

# Prevalence of Dementia in Older Japanese-American Men in Hawaii

## The Honolulu-Asia Aging Study

Lon White, MD; Helen Petrovitch, MD; G. Webster Ross, MD; Kamal H. Masaki, MD; Robert D. Abbott, PhD; Evelyn L. Teng, PhD; Beatriz L. Rodriguez, MD, PhD; Patricia L. Blanchette, MD, MPH; Richard J. Havlik, MD, MPH; Gilbert Wergowske, MD; Darryl Chiu; Daniel J. Foley, MS; Carolyn Murdaugh, PhD; J. David Curb, MD, MPH

**Objective.**—To determine prevalence of dementia and its subtypes in Japanese-American men and compare these findings with rates reported for populations in Japan and elsewhere.

**Design and Setting.**—The Honolulu Heart Program is a prospective population-based study of cardiovascular disease established in 1965. Prevalence estimates were computed from cases identified at the 1991 to 1993 examination. Cognitive performance was assessed using standardized methods, instruments, and diagnostic criteria.

**Participants.**—Subjects were 3734 Japanese-American men (80% of surviving cohort) aged 71 through 93 years, living in the community or in institutions.

**Main Outcome Measures.**—Age-specific, age-standardized, and cohort prevalence estimates were computed for dementia (all cause) defined by 2 sets of diagnostic criteria and 4 levels of severity. Prevalence levels for Alzheimer disease and vascular dementia were also estimated.

**Results.**—Dementia prevalence by *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised* ranged from 2.1% in men aged 71 through 74 years to 33.4% in men aged 85 through 93 years. Age-standardized prevalence was 7.6%. Prevalence estimates for the cohort were 9.3% for dementia (all cause), 5.4% for Alzheimer disease (primary or contributing), and 4.2% for vascular dementia (primary or contributing). More than 1 possible cause was found in 26% of cases. The Alzheimer disease/vascular dementia ratio was 1.5 for cases attributed primarily to Alzheimer disease or vascular dementia.

**Conclusions.**—Prevalence of Alzheimer disease in older Japanese-American men in Hawaii appears to be higher than in Japan but similar to European-ancestry populations. Prevalence of vascular dementia appears to be only slightly lower than in Japan, but higher than in European-ancestry populations. Further cross-national research with emphasis on standardized diagnostic methods is needed.

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PAST PREVALENCE surveys indicate that 4% to 11% of persons over the age of 65 years have some form of de-

menting illness.<sup>1</sup> The national economic impact of the dementing diseases is staggering; the human costs to patients and their families are devastating.

Research on differences in rates of dementia in diverse populations represents one approach to the identification of modifiable risk factors and, ultimately, to the prevention of dementing diseases. While overall dementia rates seem to be generally similar among nations, relative frequencies of the 2 major subtypes of dementia, Alzheimer disease (AD) and vascular dementia (VsD), vary. Alzheimer disease is the major subtype in most Western nations. In contrast, VsD has usually been reported to be the domi-

nant subtype in Japan and possibly in other Asian nations.<sup>1,2</sup> However, because case finding and classification methods have not been well standardized, these reported differences may reflect methodologic differences. Alternatively, true genetic, constitutional, social and/or environmental differences among people from distinct cultures may account for these disparate rates.

For editorial comment see p 993.

The Honolulu-Asia Aging Study (HAAS) is a member of an informal consortium of epidemiologic studies on dementia in the United States, Japan, and Taiwan that were designed collaboratively with special attention to the use of standardized methods, instruments, and diagnostic criteria.<sup>2</sup> The HAAS is conducted in cooperation with the Honolulu Heart Program (HHP), an established, longitudinal, long-term study of heart disease and stroke in Japanese-American men. In this article, we present age-specific and age-standardized prevalence estimates for total dementia, AD, and VsD in the HHP cohort.

### METHODS

The HHP is a longitudinal study of heart disease and stroke in Japanese-American men born 1900 through 1919 and living on Oahu when the study began in 1965. The World War II Selective Service Registration file was used to identify 12 417 possibly eligible men and 8006 participated in the first examination. Eighty-eight percent of the men were born in Hawaii, 12% in Japan. Continuous surveillance for mortality and hospitalizations has been carried out since the study's inception.<sup>3</sup> Research on dementia began at the fourth examination of the cohort in 1991 with the establishment of the HAAS.

