# Incidence of dementia in oldest-old with amnestic MCI and other cognitive impairments

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## ABSTRACT

**Objective:** To examine the incidence of dementia among the oldest-old people with normal cognition and different types of cognitive impairment.

**Methods:** This study included 395 participants without dementia (mean age 93.3 years) from The 90+ Study, a prospective, population-based study of aging and dementia in people aged 90 years and older. The participants had evaluations for dementia every 6 months, and their average follow-up was 2.5 years. We examined the incidence of all-cause dementia in participants stratified into 4 cognitive groups: normal, amnestic mild cognitive impairment (aMCI), nonamnestic mild cognitive impairment (naMCI), and other cognitive impairment (OCI).

**Results:** Dementia incidence was highest for participants with aMCI (31.4% per year) and OCI (39.9% per year). Participants with naMCI had an incidence of 14.1% per year, and participants with normal cognition had an incidence of 8.4% per year. Dementia incidence was associated with increasing age in both normal and cognitively impaired participants; however, an *APOE*4 allele was associated with a higher dementia incidence only in participants with baseline cognitive impairment.

**Conclusions:** The risk of developing dementia in the oldest-old is high and increases to higher rates when cognitive impairment is present. Similar to results of studies in younger elderly individuals, cognitive impairment and increasing age were related to increased dementia incidence. High dementia incidence rates in the oldest-old individuals, particularly when cognitively impaired, emphasize the need to further study cognitive impairment and dementia in this rapidly expanding age group. ***Neurology*® 2011;77:1906–1912**

## GLOSSARY

**AD** = Alzheimer disease; **CI** = confidence interval; ***DSM-IV*** = *Diagnostic and Statistical Manual of Mental Disorders, fourth edition*; **aMCI** = amnestic mild cognitive impairment; **MMSE** = Mini-Mental State Examination; **naMCI** = nonamnestic mild cognitive impairment; **OCI** = other cognitive impairment; **RR** = relative risk; **VaD** = vascular dementia.

Less than 1% of people aged 65–70 years develop dementia each year,[1] and incidence approximately doubles with every 5 years of increasing age.[2] A previous study of the current cohort[3] found that the doubling of incidence extends to ages 90 and older (the oldest-old), with 13% of 90- to 94-year-old, 21% of 95- to 99-year-old, and 41% of 100-year-old individuals developing dementia each year. Hence, dementia incidence is very high in the oldest-old, the fastest growing age group in the United States.[4]

Compared with normal individuals, cognitively impaired individuals, particularly those with memory impairments, have an increased risk of developing dementia. Population studies have found that approximately 6%–15% of 80-year-old individuals with mild cognitive impairment (MCI) develop dementia each year compared with 1%–2% per year of elderly individuals with normal cognition.[5–8] Few studies have examined dementia incidence in oldest-old individuals with different types of cognitive impairment.

This study examined the incidence of dementia in the oldest-old stratified into 4 groups: normal, amnestic mild cognitive impairment (aMCI), nonamnestic mild cognitive impairment

Supplemental data at www.neurology.org

Supplemental Data

From the Institute for Memory Impairments and Neurological Disorders (C.P., M.M.C., D.J.B., C.H.K.), Department of Neurology (M.M.C., C.H.K.), and Department of Neurobiology and Behavior (C.H.K.), University of California, Irvine, Irvine.

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(naMCI), and other cognitive impairment (OCI). Our hypothesis was that cognitive impairment, particularly memory impairment, would increase the incidence of dementia. Alternatively, cognitive impairment in the oldest-old could be due to physical comorbidities, and, thus, no increase in dementia incidence with cognitive impairment would be found. We also determined whether risk factors for dementia were related to dementia incidence in the oldest-old. Finally, we compared dementia types in each cognitive group to determine whether having a memory deficit was related to Alzheimer disease (AD) rather than to another dementia type.

