Prevalence of Alzheimer's Disease in a Community Population of Older Persons

Higher Than Previously Reported

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Clinically diagnosed Alzheimer's disease and other dementing illnesses were assessed in a geographically defined US community. Of 3623 persons (80.8% of all community residents over 65 years of age) who had brief memory testing in their homes, a stratified sample of 467 persons underwent neurological, neuropsychological, and laboratory examination. Prevalence rates of Alzheimer's disease were calculated for the community population from the sample undergoing clinical evaluation. Of those over the age of 65 years, an estimated 10.3% (95% confidence limits, 8.1% and 12.5%) had probable Alzheimer's disease. This prevalence rate was strongly associated with age. Of those 65 to 74 years old, 3.0% (95% confidence limits, 0.8 and 5.2) had probable Alzheimer's disease, compared with 18.7% (95% confidence limits, 13.2 and 24.2) of those 75 to 84 years old and 47.2% (95% confidence limits, 37.0 and 63.2) of those over 85 years. Other dementing conditions were uncommon. Of community residents with moderate or severe cognitive impairment, 84.1% had clinically diagnosed Alzheimer's disease as the only probable diagnosis. These data suggest that clinically diagnosed Alzheimer's disease is a common condition and that its public health impact will continue to increase with increasing longevity of the population.

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MOST studies of Alzheimer's disease have been conducted among outpatients referred for evaluation or among persons admitted to tertiary-care medical centers, chronic-care institutions, or psychiatric hospitals. The findings of such studies can be influenced by selection factors such as recognition of the problem by someone close to the individual, access to medical care, severity of impairment, presence of atypical clinical features, and the clinical interests of the institution. Thus, studies of institutional groups may not reflect occurrence of this disease in the general population.

For editorial comment see p 2591.

We sampled individuals for detailed neurological, neuropsychological, and laboratory evaluation for dementing illness from residents 65 years of age and older of a defined community. These data permit us to address three issues as follows: the conditions responsible for cognitive impairment in this community population, the overall prevalence of clinically diagnosed Alzheimer's disease in the age group over 65 years in this community, and the relation of age to the prevalence of Alzheimer's disease within this group.

METHODS

The study employed a two-stage design (Fig 1). In the first stage, a brief performance test of cognitive function was administered to all participating residents over the age of 65 years in a defined community. Persons were sampled from all levels of performance on this brief test to undergo clinical evaluation for dementing illness. The results of the clinical evaluation could then be referred back to the community population. The brief screening test was used only for sampling and not to determine disease status.

The Study Community and Population Survey

The study was conducted in East Boston, Mass, a geographically defined, urban, working-class community of approximately 32 000 persons. East Boston is one of four centers of the US National Institute on Aging Established Populations for Epidemiologic Studies of the Elderly project.[1] The study was done with the support of the East Boston Neighborhood Health Center, the major source of primary medical care within the community. Beginning in January 1982, a community census was performed. All dwelling units were visited by interviewers to ascertain the

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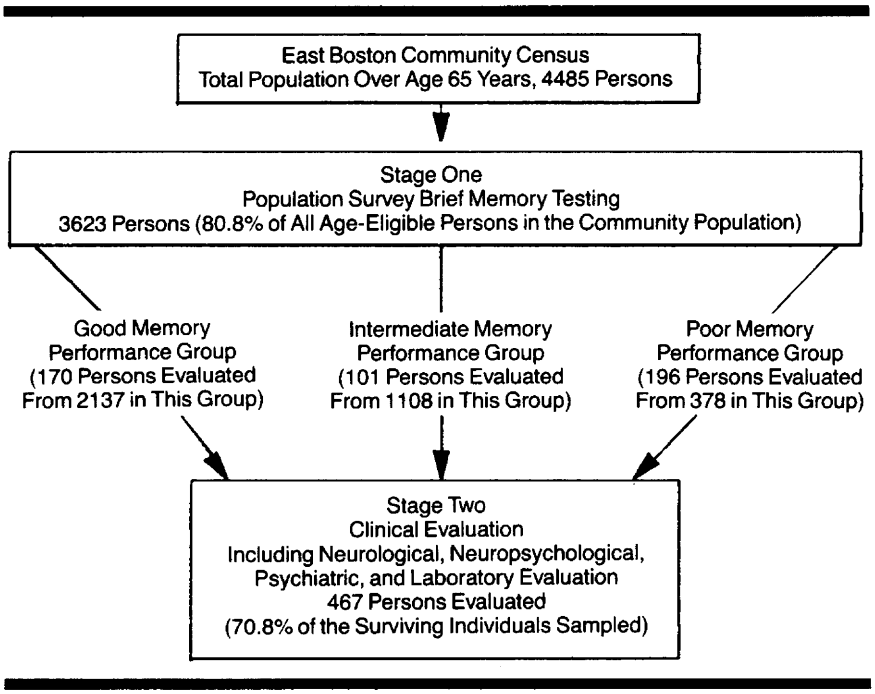

