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Older Adults' Attitudes Toward Enrollment of Noncompetent Subjects Participating in Alzheimer's Research

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Recommended Citation

Karlawish, J., Rubright, J., Casarett, D., Cary, M., Ten Have, T., & Sankar, P. (2009). Older Adults' Attitudes Toward Enrollment of Noncompetent Subjects Participating in Alzheimer's Research. Retrieved from http://repository.upenn.edu/bioethics_papers/64

Reprinted from:

Karlawish J, Rubright J, Casarett D, Cary M, Ten Have T, Sankar P. Older Adults' Attitudes Toward Enrollment of Non-competent Subjects Participating in Alzheimer's Research. *American Journal of Psychiatry*. 2009; 166: 182-8. Epub 2008 Oct 15.

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<http://ajp.psychiatryonline.org/cgi/content/abstract/166/2/182>

doi: 10.1176/appi.ajp.2008.08050645

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Older Adults' Attitudes Toward Enrollment of Noncompetent Subjects Participating in Alzheimer's Research

Abstract

OBJECTIVE: Research that seeks to enroll noncompetent patients with Alzheimer's disease without presenting any potential benefit to participants is the source of substantial ethical controversy. The authors used hypothetical Alzheimer's disease studies that included either a blood draw or a blood draw and lumbar puncture to explore older persons' attitudes on this question.

METHOD: Face-to-face interviews were conducted with 538 persons age 65 and older. Questions explored participants' understanding of research concepts, their views on enrolling persons with Alzheimer's disease in research, and their preferences regarding having a proxy decision maker, granting advance consent, and granting their proxy leeway to override the participant's decision. Additional questions assessed altruism, trust, value for research, and perceptions of Alzheimer's disease.

RESULTS: The majority (83%) were willing to grant advance consent to a blood draw study, and nearly half (48%) to a blood draw plus lumbar puncture study. Most (96%) were willing to identify a proxy for research decision making, and most were willing to grant their proxy leeway over their advance consent: 81% for the blood draw study and 70% for the blood draw plus lumbar puncture study. Combining the preferences for advance consent and leeway, the proportion who would permit being enrolled in the blood draw and lumbar puncture studies, respectively, were 92% and 75%. Multivariate models showed that willingness to be enrolled in research was most strongly associated with a favorable attitude toward biomedical research.

CONCLUSIONS: Older adults generally support enrolling noncompetent persons with Alzheimer's disease into research that does not present a benefit to subjects. Willingness to grant their proxy leeway over advance consent and a favorable attitude about biomedical research substantially explain this willingness.

Keywords

research ethics, proxy consent, Alzheimer's disease

Disciplines

Bioethics and Medical Ethics | Geriatrics

Comments

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© 2009 American Psychiatric Association. The official published article is available online at:

<http://ajp.psychiatryonline.org/cgi/content/abstract/166/2/182>

doi: 10.1176/appi.ajp.2008.08050645

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Older adults' attitudes toward noncompetent subjects participating in Alzheimers research

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Published in American Journal of Psychiatry,
Volume 166, February 2009, pages 182-188.

Word count: 3497

Tables: 3

Figures: 1

Older adults' attitudes toward noncompetent subjects participating in Alzheimers research

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This research supported by National Institute of Mental Health grant # R01-MH071643, a Greenwall Faculty Scholars Award in Bioethics to Dr. Karlawish, and The Marian S. Ware Alzheimer Program.

All authors report no competing interests.

Short title: proxy preferences

Key words: research ethics, proxy consent, Alzheimers disease

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Abstract.

Objective: Since research that enrolls noncompetent patients with Alzheimers disease and does not present potential benefit to subjects is the source of substantial ethical controversy, we assessed willingness to have a proxy for research decision making, and, for each of two Alzheimers disease biomarker studies (minimal risk blood draw and a greater than minimal risk blood draw and lumbar puncture), willingness to grant an advance consent, and willingness to grant a proxy leeway over advance consent.

