Published in final edited form as:

J Am Geriatr Soc. 2013 March ; 61(3): 396–402. doi:10.1111/jgs.12132.

Health-Related Resource Use and Costs in Elderly Adults with and without Mild Cognitive Impairment

Carolyn W. Zhu, PhD^{*}, Mary Sano, PhD^{†,‡}, Steven H. Ferris, PhD[§], Peter J. Whitehouse, MD, PhD[¶], Marian B. Patterson, PhD[¶], and Paul S. Aisen, MD^{**}

^{*}Department of Geriatrics and Palliative Medicine, Alzheimer Disease Research Center, Bronx, New York

[†]Department of Psychiatry, Mount Sinai School of Medicine, Alzheimer Disease Research Center, Bronx, New York

[‡]James J. Peters Veterans Affairs Medical Center, Bronx, New York

[§]Alzheimer's Disease Center, New York University Langone Medical Center, New York

[¶]Department of Neurology, Case Western Reserve University, Cleveland, Ohio

^{**}Department of Neurosciences, University of California at San Diego, San Diego, California

Abstract

OBJECTIVES—To assess differences in resource use and cost between older adults with and without mild cognitive impairment (MCI) over time.

DESIGN—Multicenter, longitudinal study.

SETTING—Sixty-eight Alzheimer's Disease Cooperative Study (ADCS) sites in the United States.

PARTICIPANTS—Two hundred fifty-nine individuals diagnosed with MCI and 107 cognitively normal elderly adults followed annually for 3 years.

© 2013, Copyright the Authors

Address correspondence to Carolyn W. Zhu, Department of Geriatrics and Palliative Medicine, Mount Sinai School of Medicine, 130 West Kingsbridge Road, Bronx, NY 10468. carolyn.zhu@mssm.edu.

Author Contributions: Dr. Zhu: Drafting and revision of manuscript, study concept and design, analysis and interpretation of data. Dr. Sano: Drafting and revision of manuscript, study concept and design, analysis and interpretation of data. Dr. Ferris: Study concept and design, revision of manuscript. Dr. Whitehouse: Design, revision of manuscript. Dr. Patterson: Revision of manuscript, study concept and design, interpretation of data. D. Aisen: Revision of manuscript, study concept and design, analysis and interpretation of data.

Conflict of Interest: The work was supported by National Institute on Aging Grant U01AG10483. Dr. Sano serves on a scientific advisory board for Medivation, Inc. and as a consultant for Bayer Schering Pharma, Bristol-Myers Squibb, Elan Corporation, Genentech, Inc., Medivation, Inc., Medpace Inc., Pfizer Inc, Janssen, Takeda Pharmaceutical Company Limited, and United Biosource Corporation and receives research support from the National Institute on Aging (NIA), National Center for Research Resources, National Institutes of Health (NIH).

Dr. Ferris serves as a consultant or advisory board member for Accera, Baxter, Bristol Myers Squibb, Eisai, Intellect Neurosciences, Janssen Alzheimer Immunotherapy, Elan, Eli Lilly, MedAvante, Merck, Merz, Neuronix, Pfizer, and United Biosource and receives research support from Baxter, Bristol Myers Squibb, Janssen Alzheimer Immunotherapy, Eisai, Eli Lilly, Medivation, Pfizer, and the NIA, NIH.

D. Aisen serves on a scientific advisory board for NeuroPhage and as a consultant to Elan Corporation, Wyeth, Eisai Inc., Bristol-Myers Squibb, Eli Lilly and Company, NeuroPhage, Merck & Co., Roche, Amgen, Abbott, Pfizer Inc, Novartis, Bayer, Astellas, Dainippon, Biomarin, Solvay, Otsuka, Daiichi, AstraZeneca, Janssen, Medivation, Inc., Theravance, Cardeus, and Anavex and receives research support from Pfizer Inc., Baxter International Inc., and the NIH (NIA U01-AG10483 (PI), NIA U01-AG024904 (Coordinating Center Director), NIA R01-AG030048 (PI), and R01-AG16381 (Co-I)).

MEASUREMENTS—The Resource Use Instrument (RUI) was used to capture medical and nonmedical care use. Generalized linear latent and mixed models were used to estimate differences in resource use and costs in older adults with and without MCI after controlling for clinical and demographic characteristics.

