

Aging and the Occurrence of Dementia

Findings From a Population-Based Cohort With a Large Sample of Nonagenarians

Eva von Strauss, MSc; Matti Viitanen, PhD; Diana De Ronchi, MD; Bengt Winblad, PhD; Laura Fratiglioni, PhD

Context: In spite of numerous studies on the occurrence of dementia, many questions remain, such as the relation between age, aging, and dementing disorders. This question is relevant both for understanding the pathogenetic mechanism of the dementias and for the public health prospective because of the increasing number of 85-year-old or older persons in our population.

Objective: To estimate the occurrence of dementia in the very old, including nonagenarians, in relation to age, gender, and different dementia types.

Design: An epidemiological survey where all participants were clinically examined by physicians, assessed by psychologists, and interviewed by nurses. The *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R)* criteria for dementia were followed. A category of “questionable dementia” was added when all criteria were not fulfilled. A double diagnostic procedure was used for all subjects.

Setting: Community-based population, including all inhabitants of 2 areas in central Stockholm, Sweden (N = 1848).

Participants: Of the 1848 subjects in the study population, 168 (9.1%) had died and 56 (3%) moved before examination. Of the remaining subjects, 1424 (87.7%)

were examined, and the refusal rate was 12.3%.

Main Outcome Measures: Age- and gender-specific prevalence figures, and gender- and education-adjusted odds ratios were used.

Results: At the end of the diagnostic procedure, 358 clinically definite cases of dementia and 101 questionable cases of dementia were identified. Alzheimer disease (AD) contributed to 76.5%, and vascular dementia (VaD) to 17.9%. The prevalence of dementia increases from 13% in the 77- to 84-year-old subjects to 48% among persons 95 years and older (from 18% to 61% when questionable cases were included). The odds ratio for subjects 90 to 94 years and 95 years and older in comparison with 77- to 84-year-old subjects was 3.7 (95% confidence interval [CI], 2.7-5.1) and 6.5 (95% CI, 3.9-10.8) for dementia, 4.8 (95% CI, 3.3-7.0) and 8.0 (95% CI, 4.6-14.0) for persons with AD, 2.3 (95% CI, 1.3-4.2) and 4.6 (95% CI, 1.9-11.2) for VaD, respectively.

Conclusions: Dementia prevalence continues to increase even in the most advanced ages. This increase is especially evident among women and is more clear for AD. We believe that our prevalence data reflect the differential distribution of dementia risk.

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From the Stockholm Gerontology Research Center, Division of Geriatric Medicine, Neurotec, Karolinska Institute, Stockholm, Sweden (Ms von Strauss and Drs Viitanen, De Ronchi, Winblad, and Fratiglioni); and the Institute of Psychiatry, University of Bologna, Bologna, Italy (Dr De Ronchi).

IN RECENT years, several studies have addressed the issue of whether dementia is an “age- or aging-related disorder.”¹⁻³ In spite of numerous prevalence⁴⁻¹³ and incidence¹⁴⁻²² studies, it is still unclear if the exponential increase in dementia frequency with age continues, even in the advanced ages, as an inevitable feature of aging,^{9,10,13} or if the occurrence reaches a plateau in people 85 years and older.^{2,3}

Moreover, we still do not know if dementia occurs with a different age distribution in men and women, as suggested by Fratiglioni et al,^{22,23} or if the relation between dementia occurrence

and age varies according to different dementia types. Some authors^{12,24} suggested that vascular dementia (VaD) may be the major cause of dementia in the highest ages, whereas others²⁵ reached an opposite conclusion in a review article on VaD, suggesting that this type of dementing disorder may be more frequent in the youngest-old ages.

This uncertainty derives mainly from the difficulty in studying samples that include enough subjects 90 years and older to allow reliable estimations of dementia frequency in the very old. In fact, only 3 prevalence studies included more than 200 persons 90 years and older.^{6,9,11}

SUBJECTS AND METHODS

STUDY POPULATION

The study population consisted of 2 groups: (1) all the 77-year-old and older subjects living in the Kungsholmen area and (2) all persons 90 years and older registered in the contiguous area, St Görán, on January 1, 1992, whether living at home or in institutions. These are 2 homogeneous populations with the same age- and gender-distribution and similar health care system as in the Stockholm area. On average, the subjects had lived 49.6 years in the Kungsholmen area and 45.1 years in the St Görán area.

