privacy in terms of how images and records would be managed and how research would be presented, a description of the MRI procedure, and a discussion of how participant safety would be maintained. The participant was allowed to read the consent form in private. Women who provided this consent underwent screening to determine if they were acceptable candidates for MRI. Exclusion criteria included the presence of pacemakers, defibrillators, neurostimulators, prohibited medical implants, and foreign bodies (eg, bullets, shrapnel, metal slivers) that would pose a hazard to the participant during the MRI procedure. Other exclusion criteria included shortness of breath or inability to lie flat and conditions that can be exacerbated by stress (eg, anxiety/panic disorders, claustrophobia, uncontrolled high blood pressure, seizure disorders) severe enough to preclude an MRI.

Baseline Data Collection, Variable Definitions, and Data Analysis Plans

We assembled a range of factors to serve as markers of health, culture, demography, and lifestyle. We wished to explore whether there was evidence that screening consent rates differed according to these attributes. Thus, although we include diabetes among the factors examined, we view it more generally as a marker of health rather than a specific medical condition. We used the same factors to examine associations with our success in ultimately obtaining an image. In some cases, these factors were associated with eligibility criteria (eg, heart disease was related to use of a pacemaker) and thus there is some degree of causality. Factors were collected by standardized questionnaires, either self- or staff-administered, or by clinical measures obtained from trained and certified technicians, as discussed in greater detail elsewhere (10,11). These included characteristics at the time of enrollment (age, education, ethnicity, and history of stroke or transient ischemic attack or coronary heart disease) and prior treatment assignment. Self-reported medical conditions were used because conditions known to the participant would be more likely to influence behavior than events adjudicated through the WHI process. Annual Modified Mini-Mental state (3MS) exams were used to measure global cognition (19). Women were classified according to whether they had experienced declines of two standard deviations (eight units) on the 3MS during follow-up. The average time between the start of WHI data collection and the start of WHIMS-MRI enrollment was 8 years.

A subset of WHIMS-MRI women were enrolled in the Women's Health Initiative Study of Cognitive Aging, (18) which included an annual assessment of depression using the Geriatric Depression Scale-Short Form (GDS-SF) to measure nonsomatic features of depressed mood (20). We grouped these women according to whether there was evidence of depressive symptoms measured within the past year (GDS-SF score >5) or not.

Univariable and multivariable associations between these participant characteristics and the rates of consent and of successful imaging were examined with logistic regression. Backward stepwise logistic regression was used to identify important sets of factors that were mutually associated with agreement. Associations were summarized with odds ratios. Model fit was assessed with influence plots (21). Because many factors were interrelated, these approaches may not have characterized the full expression of all important multivariate relationships. Sensitivity analyses were conducted to examine the potential breadth of biases in study

outcomes that derive from selection biases we describe. A P value $< .05$ was considered significant.

RESULTS

Recruitment for the WHIMS-MRI study began in January 2005 and was completed by April 2006 (Fig 1). Over this period, 2,345 WHIMS participants were approached for enrollment in WHIMS-MRI and 1,688 (72%) consented to undergo screening for the study. Of those screened, 1,431 (61%) ultimately provided MRI scans, which was 99% of the study goal of 1,450.

Rates of Consent for WHIMS-MRI Enrollment

Table 1 presents rates that consent was provided among subgroups of women defined by markers of socio-demographic, lifestyle, and clinical factors. Rate of consent varied significantly by several factors that we examined. Consent was more frequent among women who were younger than 82 years of age, who reported more formal education, and who did not have a history of heart disease. Consent was also more frequent among women with higher levels of global cognitive function, as measured by 3MS examinations, and for women who experienced less cognitive decline during the WHIMS trial. Consent did not appear to be strongly related to ethnicity, smoking, history of cerebrovascular disease, diabetes, alcohol intake, body mass index, or WHI treatment assignment.

Backwards stepwise logistic regression was used to select a group of these factors that appeared to have the strongest independent associations with rates of consent. These included age, education, history of heart disease, and on-trial cognitive decline (Table 2). From the multi-variable model, the odds of consent were about 40% greater among women ages 70–81 than those ages 82–88. The rates were similar for women with and without a history of heart disease. The odds of consent increased steadily with education level, such that approximately 40% more college graduates consented than did those with a high school (or less education). Consent rates were approximately 40% higher among women without marked on-trial cognitive decline compared with those with cognitive decline.