RESULTS—At baseline, average annual direct medical cost per person was substantially higher for participants with MCI (\$6,499) than for those without (\$2,969) $P < .001$. Informal care use was also substantially higher (33% vs 8.4%, $P < .001$). Results from multivariate analyses of longitudinal data show that, after controlling for participant and informant characteristics, direct medical costs were 44% higher for participants with MCI than for those without. Participants with MCI were almost five times as likely to use informal care as those without. Number of medical conditions and older age were associated with higher medical cost. Worse functional and cognitive status, older age, being married, and being female were associated with higher likelihood of informal care use. Having an adult child informant was associated with higher likelihood of using informal care.

CONCLUSION—The RUI captured differences in resource use and costs between individuals with and without MCI. Clinicians who care for individuals with MCI should address informal care needs early in the disease course.

Keywords

mild cognitive impairment; case-control study; medical care; resource use; cost; informal care

Mild cognitive impairment (MCI) due to Alzheimer's disease (AD) is characterized by noticeable decline in memory that is not severe enough to significantly interfere with daily life.^{1,2} As many as 10% to 20% of people aged 65 and older are estimated to have MCI; approximately 5% to 15% of these progress to AD annually.^{3–6} Because of the large and growing number of individuals with AD and the high costs of their care, much research has focused on exploring the effects of disease severity on cost of AD, but resource use and costs for individuals with MCI are not well understood. One recent study on the direct cost of care for individuals with MCI in a primary care setting reported 16% higher direct costs for individuals with MCI than for those without.⁷

Two recent reviews noted several limitations of existing studies on cost of AD, including lack of longitudinal data, limited measures of disease severity, and limited focus on informal care.^{8,9} In light of these recommendations, the aim of this study was to further knowledge of resource use and costs in MCI in several fronts. First, a validated measure of resource use, the Resource Use Instrument (RUI), developed as part of the Alzheimer's Disease Cooperative Study (ADCS) instrument development program, was used to capture health-related resource use for older adults at various stages of cognitive decline. The RUI has been effectively administered in clinics and at home in several studies for participants with and without AD,^{10–12} but it has not been used to examine resource use in MCI. Second, a comparison group of elderly adults without MCI was included to assess excess cost due to MCI. Third, longitudinal data were used to assess whether differences in resource use changed over time, after controlling for disease severity and other participant characteristics.

METHODS

Participants

Participants with ($n = 259$) and without ($n = 107$) MCI were recruited into parallel studies using comparable methods at 68 ADCS sites. Common entry criteria were aged 55 to 90, no use of antimentia drugs or other drugs known to affect cognition, and an available informant who lived with the participant or had personal encounter with the participant at

least 6 to 8 hours more than 1 day per week and accompanied the participant to all clinic visits for the study period. Criteria specific to participants with MCI were memory complaints verified by an informant, abnormal memory function below an education-adjusted cutoff on the Logical Memory II subscale (Delayed Paragraph Recall) of the Wechsler Memory Scale,¹³ Mini-Mental State Examination (MMSE) score of 24 or less,¹⁴ Clinical Dementia Rating Scale (CDR) score of 0.5,¹⁵ and general cognition and functional performance sufficiently preserved such that the site physician could not make a diagnosis of AD at screening. Criteria specific to controls required absence of depression or other neurodegenerative conditions; absence of a memory complaint; normal cognition as indicated by a CDR score of 0, a Global Deterioration Scale score of 1, or 2,¹⁶ or a MMSE score greater than 26; and a Hamilton Depression Rating Scale score less than 1.¹⁷ Twenty percent of controls were required to be nonwhite minorities. After baseline assessment, participants were followed annually for 3 years, with follow-up evaluations performed within a 2-week period of the scheduled follow-up date. Institutional review board approval was obtained at each participating ADCS site, and written informed consent was obtained from all study participants and informants.

Instrument

A trained study coordinator recorded data on participants' resource use using the RUI in an interview with the participant and informant that took place in the clinic. The instrument and costing methods have been fully described elsewhere.¹⁰ Briefly, questions were selected to reflect the most important aspects of health care that elderly adults may use and were designed to collect information with little assistance from study staff. Direct medical care included hospitalizations, medications, health provider visits, treatments and procedures, and durable medical equipment. Nonmedical care items included paid (formal) and unpaid (informal) care. Formal care included care that home health aides, attendants, or other paid individuals provided. Informal care included care that family members, friends, volunteers, or other helpers provided for basic and instrumental activities of daily living (ADLs). Intensity of use (e.g., number of hospitalizations) was recorded for each item. The RUI did not ask whether or how much was paid by insurance or out of pocket. The perspective is from the society, and total reimbursed and un-reimbursed healthcare costs were estimated.