Methods: Face to face survey of 538 persons 65 and over who resided in the Southeastern Pennsylvania region

Results: The majority 83% (445/538) granted advance consent to a blood draw study and nearly half to a blood draw plus lumbar puncture 259 (48%). Most persons (96%) were willing to identify a proxy for research decision making and most were willing to grant their proxy leeway over their advance consent: blood draw 434 (81%), and 375 (70%) blood draw plus lumbar puncture. Combining the preferences for advance consent and leeway, the proportion who would permit being enrolled in the blood draw and spinal fluid sample studies were, respectively, 92% (497/538) and 75% (404/538). Multi-variate models showed that willingness to be enrolled in research was most strongly associated with a favorable attitude about biomedical research.

Conclusions: Older adults generally support enrolling noncompetent persons with Alzheimers disease into research that does not present a benefit to subjects. Willingness to grant their proxy leeway over advance consent and a favorable attitude about biomedical research substantially explain this willingness.

Dementia, especially dementia caused by Alzheimers disease (AD), is among the most serious public health challenges of the coming decades. The rapid aging of the U.S. population means that within 50 years the number of people with dementia will increase to 12 million.(1) To respond to this challenge, research is needed that often requires the participation of subjects who are themselves demented. But ethical norms surrounding the protection of human subjects limit vulnerable persons' participation in research that does not offer the prospect of direct medical benefit and presents more than minimal risks.(2)

To address this problem, researchers and ethicists have developed a model of proxy consent. Proxy consent allows another individual to provide consent for a subject who is not competent to provide informed consent. The ethic to guide proxy consent is a substituted judgment: a proxy should decide based on what the patient, if capable, would choose.(3) This is especially advocated in research presenting more than minimal risks and without a reasonable prospect of benefit to the subject. For this kind of research, proposed guidelines require that a noncompetent subject can be enrolled only if the subject has executed a previous written directive indicating a willingness to participate.(4)

Unfortunately, studies show only fair agreement between what a proxy thinks a patient would decide and what the patient actually decides(5, 6), and one study that found some proxies choose the opposite of what the proxies think the now noncompetent patient would have wanted.(7)

Yet, little research has examined the views of people on this controversy. Studies suggest that adults may support enrolling noncompetent persons with AD into research using proxies. Most importantly, people may be willing to grant their proxy discretion, or leeway, to decide what the proxy thinks is best, even if that proxy's decision is opposite to what the person would want.(8-10) However, these studies have focused on the views of persons already enrolled in research about protocols that have the potential to benefit subjects.

No study has examined views of older adults on the degree of leeway they would give their proxy to enroll them in AD research that does not present a reasonable prospect of benefit. In addition, no study has verified that respondents understand core concepts

about research, proxy decision making, and research risk. Hence, the available data may come from respondents who do not have an adequate understanding of the ethical issues.(11) These are complex concepts that can be especially difficult to convey because of the necessity that they be framed as future, hypothetical possibilities. Finally, we do not know the characteristics of people who are willing or not willing to allow proxy consent for research that enrolls noncompetent subjects. This is especially important for populations who have historically suffered undue burden in research and therefore may mistrust research, such as African-Americans.(12)

Until we better understand whether people are willing to participate in non-beneficial research that enrolls persons with AD and why they are willing, policymakers cannot develop research ethics policies that respect the values of the people they are designed to protect and, in turn, resolve the controversy that has some states and institutional review boards substantially limiting the practice of proxy consent for research.(13-15) This is especially important because the Office of Human Research Protections, the Federal office that writes and enforces human subjects research protections, has a working group engaged in determining whether regulations are needed for research that enrolls persons with impairments in their decisional capacity.(16)

The purpose of this study was to discover whether older adults support enrolling noncompetent persons with AD into research that does not benefit the subjects. We focused on persons 65 and over because age is one of the chief risk factors for progressive cognitive impairment and we focused on AD because it is among the most common causes of late-life cognitive impairment and there is an urgent need to identify biological markers of the disease in blood and spinal fluid. Our survey sought to determine whether older adults would want to be enrolled in non-beneficial AD research if they themselves had AD and were unable to give an informed consent. We also sought to identify the demographic and attitudinal characteristics of persons who support this practice.

Methods.