## METHODS

**Study population.** All participants were members of the Leisure World Cohort Study,[9] started in 1981 when 13,978 (61%) residents of Leisure World, a southern California retirement community, completed a health survey. On January 1, 2003, and again on January 1, 2008, all surviving Leisure World Cohort Study participants aged 90 years and older were invited to join The 90+ Study, a population-based prospective study of aging and dementia in the oldest-old. As of July 31, 2010, The 90+ Study consisted of 1,155 participants (average age 94 years) who are mostly women (77%), Caucasian (99%), and well-educated (approximately 40% have at least a college degree). These traits are similar to the demographics of the elderly population in Orange County in the early 2000s, where, according to the US Census, most people aged 90 and older were women (76%) and Caucasian (91%)[10] and one-third of people aged 65 years and older had at least a college degree (33%).[11]

**Assessments.** All participants from The 90+ Study are asked to undergo a comprehensive in-person examination. However, because of physical or cognitive impairment, some participants were examined through telephone interviews or through an informant, usually a spouse or child. Participants seen in person received evaluations every 6 months by trained neuropsychological testers and neurologic examiners (a physician or nurse practitioner) to evaluate health, functional status, and cognitive status and to update information regarding living situation, medical history, and medication usage.

The neuropsychological battery administered during the visit included the Mini-Mental State Examination (MMSE), a measure of general cognition,[12] and tests of memory (California Verbal Learning Test-II Short Form[13]), language (Category Verbal Fluency[14,15]), praxis (Constructions[15]), and executive function (Digit Span Backwards[16]) among others, as described previously.[17] Before testing, hearing and visual deficits were assessed, and participants who were extremely hard of hearing were provided amplifiers, and visual stimuli were presented in size 90 font for all participants to increase visibility.

The neurologic examiner performed an assessment of mental status using items from the MMSE and clinical judgment independent of neuropsychological testing. The examiner also assessed functional abilities to determine whether the participant had impairment in instrumental activities of daily living[18] due to cognitive difficulties. Either a blood sample or cheek swab was collected for *APOE* genotyping.

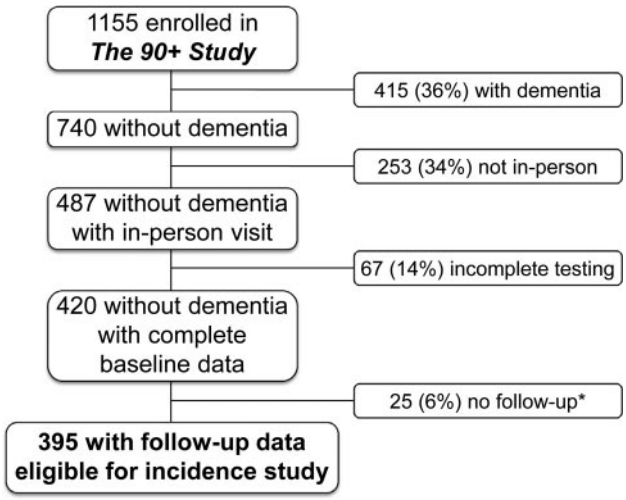
**Standard protocol approvals, registrations, and patient consents.** All procedures were approved by the institutional review board at the University of California, Irvine, and all participants gave written informed consent.

**Determination of cognitive status.** At baseline, all possible participants for this analysis were seen in person, at which time the examiner determined dementia status according to the *DSM-IV* criteria.[19] Only participants determined to not have dementia and who had complete information for all the relevant cognitive tests were included in the current study (figure).

At follow-up, cognitive status was determined during an in-person evaluation by an examiner applying *DSM-IV* criteria for dementia for most participants (71%). Approximately 94% of the follow-up in-person evaluations were completed within 5–7 months. When an in-person evaluation was impossible, we used information from the Cognitive Abilities Screening Instrument-Short Form[20] obtained over the phone or informant questionnaires to determine dementia status at follow-up. Details about how dementia criteria were applied using these instruments and their validity for dementia diagnosis have been published elsewhere.[3,21] Follow-up information was available for 96% of the participants without dementia who underwent complete testing at baseline. The follow-up rate for participants who were not deceased was 99%. Only 19 deceased participants had no follow-up as of the end of the study period (July 31, 2010).

