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Dementia Incidence Continues to Increase with Age in the Oldest Old The 90+ Study

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Abstract

Objective—The oldest old are the fastest growing segment of the US population, and accurate estimates of dementia incidence in this group are crucial for healthcare planning. Although dementia incidence doubles every 5 years from ages 65 to 90 years, it is unknown if this exponential increase continues past age 90 years. Here, we estimate age- and sex-specific incidence rates of all-cause dementia in people aged 90 years and older, including estimates for centenarians.

Methods—Participants are from The 90+ Study, a population-based longitudinal study of aging and dementia. Three hundred thirty nondemented participants aged 90 years and older at baseline were followed between January 2003 and December 2007. Age- and sex-specific incidence rates of all-cause dementia were estimated by person-years analysis.

Results—The overall incidence rate of all-cause dementia was 18.2% (95% confidence interval [CI], 15.3–21.5) per year and was similar for men and women (risk ratio, 0.94; 95% CI, 0.65–1.37). Rates increased exponentially with age from 12.7% per year in the 90–94-year age group, to 21.2% per year in the 95–99-year age group, to 40.7% per year in the 100+-year age group. The doubling time based on a Poisson regression was 5.5 years.

Interpretation—Incidence of all-cause dementia is very high in people aged 90 years and older and continues to increase exponentially with age in both men and women. Projections of the number of people with dementia should incorporate this continuing increase of dementia incidence after age 90 years. Our results foretell the growing public health burden of dementia in an increasingly aging population.

Dementia incidence increases exponentially with age between the ages of 65 and 90 years and doubles approximately every 5 years.¹ Whether this doubling of rates continues at older ages^{2,3} and whether the pattern is the same in very elderly men and women are not

known.⁴⁻⁶ The number of people aged 90 years and older was approximately 2 million in 2007⁷ but will increase to 8.7 million by the middle of the 21st century,⁸ making the oldest old the fastest growing segment of the US population. Precise estimates of dementia rates in the oldest old are therefore critical for accurate projection of the number of affected people and estimation of the social and economic impact of dementia in future years. To this end, we estimated the age- and sex- specific incidence of all-cause dementia in people aged 90 years and older, including estimates for centenarians, in The 90+ Study.

Subjects and Methods

Study Population

Participants were part of The 90+ Study, a population-based longitudinal study of aging and dementia among people aged 90 years and older. Participants were originally members of the Leisure World Cohort Study, an epidemiological health study established in the early 1980s of a retirement community in California (Laguna Woods).⁹ The cohort is mostly female, Caucasian, well educated, and upper middle class. The 1,150 individuals alive and aged 90 years and older as of January 1, 2003 were invited to participate, and 950 participants had joined as of December 31, 2007.

Assessments

Participants in The 90+ Study were asked to undergo a full in-person evaluation, either at the research office or at their home. This evaluation included a neurological examination (with mental status testing and assessment of functional abilities) by a trained physician or nurse practitioner and a neuropsychological test battery that included the Mini-Mental State Examination (MMSE).¹⁰ Some participants poor health, frailty, or disability did not allow a full in-person evaluation. Information about such participants was obtained by telephone or with informants. Participants who were evaluated by telephone completed the short version of the Cognitive Abilities Screening Instrument (CASI-short).¹¹ For participants evaluated through informants, the Dementia Questionnaire (DQ)¹²⁻¹⁴ was completed over the telephone. All participants (or their informants) completed a questionnaire that included demographics, past medical history, and medication use. In addition, informants of all participants were asked about the participant's cognitive status¹⁵ and functional abilities^{16,17} using a mailed questionnaire. Evaluations were repeated every 6 months for in-person participants and annually for participants evaluated by telephone and through informants. The DQ was completed for all participants shortly after death.