Clinical and Demographic Characteristics

Information was collected on age, sex, ethnicity, marital status, and education. Clinical characteristics included MMSE score, Alzheimer's Disease Assessment Scale—Cognitive subscale (ADAS-cog),^{18,19} and ADCS-ADL scale.²⁰ In obtaining participants' medical history, the study asked whether the participant had major psychiatric; neurological; head, eyes, ears, nose, and throat; cardiovascular; respiratory; hepatic; dermatological or connective tissue; musculoskeletal; endocrine or metabolic; gastrointestinal; hematopoietic or lymphatic; or renal or genitourinary problems, as well as allergies or drug sensitivities or malignancies and whether the participant had any major surgical procedures. These areas were summed to construct the total number of medical problems the participant had. To examine whether informant characteristics were associated with participant health-related resource use, information on the informant's age, sex, education, and relationship to the participant was included.

Analysis

Baseline characteristics, utilization rates, and cost per person of participants with and without MCI were first compared. Because responses for many resource utilization items were heavily concentrated at 0, costs per user for each item were also computed as were costs of participants with and without MCI. The chi-square test was used to compare utilization rates. Because healthcare costs are highly skewed to the right, group differences

were compared using Kruskal-Wallis tests. All costs were adjusted to 2009 dollars using the Consumer Price Index.

Generalized linear latent and mixed models were used to estimate differences in resource use and costs in participants with and without MCI. Unobserved heterogeneity within participant groups and sites were modeled using random effects.²¹ Whether rate of change in resource use and cost over time were different between participants with and without MCI were tested by including an interaction term of indicators for MCI and year, but it was statistically insignificant and therefore dropped from final analyses. All estimates were performed using STATA 9.0 (StataCorp, College Station, TX). The main independent variable, a dichotomous indicator for MCI group, was used to assess excess use and cost due to MCI. Control variables were baseline age, sex, race, marital status, and years of education of the participants. Clinical variables were ADAS-cog, ADCS-ADL, and number of medical problems, all measured at each interval. Bivariate associations between informant characteristics and participant resource use were tested. Having an adult child participate as the informant was the only informant characteristic that was statistically associated with participant resource use and was included in the analyses. Direct medical costs were log-transformed because they were highly skewed to the right. Estimated coefficients in this model are proportional changes in cost for a unit change in the explanatory variable. Informal care use was estimated because the number of participants who used informal care was small. Formal care use was not estimated because no participants without MCI used formal care any time during the study, and only 2.7% of participants with MCI at baseline and 9.1% in Year 3 used formal care.

RESULTS

Demographic and Clinical Variables at Baseline

Participants with MCI were older (mean age 73 vs 70), more likely to be male (53% vs 39%), and married (78% vs 68%) (Table 1). Participants with MCI were 93% white. Because 20% of controls were required according to study protocol to be nonwhite minorities, 69% of the control group was white. Average scores for all clinical measures were significantly worse for participants with MCI (all $P < .01$). Approximately two-thirds (64.5%) of participants with MCI completed the study, compared with 80.3% of those without ($P = .003$). Presence of medical problems were similar between participants with and without MCI except for higher proportions in MCI of renal or genitourinary (49% vs 35%), neurological (29% vs 17%), and respiratory (19% vs 8%) problems. The most commonly reported problems were head, eyes, ears, nose, and throat; musculoskeletal; or cardiovascular and having had major surgical procedures.

Compared to normal elders, informants for participants with MCI had fewer years of schooling (mean 14.6 vs 15.4, $P = .01$). They also were more likely to be spouses (71% vs 54%) but less likely to be friends (10% vs 19%) or other relations (5% vs 10%, $P < .001$). Differences in informant age and sex between participants with and without MCI were not statistically significant.

Unadjusted Resource Use and Costs at Baseline

Utilization rate of direct medical care was similar between participants with and without MCI except for slightly higher rates of prescription medication use for MCI (99% vs 95%, $P = .04$) (Table 2). Informal care use was significantly higher for participants with MCI (33% vs 8.4%, $P < .001$).