**Determination of cognitive groups.** For analysis, participants without dementia were classified into 4 cognitive groups (normal, aMCI, naMCI, and OCI) using baseline evaluation data according to criteria outlined in table 1. The main criterion for aMCI was objective memory impairment (California Verbal Learning Test-II Short Form long-delay score >1.5 SD below age- and gender-specific norms). Participants with naMCI had impairment in one or more nonmemory domains such as language, executive function, or praxis (animal fluency, digit span backwards, or constructions >1.5 SD below age-specific norms). We calculated age- and gender-specific norms from all participants without dementia with complete neuropsychological data at baseline (n = 420) to determine the 1.5 SD cutoff scores. Unlike the criteria of Petersen,[22] subjective memory com-

**Figure** Participant flowchart




*Six participants not deceased with no follow-up, 19 participants deceased with no follow-up as of the end of the study period (July 31, 2010).

**Table 1** Criteria for classification in cognitive groups

| | Memory score <1.5 SD below norms | Nonmemory score <1.5 SD below norms | MMSE score <24 | Functional impairment[a] |
|---|---|---|---|---|
| aMCI | Yes | Yes, not required | No | No |
| naMCI | No | Yes | No | No |
| OCI | Yes, not required | Yes, not required | Yes[b] | Yes[b] |
| Normal | No | No | No | No |

Abbreviations: aMCI = amnestic mild cognitive impairment; MMSE = Mini-Mental State Examination; naMCI = nonamnestic mild cognitive impairment; OCI = other cognitive impairment.
[a] Functional impairment in instrumental activities of daily living due to cognition.
[b] Participants with OCI had MMSE score <24, functional impairment, or both.

plaints were not required for MCI group inclusion. Participants were classified as OCI[23,24] if they did not have dementia but had a MMSE score <24, functional impairment in instrumental activities of daily living due to cognition, or both. Most participants who were classified as OCI received the designation due to a MMSE score <24 (82%); the remaining had normal MMSE scores but had functional impairment due to cognitive deficits. Impairment >1.5 SD in memory was found in 21.9% of participants with OCI, and 8% had impairment >1.5 SD in memory and nonmemory domains. Participants were classified as normal if they did not meet the criteria for aMCI, naMCI, or OCI.

**Statistical analysis.** All participants without dementia who had a complete neurologic examination and neuropsychological battery at baseline and follow-up data were included in the incidence analyses. The figure shows a flowchart of included participants. Demographic comparisons between the groups were made using one-way analysis of variance for continuous variables and $\chi^2$ analyses for categorical variables. Post hoc comparisons between the groups were performed on variables with a significant main effect. All-cause dementia incidence was calculated separately for each group and by gender and age category (90–94 and 95+ years) using a person-years analysis.

Participants contributed person-years and were considered at risk for dementia from the date of their baseline visit until the date of their follow-up visit when they were determined to have dementia or the date of the last visit when they were determined not to have dementia. A 95% confidence interval (CI) was computed for the incidence rate, assuming a Poisson distribution for the number of incident cases in each cognitive group, age, and sex strata. Incidence rates by age group and dementia type were compared using a Poisson regression model. The effects of gender, education, *APOE*4, and memory impairment on incidence rates were estimated using a Cox regression model with adjustment for age. All analyses used SAS 9.2 (SAS Institute, Cary, NC) and STATA 7.0 for Windows (StataCorp, College Station, TX).

**Comparison of included and excluded participants.** We excluded 253 people without dementia from these analyses because they were not seen in person. Nonparticipants were older (95.0 vs 93.3 years; $p < 0.001$), were less likely to live at home (62.8% vs 87.6%; $p < 0.001$), and were more likely to be women ($p < 0.01$) compared with included participants but did not differ in education level or number of major medical illnesses. We also did not include 92 people seen in person but without either complete baseline data (n = 67) or follow-up data (n = 25). These participants were significantly older (94.3 vs 93.3 years; $p < 0.01$) and had lower MMSE scores (25.0 vs 26.3; $p < 0.01$) than included participants.