Participants: Eligible participants were residents of the Southeastern Pennsylvania region over 65; understood spoken English; could read 14 point font text or, if visually impaired, followed a verbal reading of survey text; and provided verbal informed consent. Participants were recruited from three clinics (the Philadelphia VA, a university urban geriatrics practice, and a university suburban internal medicine practice) and a Philadelphia city senior center.

Measurements: We performed a cross-sectional, 45 to 60 minute face-to-face interview consisting of fixed-choice and open ended questions. The interview consisted of three parts and incorporated periodic reviews of responses to assure participants understood the implications of their choices.

The first part of the interview assessed understanding of basic research concepts (the proxy role, making plans for the future, research, different kinds of benefits, and informed consent) by assessing comprehension of a story read to participants. The vignette describes a woman's attitudes about research and how, at a later time, she develops AD and is recruited for a study. To assess participant understanding and reasoning about the story's core points, the interviewer asked a set of questions, such as "*Can you tell me in your own words what is research?*" and "*Who can make the decision whether Mrs. Adams should join this research study?*" These questions were based on our previous research using the MacCAT-T to assess decision making ability of persons with AD and their caregivers(10, 17, 18) and serious illness.(19, 20)

The second part was a survey of participants' views about research that enrolls persons with AD. Only participants who showed adequate understanding of core concepts continued to part two. At the beginning of part two, they were asked if they would be willing to have a proxy for research decisions:

Suppose that in the future you had Alzheimers disease and you were unable to make decisions about joining a research study. Would you want someone else to serve in the role that Mr. Adams did and make decisions for you about enrolling in research?

Next, they were presented in random order one of two studies to develop diagnostic tests for biomarkers of AD: (1) a minimal risk study that involved a blood draw, and (2) a

greater than minimal risk study that involved a blood draw plus a lumbar puncture to gather spinal fluid. For each study, the interviewer verified the participant understood the risks and benefits of the study and then asked their advance consent:

Suppose that in the future, you had Alzheimers disease and you were in the physical and mental state Mrs. Adams was in. Would you say that you would want to participate or not want to participate?

Participants who had designated a proxy were asked whether they would grant proxy leeway to override the participant's advance consent. The question was tailored to fit the participant's preference for a proxy and their advance consent. The following shows the question asked to a participant who selected his daughter as proxy and declined to grant an advance consent to the lumbar puncture:

How much leeway should your daughter have in over riding your choice and instead enroll you in the study? By "leeway" I mean your daughter should exercise freedom to choose what she thinks is best rather than follow your instructions you just told me about. Would you say she should have no leeway or at least some leeway?

Implications of participants' responses about granting leeway were reviewed, in particular, that leeway could override their advance consent. Participants could then change answers, if desired.

Part three measured relevant attitudes and collected demographic information.

Altruism. We used the 8 item Social Responsibility Scale(21) (higher scores indicating a greater degree of social responsibility). We also measured two single item measures of behaviors plausibly associated with altruism to science and healthcare: "Have you signed up to be an organ donor?" and "Have you signed up to donate your body to science?" We selected these two behaviors as they are topically related to the decision to be in research and they are readily reported and ascertained by family.

Trust. We used the 10 item Health Care System Distrust scale(22) (higher scores indicating more trust).

Value of research. Attitudes about research were assessed using the Research Attitudes Questionnaire, an 11-item measure that assesses how favorably or unfavorably one views biomedical research (higher scores indicating more favorable views).(23)

Perception of AD. We used the Perceived Threat of Alzheimers Disease Scale(24) (higher scores indicating greater perceived threat) and one single item measure of familiarity with AD: “Have you been or are you now close to someone who has Alzheimers Disease?”

Social and demographic characteristics: We collected participants’ age, gender, ethnicity, self-identified racial identity, highest grade of school, financial burden measured as how finances work out at the end of the month(25), number of living children, marital status, and whether they worked in medicine or science.

Data analyses: Primary endpoint was the participants’ willingness to participate in research that enrolled persons with AD who were not capable of consent under each of two research risk conditions. We operationalized this as a dichotomous variable called “willing to participate.”