Average annual costs per person for medical care were substantially higher for participants with MCI (\$6,499 vs \$2,969, $P < .001$). Per-person cost of hospitalizations, prescription medications, and doctor visits were each significantly higher for MCI (all $P < .02$). The largest cost component for both groups was hospitalizations, accounting for nearly half of total medical costs for participants without (\$1,293, 46.3% of total cost) and with (\$3,768, 58.0% of total cost) MCI. The second largest cost component, prescription medications, was lower for participants without (\$407, 14.6% of total cost) than with (\$1,537, 24.0% of total cost) MCI. Costs of assistive devices, outpatient tests and procedures, and doctor visits were low for both groups. Informal caregiving time was significantly higher for participants with (58 min/d) than without MCI (9 min/d) ($P < .001$). Per-person cost of formal care was nominal (\$62) for participants with MCI.

On a per-user basis, costs for hospitalizations and doctor visits were not significantly different between participants with and without MCI. Reasons for hospitalizations, categorized into major diagnostic categories, were similar between participants with and without MCI. The most frequent reasons for hospitalizations were hip and knee replacement, cardiac problems, and pneumonia. Prescription medication cost per user was significantly higher for MCI (\$1,555 vs \$427, $P < .001$). For those who used informal care, informal hours per day for participants with MCI exceeded that of controls by approximately 1 hour per day (174 vs 108 minutes), although differences were statistically not significant. For participants with MCI who used paid care, annual costs of \$2,278 were substantial.

Multivariate Analysis of Longitudinal Changes in Resource Use and Cost

Table 3 presents multivariate regression results of longitudinal effects of participant characteristics on direct medical costs and informal care use. Results show that, after controlling for other covariates, direct medical costs were 44% higher for participants with MCI than for those without ($P = .01$). Annual direct medical costs increased an average of 13.1% each year for both groups ($P < .001$). Rates of increase did not differ according to group. Each additional medical problem was associated with 14.8% greater direct medical costs ($P < .001$). Higher direct medical costs also were associated with older age (8.4% greater for every 5 years of age, $P = .04$). Variation between participants at a site (standard deviation (SD) = 0.663) and variation between sites (SD = 0.397) were smaller than variation over time within participants (SD = 1.191).

Controlling for other characteristics, participants with MCI were almost five times as likely to use informal care as controls (odds ratio (OR) = 4.62, $P = .001$). Each point increase in ADAS-cog was associated with a 5% greater likelihood of using informal care (OR = 1.05, $P = .02$), and each point increase in ADCS-ADL was associated with 10% less likelihood of using informal care (OR = .90, $P < .001$). Greater likelihood of using informal care was also associated with older age (OR = 1.22, $P = .03$ for every 5 years of age), being married (OR = 2.69, $P = .01$), being female (OR = 3.12, $P < .001$), and having an adult child as informant (OR = 3.05, $P = .01$). Variation between sites (SD = 0.985) was smaller than between participants within a site (SD = 1.157).

DISCUSSION

Few studies have examined resource use and cost of caring for individuals with MCI. As part of a clinical trial, this study showed that RUI captured variations in resource use and costs between participants with and without MCI. With few exceptions, use and costs for each resource item were higher for participants with MCI than for those without. For both groups, the largest cost component by far was for hospitalizations. Medications represented an increasingly important component of direct medical costs for participants with MCI over time. The distribution of different cost components was consistent with those reported in AD

and a recent German study in MCI.^{7,12} Differences in direct medical costs and informal care use between participants with and without MCI were examined after controlling for participant characteristics to assess excess use and cost of MCI. Results showed significantly higher direct medical cost and informal care use for participants with MCI than for those without. Because of the substantial nonmedical cost of caring for individuals with AD, it is particularly important to quantify informal care use to fully comprehend the economic effect of MCI and potential savings that might be gained by pharmacological intervention at this stage. Results from this study suggest that informal care begins to exert its toll early, before individuals develop dementia.

This study has several limitations. Participants were recruited from a clinical trial. Selection criteria for clinical trials may result in more-homogeneous samples that are younger, more white, more likely to be male, better educated, and healthier and therefore may include study participants who use fewer health services than individuals with or without MCI in the community at large and may not be representative of overall clinical populations.^{22,23} Such selection effects may also affect healthcare use and costs.^{23,24} Nevertheless, because participants with and without MCI were recruited in the same setting, although the samples themselves may not be representative of the general population, unless participation in clinical trials has a different effect on resource use and costs between participants with and without MCI, potential biases in the results from different effects on resource use and costs between participants with and without MCI that are associated with participation in clinical trials should be reduced. Still, because this study begins to set a baseline for the incorporation of pharmacoeconomic studies in clinical trials in MCI, possible different participation effects between groups should be explored in future studies.