**Table 2** Participant characteristics by cognitive group at baseline (n = 395)

| | Cognitive groups | | | | | |
|---|---|---|---|---|---|---|
| Baseline characteristics | Normal | aMCI | naMCI | OCI | All cognitive impairment[a] | Total |
| All subjects, n (%) | 260 (65.8) | 32 (8.1) | 32 (8.1) | 71 (18.0) | 135 (34.2) | 395 |
| Gender, n (%) | | | | | | |
| Women | 183 (70.4) | 14 (43.8) | 20 (62.5) | 46 (64.8) | 80 (59.3) | 263 (66.6) |
| Men | 77 (29.6) | 18 (56.2) | 12 (37.5) | 25 (35.2) | 55 (40.7) | 132 (33.4) |
| Age category, n (%) | | | | | | |
| 90–94 y | 198 (76.2) | 21 (65.6) | 24 (75.0) | 48 (67.6) | 93 (68.9) | 291 (73.7) |
| 95 + y | 62 (23.8) | 11 (34.4) | 8 (25.0) | 23 (32.4) | 42 (31.1) | 104 (26.3) |
| Education, n (%) | | | | | | |
| < College graduate | 136 (52.3) | 20 (62.5) | 20 (62.5) | 39 (54.9) | 79 (58.5) | 218 (54.5) |
| ≥ College graduate | 124 (47.7) | 12 (37.5) | 12 (37.5) | 32 (45.1) | 56 (41.5) | 182 (45.5) |
| Genotype, n (%)[b] | | | | | | |
| *APOE*4− | 207 (82.1) | 21 (70.0) | 25 (83.3) | 58 (85.3) | 104 (81.3) | 317 (82.1) |
| *APOE*4+ | 45 (17.9) | 9 (30.0) | 5 (16.7) | 10 (14.7) | 24 (18.7) | 69 (17.9) |
| Deceased at end of study, n (%) | 160 (61.5) | 22 (68.8) | 20 (62.5) | 55 (77.5) | 97 (71.9) | 257 (65.1) |
| Age, y, mean (range) | 93.0 (90–101) | 93.9 (90–102) | 93.7 (90–100) | 93.8 (90–103) | 93.8 (90–103) | 93.3 (90–103) |
| MMSE score, mean (range) | 27.4 (24–30) | 26.0 (24–29) | 26.5 (24–30) | 22.2 (17–30) | 24.1 (17–30) | 26.3 (17–30) |
| Follow-up, y, mean (range) | 2.8 (0.1–7.0) | 1.8 (0.1–5.5) | 2.2 (0.1–6.4) | 1.8 (0.3–6.2) | 1.9 (0.1–6.4) | 2.5 (0.1–7.0) |

Abbreviations: aMCI = amnestic mild cognitive impairment; MMSE=Mini-Mental State Examination; naMCI = nonamnestic mild cognitive impairment; OCI = other cognitive impairment.
[a] All participants with aMCI, naMCI, or OCI.
[b] Genotype data available on a subset of participants, n = 380.

**RESULTS** Baseline characteristics for the 395 participants combined and separated into the 4 cognitive groups are shown in table 2. The average age of all participants at baseline was 93.3 years, 66.6% were women, and 45.5% had at least a college degree. The average follow-up of all participants was 2.5 years. Participants who joined the study in 2003 had longer follow-up (average 2.76 years) than participants who joined the study in 2008 (average 1.31 years; $t_{393} = 6.71$, $p < 0.001$). Comparing characteristics among the cognitive groups, we found main effects for age ($p < 0.05$), gender ($p < 0.05$), and MMSE score ($p < 0.001$) and a trend for having died by study end ($p = 0.09$). Post hoc comparisons for the significant variables showed that normal participants were younger than participants with OCI ($p < 0.05$) or aMCI ($p = 0.06$). There were significantly more men in the aMCI group than in the normal ($p < 0.01$) and OCI ($p < 0.05$) groups. MMSE scores were significantly lower in the OCI group than in all other groups ($p < 0.001$ for all). Participants with normal cognition had higher MMSE scores than participants with aMCI ($p < 0.001$) and naMCI ($p < 0.05$). Participants with OCI were more likely to have died by study end than normal participants ($p < 0.05$). There were no differences in education ($p = 0.62$) or *APOE4* allele status ($p = 0.34$) among the groups.

Dementia incidence rates and 95% CI for all groups are shown in table 3. The highest incidence rates were found in participants with OCI and aMCI (39.9% and 31.4% per year). Participants with naMCI had an incidence rate of 14.1% per year. Participants with normal cognition had an incidence rate of 8.4% per year. To further examine the high incidence rates in participants with OCI, we separated participants into people with (22%) and without (78%) memory impairment. We found that participants with OCI with a memory deficit had an incidence rate of 61.9% per year (95% CI 33.0–105.9), whereas those without a memory deficit had an incidence rate of 35.6% per year (95% CI 25.2–48.5). Participants with OCI and memory impairment were twice as likely to develop dementia each year compared with those without (hazard ratio 2.13, $p < 0.05$).