Rates of Obtaining MRIs

Of those who consented, 5.35% were excluded because of contraindications to MRI imaging, with the presence of a pacemaker (2.38%) being the most common reason for exclusion (Table 3).

After excluding those with a contraindication, the individual factors associated with variable rates in obtaining MRI scans include all those that were associated with consent (age, education, history of heart disease, baseline cognition, and on-trial cognitive decline), as listed in Table 1. In addition, current smoking and diabetes were found to be significantly associated with reduced odds of obtaining an image.

Backwards stepwise logistic regression selected six factors as being independently associated with variable rates of obtaining scans (Table 4). The odds of completing scans were approximately 60% greater among women in the lowest two tertiles of age (e.g. ≤ 81 years), compared with the oldest tertile. Less education, heart disease, diabetes, current smoking, and an on-trial marked decrease of 3MS were each independently associated with lower odds of obtaining scans.

Associations with Depression

GDS-SF scores within the last year were available for 1,646 women who were approached about enrolling in WHIMS-MRI; 1,272 provided consent for screening. Consent for screening was lower among women with depressive symptoms (GDS-SF >5) than those without: 67% versus 78% ($P = .005$). Among women who consented to screening, MRIs were less often obtained among these women, as well: 55% versus 68% ($P = .006$).

Rates of Adverse Events

Adverse events were defined to be conditions that arose during the MRI study visit or during the scanning procedure that elicited a participant complaint or injury. These may have resulted in interruption of the scanning procedure and loss of data. Overall, 25 adverse events were encountered: 12 of claustrophobia (0.8%), 6 of difficulty breathing (0.4%), 2 each of pain while lying flat, dementia-unable to cooperate, and postnasal drip/excessive swallowing (each 0.1%), and 1 recorded as fear of scanner. These adverse events results in 12 losses of data: 6 from claustrophobia, 2 from difficulty of breathing, and 1 from each of the other reasons. No serious adverse events (ie, those that required medical treatment) were noted during this study.

DISCUSSION

The failure to obtain potential study outcomes from planned individuals, whether because of nonconsent or measurement difficulties, affects costs and introduces biases. For studies of magnetic resonance imaging, because of its intrusive nature and complexity, nonconsent and missing data may be especially important issues. It may be expected that selection biases in these studies may differ from those in other research protocols.

Rates of Consent for Screening and Imaging Yields

Table 5 summarizes the rates that participants in large cohort studies have agreed to be screened for brain MRI studies and the rates that images were ultimately collected. Consent rates varied from 71% to 90% and yields varied from 57% to 72%. Although the characteristics of cohorts and consenting protocols varied among studies, the collective experience indicates that large MRI studies are quite feasible to plan and conduct using established cohorts. The rates observed in WHIMS-MRI, 72% consenting to undergo screening and 61% ultimately being scanned, align with the reports from other studies.

Factors Associated with Missing Data

WHIMS-MRI and other studies have identified many factors that appear to be associated with differential rates of obtaining images (Table 6). Consistently, these include demographic markers (age, education, income), markers of chronic disease (cardiovascular disease, diabetes), and cognitive status. Less consistently, other factors related to risk and health (body weight, cerebrovascular disease, hypertension) may be associated with missing data. WHIMS-MRI adds to this list cognitive decline and depression. In total, these studies suggest that the factors associated with missing data in MRI studies are varied and may be complex. Because of this, and because many of the related factors are expected to have strong associations with MRI outcomes, results from MRI studies are likely to have some bias, as discussed in the following section.

In general, many of relationships suggest that brain MRI studies are likely to enroll cohorts that are of relatively lower risk for neuropathology than the targeted populations, and thus may underestimate the prevalence of disease and have diminished power for detecting risk factor relationships.

Recruitment programs for MRI studies should be sensitive to potential barriers associated with older age, cognitive declines, and chronic diseases; greater commitment of resources to recruitment may be required than for other populations. It is not surprising that these factors influence enrollment in MRI studies, even among women who previously enrolled in less “invasive” studies. Anxiety about MRI scanning has been reported to be related to fear of enclosed places, pain, the unknown, and apprehension about potential findings (23). It has been reported that as many as 20% of patients may experience claustrophobia severe enough to preclude the completion of attempted MRI, (24) and many of these would be unlikely to agree to screening.