There were statistically significant differences in demographic characteristics between participants with and without MCI. Higher proportions of men with MCI have been reported in other reports.^{25,26} Because of study requirement of at least 20% nonwhite minorities in controls, distribution of race and ethnicity differed significantly according to group. These demographic characteristics were controlled for in the multivariate analyses.

The RUI is a self-reported instrument. Studies show that self-reported healthcare use may be used when administrative data are unavailable. Higher accuracy of self-reports for more-traumatic, less-routine events such as hospitalizations, which constitute a large proportion of total costs, suggests that large portions of total costs may be accurately estimated.²⁷ Studies that have examined relationships between accuracy of self-reported resource use and socioeconomic status have reported mixed results.^{27,28} Only older age has been shown to be consistently associated with underreporting of healthcare use.²⁹ In this study, participants with MCI were older than controls, suggesting that resource use may be underreported in participants with MCI, and the results may represent a conservative estimate of differences in resource use between participants with and without MCI.

Participation of an informant was required according to study protocol and participants and informants were permitted to contribute to the report. In an earlier study using a sample of cognitively normal elderly adults, resource use of participants who reported on their own and those who reported with the help of an informant were compared.¹⁰ Results showed no difference in resource use between these two groups. Although this suggests that evaluation of resource use in normal aging can be self-administered and does not require substantial staff involvement and data monitoring, in those who later develop dementia, assessment will be increasingly difficult as cognition deteriorates. A comparison between self-reported use and Medicare claims data is needed to validate the self-report methodology to help inform relationships between self-reported use and costs and those that actually incurred with cognitive changes.

Characteristics of the informants may also have affected the RUI reports. It is possible that the degree of informant participation between participants with and without MCI could differ and may have affected the results, but the extent of informant involvement and specific contribution of each was not monitored in the study, precluding an analysis of its effect on resource use. As part of a clinical trial, standard levels of demographic information were collected on informants. All available information on the informant that might affect RUI in the analysis were controlled for, and it was found that informants' marital status and relationship to the participant were associated with participants' informal care use but not medical care costs. Ideally, analysis should also control for informant health characteristics (e.g., psychological status) that might affect RUI, but data collection on informant health is beyond the scope of clinical trials. Future studies outside the clinical trial context should consider including more-detailed data on informants to obtain a fuller picture of how participant and informant characteristics affect costs associated with MCI. MCI is an important stage in the continuum from healthy cognition to dementia. Health-related resource use and costs are important components for demonstrating the value of treatments. Assessment of the effectiveness of pharmacological agents for treating symptoms and slowing progression of AD requires better assessment methods to evaluate clinical changes in MCI. The current study demonstrated the utility of the RUI in comparing resource use and cost of individuals with and without MCI. The results suggest that clinicians who care for individuals with MCI should address individuals' informal care needs early in the disease course.

Acknowledgments

The authors thank Oregon Health & Science University, PI Jeff Kaye; University of Southern California, PI Lon Schneider; University of California at San Diego, PI Adam Fleisher; University of Michigan, Raymond Scott Turner; Mayo Clinic, Rochester, PI Ron Petersen; Seattle Institute for Biomedical and Clinical Research, University of Washington, PI Murray Raskind; Baylor College of Medicine, PI Rachelle Doody; Columbia University, PI Karen Bell; University of Alabama at Birmingham, PI Ed Zamrini; Mount Sinai School of Medicine, PI Mary Sano; Rush University Medical Center, PI David Bennett; Wien Center for Clinical Research, PI Raj Duara; Washington University, St. Louis, PI James Galvin; New York University Medical Center, PI Steve Ferris; Duke University Medical Center, PI Murali Doraiswamy; University of Pennsylvania, PI Chris Clark; University of Kentucky, PI Greg Jicha; University of Pittsburgh, PI Steve DeKosky; University of Rochester Medical Center, PI Pierre Tariot; University of California at Irvine, PI Carl Cotman; University of Texas, Southwestern MC, PI Ramon Diaz-Arrastia; Emory University, PI Allan Levey; University of California at Los Angeles, PI Jeff Cummings; Mayo Clinic, Jacksonville, PI Neil Graff-Radford; Indiana University, PI Martin Farlow; Memorial Hospital Rhode Island, Brown University, PI Brian Ott; Yale University, PI Chris Van Dyck; University of California at Davis, PI Charles DeCarli; State University of New York, Stony Brook, PI Mark Sedler; Arizona Health Sciences Center, PI Geoffrey Ahern; Memory Clinic at Southwestern Vermont Medical Center, PI Paul Soloman; Barrow Neurology; PI Jiong Shi; Northwestern University, PI Marek-Marsel Mesulam; Medical University of South Carolina, PI Jacobo Mintzer; Premiere Research Institute, PI Carl Sadowsky; Georgetown University, PI Paul Aisen; Brigham and Women's Hospital, PI Reisa Sperling; Boston University, PI Robert Green; Howard University, PI Thomas Obisesan; Case Western Reserve University, PI Alex Auchus; Neurological Care of CNY, PI Smita Kittur; MD Clinical, PI Kerri Wilks; Stanford, PI Jerome Yesavage; State University of New York Downstate, PI Howard Crystal.