For each of the research conditions, we defined persons not willing to participate as a person who did not want a proxy for research and did not grant an advance consent, or a person who did want a proxy, did not grant an advance consent, and did not grant their proxy leeway over that advance directive. All other persons were defined as willing to participate because the net effect of their preferences was willingness to be enrolled. For example, a person was willing to participate if their advance consent for the greater than minimal risk spinal fluid sample study was “would not want to enroll” but that person had been willing to appoint a proxy and to grant proxy leeway over this decision.

We used logistic regression to examine associations between participant characteristics and willingness to allow proxy consent for each research risk condition. The binary participation outcome for both high and low risk was analyzed in Stata version 10 using a logistic regression model estimated with generalized estimating equations (GEE).(26) Accordingly, standard errors of effect estimates were obtained with the sandwich variance estimator to adjust for correlated high and low risk observations. We did not include order of scenario presentation in the models because it was not conceptually a confounder on the effects of interest with willingness to participate.

Moreover, the interaction of order of presentation with scenario was a not significant ($p=0.25$). Multivariate GEE models were used to evaluate whether self-reported minority status impacts willingness to enroll above and beyond other demographic and attitudinal co-variates, as some studies suggest race and attitudes about research may influence willingness.(12)

Scale scores missing less than 20% of items were pro-rated; missing items were assigned the average value of non-missing items and added to the scale. Participants with any individual scale having greater than 20% missing items were not included.

Human subjects protections: After description of the study to subjects, verbal informed consent was obtained to participate in this institutional review board approved research. Participants received a \$20 gift certificate to compensate for time and effort.

Results.

Participant characteristics: As shown in figure 1, 598 of eligible persons agreed to an interview (57%). Women were more likely than men to participate (61% versus 53%, $\chi^2=7.8$, $p=0.005$), but no differences existed in the race of participants versus non-participants. Among participants, 93% passed the core concepts assessment. After removing 20 participants who did not complete all co-variate scales, the final sample consisted of 538 participants. Comparing those 20 removed to the remaining participants showed no significant differences in the outcome measures, attitudes or demographics. Data were collected from December 2005 to December 2007.

Table 1 summarizes demographic and attitudinal characteristics. One-third (37%) were African-American, 59% female, 38% had no more than 12 years of education, and more than one-quarter (29%) reported either just enough or not enough money at the end of the month.

Willingness to be enrolled in AD research that does not present benefit to the subjects: Table 2 shows that most 517 (96%) people were willing to designate a proxy for research decision making (one person wanted a proxy for the greater than minimal risk study but not for the minimal risk study). The majority 445 (83%) granted advance consent to a blood draw study and nearly half to a blood draw plus lumbar puncture 259 (48%). For both research risk conditions, most persons were willing to grant leeway over advance consent: blood draw study 434 (81%), and 375 (70%) lumbar puncture study.

When combining preferences for advance consent and, in the case of persons who wanted a proxy, whether they would grant the proxy leeway, we found that 497/538 (92%) had preferences that would allow enrollment in the blood draw study and 404/538 (75%) in the lumbar puncture study.

Participants' willingness to grant proxy leeway over their advance consent substantially contributed to this willingness. Without including participants decision to grant their proxy leeway over their advance consent, the proportion whose preferences suggest that they would be willing to be enrolled in the lumbar puncture study would have decreased from 75% to 52% and the proportion for the blood draw study would have decreased from 92% to 83%.

Characteristics associated with supporting participation in research that does not present benefit to the subjects: Table 3 shows that in both research risk conditions, willingness to be enrolled was associated with higher scores on the social responsibility scale (minimal risk OR=1.18, 95% CI 1.07 to 1.29, p=0.001; greater than minimal risk OR=1.06, 95% CI 1.00 to 1.12, p=0.04), trust in the health care system (minimal risk OR=1.10, 95% CI 1.03 to 1.18, p=0.005; greater than minimal risk OR=1.09, 95% CI 1.05 to 1.14, p<0.001) and favorable attitudes about research (minimal risk OR=1.27, 95% CI 1.17 to 1.38, p<0.001; greater than minimal risk OR=1.18, 95% CI 1.12 to 1.24, p<0.001). In addition, participants who self-reported behaviors associated with these attitudes were more willing to permit proxy consent for research that does not present a benefit, specifically, persons who reported they were organ donors (minimal risk OR=6.28, 95% CI 2.20 to 17.90, p=0.001; greater than minimal risk OR=2.65, 95% CI 1.69 to 4.16, p<0.001) and, in the case of greater than minimal risk research, had donated their body to science (OR=3.28, 95% CI 1.15 to 9.37, p=0.03).