Each subject was sent a personal letter explaining the study and the importance of participation but clearly stating that it was voluntary and that at any time they could discontinue participation.^{27,28} The study has been approved by the ethics committee of the Karolinska Institute.

DATA COLLECTION

All participants were examined following a standardized protocol, including a social interview performed by nurses, a neuropsychological battery, and a clinical examination. The psychological battery included the Mini-Mental State Examination (MMSE),²⁹ free recall and recognition of random words,³⁰ and digit span.³¹ These tests were chosen as they had been proven to best discriminate between subjects with and without dementia in the first wave of our project.³² All subjects were examined by physicians who assessed the elderly person's general, neurologic, cognitive, and psychiatric status, as well as medication use. The clinical examination was similar to a normal geriatric examination usually performed in clinical practice but structured and defined with scoring criteria. Depression was assessed with the Comprehensive Psychopathological Rating Scale.³³ Several cognitive functions were tested, such as semantic and episodic memory, language, abstract thinking, praxis, visuospatial ability, calculation, and gnosis.²²

To differentiate among various types of dementia, laboratory tests were performed (albumin, glucose, ferritin, vitamin B₁₂, and thyroid functions). As neuroimaging was not available in all cases, these data were not taken into account in the diagnosis. An informant interview was carried out in 92% of the cases—it covered clinical and family history, current health status, and changes in cognitive and memory functioning.

The clinical examination was completed in April 1993. The average time between the onset of the study and the examination was 8.0 ± 5.2 months; 41% of the subjects were examined within 6 months and 80% in 12 months.

DEMENTIA AND DEMENTIA-TYPE DIAGNOSIS

The *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R)* diagnostic criteria,³⁴ with some modifications,³⁵ were used for the clinical diagnosis of dementia and different dementia types. The cases fulfilling the *DSM-III-R* criteria were denominated “clinically

definite dementia,” in contrast to a category of “questionable dementia,” which was used when there was evident memory impairment and daily life was affected but dysfunction of a second cognitive ability was questionable.²²

Special attention was given to the definition of “social and work activities.” According to the *DSM-III-R* criteria, cognitive disturbances can be diagnosed as dementia only if they interfere with such activities. As work activities, we considered daily activities in the home (preparing food, shopping, managing light household tasks, balancing a checkbook, and handling money), hobbies, and leisure activities. Social activities were defined as relationship with relatives and friends. The subject and a close relative were asked specifically to judge if any changes from previous levels of performance had occurred and, if so, to describe when and how.

Differential diagnosis between Alzheimer disease (AD) and VaD was based only on clinical data, including information from a relative concerning clinical history. More specifically, for a diagnosis of AD, gradual onset and progressive deterioration of dementia were required and all other specific causes of dementia had to be excluded. The diagnosis of VaD was based on clinical features of dementia with abrupt onset and stepwise deterioration; a history of stroke and/or focal deficits were required. The Hachinski scale³⁶ was also used to support the differential diagnosis between AD and VaD. All subjects with a clinical dementia syndrome characteristic of AD but with a history of stroke were classified in the diagnostic category of “mixed dementia.” When it was impossible to define the dementia type, a category of “unspecified type of dementia” was used. The diagnostic process has already been described, and the same double diagnostic procedure was used for all subjects.^{22,35} Information on the duration of the disease was obtained by asking the relative when the first dementia-related symptoms appeared. Dementia severity was measured according to the Washington University Clinical Dementia Rating Scale (CDR)³⁷ and was done by 1 physician.

DATA ANALYSIS

The relationship between dementia occurrence and aging was explored separately for both clinically definite and questionable dementia by using the following measures:

1. Age- and gender-specific prevalence figures were calculated using as the numerator all cases with a final diagnosis and, as the denominator, the number of inhabitants of the 2 areas on the prevalence day. Ninety-five percent confidence intervals (95% CIs) were computed based on the binomial distribution.³⁸ For clinically definite dementia the same analysis was performed for AD and VaD.

2. Gender- and education-adjusted odds ratios (ORs) due to increasing age were derived from logistic regression analyses.³⁹ Categories of education used were “elementary/vocational” and “high school/university.” Age was entered as a continuous variable in 2 models (1-year or 5-year increment). Another model treated age as an indicator variable, comparing 3 age groups (85-89, 90-94, and ≥95 years) to the reference category (77-84 years). Similar analyses were repeated for AD and VaD separately.