Sponsor's Role: None.

References

1. Petersen RC. Mild cognitive impairment as a diagnostic entity. *J Intern Med.* 2004; 256:183–194. [PubMed: 15324362]
2. Winblad B, Palmer K, Kivipelto M, et al. Mild cognitive impairment—beyond controversies, towards a consensus: Report of the International Working Group on Mild Cognitive Impairment. *J Intern Med.* 2004; 256:240–246. [PubMed: 15324367]
3. Petersen RC, Thomas RG, Grundman M, et al. Vitamin E and donepezil for the treatment of mild cognitive impairment. *N Engl J Med.* 2005; 352:2379–2388. [PubMed: 15829527]

4. Ritchie K. Mild cognitive impairment: An epidemiological perspective. *Dialogues Clin Neurosci*. 2004; 6:401–408. [PubMed: 22034212]
5. Bruscoli M, Lovestone S. Is MCI really just early dementia? A systematic review of conversion studies. *Int Psychogeriatr*. 2004; 16:129–140. [PubMed: 15318760]
6. Luck T, Riedel-Heller SG, Kaduszkiewicz H, et al. Mild cognitive impairment in general practice: Age-specific prevalence and correlate results from the German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe). *Dement Geriatr Cogn Disord*. 2007; 24:307–316. [PubMed: 17848793]
7. Luppá M, Heinrich S, Matschinger H, et al. Direct costs associated with mild cognitive impairment in primary care. *Int J Geriatr Psychiatry*. 2008; 23:963–971. [PubMed: 18416451]
8. Jonsson L, Wimo A. The cost of dementia in Europe: A review of the evidence, and methodological considerations. *Pharmacoeconomics*. 2009; 27:391–403. [PubMed: 19586077]
9. Mauskopf J, Racketa J, Sherrill E. Alzheimer's disease: The strength of association of costs with different measures of disease severity. *J Nutr Health Aging*. 2010; 14:655–663. [PubMed: 20922342]
10. Sano M, Zhu CW, Whitehouse PJ, et al. ADCS Prevention Instrument Project: Pharmacoeconomics: Assessing health-related resource use among healthy elderly. *Alzheimer Dis Assoc Disord*. 2006; 20(4 Suppl 3):S191–S202. [PubMed: 17135812]
11. Zhu CW, Leibman C, McLaughlin T, et al. Patient dependence and longitudinal changes in costs of care in Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2008; 26:416–423. [PubMed: 18946219]
12. Zhu CW, Scarmeas N, Torgan R, et al. Longitudinal study of effects of patient characteristics on direct costs in Alzheimer disease. *Neurology*. 2006; 67:998–1005. [PubMed: 16914696]
13. Wechsler, D. WMS-R Wechsler Memory Scale—Revised Manual. New York, NY: Psychological Corporation, Harcourt Brace Jovanovich Inc; 1987.
14. Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975; 12:189–198. [PubMed: 1202204]
15. Morris JC. The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology*. 1993; 43:2412–2414. [PubMed: 8232972]
16. Reisberg B, Ferris SH, de Leon MJ, et al. The Global Deterioration Scale for assessment of primary degenerative dementia. *Am J Psychiatry*. 1982; 139:1136–1139. [PubMed: 7114305]
17. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960; 23:56–62. [PubMed: 14399272]
18. Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. *Am J Psychiatry*. 1984; 141:1356–1364. [PubMed: 6496779]
19. Mohs RC, Knopman D, Petersen RC, et al. Development of cognitive instruments for use in clinical trials of antidementia drugs: Additions to the Alzheimer's Disease Assessment Scale that broaden its scope. *The Alzheimer's Disease Cooperative Study Alzheimer Dis Assoc Disord*. 1997; 11 (Suppl 2):S13–S21.
20. Galasko D, Bennett D, Sano M, et al. An inventory to assess activities of daily living for clinical trials in Alzheimer's disease. *The Alzheimer's Disease Cooperative Study Alzheimer Dis Assoc Disord*. 1997; 11(Suppl 2):S33–S39.
21. Muthén, B. Latent variable modeling of longitudinal and multilevel data. In: Raftery, A., editor. *Sociological Methodology*. Boston, MA: Blackwell Publishings; 1997. p. 453–480.
22. Schneider LS, Olin JT, Lyness SA, et al. Eligibility of Alzheimer's disease clinic patients for clinical trials. *J Am Geriatr Soc*. 1997; 45:923–928. [PubMed: 9256842]
23. Albert SM, Sano M, Marder K, et al. Participation in clinical trials and long-term outcomes in Alzheimer's disease. *Neurology*. 1997; 49:38–43. [PubMed: 9222167]
24. Kennedy WA, Laurier C, Malo JL, et al. Does clinical trial subject selection restrict the ability to generalize use and cost of health services to "real life" subjects? *Int J Technol Assess Health Care*. 2003; 19:8–16. [PubMed: 12701935]