A total of 4678 surviving men were

From the National Institute on Aging (Drs White and Havlik and Mr Foley), National Institute for Nursing Research (Dr Murdaugh), National Institutes of Health, Bethesda, Md; Honolulu-Asia Aging Study, Kuakini Medical Center, Honolulu, Hawaii (Drs Petrovitch, Masaki, Rodriguez, and Curb and Mr Chiu); Department of Veterans Affairs, Honolulu (Dr Ross); Department of Medicine, University of Hawaii, John A. Burns School of Medicine, Honolulu (Drs Petrovitch, Ross, Masaki, Rodriguez, Blanchette, Wergowske, and Curb); Division of Biostatistics, University of Virginia, Charlottesville (Dr Abbott); and University of Southern California, Los Angeles (Dr Teng).

Reprints: Lon White, MD, Honolulu Heart Program, Honolulu-Asia Aging Study, 347 N Kuakini St, Honolulu, HI 96817.

eligible to participate in the fourth examination. All but 5 were found and invited to participate. Of 3741 men who were seen at the fourth examination, 3734 participated in phase 1 of the dementia case-finding effort. Ages ranged from 71 through 93 years (average, 78 years). Average years of education were 10.5. Thirteen percent had fewer than 8 years, and 45% had completed 12 or more years of education.

Interviews and testing were conducted in the participant's preferred language, English or Japanese. Subjects were fully informed regarding study participation and signed informed consent forms.

### Dementia Case-Finding Methods

Dementia case-finding occurred in 3 phases (Figure 1). A total of 3734 participants (80% of the eligible cohort) were administered the Cognitive Abilities Screening Instrument (CASI) at phase 1. Eighty-five percent were seen at the clinic, 13% at home, and 2% in nursing homes. The CASI has been validated as a screening instrument for dementia in the United States and Japan, in both English and Japanese languages.<sup>4</sup> Designed for use in comparative cross-national studies of dementia in the United States and Japan, it is a composite of the Hasegawa Dementia Screening Scale (widely used in epidemiologic studies in Japan),<sup>5</sup> the Folstein Mini-Mental State Examination,<sup>6</sup> and the Modified Mini-Mental State Test.<sup>7</sup> The CASI includes tasks assessing attention, concentration, orientation, short- and long-term memory, language ability, visual construction, word list generation, abstraction, and judgment. The score range is 0 to 100.

Phase 1 CASI score was used to stratify the cohort into low scorers (CASI <74), intermediate scorers (CASI = 74-81.9), and high scorers (CASI ≥ 82). All low scorers and men aged 85 years or older were invited back for the phase 2 examination. Participants were sampled from intermediate- and high-scoring groups by a probability sampling system. Of 1063 subjects invited to return, 948 (89%) completed phase 2. Most were examined within 12 weeks of their phase 1 appointment.

The phase 2 examination included a second CASI, neurologic examination, and testing of the participant's hearing and vision. Examiners were shielded from information obtained at phase 1. An informant (usually the wife) was given a standardized interview that included the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), to assess changes in cognitive function and behavior over the prior 10 years. An IQCODE score of 3.6 or higher is a strong indicator of dementia.<sup>8,9</sup>

Participants invited for phase 3 assessment included individuals with persistently low CASI scores (better of 2 scores <75) or IQCODE score greater than 3.6, plus a probability sample of remaining participants. Of the 507 subjects selected, 426 (84%) received the full phase 3 dementia evaluation.

Phase 3 examination included a standardized interview and neurologic examination by a neurologist with advanced training in behavioral neurology and dementia research, as well as the neuropsychological test battery from the Consortium to Establish a Registry for Alzheimer's Disease (CERAD).<sup>10,11</sup> The neurologist obtained a structured history from the informant based on CERAD clinical evaluation protocol.<sup>10</sup> Phase 3 examiners were shielded from information obtained at phases 1 and 2.

Those participants judged by the study neurologist to meet *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*<sup>12</sup> (*DSM-III-R*) criteria for dementia had brain computed tomographic (CT) scans and blood tests (complete blood cell count, chemistry profile, vitamin B<sub>12</sub> level, folate level, rapid plasma reagin, and thyroid function tests).