We were able to determine dementia etiology only for participants diagnosed in person (82% of those with dementia). Overall, dementia etiology was 62% AD, 19% vascular dementia (VaD), 12% mixed AD/VaD, and 8% other or unspecified dementia. The incidence rates for AD and VaD by cognitive group at baseline are shown in table 3. Dementia incidence rates were not estimated in participants with mixed AD/VaD or other dementias because of the small numbers. Participants were more likely to develop AD than VaD in all cognitive groups except naMCI (normal: relative risk [RR] 2.25, $p < 0.05$; aMCI: RR 3.03, $p = 0.15$; naMCI: RR 0.91, $p = 0.90$; OCI: RR 2.28, $p = 0.06$).

Table 4 shows age-specific all-cause dementia incidence rates for normal and cognitively impaired participants. All participants with cognitive impairment were collapsed into one group because of the few incident cases in the MCI groups. Incidence approximately doubled between ages 90–94 and 95+ for the normal and the cognitively impaired groups (normal $p < 0.001$; cognitively impaired $p < 0.05$). Dementia incidence did not differ in the normal or cognitively impaired participants by gender or education.

*APOE* genotype was available for 96% of participants (n = 380). Table 4 shows incidence for normal and cognitively impaired *APOE4*− and *APOE4*+ participants. Normal *APOE4*+ participants did not have an increased risk of dementia compared with *APOE4*− participants ($p = 0.91$). However, cognitively impaired *APOE4*+ participants were twice as likely to develop dementia as cognitively impaired *APOE4*− participants ($p < 0.05$).

We performed a sensitivity analysis to examine whether there were differences in incidence rates be-

**Table 3** Incidence of all-cause, Alzheimer disease, and vascular dementia by baseline cognitive group

| Cognitive groups | Incident cases | Person-years | Incidence per 100 person-years (95% CI) |
|---|---|---|---|
| **All-cause dementia** | | | |
| Normal | 61 | 726.6 | 8.4 (6.4–10.8) |
| aMCI | 18 | 57.3 | 31.4 (18.6–50.0) |
| naMCI | 10 | 71.1 | 14.1 (6.8–25.9) |
| OCI | 52 | 130.5 | 39.9 (29.6–52.0) |
| All cognitive impairment[a] | 80 | 258.9 | 30.9 (24.5–38.4) |
| **Alzheimer dementia[b]** | | | |
| Normal | 24 | 468.7 | 5.1 (3.3–7.6) |
| aMCI | 11 | 35.2 | 31.3 (15.7–56.2) |
| naMCI | 4 | 39.3 | 10.2 (2.8–26.3) |
| OCI | 33 | 78.5 | 42.0 (28.8–58.7) |
| All cognitive impairment[a] | 48 | 153.0 | 31.4 (23.1–41.6) |
| **Vascular dementia[b]** | | | |
| Normal | 10 | 440.1 | 2.3 (1.1–4.2) |
| aMCI | 2 | 19.4 | 10.3 (1.3–38.0) |
| naMCI | 4 | 35.8 | 11.2 (3.0–28.4) |
| OCI | 6 | 32.5 | 18.5 (6.7–39.6) |
| All cognitive impairment[a] | 12 | 87.7 | 13.7 (7.0–23.8) |

Abbreviations: aMCI = amnestic mild cognitive impairment; CI = confidence interval; naMCI = nonamnestic mild cognitive impairment; OCI = other cognitive impairment.
[a] All participants with aMCI, naMCI, or OCI.
[b] Data available on 115 of 141 cases of incident dementia.