25. Grundman M, Petersen RC, Ferris SH, et al. Mild cognitive impairment can be distinguished from Alzheimer disease and normal aging for clinical trials. *Arch Neurol*. 2004; 61:59–66. [PubMed: 14732621]
26. Ganguli M, Dodge HH, Shen C, et al. Mild cognitive impairment, amnesic type: An epidemiologic study. *Neurology*. 2004; 63:115–121. [PubMed: 15249620]
27. Short ME, Goetzel RZ, Pei X, et al. How accurate are self-reports? Analysis of self-reported health care utilization and absence when compared with administrative data. *J Occup Environ Med*. 2009; 51:786–796. [PubMed: 19528832]
28. Marshall SF, Deapen D, Allen M, et al. Validating California teachers study self-reports of recent hospitalization: Comparison with California hospital discharge data. *Am J Epidemiol*. 2003; 158:1012–1020. [PubMed: 14607810]
29. Raina P, Torrance-Rynard V, Wong M, et al. Agreement between self-reported and routinely collected health-care utilization data among seniors. *Health Serv Res*. 2002; 37:751–774. [PubMed: 12132604]

Table 1**Baseline Demographic and Clinical Characteristics Group**

Characteristic	Control (n = 107)	MCI (n = 259)
Participant		
Demographic		
Age, mean $\pm$ SD	70.1 $\pm$ 8.3	72.9 $\pm$ 7.6 ^b
Male,%	39.3	53.3 ^a
White,%	69.2	93.1 ^b
Married,%	68.2	78.4 ^a
Education, years, mean $\pm$ SD	14.8 $\pm$ 3.2	14.7 $\pm$ 3.1
Clinical, mean $\pm$ SD		
Alzheimer's Disease Assessment Scale Cognitive Subscale	5.6 $\pm$ 3.2	11 $\pm$ 4.3 ^b
Alzheimer's Disease Cooperative Study Activity of Daily Living Scale	50.7 $\pm$ 2.6	45.7 $\pm$ 5.3 ^b
Mini-Mental State Examination	29 $\pm$ 1.3	27.4 $\pm$ 1.8 ^b
Clinical Dementia Rating-Sum of Boxes	0.1 $\pm$ 0.2	1.9 $\pm$ 0.8 ^b
Global Deterioration Scale	1.2 $\pm$ 0.4	2.7 $\pm$ 0.6 ^b
Number of medical problems, mean $\pm$ SD	2.4 $\pm$ 1.6	3.0 $\pm$ 1.8 ^b
Major surgical procedures,%	81.3	73.7
Head, eyes, ears, nose, throat,%	66.4	68.0
Musculoskeletal,%	58.9	63.3
Cardiovascular,%	50.5	59.1
Allergies or drug sensitivities,%	39.3	32.4
Gastrointestinal,%	38.3	45.2
Renal or genitourinary,%	34.6	49.0 ^a
Endocrine or metabolic,%	32.7	37.1
Dermatologic or connective tissue,%	28.0	30.1
Neurologic,%	16.8	29.3 ^a
Malignancy,%	13.1	15.1
Psychiatric,%	11.2	17.8
Hematopoietic or lymphatic,%	10.3	6.9
Respiratory,%	8.4	19.3 ^a
Hepatic,%	5.6	5.0
Informant		
Age, mean $\pm$ SD	63.0	66.0 ^a
Male,%	44.0	35.4
Years of schooling, mean $\pm$ SD	15.3	14.6 ^a
Relationship to participant,%		^a