Fig 1.—Outline of design of this study of clinically diagnosed Alzheimer's disease in a community population of persons 65 years of age and older.

identity, sex, and age of each resident. All noninstitutionalized individuals aged 65 years or older were invited to participate in the study by responding to a structured questionnaire administered in their homes by trained interviewers. Because some community residents usually spoke Italian, a version of the questionnaire in this language was used for 323 individuals.

The questionnaire included a broad range of items concerning medical and social problems of older persons as well as brief performance tests of selected areas of cognitive function,[2] including immediate and delayed memory. Memory was tested by having the interviewer read to the participant a brief story composed of three short sentences, each of which contained two ideas. The participant was asked to retell the story immediately after its presentation. The response was scored by recording the number of specified ideas recalled. The maximum score was 6. Those recalling four or fewer ideas on immediate memory testing had delayed memory tested by asking them to recall the story again following a distracting task of approximately 2-minutes duration.

Virtually all (99.8%) households in the study community were censused. Of 4485 age-eligible residents, 3811 (85.0%) participated in the population survey. Of these participants, 3623 had memory testing (80.8% of the age-eligible residents of the community), while 188 persons did not receive memory testing and were not included in this study, either because they participated through proxy respondents (117 persons) or declined to respond to the memory test items (71 persons).

Sampling for Clinical Evaluation

The sampling plan is outlined in Fig 1. Sampling was designed both to allow the results from the sample undergoing clinical evaluation to be referred to the community population and to generate cohorts of affected and unaffected individuals for further study. Each population survey participant was placed in one of three groups according to performance on the brief test of memory. Individuals were then selected for clinical evaluation from all three levels of performance. The good memory performance group was composed of those having zero to two errors on immediate memory testing. The poor performance group was composed of those with four or more errors on immediate memory testing and six errors (of six possible) on delayed memory testing. The intermediate performance group was composed of those with memory test results between those of good and poor performance groups. Individuals were selected randomly from the poor and intermediate performance groups, with much heavier sampling from the poor performance group. As expected, the good performance group was the major source of unaffected persons and the poor performance group was the major source of affected individuals. Since simple random selection from the good performance group would have led to a young sample and greatly decreased the efficiency of comparisons between affected and unaffected persons, we instead sampled the good performance group on age and gender to ensure comparability between affected and unaffected individuals.

Of 3623 persons receiving brief memory testing at the population survey, 2137 were in the good, 1108 in the intermediate, and 378 in the poor performance group. Of 714 persons sampled for clinical evaluation, 54 died prior to being invited to undergo evaluation; 467 (70.8% of the surviving eligible individuals) were evaluated; and 193 declined evaluation. Of the 467 persons undergoing clinical evaluation, 170 were from the good, 101 from the intermediate, and 196 from the poor performance group. The average interval between the date of the population survey interview and the clinical evaluation was 16.3 months.

Content of the Clinical Evaluation

The clinical evaluation included neuropsychological testing, neurological examination, brief psychiatric evaluation, laboratory evaluation, brief review of the medical history, and interview of another informant for each participant. All prescription and over-the-counter medications used during the previous 2 weeks were inspected and identified. Each clinical evaluation required, on average, approximately 2½ hours. Structured instruments were used, and examiners were blinded to the subjects' performance on the population survey cognitive testing.

A major purpose of the neurological examination component was to diagnose conditions other than Alzheimer's disease that might result in cognitive impairment, such as strokes, Parkinson's disease, and hydrocephalus. It was performed by one of three senior neurologists (H.H.F. and two others). It was similar to a comprehensive neurological examination in clinical practice and also included alternate and sequenced hand positions, finger-tapping speed, and a brief assessment of language and praxis. The examination was highly structured, with defined scoring criteria.

The neurologist also conducted the brief psychiatric evaluation. Its major purpose was to recognize the presence of psychiatric disorders that might produce cognitive impairment in older persons, especially depression and major thought disorders. The depression section of the Schedule for Affective Disor-

ders and Schizophrenia—Lifetime Version[3] was used to elicit information concerning both major and minor depressive symptoms. In addition, the Brief Psychiatric Rating Scale of Overall and Gorham[4] was completed by the examiner.