We find it of interest that among these studies, enrollment rates appeared to be fairly uniform across ethnic groups. Historically, many barriers have been described in recruiting individuals from ethnic minorities into clinical research (25-28).

Potential Impact of Nonconsent on Findings

The goal of the WHIMS-MRI is to identify relationships that hormone therapy and cognitive risk factors have with silent infarcts and other neuroradiologic outcomes. Yields across the four arms of the WHIMS trials were fairly similar, which provides some reassurance that intention-to-treat comparisons may provide balanced assessments of relative differences. Secondary goals of the WHIMS-MRI, however, include examining relationships that suspected risk factors have with MRI outcomes. For these, selection biases may complicate analyses. Consider the table in Fig 2. MRI data are not available for the lower panel; however, within the context of an established cohort, data on the risk factor would be expected to be available.

If MRI data are missing completely at random (ie, the probability of missing data is unrelated to MRI outcomes), the lower panel of Fig 2 may be ignored in analyses. WHIMS-MRI data suggest that this may not be the case because “missingness” is related to many factors that have associations with neuropathology. If missingness is indeed related to the risk factor or MRI outcome, ignoring the lower panel may result in bias. In such cases, it may be possible to develop models that statistically account for these relationships. If successful, this approach yields data that are “missing at random,” for which many analytical approaches are appropriate (29). If data are missing at random and if data collection rates are fairly high, estimation bias can be controlled to be relatively modest through the use of statistical methods (30). If models cannot be found to account for relationships, missing data are not ignorable. In such cases, expected bias is related to the rate of consent and the strength of associations causing the “non-ignorability” (31).

Sensitivity analyses may be used to examine the potential breadth of biases. As an example of these, we consider a situation in which rates of missing data are conditionally independent of whether an MRI scan is performed, but vary depending on an intermediate or confounding variable and a risk factor that are both linked to MRI outcomes. An example may be cognitive decline, which may be associated both with MRI risk factors and MRI outcomes. We simulated data ($n = 100,000$) in which the odds ratio relating a risk factor to an MRI outcome was 4.0 both among individuals with and without the confounding factors. We examined situations in which the confounding factor had relationships with the risk factor and MRI outcome described by odds ratios of 2.0 and 3.0, respectively, and in which the overall prevalence of the risk factor, MRI outcome, and confounding factor were all 50%. (The range of associations associated with odds ratios of 2.0 to 4.0 may be described as moderate to large) (32). We then randomly withdrew individuals from the cohort at rates that varied depending on the confounding factor (as if their MRI scans were not completed). We considered the impact of analyses on the remaining cohort (relative to an analysis based on the entire cohort), when rates of missing MRI scans ranged from 20% to 40% for individuals with or without the confounding factor and according to the status of the risk factor, as displayed in Table 6. The range of assumptions

we explored produced non-ignorable missing data in some cases and was sufficient to introduce biases ranging from -17% to 19% in estimates of odds ratios relating risk factors to outcomes. Thus, analyses limited to women providing MRI scans may both under- and overestimate the strength of relationships between risk factors and outcomes in the target population. In our example, the magnitude of this bias may be as large as 19%.

Adverse Events

The low frequency of adverse events may be associated with the WHIMS-MRI screening procedures and the use of special guidelines for participants with a history of claustrophobia. Even when rigorous exclusion criteria are used, however, some adverse events must be expected. Therefore, in addition to careful documentation and categorization of adverse study events, safety protocols should be in place for managing these as they occur.

Limitations

Our analyses are limited to women who have met the criteria for participation in the WHI and WHIMS clinical trials and who had previously agreed to participate in these trials. As documented, these women may not be representative of the general US population, tending to be healthier, better educated, and having already committed to participating in rigorous clinical trials (12,33). Enrollment in WHIMS-MRI was from an existing cohort with a history of volunteerism for medical research. The rates we report likely exceed those associated with de novo recruitment, and other selection biases may occur (5,22).

CONCLUSIONS

Enrollment of older individuals from established cohorts into brain MRI studies appears to be very feasible. Selection factors differ from those for other biomedical studies and may, if not addressed, introduce moderate levels of bias in findings.