Determination of Cognitive Status

For all participants in this analysis, cognitive status at baseline was determined from an in-person evaluation, either a neurological exam (94%) or MMSE score (6%). Cognitive status at follow-up was also determined from an in-person evaluation for most participants (70%). However, since an in-person evaluation at follow-up was not always possible, we used any available information in the following hierarchical order: (1) neurological exam, (2) MMSE, (3) informant questionnaires, and (4) CASI-short. The neurological examiner determined cognitive status applying Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria for dementia.¹⁸ For the MMSE, we used age- and education-specific cutoff scores for dementia derived from this cohort.¹⁹ Computer algorithms were used to apply DSM-IV criteria for dementia to the questionnaires obtained from informants. For the CASI-short, we used a score ≥ 25 as the cutoff score for dementia.¹¹ Details about the application of the algorithms and the validity of these methods are published elsewhere.²⁰

Statistical Analyses

We restricted our analyses to the 330 participants who were not demented at baseline, as ascertained by an in-person evaluation, and who had at least 1 additional follow-up evaluation. Figure 1 shows a flow chart of participants included in the incidence estimates.

Incidence rates were computed for strata of sex and 5-year age categories (90–94, 95–99, and 100+ years) using a person-years analysis. Participants were considered at risk and contributed person-years from the date of their baseline evaluation until the date of the follow-up evaluation when determined to be demented or the date of last follow-up evaluation when determined not to be demented. A 95% confidence interval (CI) for the incidence rate was computed assuming a Poisson distribution for the number of incident cases in each age and sex strata. To obtain an age-specific incidence curve, we calculated incidence rates using single years of age (from age 90 to age 106 years) and then modeled incidence rates (in the log scale) as a function of age using a Poisson regression. The effects of sex and education were assessed by fitting an additional Poisson regression model that included age, sex, and education. All analyses were done using SAS 9.1 (SAS Institute, Cary, NC) and STATA 7.0 (StataCorp, College Station, TX) for Windows.

Results

Table 1 shows characteristics of the 330 participants included in the analyses. The average age at baseline was 94.2 years (range, 90–103 years), most participants were women (69.7%), and most had at least some college education (70.6%). A total of 140 incident cases of dementia were identified during follow-up. Of those diagnosed as demented by a neurological examiner (81% of demented), the etiology of dementia was 60% Alzheimer disease (AD), 22% vascular dementia, 9% mixed AD and vascular dementia, and 9% other or unspecified dementia. We could not determine dementia etiology for participants diagnosed by an informant questionnaire or a single cognitive test. Table 1 also compares clinical characteristics of those who developed dementia during follow-up to those who did not. At baseline and follow-up, incident cases had lower MMSE scores ($p < 0.001$) and higher Clinical Dementia Rating scores ($p < 0.001$). Incident cases were more likely to have a medical history of depression ($p = 0.03$) but less likely to have hypertension ($p = 0.007$). There was no difference by presence or absence of an apolipoprotein E (APOE) $\epsilon 4$ allele ($p = 0.36$).

We excluded from analyses 230 people who were nondemented at baseline but either did not have a baseline in-person examination or died before they could be re-examined. Compared with the 330 participants used in the analyses, excluded participants were older (95 vs 93 years, $p < 0.001$), more likely to be women (79% vs 70%, $p < 0.01$), less educated ($p < 0.01$), and less likely to live independently ($p < 0.001$).

Our overall incidence rate based on 770 person-years of follow-up was 18.2% per year (95% CI, 15.3–21.5) (Table 2). Rates increased with age from 12.7% per year in the 90–94-year age group, to 21.2% per year in the 95–99-year age group, to 40.7% per year in the 100+-year age group, almost doubling every 5 years. Figure 2 shows incidence rates for the 5-year age categories and the age-specific incidence curve for dementia. Incidence rates increased with age ($p < 0.001$), and this age effect was linear on the log scale. We tested for a nonlinear age effect by including an age-squared term in the Poisson regression, but it was not significant ($p = 0.95$). The estimated doubling time for the incidence rates was 5.5 years.

Table 2 also shows age- and sex-specific incidence rates of dementia. Incidence was similar between men and women in the 90–94-year ($p = 0.89$) and the 95–99-year ($p = 0.87$) age categories, but somewhat higher for men than women in the 100+-year age category,

although not significantly ($p = 0.40$). The estimated risk ratio (RR) from the Poisson regression showed men and women with a similar risk of dementia (RR = 0.94; $p = 0.77$) (Table 3). A suggestion of an association between increased education and lower dementia risk was seen in women but not men. Women who attended graduate school had a 41% lower risk than those with a high school education or less (RR = 0.59; $p = 0.09$) (see Table 3).