The neuropsychological test battery, administered by a trained technician, tested several functional areas. Tests of memory included a delayed recognition memory span test[5] that required the participant to recall the spatial arrangement of an increasing series of disks on a checkerboard surface and had a maximum score of 17, a matching form of the Benton Visual Retention Test[6] with a maximum score of 6, and a short-story recall test identical to that used in the population survey with a maximum score of 6. Other areas of cognitive function tested included confrontation naming, visuospatial ability, abstraction, and set maintenance. The test of confrontation naming consisted of 15 line drawings of objects taken from the Boston Naming Test.[7] Tests of visuospatial ability included copying geometric figures and a task requiring matching of simple geometric figures, with a maximum score of 11. Abstraction was assessed by the ability to identify similarities and differences among sets of geometric figures.[8] The test of set maintenance required the participant to copy a sawtooth design of alternating triangles and squares,[8] and then continue the alternating pattern across the page, having a maximum score of 8. Attention was formally assessed by an auditory continuous performance task in which the participant was asked to listen to a recorded series of letters and to identify every instance of the letter "*A*" being spoken.[9]

Laboratory tests included a serological test for syphilis and serum concentrations of vitamin B_{12}, folic acid, and thyroxine. In addition, a white blood cell count and differential; hemoglobin; serum concentrations of glucose, sodium, potassium, total protein, albumin, bilirubin, creatinine, calcium, and phosphorus; and an electrocardiogram were included to help detect major nonneurological illnesses that might influence cognitive function.

Classification of Participants

We used diagnostic criteria for Alzheimer's disease consistent with the criteria for the clinical diagnosis of probable Alzheimer's disease developed by the joint Work Group of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association[10] as well as those for primary degenerative dementia in the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition*, of the American Psychiatric Association.[11] One adaptation of *Diagnostic and Statistical Manual of Mental Disorders, Third Edition* criteria was required for this study. These criteria require that there be "a loss of intellectual abilities sufficient to interfere with social or occupational functioning."[10] This criterion may be applied in the typical medical setting in which individuals are brought to attention by family or care givers, usually because such an impairment of social function has been noted. It is difficult to apply this criterion in a uniform, meaningful way in a community study, such as the present one, in which we actively identified cases. In the community, participants differ both with regard to the availability of family or friends and the sensitivity of these persons to manifestations of disease. Therefore, we used objective tests to assess cognition and addressed this concept by establishing the presence of cognitive impairment of substantial magnitude so that interference with these functions would be expected.

The National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria for probable Alzheimer's disease require dementia confirmed by neuropsychological testing with deficits in two or more areas of cognition. In this study, we implemented these requirements by requiring for this diagnosis evidence of memory impairment with a score of 2 or less on the delayed memory test or a score of 7 or less on the delayed recognition memory span test or a decrement of two or more between immediate and delayed memory. In addition evidence was required of impairment in at least one of three other areas of cognitive function as follows: language, spatial ability, or abstraction with a score of 10 or less on naming, 5 or less on figure copying, or 6 or less on visual abstraction. Further, the diagnosis of probable Alzheimer's disease required absence of a history of abrupt onset of symptoms from the informant and clear state of consciousness judged by the neurologist and psychological test technician on the ability to maintain focus. Finally, in applying these criteria, the neurologist and neuropsychologist considered factors that might limit performance, including visual and hearing deficits.

Although, each participant was classified by both the examining neurologist and, independently, by a neuropsychologist (M.S.A.) who used only recorded data, we have used the neurologist's opinion in this article both for conciseness and because this examiner actually conducted the evaluation. The Pearson correlation coefficient between the neurologist and neuropsychologist diagnoses was .70 ($P<.0001$).

Since many diseases other than Alzheimer's disease may cause cognitive impairment and since individuals with Alzheimer's disease or other dementing conditions vary in severity of disease manifestations, level of cognitive impairment was rated for each participant, both those with and without Alzheimer's disease, prior to assigning a diagnosis. The degree of cognitive impairment was assessed solely from the results of the cognitive performance tests administered at clinical evaluation. The results of the in-home population screening tests were not used for this purpose. Those who passed all cognitive tests administered at the clinical evaluation or failed only 1 test with a near-passing score were rated as having no evidence of cognitive impairment. Those who clearly failed 2 or more tests or failed 3 or more tests with near-passing scores were classified as having mild cognitive impairment. To be classified as having moderate cognitive impairment required failing scores on between 5 and 8 of the cognitive function tests, not including the auditory continuous performance test. Those failing either 9 or all 10 of the cognitive tests were classified as having severe cognitive impairment. Although it was not used as a classification criterion, all those with severe cognitive impairment also had substantial difficulty comprehending and expressing simple ideas outside of the formal testing situation.