To shed more light on this topic, we examined the occurrence of dementia and different dementia types using data gathered from the second wave of the longitudinal study carried out in the Kungsholmen district in Stockholm, Swe-

den.²⁶ During this phase, to attain a higher precision in estimating dementia occurrence among the oldest old, the study population had been enlarged by adding all the 90-year-old and older inhabitants of a contiguous area.

Table 1. Study Population, Dropouts by Causes, and Participants (Clinically Examined), Distribution by Age and Gender

Age Group, y	Study Population	Dropouts			Clinically Examined
		Moved	Refused	Died	
Men					
77-84	186	4	16	11	155
85-89	93	4	11	7	71
90-94	103	1	11	16	75
≥95	17	0	2	5	10
Total	399	9	40	39	311
Women					
77-84	544	12	66	28	438
85-89	327	7	39	23	258
90-94	450	21	46	50	333
≥95	128	7	9	28	84
Total	1449	47	160	129	1113
All	1848	56	200	168	1424

RESULTS

Of the 1848 subjects in the study population, 9.1% died, 3% had moved from the area before examination, and 12.3% refused to participate. Thus, 1424 persons were clinically examined and of them 502 persons were more than 89 years old (**Table 1**). Forty-five percent of the men and 36% of the women had more than 7 years of schooling.

Number and clinical characteristics of questionable and clinically definite dementia by type are reported in **Table 2**. The other dementias were 4 cases of dementia in subjects with Parkinson disease, 2 cases of other neurologic diseases, 6 cases of alcohol dementia, and 8 cases with unspecified dementia type. Only 9 subjects with clinically definite dementia had an MMSE score above 23. Mild cases accounted for 85.1% among questionable dementia cases, while moderate and severe forms accounted for 66.5% of all the clinically definite dementia cases. Mild dementias were more frequently reported among the youngest age groups, both among questionable and definite dementia cases (32.6% and 31.7% in the 77- to 84-year-old age group decreasing to 12.8% and 8.3% in the ≥95-year-old age group, $P = .01$ and $P < .001$, respectively). Alzheimer disease and VaD had similar percentages of severe forms of dementia, as well as mean MMSE scores.

The age- and gender-specific prevalence per 100 population, and adjusted ORs for clinically definite dementias are presented in **Table 3**. The prevalence of clinically definite dementia increases with age even in the most advanced ages. This increase was more pronounced for women than for men. The crude ORs for all clinically definite dementias were 2.2 (95% CI, 1.6-3.1) for the 85- to 89-year-old group; 4.1 (95% CI, 3.0-5.6) for the 90- to 94-year-old group; and 7.3 (95% CI, 4.5-12.0) for the 95-year-old and older group, with age group 77 to 84 years as the reference level. When gender and education were introduced into the logistic regression model, the asso-

Table 2. Number of Cases, Cognitive Impairment (MMSE Score), Disease Severity (CDR), and Appearance of First Symptoms (Years) of Dementia Cases Separately for Questionable and Clinically Definite Forms*

	Questionable Dementia	Clinically Definite Dementia			
		AD	VaD	Other	All
No. of cases	101	274	64	20	358
MMSE score					
Mean	20.0	11.7	10.5	8.4	11.3
SD	6.6	7.9	8.4	8.5	8.1
CDR, %					
Mild (0.5-1)	85.1†	34.7	29.7	30.0	33.5
Moderate (2)	...	32.8	42.2	15.0	33.5
Severe (3)	...	32.5	28.1	55.0	33.0
Appearance of first symptoms, y‡					
Mean	2.2	5.4	5.3	6.0	5.4
SD	2.3	3.8	4.4	4.2	3.9

*MMSE indicates Mini-Mental State Examination; CDR, Clinical Dementia Rating Scale; AD, Alzheimer disease; and VaD, vascular dementia. Ellipses indicate data not applicable.

†Missing information for 15 cases.

‡Missing information for 49 cases.

ciation with increasing age was still present (**Table 3**). Analyzing age as a continuous variable, the adjusted OR for the 1-year age increment was 1.1 (95% CI, 1.1-1.2) and for the 5-year increment, 1.9 (95% CI, 1.7-2.2).