Discussion

Our study estimated the overall incidence rate of all-cause dementia in people aged 90 years and older as 18% per year. Rates increased with age and doubled approximately every 5 years with estimates as high as 41% per year in centenarians. Incidence rates were similar for men and women. These contrast sharply with many previous studies that have suggested a slowing of the increase in incidence with age or different rates for men and women.

Most studies of age-specific dementia incidence rates have not reported rates for people older than 90 years or have few participants at very old ages and therefore combine all people aged 90 years and older into 1 age category. The ability to separate older participants into smaller age categories allows for more accurate incidence estimates and projections. Besides ours, the handful of studies that have reported age-specific dementia incidence rates for ages 90 years and above include the Lundby Study,²¹ a study in Munich, Germany,²² the Canadian Study of Health and Aging (CSHA),²³ the Rotterdam study,⁵ the Rochester Epidemiology Project,⁶ the Cache County Study (CCS),³ and the Bronx Aging Study (BAS).²⁴ These studies show a wide range of dementia incidence rates for ages 90 years and above (6%⁵ to 21%²² per year). Estimates from meta-analyses range from 7% to 9% per year.^{2,4,25}

Our overall estimate of 18.2% per year is higher than most studies. This difference is primarily apparent at the oldest age categories. For ages 90–94 years, our rate of 12.7% per year falls within the range of previous studies (5–19% per year) and is similar to that of CCS,³ CSHA,²³ and BAS.²⁴ For ages 95 years and older, incidence rates in other studies range from 7% to 17% per year, with 1 small study (7 person-years of observation) having a rate of 30% per year.²² Our rate of 23.7% per year is higher than almost all these studies.

Our estimate of dementia incidence in centenarians (40.7% per year) is particularly high. Few studies have estimated incidence in centenarians.^{21,26} The Lundby study²¹ reported no incident cases among 3 person-years of observations. In a Liverpool study,²⁶ of 8 nondemented centenarians, 4 died, 1 refused to be reexamined, and 3 remained nondemented after 2 years of follow-up. Our study was considerably larger than these, with 49 person-years of observation at ages 100 years and older.

We observed a consistent increase in incidence after age 90 years, with rates doubling every 5.5 years. Although the effect of age on incidence rates of dementia is well known before age 90 years, with rates increasing exponentially with age from age 65 to age 90 years and doubling every 5 years,¹ the pattern is not clear at older ages. Most studies found a slowing in the increase of incidence rates after age 90 years,^{5,6,23,24} and 1 study found a decline in rates between 90–92 and 93 + years of age.³ A meta-analysis of 12 studies of dementia found that the increase in incidence rates slowed with age; rates tripled every 5 years before age 63 years, doubled every 5 years between ages 64 and 75 years, and increased by 1.5× around age 85 years.²

We found almost identical dementia incidence rates increasing significantly with age after age 90 years in men and women. In contrast, several studies have suggested that the pattern of increasing dementia incidence after age 90 years is not the same in men and women. In

women, most studies show dementia incidence increasing with age after age 90 years,^{5,6,23,24} with 1 exception³ where rates slightly decreased. For men, on the other hand, most studies show incidence rates decreasing with age,^{3,5,6,24} with 1 study showing rates increasing slightly.²³

We previously published sex- and age-specific dementia prevalence for the 90+ Study cohort.²⁰ Our prevalence study found higher estimates of dementia prevalence in women (45%) compared with men (28%), a result also seen in other studies. Based on our current findings of virtually identical incidence rates of dementia in men and women, we believe sex differences in prevalence are due to shorter survival of men after a diagnosis of dementia, as previously reported in younger elderly.^{27,28} We will directly measure survival after a dementia diagnosis in this cohort after accrual of adequate follow-up time.

A sex difference in our study was the slightly lower risk of dementia among women with higher levels of education, but not among men. A meta-analysis of European studies²⁹ found a similar result in participants younger than 90 years. This difference may be due to unmeasured confounding factors related to education and risk for dementia that may be distributed differently in men and women. Women in this study, who obtained their advanced education in the 1920s and 1930s, may have had a variety of characteristics different from men, such as socioeconomic status, early-life exposures, access to healthcare, and nutrition.