### Diagnostic Methods and Criteria

Dementia was defined using 2 independent sets of diagnostic criteria: those of Cummings and Benson<sup>13</sup> and the *DSM-III-R*.<sup>12</sup> The Cummings and Benson criteria define dementia as acquired impairment in at least 3 of 5 neuropsychological domains (memory, speech/language, visuospatial function, higher cognition, and mood/personality). Impairment in a specific domain was a clinical decision based on the neurologist's evaluation and neuropsychological test scores. The *DSM-III-R* criteria require impairment in both long- and short-term memory and 1 other domain, with the additional requirement that the impairment be severe enough to interfere with social or occupational functioning. Semistructured guidelines were used to define functional impairment that required: (a) an informant's assessment of social/occupational expectations and capabilities of the participant prior to and after the onset of cognitive decline and (b) the decline in functioning be related to cognitive impairment and not physical disability.

Final diagnosis and clinical dementia rating (CDR)<sup>14</sup> index were assigned by a panel consisting of the study neurologist and at least 2 other physicians with expertise in geriatric medicine and dementia. The panel was provided with all information accrued at phase 3, including CT scans, laboratory results, and the neurologist's diagnostic impression.

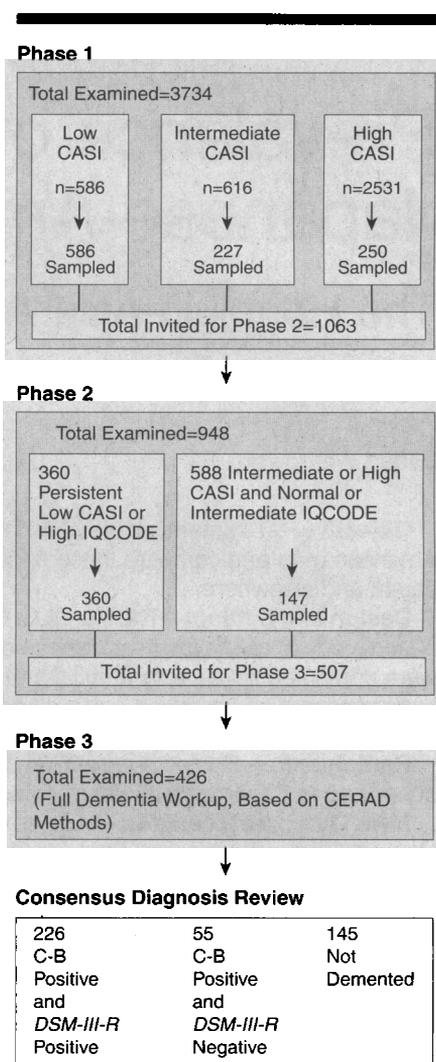


Figure 1.—Outline of study design. CASI indicates Cognitive Abilities Screening Instrument; IQCODE, Informant Questionnaire on Cognitive Decline; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; *DSM-III-R* positive, meeting criteria for dementia of the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*; *DSM-III-R* negative, not meeting criteria for dementia of the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*; and C-B positive, meeting Cummings and Benson criteria for dementia.

The panel was shielded from information gathered during phases 1 and 2. For those participants meeting *DSM-III-R* criteria for dementia, diagnostic subtypes were also determined. Alzheimer disease was diagnosed according to the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA).<sup>15</sup> Criteria for VsD were based on those proposed by the California Alzheimer's Disease Diagnostic and Treatment Centers (AD-DTC).<sup>16</sup> Dementia due to a degenerative parkinsonian disorder was diag-

Table 1.—Estimated Age-Specific and Age-Standardized Prevalence for Dementia (All Cause), Alzheimer Disease, and Vascular Dementia\*