The same pattern was found when questionable dementia cases were analyzed (**Table 4**). Due to the small number of cases, we could not stratify questionable dementia by gender. Moreover, we repeated the logistic regression analysis as described above, adding questionable dementia to clinically definite dementia in a first model and then adding questionable dementia to the group without dementia in a second model. The results did not change substantially.

A stronger association between increasing age and dementia prevalence was observed for AD than for VaD (**Figure 1**). For AD, the prevalence was higher for women than men in each age stratum but especially among the oldest old.

Crude ORs for AD were 3.0 (95% CI, 2.0-4.5) for the 85- to 89-year-old group, 5.3 (95% CI, 3.7-7.7) for the 90- to 94-year-old group, and 9.3 (95% CI, 5.4-16.1) for the 95-year-old and older group, when using age up to 84 years as the reference level. When gender and education were introduced into the model, the association with increasing age was still strong. An association between VaD and increasing age was also observed but only in the 90-year-old and older group. The same analyses were also performed separately for men and women, and the association with increasing age remained among women, whereas it was less clear among men (**Figure 2**).

COMMENT

The present study is one of the few in which the relationship between the occurrence of dementia and different dementia types has been explored in a community population with a large sample of 90-year-old and older

Table 3. Number of Cases, Prevalence per 100 Population, and Adjusted Odds Ratios (aORs) for Clinically Definite Dementia of All Types, Distribution by Age and Gender*

Age Group, y	Men			Women			All		
	No.	Prevalence (95% CI)	aOR† (95% CI)	No.	Prevalence (95% CI)	aOR† (95% CI)	No.	Prevalence (95% CI)	aOR‡ (95% CI)
77-84	18	11.6 (6.6-16.7)	1.0	62	14.2 (10.9-17.4)	1.0	80	13.5 (10.7-16.2)	1.0
85-89	14	19.7 (11.2-30.9)	2.0 (0.9-4.3)	67	26.0 (20.6-31.3)	2.2 (1.5-3.2)	81	24.6 (20.0-29.3)	2.1 (1.5-3.0)
90-94	18	24.0 (14.9-35.3)	2.6 (1.3-5.5)	134	40.2 (35.0-45.5)	4.0 (2.8-5.7)	152	37.3 (32.6-41.9)	3.7 (2.7-5.1)
≥95	3	30.0 (6.7-65.3)	3.1 (0.6-17.8)	42	50.0 (38.9-61.1)	7.1 (4.2-12.2)	45	47.9 (37.5-58.4)	6.5 (3.9-10.8)

*CI indicates confidence interval.

†Adjusted for education.

‡Adjusted for gender and education.

Table 4. Number of Cases, Prevalence per 100 Population, and Adjusted Odds Ratios (aORs) for Questionable Dementia of All Types*

Age Group, y	No.	Prevalence (95% CI)	aOR (95% CI)†
77-84	30	5.1 (3.3-6.8)	1.0
85-89	28	8.5 (5.5-11.5)	2.0 (1.2-3.4)
90-94	31	7.6 (5.0-10.2)	2.1 (1.3-3.6)
≥95	12	12.8 (6.8-21.2)	4.9 (2.3-10.4)

*CI indicates confidence interval.

†Adjusted for age and education.

persons and in which all subjects were clinically examined. We found a steady increase of dementia prevalence with age, even in the most advanced ages. Our prevalence rates were 37% among persons aged 90 to 94 years and 48% among persons 95 years and older, and these figures would have increased up to 45% and 61%, respectively, if questionable dementia had been taken into account. This increase was evident among women but unclear among men. A similar pattern was found for AD; for VaD such a pattern was questionable. In all age strata, AD prevalence values were higher than VaD figures.

Several questions arise from these findings:

1. Is the positive association between dementia prevalence and age due to a continuous increase of dementia incidence with age? As prevalence is determined by both incidence and duration of the disease, differential survival at different ages among subjects with dementia has been suspected of affecting the age distribution of dementia prevalence.⁴⁰ We attempted to verify the influence of the differential survival by estimating dementia incidence from prevalence figures and disease duration.⁴¹ Information on duration was gathered from a previous study⁴² in which incident dementia cases were followed up from diagnosis to death in a 5-year period. We found that for both men and women, the estimated incidence rates continued to increase with age even after 85 years. The frequency of questionable dementia also increased with age, and prevalence figures of questionable dementia are likely to be less affected by differential disease duration for different age groups. In conclusion, we believe that the increase of dementia prevalence is a result of an increased incidence of the disease with increasing age. Almost all the recent incidence studies,