We did not find a relationship between support for proxy consent and the perceived threat of AD, being close to someone with AD, or a history of working in the medical or scientific fields.

Demographic characteristics associated with willingness to be enrolled in research with proxy consent varied depending upon degree of research risk. Persons who chose a spouse or partner as their research proxy (OR=4.20, 95% CI 1.62 to 10.88, p=0.003), reported more years of education (OR=1.11, 95% CI 1.01 to 1.22, p=0.03), or reported less financial burden (OR=0.56, 95% CI 0.36 to 0.88, p=0.01) were more willing to be enrolled in the minimal risk research, but these associations were not seen in the greater than minimal risk condition. Persons who reported being a racial minority were less willing to be enrolled in greater than minimal risk research (OR=0.59, 95% CI 0.40 to 0.87, p=0.008).

Multivariate analyses to examine the relative effects of attitudes and characteristics found that, in the greater than minimal risk scenario, minority status was the only demographic associated with a reduced willingness to participate. Other demographic measures (years of education, financial burden, and gender) did not attenuate this association (OR=0.63, 95% CI 0.42 to 0.96, p=0.03). Minority status was

not significant in the minimal risk scenario, though the effect was in the same direction (OR=0.58, 95% CI 0.31 to 1.10, p=0.09).

Similarly, favorable attitudes about research was the only attitudinal characteristic associated with willingness to participate in multivariate models, and the addition of other attitudinal variables (Social Responsibility, Health Care System Distrust, Alzheimer's Disease Perceived Threat) did not attenuate this effect in either the high risk (OR=1.19, CI 1.13 to 1.27, p<0.001) or low risk (OR=1.19, CI 1.13 to 1.27, p<0.001) scenarios.

Models examining the combined effect of the Research Attitude Questionnaire and minority status for the greater than minimal risk scenario showed the effect for minority status disappear (Research Attitude Questionnaire OR=1.20, CI 1.14-1.26, p<0.001; minority status OR=0.84, CI 0.55-1.28, p=0.42).

Discussion.

Our results suggest that older adults support enrolling noncompetent patients with AD in non-beneficial research. Even in the greater than minimal risk lumbar puncture study, three-quarters of participants had preferences permitting their enrollment in research if they had AD and could not provide informed consent. We discuss four key findings.

It is notable that preference to grant a proxy leeway over advance consent substantially contributed to willingness to be enrolled. These results suggest that many people who do not want to participate in certain kinds of medical research are still willing to appoint a proxy with the ability to override that decision. These results are supported by a study of persons with AD showing that preferences about granting proxy leeway over an advance consent decision are a critical element of how elderly people formulate advance planning preferences.(8)

The second key finding is that participants' favorable attitudes about research, sense of social responsibility and trust in the health care system were associated with support for proxy consent, but experiences with AD were not. This result expands the finding among a postal survey of elderly persons that the strongest association with support for proxy consent for research was favorable attitudes about research.(23) Neither that study, nor a telephone survey of caregivers of persons with AD,(9) found that attitudes about AD were associated with support for proxy consent. Collectively, these results suggest that overarching values such as trust and altruism shape attitudes about the ethics of research that enrolls noncompetent subjects, not specific views on the disease under study.

Third, persons who reported being a racial minority were less likely to support enrolling noncompetent persons in greater than minimal risk research. Notably, this association was independent of age, education and financial burden, yet dropped out of models that adjusted for attitudes about research. These results suggest that favorable attitudes about research, more so than trust or altruism, largely explain racial differences in support for research that enrolls noncompetent subjects.

Finally, most participants (93%) generally understood the core concepts of the proxy role, making plans for the future, research, different kinds of benefits in research,

and informed consent. This finding is encouraging. It suggests that older adults can participate in research advance planning.