Characteristic	Control (n = 107)	MCI (n = 259)
Spouse	54.2	74.9
Adult child or child in law	15.9	13.5
Friend	19.6	7.7
Other	10.3	3.9

Group differences between participants with and without mild cognitive impairment (MCI) significant at

^a $P < .05$,

^b $P < .01$.

SD = standard deviation.

Table 2**Unadjusted Baseline Resource Use and Cost According to Group**

Resource Use and Cost	Control, n = 107	MCI, n = 259
Utilization rate, %		
Direct medical care		
Hospitalizations	2.8	6.9
Prescription medications	95.3	98.8 ^a
Assistive device	28.0	28.2
Outpatient treatment and procedures	45.8	52.5
Doctor visit	77.6	69.1
Nonmedical care		
Unpaid informal care	8.4	33.2 ^b
Paid formal care	0.0	2.7
Per-person costs, mean ± SD		
Direct medical care		
Total	2,969 ± 9,843	6,499 ± 15,959 ^b
Hospitalizations	1,293 ± 9,087	3,768 ± 15,069 ^a
Prescription medications	407 ± 601	1,537 ± 1,909 ^b
Assistive device	345 ± 1,531	438 ± 1,291
Outpatient treatment and procedures	350 ± 691	21 ± 222 ^b
Doctor visit	399 ± 614	531 ± 540 ^b
Nonmedical care		
Unpaid care per day, minutes	9 ± 35	58 ± 131 ^b
Paid formal care, \$	0	62 ± 609
Per-user costs, mean ± SD		
Direct medical care, \$		
Hospitalizations	46,131 ± 35,687	36,932 ± 28,923
Prescription medications	427 ± 609	1,555 ± 1,913 ^b
Assistive device	1,107 ± 2,748	1,237 ± 2,069
Outpatient treatment and procedures	684 ± 877	40 ± 305 ^b
Doctor visit	514 ± 654	510 ± 464
Nonmedical care		
Unpaid care per day, minutes	108 ± 60	174 ± 174
Paid, formal care, \$	0	2,278 ± 3,172

Group differences between normal and MCI significant at

^a $P < .05$,

^b $P < .01$.

SD = standard deviation.

Table 3

Multivariate Regression Results of Direct Medical Cost and Informal Care Use over Time (N = 997)

Variable	Direct Medical Cost	Informal Care Use	Odds Ratio
	Coefficient (Standard Error)		
Interval	0.131 (0.038) ^b	0.073 (0.084)	1.076
MCI (reference no MCI)	0.440 (0.171) ^a	1.531 (0.476) ^b	4.624
Alzheimer's Disease Assessment Scale Cognitive Subscale	0.004 (0.010)	0.051 (0.021) ^a	1.052
Alzheimer's Disease Cooperative Study Activity of Daily Living Scale	0.004 (0.009)	-0.108 (0.021) ^b	0.898
Age in 5-year increment	0.084 (0.040) ^a	0.195 (0.089) ^a	1.215
Male (reference female)	-0.134 (0.128)	-1.138 (0.283) ^b	0.321
White (reference nonwhite)	0.098 (0.203)	0.584 (0.526)	1.793
Married (reference unmarried)	-0.119 (0.174)	0.990 (0.401) ^a	2.690
Years of schooling	0.028 (0.019)	-0.069 (0.043)	0.933
Number of medical problems	0.148 (0.035) ^b	-0.054 (0.074)	0.948
Having an adult child informant	-0.274 (0.202)	1.114 (0.454) ^a	3.048

^a $P < .05$,^b $P < .01$.

MCI = mild cognitive impairment.