Similar to studies in younger elderly, we found depression (at baseline) more common among incident dementia cases.³⁰ However, we found no association with other factors typically related with increased risk of dementia in younger populations, including history of stroke, transient ischemic attack, Parkinson disease, heart disease, and diabetes, or the presence of an APOE e4 allele. This last finding is consistent with studies suggesting that the association between APOE e4 and dementia decreases with age^{31,32} or even disappears in the very elderly. In contrast, a history of hypertension was less frequent among incident cases. As we looked only at history of these conditions without regard to treatment or duration, these results are preliminary and deserve more study.

A major strength of our study is the short interval (6 months) between evaluations. In other studies, this interval has ranged from 1 to 5 or more years, with the larger studies typically having an interval of 3 or more years. With a long interval, some participants who develop dementia may die before the next scheduled evaluation and therefore not be counted as demented, resulting in lower and underestimated incidence. This is more likely to affect the results for men, who have shorter survival after a dementia diagnosis than women, at least among younger elderly.²⁸ Some studies try to minimize the possibility of loss to follow-up by using information from death certificates, informants, and medical records.^{5,23} Our short 6-month interval between evaluations, almost complete follow-up (96%), and use of information from surrogates particularly after death are strengths of our study and considerably minimized the possibility of missing participants who developed dementia and died between evaluations. To test the hypothesis that lower incidence estimates may be due to a long interval between evaluations, we estimated incidence rates after simulating the longer interval in other studies by ignoring evaluations <2 years apart and information obtained from relatives after a participant's death. In this simulation, our overall incidence rate dropped from 18.2% to 11.7% per year ($p = 0.003$), with rates slightly lower for men (10.0% per year) than for women (12.5% per year). The pattern of incidence increasing with age and doubling every 5 years remained, with estimates of 7.9% per year at ages 90–94 years, 14.3% per year at ages 95–99 years, and 27.0% per year at ages >100 years. This simulation confirmed that a long interval between evaluations may underestimate dementia

incidence but did not explain the slowing down or decrease in rates with age seen in other studies.

Another strength of our study is the inclusion of a relatively large number of centenarians. We had 17 centenarians at baseline and 39 by the end of follow-up, with 49 person-years of observation at ages 100 years and older. This high number of centenarians may also explain in part our higher incidence rates. As we observed, centenarians have a high risk of dementia, and inclusion of a greater number of participants at these extreme ages would result in higher estimates of incidence. Other studies may have underestimated dementia incidence above age 95 years because of a lack of extremely old people.

Although we would have preferred to calculate incidence rates using information collected from in-person examinations during follow-up, as we did for the baseline evaluation, this was not always possible in participants who had become ill or frail. This is a limitation of our and other studies evaluating very elderly participants. Rather than exclude these participants and potentially underestimate our incidence rates, we used any available information (ie, telephone interviews and informant interviews) to determine cognitive status at follow-up. The use of a variety of assessment methods may have contributed to our high incidence estimates. To explore this, we performed analyses using only the 305 participants who had in-person evaluations at both baseline and follow-up for determination of cognitive status. The overall incidence rate of 16.9% per year (117 incident cases among 694 person-years) was slightly lower but not significantly different from the original analysis (18.2% per year, $p = 0.55$). We also estimated incidence rates with the 437 nondemented participants who had enough information for determination of cognitive status at baseline and follow-up, whether or not it was obtained in-person. The overall incidence rate of 18.8% per year (194 incident cases among 1,033 persons) was not different from the original estimate (18.2% per year, $p = 0.77$).

Another limitation of our study may be the potential for diagnostic misclassification. First, diagnostic criteria for various dementias are not clearly established for the very elderly. Second, sensory deficits, fatigue, motor limitations, and medical comorbidities complicate the administration and may confound the interpretation of diagnostic assessments.³⁵ Thus, we may have assigned a diagnosis of dementia to nondemented participants. However, our incidence rates for ages 90–94 years are consistent with previous studies, and our estimates of prevalence of dementia in the same cohort,²⁰ obtained with similar methodologies, are consistent with other studies of the oldest old. We also note that although we applied DSM-IV dementia criteria, most previously cited studies used DSM-III-R³⁶ criteria. Evidence suggests that slightly lower estimates are obtained with DSM-IV criteria, compared with DSM-III-R criteria,^{37,38} making direct comparisons between studies difficult.