The strengths of this study are that all respondents demonstrated adequate understanding of the core concepts required for informed research participation, and the interview was designed to assure that participants understood the consequences of their preferences. Previous research in advance planning has been limited by failure to assure that participants understood the complex future oriented issues at stake.(11) Second, the sample reflected the ethnic diversity of the Philadelphia region and we measured relevant attitudes that might explain preferences about proxy consent.

Limitations include the focus on research to develop biomarkers for AD. Hence, results may not apply to research involving other kinds of conditions, such as critical illness. In addition, our sample was limited to persons at plausible risk for developing AD: persons 65 and older. While this design choice respected the need to have a real world scenario, it is entirely possible that a younger cohort would have different views on proxy consent. Future studies should investigate views of persons at risk for critical illness and younger persons.

At present, research -- especially greater than minimal risk research -- that seeks to enroll noncompetent persons with proxy consent is the source of substantial controversy. Some states and institutions restrict the practice;(27) federal research regulations offer no guidance on the matter; and past efforts to develop guidance have collapsed.(4, 28) The Office of Human Research Protections, the Federal office that writes and enforces human subjects research protections, has a working group engaged in determining whether regulations are needed for research that enrolls persons with impairments in decision making capacity.(16)

Our results have important implications on that effort. They suggest that, in general, elderly people support enrolling noncompetent patients in research that studies the patients' disease even though that research will not benefit the subjects' health and well being but instead, the research might benefit others. This support reflects a willingness to grant a proxy leeway over an advance consent. Hence, policies that require a proxy to exercise a strict substituted judgment based upon past consent preference do not respect how people want their proxies to make decisions. It also suggests that

researchers and their funders focus on how their behaviors shape people's attitudes about research.

Acknowledgements.

Authors wish to thank James Beaver, Paige Brookstein, Maysa DeSousa, Lauren Fisher, Kristin Harkins, Margaret Rice, Samantha Schwartz, and Elizabeth Taylor for their assistance in data collection. Authors especially thank the participants who participated in this study.

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Tables.

Table 1. Subject Characteristics (N = 538).	
<i>Demographics</i>	
Gender	
Male	222 (41.3%)
Female	316 (58.7%)
Race	
Caucasian	329 (61.2%)
African-American	198 (36.8%)
Asian	9 (1.7%)
American Indian	1 (<1%)
Pacific Islander	1(<1%)
Ethnicity	
Latino	7 (1.3%)
Not Latino	531 (98.7%)
Living Situation	
Married	255 (47.4%)
Widowed	160 (29.7%)
Living with someone else	15 (2.8%)
Divorced	56 (10.4%)
Single	52 (9.7%)
Financial Burden	
Some money left over	383 (71.2%)
Just enough to make ends meet	119 (22.1%)
Not enough to make ends meet	36 (6.7%)
Age in years	76.8 ± 6.7 (65-96)
Years of education	14.5 ± 3.4 (4-21)
<i>Attitudinal Characteristics</i>	
Social Responsibility Scale (8-40)	31.7 ± 3.7 (22-40)
Is an organ donor	
Yes	205 (38.1%)
No	333 (61.9%)
Has donated body to science	
Yes	41(7.6%)
No	497 (92.4%)
Health Care System Distrust Scale (10-50)	33.0 ± 4.8 (19-50)
Has/had a job in medical or scientific field	
Yes	173 (32.2%)
No	365 (67.8%)
Research Attitudes Questionnaire (11-55)	39.9 ± 4.1 (23 – 54)

Is/was close to someone with Alzheimers Disease	
Yes	266 (49.4%)
No	272 (50.6%)
<hr/>	
Alzheimer's Disease Perceived Threat Scale (7-35)	17.2 ± 5.5 (7-33)
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AD Threat- Likelihood Subscale (2-10)	4.0 ± 1.9 (2-10)
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AD Threat- Concern Subscale (3-15)	7.2 ± 3.4 (3-15)
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AD Threat- Consequence Subscale (2-10)	6.1 ± 2.1 (2-10)
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Table 2. Willingness to be enrolled in minimal risk and greater than minimal risk research if they had Alzheimers Disease and were not capable of informed consent^a.