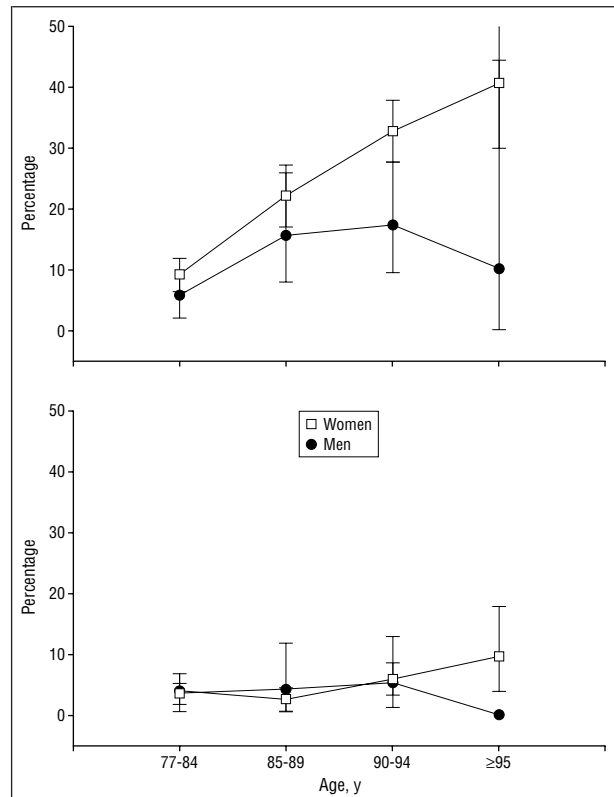


Figure 1. Prevalence per 100 population and 95% confidence intervals (bars) of clinically definite Alzheimer disease (top) and definite vascular dementia (bottom). Distribution is by age and gender.

although limited by small numbers of nonagenarians, have shown a tendency toward an increase even after age 90 years.^{17,18,20,22}

Our findings are in complete agreement with other studies in Canada,⁹ Germany,¹⁰ and the United States,¹² where similar prevalence figures and the same relationship with age were found. These findings support the hypothesis that dementia is an aging-related process, as suggested first by Jorm et al⁴³ in 1987. Only 2 studies have reported data showing a plateau of dementia prevalence at the age of 85 years.^{2,7} This disagreement could be due to methodological issues.⁴⁴

2. Is the higher occurrence of dementia in old age due to differential misclassification in different age groups? Dementia diagnosis in population studies is always dif-

ficult,^{19,35,44,45} especially in old age.¹⁰ In the oldest-old people, it may be problematic to distinguish between early manifestations of dementia and changes associated with “normal aging.” Although the *DSM-III-R* criteria were strictly followed in our study, some cases could not be classified with certainty, and, therefore, a category of questionable dementia was used.²² The interference with work and social life, as requested by the *DSM-III-R*, can sometimes be arduous to evaluate in old-old subjects. We tried to overcome these difficulties by asking the person and his or her family about any changes in daily activities, hobbies, and social activities. Moreover, each diagnosis was made twice, separately, by experienced clinicians (L.F. and M.V.) (geriatricians and neurologists). If a differential misclassification was present, it is more likely to have led to an underestimation of the prevalence among old subjects, as mild cases may be easily missed in this age group. In fact, the oldest-old persons are not expected to perform complicated activities as well as younger-old adults. Therefore, mild cognitive dysfunction does not interfere as much with social activities. A previous study⁸ pointed out that mild dementia decreased with age from 36% at 75 years to 13% at 85 years. In our study, we also found that the prevalence of mild dementia according to CDR criteria was lower in the oldest-old (8.3% vs 31.7%).

3. Is the differential age distribution of dementia prevalence between men and women true, or is it due to the small sample size of men? In our study, dementia prevalence continued to increase with age clearly among women, but not among men, and in all age strata women had higher prevalence than men. At the age of 95 years, the prevalence of dementia among women was 50% (62% if questionable dementia cases were included), whereas the corresponding figure for men was 30% (50% when questionable cases were included). Unfortunately, in spite of the enlargement of the nonagenarian stratum in the study population, there was still a limited number of male survivors when ages 85 years or older were considered. Thus, all our estimates for men, both the prevalence and the OR, lack precision. The increased prevalence of dementia among women reported in previous studies^{6,12} has been attributed to their low educational attainment,¹³ but we found a higher prevalence among women even after adjustment for age and education.