**Table 4** All-cause dementia risk factors by baseline cognitive group

| | Normal cognition | | | | All cognitive impairment[a] | | | |
|---|---|---|---|---|---|---|---|---|
| Characteristic | Incident cases | Person-years | Incidence per 100 person-years (95% CI) | HR (95%CI) | Incident cases | Person-years | Incidence per 100 person-years (95% CI) | HR (95%CI) |
| **Age category, y** | | | | | | | | |
| 90–94 | 17 | 360.2 | 4.7 (2.8–7.6) | 1.0 (reference) | 31 | 137.4 | 22.6 (15.4–32.1) | 1.0 (reference) |
| 95+ | 44 | 366.3 | 12.0 (8.7–16.1) | 2.55 (1.5–4.5) | 49 | 121.4 | 40.4 (30.0–53.5) | 1.79 (1.1–2.8) |
| **Gender** | | | | | | | | |
| Men | 15 | 212.9 | 7.05 (3.9–11.6) | 1.0 (reference) | 28 | 99.6 | 28.1 (18.6–40.5) | 1.0 (reference) |
| Women | 46 | 513.7 | 8.95 (6.6–11.9) | 1.22 (0.7–2.2) | 52 | 159.3 | 32.6 (24.4–42.9) | 1.11 (0.7–1.8) |
| **Education** | | | | | | | | |
| < College graduate | 36 | 373.1 | 9.65 (6.8–13.4) | 1.0 (reference) | 50 | 166.3 | 30.1 (22.4–39.7) | 1.0 (reference) |
| ≥ College graduate | 25 | 353.5 | 7.07 (4.6–10.4) | 0.72 (0.4–1.2) | 30 | 91.5 | 32.8 (22.0–46.6) | 1.03 (0.6–1.6) |
| ***APOE* genotype[b]** | | | | | | | | |
| *APOE4*– | 49 | 563.7 | 8.7 (6.4–11.5) | 1.0 (reference) | 57 | 214.7 | 26.6 (20.1–34.3) | 1.0 (reference) |
| *APOE4*+ | 10 | 145.3 | 6.9 (3.3–12.7) | 0.96 (0.5–1.9) | 17 | 34.7 | 49.0 (28.3–77.8) | 2.03 (1.2–3.6) |

Abbreviations: CI = confidence interval; HR = hazard ratio.
[a] All participants with amnestic mild cognitive impairment, nonamnestic mild cognitive impairment, or other cognitive impairment.
[b] Genotype data available on a subset of participants, n = 380.

tween participants diagnosed in person by a neurologic examiner and those diagnosed by all methods, including telephone and informant questionnaires. The incidence rates of participants diagnosed in person (n = 280) are shown in table e-1 on the *Neurology*® Web site at www.neurology.org. Although the incidence rates for the in-person dementia diagnoses were slightly higher than the rates including all diagnostic methods, the rates were not significantly different in any of the cognitive groups ($p > 0.1$ for all).

**DISCUSSION** Cognitively impaired oldest-old participants had an increased all-cause dementia incidence compared with that of normal participants. Participants with OCI and aMCI had the highest rates of dementia incidence, which were 4 times higher than those in participants with normal cognition. Approximately one-third of participants with OCI and aMCI developed dementia each year. Participants with naMCI had half the rate of dementia incidence compared with participants with OCI and aMCI, but nearly double the rate compared with individuals with normal cognition.

Few studies have examined whether MCI increases dementia incidence in the oldest-old, who already have very high rates of dementia incidence, and they have noted mixed results. One study showed that MCI did not predict future dementia in a relatively large group of Swedish elderly individuals with an average age of 83 years at baseline[25]; however, another investigation found that cognitive impairment was associated with increased dementia incidence.[26] Both of these studies had fewer participants than the current study.

When we examined subtypes of MCI, we found that 31% of participants with aMCI developed dementia each year compared with 8% of normal oldest-old participants. The 4-fold increase in dementia incidence we found in participants with aMCI compared with participants with normal cognition is of a magnitude similar to the increase found in previous studies with younger elderly participants.[5–8] We also found a higher dementia incidence in the oldest-old participants with aMCI compared with naMCI, which is consistent with other studies of younger participants.[5,27,28]

Participants with OCI had the highest incidence of dementia in our study. These participants had a low MMSE score (82%) or functional impairment due to cognition (18%) and were more impaired than either MCI group, although they did not meet *DSM-IV* criteria for dementia at baseline. Other studies have also found that participants without dementia who have more severe impairment are more likely to progress to dementia.[23,24] However, it is possible that some participants with OCI are misdiagnosed as having dementia because of the difficulty in assessing functional loss due to cognition in the oldest-old, many of whom have overlapping physical and cognitive disabilities.[29]