Statistical Methods

The prevalences of cognitive impairment and of Alzheimer's disease in the population were estimated from the stratified sample of persons undergoing clinical evaluation. The prevalence was estimated as a weighted average of the proportions with the disease in the individual memory groups.[12] For the good performance group, which was selected by age and gender, this proportion was estimated from a logistic regression model including terms for age and gender.[13]

RESULTS

Prevalence of Alzheimer's Disease Among Those Over Age 65 Years in the Community

Of the 467 persons in the sample undergoing clinical evaluation, 134 had probable Alzheimer's disease, 166 possible Alzheimer's disease, and 167 no

evidence of Alzheimer's disease. The population memory-performance groups and the diagnostic categories for Alzheimer's disease of the individuals undergoing clinical evaluation are shown in Table 1. Most, but not all, of those with probable Alzheimer's disease were from the poor memory performance group. Of those with probable Alzheimer's disease, 35 (26%) had severe cognitive impairment, 68 (51%) moderate cognitive impairment, and 31 (23%) mild cognitive impairment. These numbers, in themselves, reveal little about prevalence of Alzheimer's disease in the community, because the sample was heavily weighted with individuals with poor screening memory performance who were likely to have Alzheimer's disease. Taking the sampling into account, the prevalence rate for probable Alzheimer's disease among those over the age of 65 years was 10.3% (95% confidence limits [CL], 8.1% and 12.5%).

Relation of Age to Prevalence of Alzheimer's Disease in the 65 Years and Older Age Group in the Community

Prevalence rates for Alzheimer's disease for the 65 to 74, 75 to 84, and 85 years and older age subgroups of the community population showed a strong association with age (Fig 2). Among those 65 to 74 years old, the prevalence rate for probable Alzheimer's disease was 3.0% (95% CL, 0.8 and 5.2). For those 75 to 84 years of age, it was 18.7% (95% CL, 13.2 and 24.2), and among those 85 years or older, 47.2% (95% CL, 37.0 and 63.2).

Other Dementing Conditions in the Community Population

Conditions other than Alzheimer's disease that caused moderate or severe cognitive impairment included multiple cerebral infarcts, alcoholic dementia, parkinsonian dementia, depression, psychosis, mental retardation, and subacute combined degeneration. None of these other causes was common in this community sample (Table 2). Of the 113 persons with moderate or severe cognitive impairment and a probable diagnosis, 95 (84.1%) had Alzheimer's disease alone. Ten (8.8%) had only a cause of dementia other than Alzheimer's disease, and 8 (7.1%) had both Alzheimer's disease and another cause of dementia. The single most common cause of dementia apart from Alzheimer's disease was multiple cerebral infarcts, present in five persons with moderate or severe impairment, three with multiple cerebral emboli and two with lacunar infarcts.

Table 1.—Population Screening Memory Performance Group and Alzheimer's Disease Diagnostic Category for the Sample of Persons Undergoing Clinical Evaluation

Memory Test Screening Group	Diagnosis at Clinical Evaluation		
	Probable Alzheimer's Disease	Possible Alzheimer's Disease	No Evidence of Alzheimer's Disease
Good	14	65	91
Intermediate	16	34	51
Poor	104	67	25
Total	**134**	**166**	**167**