4. May misdiagnosis lead to the differential age distribution in the occurrence of AD and VaD? Our results show that the continuing increase in dementia prevalence with increasing age is especially evident for AD, whereas it is more questionable for VaD. In the present study, the dementia diagnoses were based on clinical data only and not supported by neurologic investigations, such as computed tomography, magnetic resonance imaging, or autopsy. Thus, it is possible that VaD may have been underestimated but not necessarily in different ways in different age groups. Moreover, other studies have shown that both *DSM-III* and NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association) criteria have good validity when the clinical diagnosis of dementia and AD are compared with findings on autopsy.⁴⁶ Recently, a meta-analysis of validation studies concerning the use of the Hachinski scale reported an accuracy rate of 89%.⁴⁷ We, therefore, believe that our diagnoses

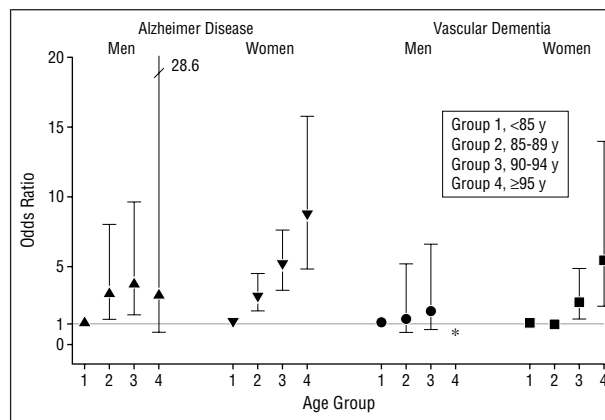


Figure 2. Association of age and gender with Alzheimer disease and vascular dementia (adjusted for education) expressed as odds ratio and 95% confidence interval (bars). The group younger than 85 years is the reference level. The asterisk indicates no cases.

are sufficiently accurate to verify our hypothesis, although less accurate than the diagnoses made in a special clinical setting. Most studies in Western countries agree that the steep increase in dementia prevalence up to the age of 85 years is a result of the age distribution found in AD.^{5,9,11,13,48,49} Our data support these findings, even after the age of 90 years. In contrast, Skoog et al,²⁴ who examined an 85-year-old population in Sweden, found that 47% of all dementia cases were affected by vascular or mixed dementia, suggesting that a vascular cause of dementia may be more common in old age than previously thought. The diagnostic procedure in the study by Skoog et al also used information from neuroimaging. Probably, in oldest-old ages, both vascular and degenerative mechanisms contribute to the development of dementia^{50,51} that can be attributed to one or the other subtype of dementia, depending on the diagnostic tools.

5. Could selection bias due to dropouts have determined some of our results? Refusal rate in our study was very low (12%). The subjects who refused had age- and gender distribution similar to that of the participants, so it is not likely that the refusals affected our results. However, it is not possible to say whether men at early stages of dementia are more likely to refuse a clinical examination than women in the same clinical situation. Of the study population, 168 (9%) died before being examined. This may have affected our results toward an underestimation of the dementia prevalence but not the differential distribution with age and gender. The information obtained from medical records and death certificates led to the identification of 1 case of dementia among the 39 men and 12 cases among the 129 women, leading to a higher percentage of dementia among dead women (9.4%) than among dead men (2.8%).

In conclusion, we found that dementia prevalence continues to increase with increasing age, even in the most advanced ages; the probability of having dementia increased by 10% each year, and 90% every 5 years. This increase is especially evident among women, and this pattern is more clear for AD than for VaD and is probably due to differential disease incidence. It is unlikely that misclassification and selection biases have contributed to these findings. Finally, the high prevalence of demen-

tia and more severe cases among the oldest-old underscore the need for appropriate health care planning in our Western societies, as persons 85 years or older are the age group in the population who have and will experience the most dramatic increase.⁵²

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Corresponding author: Eva von Strauss, MSc, Stockholm Gerontology Research Center, Box 6401, S-113 82 Stockholm, Sweden (e-mail: Eva.von.Strauss@neurotec.ki.se).

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