Previous studies suggested that cognitively impaired people with a memory deficit, such as aMCI, may be more likely to develop AD, whereas cogni-

tively impaired people without a memory deficit, (i.e., naMCI), may be more likely to develop other types of dementia such as VaD or frontotemporal dementia.[5,27] Consistent with this suggestion, we found that AD was the most frequent dementia subtype in all groups except the naMCI group. Participants with naMCI were equally likely to develop VaD as AD. This result extends our previous study examining the relationship between cardiovascular risk factors and prevalent cognitive impairment,[29] in which participants with naMCI were more likely to have a history of hypertension than participants in other cognitive impairment groups.

We examined several risk factors shown to increase dementia incidence in younger participants. A doubling of incidence with every 5 years of age was found in normal and cognitively impaired participants, even within the restricted age range of this study. In addition, we found that in cognitively impaired participants, being *APOE4*+ doubled the dementia incidence compared with participants who were *APOE4*−. This relationship was not present in participants with normal cognition. Consistent with our results, most studies have shown a strong relationship between *APOE4*+ status and dementia incidence in participants with cognitive impairment,[30–32] but not all studies have found the relationship.[33,34]

We found memory impairment to be an important factor leading to higher rates of incident dementia, particularly AD. Participants with aMCI progressed to dementia at a high rate of 31% per year, whereas participants with OCI progressed to dementia at nearly 40% per year. When we separated the OCI group into participants with and without memory impairment, we found that participants with OCI with a memory deficit were twice as likely to progress to dementia each year compared with those without. This high rate, along with the rate of the aMCI group compared with that of the naMCI group, indicates that having a memory deficit greatly increases dementia incidence in the oldest-old as in younger elderly.[5,27,28]

This study has several strengths. It is a population-based, epidemiologic cohort, which makes the data more generalizable to the overall population of oldest-old. Studies with relatively large numbers of oldest-old participants are rare, and, thus, most are not able to examine incident dementia. In addition, this study boasts high follow-up rates and frequent follow-up visits, which optimize detection of cognitive changes that may occur rapidly in this age group.

Limitations of this study include the necessarily selective nature of subject inclusion. To sort participants into the 4 cognitive groups, we could only include those with complete, in-person testing at baseline and follow-up evaluations. This eliminated people who were not able to be seen in person, complete testing, or participate in follow-up examinations. People not seen in person were older and were less likely to live at home. People without complete testing were older and had lower MMSE scores. Thus, if exclusion of these people affects the results, it would result in underestimation of the actual dementia incidence values.

Another limitation may be diagnostic misclassifications. Some participants classified as cognitively impaired at baseline may have performed poorly because of sensory loss rather than cognitive impairment, despite the considerable effort made to compensate for sensory losses. Including these normal but sensorially impaired participants in the cognitively impaired group rather than the normal group could have lead to lower rates of incident dementia in the cognitively impaired group. In addition, compared with the entire population of oldest-old in the United States, our sample may be more highly educated. Although we did not find a relationship between education and dementia incidence in this study, it is possible that if the educational attainment of our participants was more comparable to that of all oldest-old, the dementia incidence rates would be higher.

The risk of developing dementia in the oldest-old is extremely high and, similar to that in younger elderly, increases when cognitive impairment is present. The oldest-old participants with aMCI and OCI are more than 4 times more likely to develop dementia each year than those with normal cognition. However, the magnitude of the incidence rate in all groups with cognitive impairment is very high. These findings emphasize the need to further study cognitive impairment and dementia in this rapidly expanding age group.

## AUTHOR CONTRIBUTIONS

Study concept and design: Dr. Peltz and Dr. Kawas. Acquisition of data: Dr. Peltz. Analysis and interpretation of data: Dr. Peltz, Dr. Corrada, Dr. Berlau, and Dr. Kawas. Statistical analysis: Dr. Peltz and Dr. Corrada. Drafting of the manuscript: Dr. Peltz, Dr. Corrada, Dr. Berlau, and Dr. Kawas. Obtained funding: Dr. Kawas, Dr. Corrada, and Dr. Peltz. Study supervision: Dr. Kawas and Dr. Corrada.

## DISCLOSURE

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