Advance Consent	Proxy		No proxy	Total
	No Leeway	Leeway		
<i>Minimal risk study: blood draw</i>				
No	28 (5.2%)	52 (9.7%)	13 (2.4%)	93 (17.3%)
Yes	56 (10.4%)	382 (71.0%)	7 (1.3%)	445 (82.7%)
Total	84 (15.6%)	434 (80.7%)	20 (3.7%)	538 (100%)
<i>Greater than minimal risk study: blood draw and spinal fluid sample</i>				
No	115 (21.4%)	145 (27.0%)	19 (3.5%)	279 (51.9%)
Yes	27 (5.0%)	230 (42.7%)	2 (0.4%)	259 (48.1%)
Total	142 (26.4%)	375 (69.7%)	21 (3.9%)	538 (100%)

^aThe proportion of subjects who are not willing to participate is the sum of cells described by “No advance consent/No leeway” and “No advance consent/No proxy”.

Table 3. Associations between subjects' demographics and attitudinal characteristics and their willingness to be enrolled in research if they had Alzheimers Disease and were not capable of informed consent.

Characteristic	Willingness to be enrolled in minimal risk study		Willingness to be enrolled in greater than minimal risk study	
	Odds Ratio ^a (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Female	1.12 (0.59-2.14)	0.72	0.80 (0.54-1.20)	0.28
Reports non-white race ^b	0.58 (0.31-1.10)	0.09	0.59 (0.40-0.87)	0.008
Financial burden	0.56 (0.36-0.88)	0.01	0.75 (0.55-1.01)	0.06
Age in years	0.99 (0.94-1.04)	0.61	1.00 (0.97-1.03)	0.82
Years of education	1.11 (1.01-1.22)	0.03	1.03 (0.97-1.09)	0.31
Social Responsibility Scale ^c	1.18 (1.07-1.29)	0.001	1.06 (1.00-1.12)	0.036
Is an organ donor	6.28 (2.20-17.90)	0.001	2.65 (1.69-4.16)	<0.001
Has donated body to science	1.66 (0.39-7.14)	0.50	3.28 (1.15-9.37)	0.03
Health Care System Distrust Scale ^d	1.10 (1.03-1.18)	0.005	1.09 (1.05-1.14)	<0.001
Research Attitudes Questionnaire ^e	1.27 (1.17-1.38)	<0.001	1.18 (1.12-1.24)	<0.001
Has/had a job in medical or scientific field	1.32 (.64-2.70)	0.45	1.15 (.75-1.76)	0.51
Is/was close to someone with Alzheimers Disease	0.83 (0.44-1.58)	0.58	1.01 (0.68-1.49)	0.96
Perceived Threat of Alzheimers Disease Scale ^f	1.01 (0.95-1.07)	0.83	1.02 (0.99-1.06)	0.25
Chose spouse as research proxy	4.20 (1.62-10.88)	0.003	1.13 (0.75-1.71)	0.56

^aOR > 1 indicates a characteristic that is associated with willingness to be enrolled.

^bAfrican American (n=198), Asian (n=9), American Indian (n=1), Pacific Islander (n=1).

^cHigher scores indicate more altruism.