	Age Group, y				Overall (426/3734)	Age-Standardized‡ ≥65 y
	71-74 (34/1084)†	75-79 (122/1528)	80-84 (107/705)	85-93 (163/417)		
<b>Dementia (All Cause) by Diagnostic Criteria</b>						
Cummings-Benson %	3.0	9.2	17.2	46.2	13.0	10.3
95% CI	0.0-19.7	4.5-16.6	10.2-26.4	38.1-54.6	9.8-16.8	7.4-13.7
Cases identified at phase 3 evaluation	18	66	74	123	281	...
<b>DSM-III-R</b>						
%	2.1	6.2	12.9	33.4	9.3	7.6
95% CI	0.0-15.4	2.3-12.6	6.6-21.0	25.9-41.6	6.5-12.6	5.1-10.8
Cases identified at phase 3 evaluation	17	51	60	98	226	...
<b>DSM-III-R Positive Dementia by Cause</b>						
<b>Alzheimer disease§</b>						
%	0.9	3.7	7.0	20.6	5.4	4.7
95% CI	0.0-15.4	0.9-9.4	2.6-14.3	14.3-28.0	3.4-8.3	2.8-7.5
Cases identified at phase 3 evaluation	8	25	28	61	122	...
<b>Vascular dementia  </b>						
%	1.1	2.3	6.4	15.9	4.2	3.8
95% CI	0.0-15.4	0.1-7.1	2.0-13.1	10.1-22.5	2.3-6.6	2.1-6.4
Cases identified at phase 3 evaluation	8	25	35	47	115	...

\*CI indicates confidence interval; and *DSM-III-R*, *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*.<sup>12</sup>

†Participants at phase 3/participants at phase 1.

‡Standardized to the 1990 US population age distribution.

§Includes all cases with Alzheimer disease as the sole or contributory cause.

||Includes all cases with vascular dementia as the sole or contributory cause.

nosed if the subject had a clearly defined parkinsonian syndrome (any 2 of rest tremor, bradykinesia, rigidity, or postural instability) not related to medication or cerebrovascular disease, that preceded or occurred simultaneously with onset of cognitive impairment. No separate category of cortical Lewy body disease was made because of the difficulty in making this diagnosis without benefit of autopsy findings.

Mixed dementia involving AD was defined as possible AD (NINCDS-ADRDA criteria) with a second disorder sufficient to cause dementia.<sup>15</sup> Mixed dementia involving VsD was defined according to ADDTC criteria.<sup>16</sup> Other mixed cases were defined using the best clinical judgment of the consensus panel. An effort was made to designate the condition that was primary (most important).

### Statistical Methods

Prevalence estimate computations used standard methods for a 2-stage stratified probability sampling strategy.<sup>17</sup> At the first stage, a stratified random sample of men who had participated in phase 1 were invited to return for the phase 2 examination (Figure 1). A second stratified random sample of men who participated in phase 2 were invited to return for the phase 3 examination (Figure 1). Preliminary prevalence estimates for each phase 2 sampling stratum were computed using data from subjects seen at phase 3. Estimates were then computed for the full cohort of phase 1 participants. Ninety-five per-

cent confidence limits for the final prevalence estimates were derived from exact methods for a binomial parameter.<sup>18</sup> Logistic regression models were also fit to the estimated prevalence rates across age groups using the method of maximum likelihood.<sup>19</sup> Age-specific prevalence rates derived from these models were applied to the United States population age structure for men only and for both sexes combined (all ethnicities) age 65 years and older based on the 1990 census.

### RESULTS

As illustrated in Figure 1, 3734 men received an evaluation of cognitive functioning at the phase 1 examination, 948 participated in the phase 2 examination, and 426 received a full dementia evaluation at phase 3. Subjects who declined to return for phase 2 or 3 examination tended to be somewhat older and had slightly poorer CASI scores than those who did participate. We requested supplementary information about these men from their personal physicians. Responses were received from 120 of 149 physicians queried. Eighty-four physicians stated that their patient was not demented, 19 stated that the patient was demented, and 17 were uncertain. These data indicate that dementia was probably more prevalent among nonresponders compared with fully participating cohort members. Thus, prevalence estimates given below may slightly underestimate true prevalence levels in the full study population.

We identified 281 men who met Cum-

mings and Benson criteria for dementia; 55 of these failed to meet *DSM-III-R* criteria. All 226 men who met *DSM-III-R* criteria also met Cummings and Benson criteria. Twelve participants could not be evaluated because of severe aphasia or were judged to be severely impaired consequent to a single catastrophic event such as brainstem stroke. These individuals were not included as dementia cases.

Age-specific prevalence estimates for dementia defined by *DSM-III-R* and Cummings and Benson diagnostic criteria are presented in Table 1. Consistent with prior dementia surveys, change in prevalence estimates with age had an exponential appearance. For dementia defined using *DSM-III-R* criteria, prevalence increased from 2.1% at aged 71 through 74 years to 33.4% in participants older than 85 years. Overall prevalence in the study cohort was 9.3% and 13% for *DSM-III-R* and Cummings and Benson criteria respectively.