APPENDIX A

Roster of WHIMS-MRI Sites and Staff

Clinical Centers:—Albert Einstein College of Medicine, Bronx, NY: Sylvia Wassertheil-Smoller, Mimi Goodwin, Richard DeNise, Michael Lipton, James Hannigan; Medical College of Wisconsin, Milwaukee: Jane Morley Kotchen, Diana Kerwin, John Ulmer, Steve Censky; Stanford Center for Research in Disease Prevention, Stanford University, Stanford, CA: Marcia L. Stefanick, Sue Swope, Anne Marie Sawyer-Glover; The Ohio State University, Columbus: Rebecca Jackson, Rose Hallarn, Bonnie Kennedy; University of California at Davis, Sacramento: John Robbins, Sophia Zaragoza, Cameron Carter, John Ryan; University of California at Los Angeles: Lauren Nathan, Barbara Voigt, Pablo Villablanca, Glen Nyborg; University of Florida, Gainesville/Jacksonville: Marian Limacher, Sheila Anderson, Mary Ellen Toombs, Jeffrey Bennett, Kevin Jones, Sandy Brum, Shane Chatfield; University of Iowa, Davenport: Jennifer Robinson, Candy Wilson, Kevin Koch, Suzette Hart; University of Massachusetts, Worcester: Judith K.Ockene, Linda Churchill, Sharon Jackson, Douglas Fellows, Anthony Serio; University of Minnesota, Minneapolis: Karen Margolis, Cindy Bjerk, Chip Truwitt, Margaret Peitso; University of Nevada, Reno: Robert Brunner, Ross Golding, Leslie Pansky; University of North Carolina, Chapel Hill: Carol Murphy, Maggie Morgan, Mauricio Castillo, Thomas Beckman; University of Pittsburgh, Pittsburgh, PA: Lewis Kuller, Pat McHugh, Carolyn Meltzer, Denise Davis.

Clinical Coordinating Center:—Wake Forest University Health Sciences, Winston-Salem, NC: Sally Shu-maker, Mark Espeland, Steve Rapp, Claudine Legault, Laura Coker, Maggie

Dailey, Josh Tan, Debbie Felton, LeeAnn Andrews, Julia Robertson, Patricia Hogan, Sarah Jaramillo, Jeff Williamson.

WHIMS-MRI Quality Control Center:—University of Pennsylvania, Philadelphia, PA: Nick Bryan, Christos Davatzikos, Lisa Desiderio.

U.S. National Institutes of Health:—National Institute on Aging, Baltimore, MD: Susan Resnick.

U.S. National Institutes of Health: National Heart, Lung, and Blood Institute, Bethesda, MD:—Jacques Rossouw, Linda Pottern; National Institute on Aging: Neil Buckholtz, Susan Molchan.

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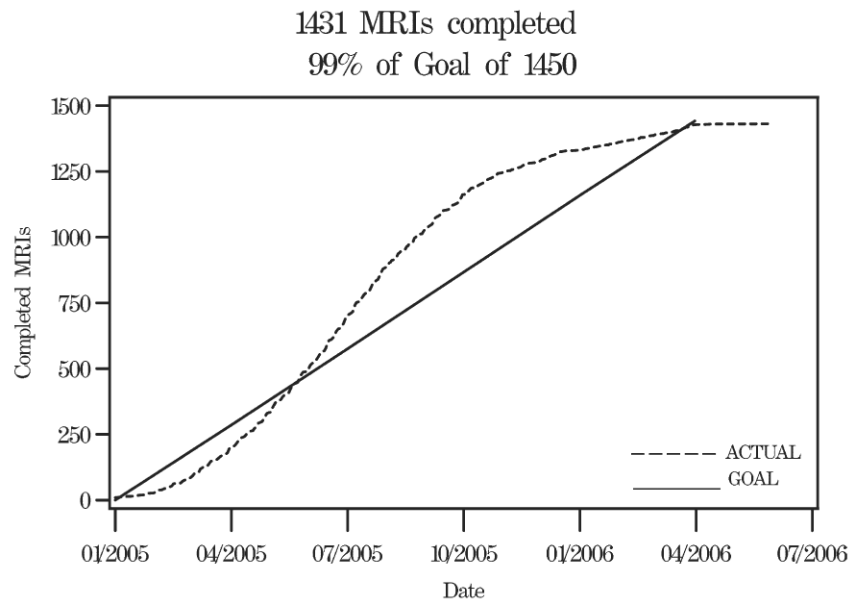


Figure 1. Enrollment Women's Health Initiative Memory Study Magnetic Resonance Imaging Study over time.