The 90+ Study comprises a predominantly female, white population of high education and socioeconomic level, characteristics that could potentially limit the generalizability of our results. According to the 2000 US Census, most people aged 90 years and older were women (76%) and Caucasian, both in Orange County, CA (90%) and in the whole United States (89%).³⁹ Thus, despite the lack of representation of minority subjects (1%) and having mostly women (70%) in the cohort, the composition of the 90+ Study cohort does reflect that of people aged 90 years and older in the county and the United States.

The 90+ Study is 1 of only a few studies to report incidence of dementia by sex and age in participants aged 90 years and older and the first to have sufficient participants to report rates in centenarians. Our study found that incidence continues to increase exponentially with age in both men and women past the age of 90 years. This is in sharp contrast with most studies that have seen a slowing of the increase in incidence with age in the oldest old

and a decline in rates among men. Although medical progress has helped more individuals live to extreme ages, those extra years of life are likely not dementia free. Thus, dementia in the oldest old threatens to become an epidemic with enormous public health impact. Projections of the number of people with dementia should account for the possibility that incidence of dementia continues to increase with age after the age of 90 years. The accuracy of these estimates will be crucial for adequate planning of healthcare resources.

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Figure 1.

Flow chart for participant inclusion in incidence estimates. ^aOf the 411 participants with no in-person evaluation at baseline, using other sources of information available we determined that 201 were demented at baseline, 107 were not demented at baseline and had a follow-up evaluation, 88 were not demented at baseline but did not have a follow-up evaluation, and 15 did not have enough information for a cognitive status determination.

Figure 2.

Age-specific incidence rates and 95% confidence intervals of all-cause dementia in the 90+ Study: January 1, 2003 to December 31, 2007. Incidence rates were computed for 3 age categories using a person-years analysis and are plotted at the average age for each age category: 92.7 years for the 90–94-year category, 96.4 years for the 95–99-year category, and 101.3 years for the 100+-year category. The incidence curve is from a Poisson regression with age as a continuous variable. The time for the incidence rates to double was estimated at 5.5 years.

Table 1
Characteristics of Participants by Dementia Status at Follow-up in the 90+ Study: January 1, 2003 to December 31, 2007

Characteristic	Total No. ^a	All Participants (N = 330)	Not Demented at Follow-up (not incident cases) (n = 190)	Demented at Follow-up (incident cases) (n = 140)	p ^b
Age at baseline, yr, mean (SD)	330	94.2 (2.7)	94.0 (2.4)	94.4 (3.1)	0.13
Follow-up, yr, mean (SD)	330	2.3 (1.3)	2.6 (1.4)	2.0 (1.2)	<0.001
MMSE score, mean (SD)					
At baseline	328	26.1 (2.8)	27.1 (2.3)	24.8 (2.8)	<0.001
At follow-up	226	24.3 (4.6)	26.7 (2.3)	22.0 (5.1)	<0.001
Women, No. (%)	330	230 (69.7)	130 (68.4)	100 (71.4)	0.63
Education, No. (%)	330				0.20
High school		97 (29.4)	51 (26.8)	46 (32.9)	
Any college		149 (45.2)	84 (44.2)	65 (46.4)	
Any graduate school		84 (25.4)	55 (29.0)	29 (20.7)	
Living situation at baseline, No. (%)	330				0.05
Living alone		180 (54.6)	115 (60.5)	65 (46.4)	
In household with relatives or caregiver		95 (28.8)	49 (25.8)	46 (32.9)	
Group quarters		48 (14.5)	24 (12.6)	24 (17.1)	
Nursing home		7 (2.1)	2 (1.1)	5 (3.6)	
APOE e4 allele present, No. (%)	310	51 (16.5)	26 (14.7)	25 (18.8)	0.36
CDR score, No. (%)					
At baseline	289				<0.001
0		175 (60.6)	125 (75.3)	50 (40.7)	
0.5		114 (39.4)	41 (24.7)	73 (59.4)	
At follow-up	228				<0.001
0		71 (31.1)	69 (60.5)	2 (1.8)	
0.5		112 (49.1)	44 (38.6)	68 (59.7)	
1		33 (14.5)	1 (0.9)	32 (28.1)	
2 or 3		12 (5.3)	0 (0)	12 (10.5)	
Medical histories at baseline, No. (%)					