Participant ages ranged from 71 to 93 years (average, 78 years). Most other surveys have been conducted in populations aged 65 years and older. Logistic curves, extended from age 65 years, were fit to available data for participating cohort members to generate comparable prevalence estimates for Japanese-American men in Hawaii (Figure 2). Application of these curves to the United States population aged 65 years and older (1990 census) yielded age-standardized dementia prevalence estimates of 7.6% (*DSM-III-R* criteria) and 10.3% (Cummings and Benson criteria) (Table

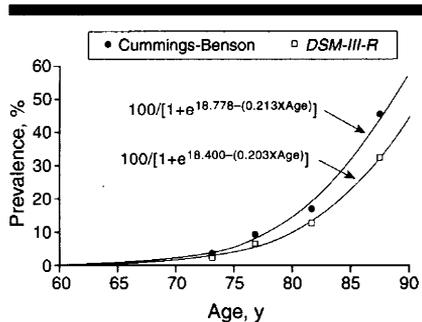


Figure 2.—Estimated age-specific prevalence curves for Japanese-American men in Hawaii aged 60 to 93 years. Dementia defined respectively by Cummings-Benson and *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R)* criteria. The upper and lower logistic equations were used to model the percent prevalence of dementia according to the Cummings-Benson and *DSM-III-R* criteria, respectively.

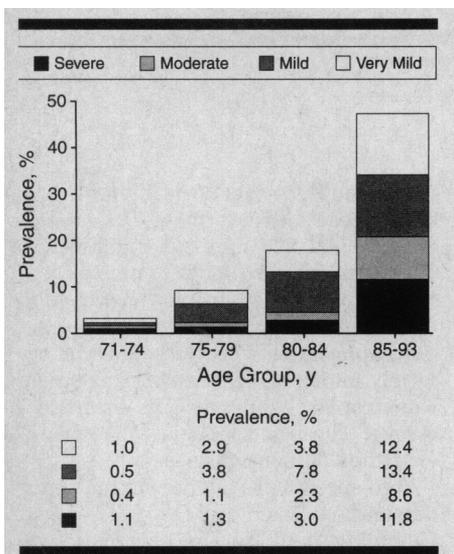


Figure 3.—Age-specific prevalence of dementia by severity among men aged 71 to 93 years old. Rates are estimated from 281 cases meeting Cummings-Benson criteria. Very mild is equivalent to a clinical dementia rating (CDR) index of 0.5; mild, CDR index of 1.0; moderate, CDR index of 2.0; and severe, CDR index of 3.0 or greater.

1). When the reference population included only males the standardized prevalence estimates fell to 6.1% and 8.3%, respectively, reflecting the lesser numbers of men in the oldest age strata of the general population.

To compare our results with those of other surveys in which prevalence values were reported according to dementia severity, we estimated age-specific prevalence at 4 levels of severity (defined by CDR index) using all the 281 cases identified by application of Cummings and Benson diagnostic criteria. The subset of very mild (CDR index=0.5) cases is represented by the top segment of each bar of Figure 3. This subset corresponds nearly perfectly with dementia cases who met Cummings and Benson

Table 2.—Specific Diagnosis Classification for 226 Cases of Dementia Meeting *DSM-III-R* Criteria\*

Classification	No.
Probable Alzheimer disease	69
Possible Alzheimer disease (atypical course)	8
Probable vascular dementia	49
Possible vascular dementia	19
Mixed dementia: possible Alzheimer disease primary cause with	41
Vascular dementia	22
Vascular dementia + other†	8
Vitamin B <sub>12</sub> deficiency	8
Subdural hematoma	1
Depression	1
Chronic alcohol use	1
Mixed dementia: probable vascular dementia primary cause with	7
Alzheimer disease	3
Vitamin B <sub>12</sub> deficiency	1
Vitamin B <sub>12</sub> deficiency plus Parkinson disease	1
Subdural hematoma	1
Neurosyphilis	1
Mixed dementia: possible vascular dementia primary cause with	5
Alzheimer disease	1
Vitamin B <sub>12</sub> deficiency	2
Parkinson disease	1
Progressive supranuclear palsy	1
Other dementia	22
Parkinson disease	7
Parkinson disease + other‡	5
Progressive supranuclear palsy	4
Progressive supranuclear palsy + vascular dementia	1
Subdural hematoma	2
Trauma	2
Vitamin B <sub>12</sub> deficiency	1
Dementia cause undetermined	6

\**DSM-III-R* indicates *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*.<sup>12</sup>

†Subdural hematoma (n=2), vitamin B<sub>12</sub> deficiency (n=2), folate deficiency (n=1), depression plus Parkinson disease (n=1), chronic alcohol use (n=2).