		Risk Factor	MRI Outcome	
			X	Not X
MRI Completed	No			
	Yes			
MRI Not Completed		Risk Factor	X	Not X
		No	MRI Outcome Unknown	
		Yes	MRI Outcome Unknown	

Figure 2.
Observed and unobserved data.

Table 1
 Characteristics of Participants Enrolled in WHIMS Grouped by Whether They Provided at Least Some Level of Consent to Participate in the WHIMS-MRI Study

Characteristic	n	Consent for Screening		MRI Obtained	
		Percent Providing Consent	Chi-square P Value	Percent MRI Obtained	Chi-square P Value
Overall	2,345	72%		61%	
Age					
70–75	766	74%		64%	<.001
76–81	1,144	73%		63%	
82–88	435	64%		50%	
Education, years					
<12 (high school)	136	63%	.001	50%	<.001
High school	574	68%		57%	
Some college	1,149	72%		61%	
College diploma	486	77%		67%	
Race/ethnicity					
African-American	105	70%		62%	
American Indian	6	67%		67%	
Asian	31	81%	.594	74%	.447
White	2,141	72%		61%	
Hispanic	31	84%		68%	
Other/multiple	23	70%		48%	
Smoking					
Never	1,324	73%		62%	
Former	877	71%	.123	61%	.025
Current	120	64%		49%	
History of cerebrovascular disease					
No	2,280	72%	.064	61%	.364
Yes	65	62%		55%	
History of heart disease					
No	2,103	73%	.008	62%	<.001
Yes	242	64%		48%	
History of diabetes					
No	2,193	72%	.062	61%	.013
Yes	152	65%		51%	
Alcohol intake					
None	1,078	71%		58%	
<1/day	421	73%	.684	65%	.084
2–3/day	422	73%		64%	
4+/day	419	73%		60%	
Physical activity (METs/wk)					
<3.5	772	71%		60%	
3.6–12.5	801	70%	.183	59%	.081
12.6+	772	74%		64%	
Body mass index (kg/m ²)					
<20.0	62	68%		58%	
20.0–24.9	643	71%		60%	
25.0–29.9	861	72%	.86	62%	.612
30.0–34.9	493	73%		62%	
35.0+	275	73%		57%	
Drop in 3MS score from baseline					
<8 (<2 SD)	2,138	73%	.005	62%	.003
8+ (≥2 SD)	207	63%		51%	
Baseline 3MS score					

Characteristic	n	Consent for Screening		MRI Obtained	
		Percent Providing Consent	Chi-square P Value	Percent MRI Obtained	Chi-square P Value
95-100	1,720	73%		63%	
90-94	451	69%	.025	57%	.005
<90	157	65%		51%	
Former treatment assignment					
E+P	719	72%		62%	
E+P placebo	725	71%	.604	63%	.334
E-alone	447	74%		58%	
E-alone placebo	454	70%		59%	

METS: metabolic equivalents; SD: standard deviation; 3MS: Modified Mini-Mental state; E = estrogen; P = progestin.

Table 2

Factors Selected by Backward Stepwise Logistic Regression as being Strongly and Independently Associated with Agreement to Participate in Screening

Characteristic	Odds Ratio	95% Confidence Interval	P Value
Age			
70–75	1.48	(1.14–1.92)	.004
76–81	1.47	(1.15–1.87)	
82–88	1.00	—	
Education, years			
<12 (high school)	0.51	(0.34–0.78)	.001
High school	0.62	(0.47–0.82)	
Some college	0.78	(0.61–1.01)	
College diploma	1.00	—	
Heart disease			
No	1.38	(1.04–1.83)	.028
Yes	1.00	—	
Drop in 3MS score from baseline			
<8 (<2 SD)	1.38	(1.02–1.88)	.039
8+ (≥2 SD)	1.00	—	

SD: standard deviation; 3MS: Modified Mini-Mental state.