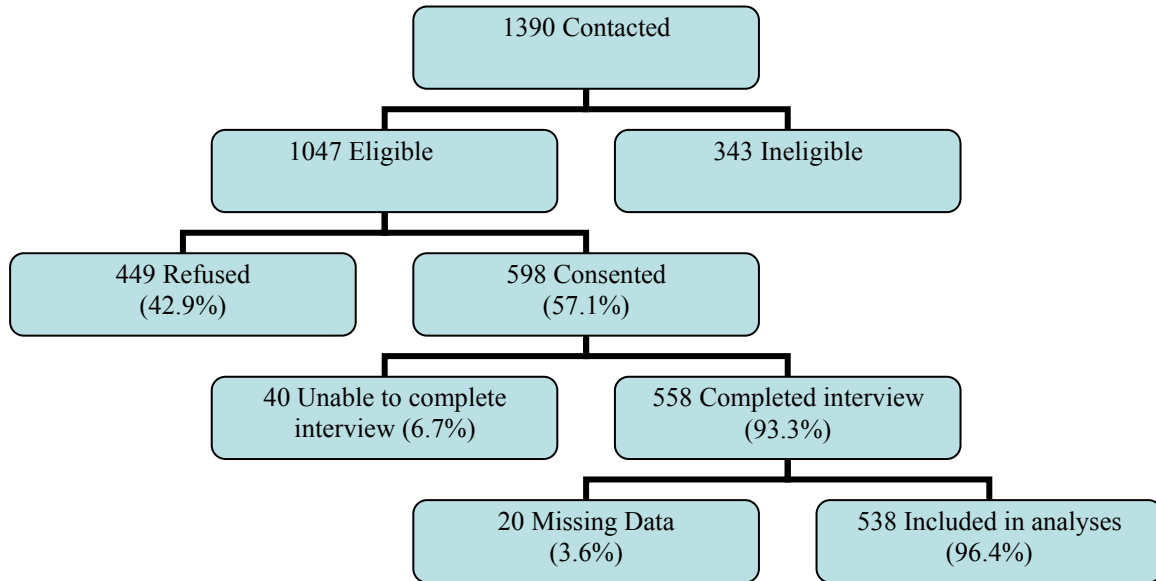
^dHigher scores indicate more trust in healthcare system.

^eHigher scores indicate more favorable views towards biomedical research.

^fHigher score indicates higher perceived threat of Alzheimers Disease.

Figures.

Figure 1. Disposition of subject recruitment.



Greater than minimal risk study description.**A study to develop a new test to diagnose Alzheimers Disease**What is the purpose of this study?

The purpose is to develop a new test to detect Alzheimers Disease. The study will compare the protein levels in the blood and spinal fluid of people who have Alzheimers Disease with people who do not have Alzheimers. These proteins are released by nerve cells as they die. These proteins may be high in persons with Alzheimers, and they may be low in persons without Alzheimers.

Who is being enrolled in this study?

The researchers are inviting two kinds of people to join this study: people who have Alzheimers disease and people who do not.

What will happen to people who join this study?

This study will take about three hours.

People who join this study will have a single blood draw of 2 tablespoons of blood and a lumbar puncture. A lumbar puncture is also called a spinal tap.

A lumbar puncture is a routine medical procedure. It allows the physician to get a sample of fluid that surrounds the brain and spinal cord. The procedure is done at a Clinical Research Center. An injection of local anesthetic is put in the skin and the muscle around the areas of the lower back. When the area is numb, the physician inserts a thin needle through the skin and muscle into the spinal canal in the lower back. This is done in a place that is well below the end of the spinal cord. Two tablespoons of spinal fluid are removed.

What are the risks of this research?

The risks of a spinal tap are pain at the site of the needle puncture, a slight risk of infection, a rare risk of allergic reaction to the local anesthetic, and a headache. Headache occurs in about 3% of the people who have the procedure. It usually lasts for 1 to two days. In unusual cases, headaches may be moderately severe and last for several days. These headaches may be treated.

The risks of the blood test are pain and discomfort at the site of the needle.

What are the benefits of this research?

People who join this study will not benefit. The results of this research may help develop a test to make an accurate and early diagnosis of Alzheimers disease.

Minimal risk study description.

A study to develop a new test to diagnose Alzheimers Disease

What is the purpose of this study?

The purpose is to develop a new test to detect Alzheimers Disease. The study will compare the protein levels in the blood of people who have Alzheimers with people who do not have Alzheimers. These proteins are released by nerve cells as they die. These proteins may be high in persons with Alzheimers, and they may be low in persons without Alzheimers.

Who is being enrolled in this study?

The researchers are inviting two kinds of people to join this study: people who have Alzheimers disease and people who do not.

What will happen to people who join this study?

This study will take about 15 minutes.

People who join this study will have a single blood draw of 2 tablespoons of blood.

What are the risks of this research?

The risks of the blood test are pain and discomfort at the site of the needle.

What are the benefits of this research?

People who join this study will not benefit. The results of this research may help develop a test to make an accurate and early diagnosis of Alzheimers disease.

Questions to assess study comprehension.

Do you have any questions about this?

Understands the risks of the study: "Can you tell me the risks of this study?"

Understands the benefits of the study: "Can you tell me the benefits of this study?"