‡Vascular dementia (n=3), vascular dementia plus subdural hematoma (n=1), chronic alcohol use (n=1).

criteria but failed to meet *DSM-III-R* criteria. Prevalence estimates that included mild, moderate, and more severe cases (CDR index  $\geq 1$ ) closely approximated estimates based on dementia cases defined by *DSM-III-R* diagnostic criteria. Approximately half of the *DSM-III-R* positive cases of dementia had CDR indexes of 1 (mild dementia).

Specific diagnoses for the 226 cases of dementia meeting *DSM-III-R* criteria are shown in Table 2. Alzheimer disease was identified as sole cause of dementia (ie, all probable AD plus possible AD without other contributing cause) in 77 cases (34%). Among mixed cases, AD was the primary cause in 41 cases and the secondary cause in 4 cases. Overall, AD was identified in 122 (54%) of the 226 dementia cases.

Cerebrovascular disease was the only apparent cause for dementia in 68 cases (30%). Among mixed cases, VsD was the primary cause in 12 cases, and the secondary cause in 35 cases. Overall, VsD was present in 115 cases (51%).

ADDC criteria specify that mixed dementia cases may be classified as either probable or possible VsD. Of the 226 dementia cases, 66 met the ADDTC

criteria for probable VsD while another 49 met criteria for possible VsD. Focal signs supporting prior stroke were noted for 67% of probable and possible cases. History of sudden onset or stepwise progression of cognitive problems was obtained for 49% of probable cases and 25% of possible cases. The CT scans showed multiple strokes for 64 (97%) of probable cases; the other 2 cases showed evidence of a single stroke judged to be of a size and location sufficient to explain the dementia. The most common strokes noted in the probable VsD group were lacunes in basal ganglia, thalamus, or frontal white matter. The CT scan and clinical picture were evidence for a diagnosis of Binswanger disease (as a type of VsD) for 1 person with probable VsD (who also had multiple strokes) and for 6 others with possible VsD.

Figure 4 shows age-specific prevalence estimates for VsD in the study cohort. The solid component and lowest cross-hatched component of the bars together represent cases meeting ADDTC criteria for probable or possible VsD with no other apparent cause. The top 2 components represent VsD with concurrent AD or some other disease possibly contributing to the dementia. The component for concurrent AD and cerebrovascular disease represents exactly the same cases as in the corresponding bar components of Figure 5. The cohort prevalence for VsD either alone or in conjunction with another possible cause (such as AD or Parkinson disease) was 4.2%.

Figure 5 shows age-specific prevalence estimates for probable or possible AD. Overall prevalence of probable or possible AD in the cohort (including cases in which AD was designated a contributing cause) was 5.4%.

Prevalence estimates for AD and VsD are summarized in the lower half of Table 1. There is substantial overlap between AD and VsD because individuals with both processes are counted in both categories. As shown, age-standardized prevalence estimates were 4.7% for AD and 3.8% for VsD. When the reference population was defined to include only men, estimates fell to 3.7% for AD and 2.9% for VsD.

## COMMENT

Variations in the observed prevalence of dementia across populations may reflect differences in age, sex, education, and ethnicity composition. Our study cohort consists of Japanese-American men aged 71 through 93 years. Since the decision to exclude women from the HHP cohort was made more than 30 years ago, we are able to provide estimates only for men. Several but not all surveys have reported a slightly higher de-

mentia prevalence in women.<sup>20,24</sup> The distribution of education in the HHP cohort is roughly similar to that of other older American populations, with an average of 10.5 years of schooling completed. As in other populations, the oldest participants reported fewer years of schooling completed.<sup>25-27</sup>