Table 3
 Contraindications to Magnetic Resonance Imaging: Frequency and Prevalence Rate and Responding Participants

Report Detailed and/or Summarized Report Contraindication	Frequency	Percent
Pacemakers	40	2.38
Other implantable devices*	4	0.24
Intracranial aneurysm clip	4	0.24
Cochlear implant	3	0.18
Harrington rods	2	0.12
McGee stapes implant	2	0.12
Defibrillator	1	0.06
Other†	9	0.54
Not specified	26	1.55
Total	91	5.41

* Defibrillator, transcutaneous electrical nerve stimulation (TENS) unit, and pump ($n = 2$).

† Two metal plates, three stents, two implants, one rod, one prosthetic device.

Table 4
 Factors Selected by Backward Stepwise Logistic Regression as being Strongly and Independently Associated with Ultimately Obtaining a Study Magnetic Resonance Image

Characteristic	Odds Ratio	95% Confidence Interval	P Value
Age			
70–75	1.74	(1.36–2.23)	
76–81	1.66	(1.32–2.10)	<.001
82–88	1.00	—	
Education, years			
<12 (high school)	0.51	(0.34–0.76)	
High school	0.61	(0.47–0.79)	<.001
Some college	0.75	(0.60–0.95)	
College diploma	1.00	—	
Heart disease			
No	1.58	(1.20–2.08)	.001
Yes	1.00	—	
Diabetes			
No	1.50	(1.07–2.11)	.020
Yes	1.00	—	
Smoking			
Never	1.90	(1.29–2.78)	
Past	1.78	(1.20–2.62)	.005
Current	1.00	—	
Drop in 3MS score from baseline			
<8 (<2 SD)	1.36	(1.01–1.83)	.423
8+ (≥2 SD)	1.00	—	

Characteristics Reported to be Associated with Lower Rates of Brain MRI Collection Across the Cohort Targeted for Enrollment

Table 5

Study	Characteristics of Targeted Cohort	Consent Rate	Image Collection Rate	Characteristics Associated with Lower Rates	Factors Not Associated with MRI Scan Rates
Cardiovascular Health Study (6)	<i>n</i> = 5,888 men and women aged ≥69 years	88%	72%	Older age, less education, lower family income, history of smoking, cardiovascular disease, cerebrovascular disease, diabetes, hypertension	Ethnicity, gender
Atherosclerosis Risk in Communities (3)	<i>n</i> = 4,474 men and women aged 55–74 years	73%	67%	Younger age, less education, greater body weight, lower high density lipoprotein cholesterol	Blood pressure, glucose, triglycerides
Rotterdam Scan Study (7)	<i>n</i> = 1,904 men and women aged 60–90 years	90%	57%	Older age, less education, lower cognitive function	Cholesterol, body weight, blood pressure
Honolulu-Asia Aging Study (8)	<i>n</i> = 845 men with mean age 82 years	71%	68%	Older age, cerebrovascular disease, dementia, ApoE4 genotype	
Framingham Scan Study (9)	<i>n</i> = 4,100 men and women aged 32–103 years	80%*	71%*	Older age, higher blood pressure, hypertension, greater body weight, diabetes, higher glucose, cardiovascular disease, cerebrovascular disease	Gender, cholesterol, high density lipoprotein-cholesterol, smoking, alcohol intake
WHIMS-MRI	<i>n</i> = 2,345 women aged 70–88 years	72%	61%	Older age, lower education, history of smoking, cardiovascular disease, diabetes, cognitive function, cognitive decline, depression	Ethnicity, history of cerebrovascular disease, alcohol intake, physical activity, body weight

MRI: Magnetic resonance imaging.

* Projected.

Table 6

Expected Relative Bias Associated with Missing MRI Scans When Rates of Missing Data Depend on a Confounding Factor. The Prevalence of the Risk Factor, MRI Outcome, and Confounding Factor were Each Assumed to be 50%

Risk Factor				Expected Relative Bias in Estimated Odds Ratio Relating Risk Factor to Outcome
Absent		Present		
Confounding Factor		Confounding Factor		
Absent	Present	Absent	Present	
20%	20%	20%	20%	0%
		40%	40%	-9%
		20%	20%	9%
	40%	20%	40%	-1%
		20%	20%	9%
		40%	40%	-1%
40%	20%	20%	20%	19%
		40%	40%	8%
		20%	20%	-9%
	40%	20%	40%	-17%
		20%	20%	0%
		40%	40%	-9%
	20%	20%	20%	-1%
		40%	40%	-10%
	40%	20%	20%	9%
		40%	40%	0%