Characteristic	Total No. ^a	All Participants (N = 330)	Not Demented at Follow-up (not incident cases) (n = 190)	Demented at Follow-up (incident cases) (n = 140)	p ^b
Heart disease ^c	316	147 (46.5)	82 (44.3)	65 (49.6)	0.36
Transient ischemic attack	314	48 (15.3)	24 (13.2)	24 (18.2)	0.27
Stroke	327	38 (11.6)	20 (10.6)	18 (13.0)	0.49
Parkinson disease	329	1 (0.3)	0 (0)	1 (0.7)	0.42
Hypertension	325	172 (52.9)	112 (59.6)	60 (43.8)	0.007
Depression	324	37 (11.4)	15 (8.0)	22 (16.1)	0.03
Diabetes	327	14 (4.3)	8 (4.2)	6 (4.4)	0.99

^aFor some variables, the total number is <330 because people whose cognitive status determination at follow-up was not done with an in-person examination did not receive a full evaluation and had some information missing.

^bp Values are from t tests for continuous variables, Fisher exact tests for binary variables, and Pearson chi-square tests for categorical variables and to compare people who developed dementia during follow-up with those who did not develop dementia during follow-up.

^cHistory of heart disease includes history of any of the following: coronary artery disease, myocardial infarction, atrial fibrillation or other arrhythmias, heart valve disease, and congestive heart failure. SD = standard deviation; MMSE = Mini-Mental State Examination; APOE = apolipoprotein E; CDR = Clinical Dementia Rating.

Table 2
Age- and Sex-specific Incidence Rates of All-Cause Dementia in the 90+ Study: January 1, 2003 to December 31, 2007

Age Interval, yr	No. of New Cases	Person-Years	Incidence Rate per 100 Person-Years (95% CI) ^a
Men			
90–94	14	114.3	12.3 (6.7–20.6)
95–99	20	97.8	20.5 (12.5–31.6)
100 +	6	10.9	55.2 (20.3–120.2)
Total (90 +)	40	222.9	17.9 (12.8–24.4)
Women			
90–94	35	271.1	12.9 (9.0–18.0)
95–99	51	237.6	21.5 (16.0–28.2)
100 +	14	38.3	36.6 (20.0–61.3)
Total (90 +)	100	547.0	18.3 (14.9–22.2)
All			
90–94	49	385.4	12.7 (9.4–16.8)
95–99	71	335.3	21.2 (16.5–26.7)
100 +	20	49.2	40.7 (24.9–62.8)
Total (90 +)	140	769.9	18.2 (15.3–21.5)

^aThe annual probability of dementia can be calculated from the incidence rate, i , using an exponential model $1 - \exp(-i)$.

CI = confidence interval.

Table 3
Estimated Risk Ratios for Incident All-Cause Dementia in the 90+ Study: January 1, 2003 to December 31, 2007

Variable	All (n = 330)		Men (n = 100)		Women (n = 230)	
	Risk Ratio (95% CI) ^a	p	Risk Ratio (95% CI) ^b	p	Risk Ratio (95% CI) ^b	p
Age (per 5-year increase)	1.89 (1.45–2.48)	<0.001	2.12 (1.21–3.73)	0.009	1.82 (1.34–2.47)	<0.001
Education						
High school	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Any college	0.89 (0.61–1.30)	0.56	0.98 (0.45–2.12)	0.96	0.86 (0.56–1.33)	0.51
Any graduate school	0.68 (0.42–1.09)	0.11	0.84 (0.39–1.84)	0.67	0.59 (0.32–1.09)	0.09
Sex						
Men	1.00 (reference)	—	—	—	—	—
Women	0.94 (0.65–1.37)	0.77	—	—	—	—

^aFrom a Poisson regression including age (continuous variable), sex, and education as covariates.

^bFrom a Poisson regression including age (continuous variable) and education as covariates.

CI = confidence interval.