Participants chosen to receive dementia evaluations were identified using stratified random sampling methods. This allowed estimation of the number of cases in all strata. Previous surveys that have used an initial screening step with less than 100% sensitivity and have not sampled subjects who scored above the cut-point are likely to have underestimated the true prevalence of dementia. The magnitude of underestimation can be substantial, as noted in a survey conducted in Stockholm, Sweden. When adjustment was made for cases missed because of false-negative screening test scores, prevalence among men aged 75 through 84 years doubled.<sup>23</sup>

In our study, approximately 80% of dementia cases identified with Cummings and Benson criteria also met *DSM-III-R* criteria. Those who did not were nearly all very mildly demented (CDR index=0.5). The definition of dementia used in the East Boston Study appears to approximate that achieved with Cummings and Benson criteria.<sup>28</sup> Using Cummings and Benson criteria, our age-standardized prevalence estimate for dementia (10.3%) is still below the prevalence of dementia (approximately 12.2%) attributable to all causes among noninstitutionalized residents of East Boston.<sup>28,29</sup> Using *DSM-III-R* dementia criteria, our age-standardized prevalence estimate is close to recent estimates from Stockholm<sup>23,30</sup> and Japan.<sup>21,31-33</sup>

Variability in prevalence estimates among studies may also be related to different severity thresholds used in the definition of a case. In the Framingham Dementia Study the reported prevalence of 3% among men was based on moderate to severely demented subjects, ie, with CDR indexes greater than 1.<sup>20</sup> Our age-standardized prevalence estimate for men (referenced to American males aged 65 years or older) is 6.1%. When only cases of moderate or greater severity (CDR index >1) are included (as in the Framingham study), our prevalence levels are lowered by about half at every age. Thus, once differences in population age distributions and severity criteria are taken into account, prevalence rates are similar in the 2 cohorts.

In contrast to most previous reports, we found a rather high proportion (26%) of cases having more than a single contributing cause. Of these, over half were classified as mixed AD and VsD. High

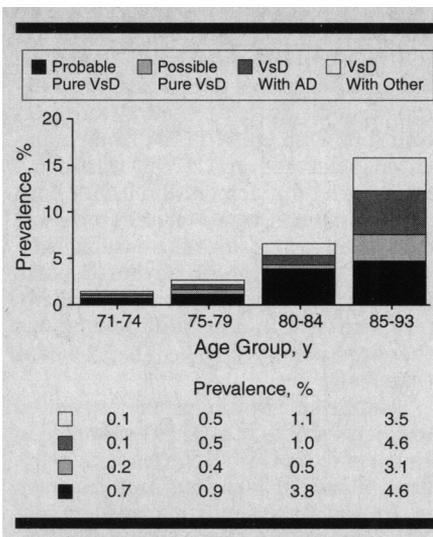


Figure 4.—Age-specific prevalence of vascular dementia (VsD) among men aged 71 to 93 years. Rates are estimated from 226 cases meeting *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised* criteria for dementia. Pure VsD defined by California Alzheimer's Disease Diagnostic and Treatment Centers criteria. In addition to meeting criteria for probable or possible VsD, cases defined as pure VsD required the absence of other systemic disorders that could account for the dementia. Mixed cases include probable or possible VsD with Alzheimer disease (AD) and other dementias.

proportions (12% and 13%) of mixed AD and VsD have recently been reported from community surveys conducted in the United States and Canada.<sup>20,22</sup> Others have reported lower proportions of mixed dementia; from 0% to 7%.<sup>21,23,28</sup> Because both AD and VsD become increasingly more prevalent with aging, the chance of having both is likely to be much greater in older populations. This may partially explain the high proportion of mixed cases in our study and in the Canadian study where subjects were over age 71 years and 85 years, respectively. In a study of 85-year-olds in Sweden, 69 of 118 demented subjects were thought to have VsD, including 12 of mixed cause.<sup>30</sup> A second factor that might contribute to the high rates of mixed AD/VsD in the present study is an enhanced recognition of cerebrovascular disease as a result of routine use of CT scans for diagnostic classification. A lack of neuroimaging data may have contributed to underrecognition of mixed AD and VsD in the Stockholm and East Boston studies.<sup>23,28</sup>

Ratios of prevalence of AD to prevalence of VsD are useful as a means for identifying differences across populations. In a majority of reports from the United States and Europe, the AD/VsD ratio has been in the range of 2 or greater. In contrast, lower AD/VsD ratios (usually <1) have been reported in many surveys conducted in Japan during the past 2 decades.<sup>21,34-36</sup> We found

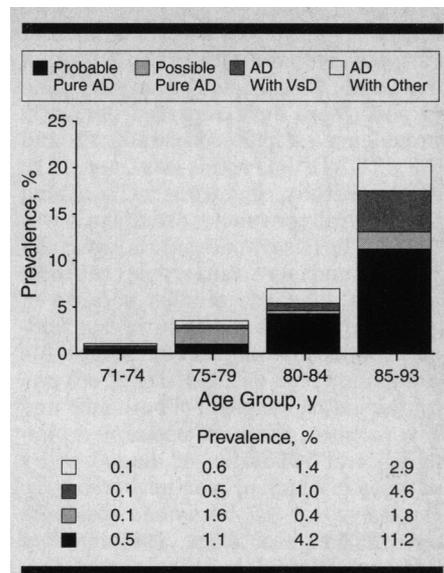


Figure 5.—Age-specific prevalence of Alzheimer disease (AD) among men aged 71 to 93 years. Rates are estimated from 226 cases meeting *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised* (DSM-III-R) criteria for dementia. Probable and possible AD defined by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer Disease and Related Disorders Association criteria. Possible AD subdivided into pure cases and mixed cases including vascular dementia (VsD) and other dementias.

118 men whose dementia was attributed solely or primarily to AD, and 80 whose dementia was attributed solely or primarily to VsD. In this group of cases, the AD/VsD ratio was 1.5, intermediate between most prior American and Japanese reports.

Age-specific and age-standardized prevalence values for AD in the HAAS population are quite close to estimates reported from several other surveys in North America and Europe.<sup>1,23,36,37</sup> Reported prevalence of AD in East Boston is more than double the AD prevalence in Hawaii and in most other surveys.<sup>28</sup> The lower prevalence of AD in Framingham reflects the stringent severity criteria used to define cases in that study; when the reported prevalence in Framingham is compared with Honolulu prevalence estimates based on AD cases of at least moderate severity (CDR index >1), rates are similar.

In contrast, estimated prevalence of VsD in Honolulu is substantially higher than in Framingham and other populations in North America and Europe.<sup>1,20,23,37</sup> Although prevalence of VsD was not specified in the East Boston Dementia Study, a possible vascular cause was noted in only about 5% of persons with moderate or severe dementia, much lower than found in Honolulu.<sup>28</sup>

Although data from fully comparable studies in Japan are not yet available, there is no lack of published prevalence

reports from Japan using methods of variable comparability to those used in our study. Most Japanese surveys done in past years have reported dementia prevalence estimates between 4% and 6% with AD/VsD ratios less than 1.<sup>34</sup> In a recent study conducted in Hisayama City, overall prevalence of dementia was 6.7%.<sup>21</sup> The Hisayama study is especially relevant and more comparable than most previous Japanese studies because of the thoroughness of dementia case finding, conduct of the survey in a stable community, use of *DSM-III-R* criteria for dementia, inclusion of both mild and severe cases, frequent use of neuroimaging, and validation of diagnoses by autopsy in a high proportion of cases. In the survey of 887 Hisayama residents aged 65 years or older, prevalence of AD was 1.5%, and the prevalence of clinically diagnosed VsD was 3.2% (overall AD/VsD ratio, 0.47). While diagnoses during life were based on clinical find-

ings, including a low Hachinski score, the relative infrequency of AD as a cause of dementia in this population was neuropathologically confirmed. A more recent follow-up study in the same population generated an AD/VsD ratio of 0.4 for men, 1.2 for women, and 0.8 for both sexes combined, based on new (incident) cases developing since the baseline survey.<sup>25</sup> Together, the 2 Hisayama reports strongly support the veracity of many prior surveys in Japanese populations that have found AD to be less prevalent than VsD.

Despite substantial problems related to comparability of studies conducted in Japan and the United States, it appears likely that older Japanese-American men in Hawaii experience a prevalence of AD approaching that of European-ancestry Americans and a prevalence of VsD only slightly below that observed in Japan. These observations lead us to speculate that environmental or cultural

exposures associated with migration from Japan to Hawaii may have influenced the development of AD in HAAS cohort members, while factors involved in the pathogenesis of VsD have remained relatively unaffected. These speculations underscore the need for further well-standardized studies specifically intended to allow comparisons of rates and risk factors for dementia in these diverse populations.

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