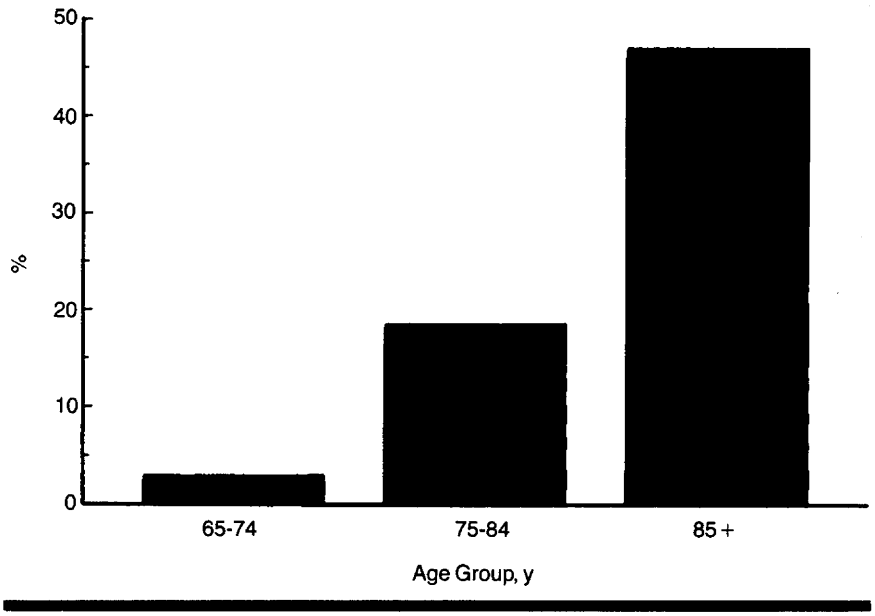

Fig 2.—Prevalence rates for probable Alzheimer's disease according to age group in a community population of persons 65 years of age and older.

Table 2.—Probable Diagnosis of Conditions Causing Moderate or Severe Cognitive Impairment in Individuals Sampled From a Defined Community Population of Persons 65 Years of Age and Older

Clinical Diagnoses	No. of Individuals
Alzheimer's disease alone	95

Other Diagnoses	No. of Individuals	
	Without Alzheimer's Disease	Accompanied by Alzheimer's Disease
Multiple cerebral infarcts		
Lacunar infarcts	1	1
Cerebral emboli	2	1
Alcoholic dementia	2	1
Parkinsonian dementia	1	2
Psychosis	2	...
Depressive dementia	1	1
Mental retardation	1	1
Subacute combined degeneration	...	1
Total	**10**	**8**

COMMENT

These data from uniform, structured, clinical evaluations of individuals from a defined community population indicate that clinically diagnosed Alzheimer's disease is a common condition that increases strongly in prevalence with age among those more than 65 years old. Most cognitive impairment in this population was due to Alzheimer's disease. Only a few individuals had dementia due to potentially reversible conditions. The

number with dementia due to strokes was also relatively low.

Previous studies providing diagnoses of the conditions responsible for cognitive impairment have usually been conducted among selected persons admitted to institutions or referred for clinical care because of symptoms.[14-21] Fewer studies[22-31] providing such diagnoses have been carried out in large, free-living populations. Most population-based studies[32-45] have investigated cognitive impairment or dementia only in general terms and have not reached clinical diagnoses.

Our overall estimate of Alzheimer's disease prevalence of 10.3% among those over the age of 65 years is somewhat higher than some previous reports. It is slightly lower, however, than two earlier indirect estimates of prevalence in the US population made by different methods. Rocca et al[46] estimated prevalence of Alzheimer's disease in the United States among those over 65 years as 11.2% by applying age- and sex-specific prevalence rates of senile dementia from a Scottish study[28] to US population estimates. Pfeffer et al[29] also estimated Alzheimer's disease prevalence to be 11.2% in the over 65-year-old age group by applying age-specific prevalence rates of clinically diagnosed Alzheimer's disease from a California retirement community to 1980 US census data for whites over age 65 years.

Relatively small differences in disease criteria may be a major reason for differing estimates of Alzheimer's disease prevalence among various studies. While there is consensus[10] on the concepts that should enter into the clinical diagnosis of Alzheimer's disease, the translation of these concepts into specific operational criteria is not a matter of secure agreement.[43,47] Such specific criteria will range along a spectrum, and prevalence estimates may vary substantially according to where along this continuum one places diagnostic cut points, especially in community populations in which mild disease that is difficult to separate from normal may be expected to predominate. Thus, prevalence estimates for Alzheimer's disease from all studies must be interpreted with some caution. Some community-based studies[24,26,27] and one indirect estimate[48] of Alzheimer's disease prevalence in the US population have restricted consideration to cases of severe dementia. The prevalence estimates from such studies restricted to severe disease are lower than the estimate from the present study, which includes more mildly affected persons as well. The US Congress Office of Technology Assessment[48] summarized existing general population prevalence estimates restricted to severe dementia as 5% to 7% of those over 65 years old. Of the individuals with probable Alzheimer's disease in the present study, 26% had severe cognitive impairment, 51% moderate impairment, and 23% mild impairment.

Methodological differences may also have led to lower prevalence estimates from other studies compared with the present investigation. Some previous studies have confined selection of subjects for clinical evaluation to those who scored poorly on population screening instruments. This leads to a substantial underestimate of disease prevalence in the population because the large group of individuals passing the screening tests includes a number of persons with disease. In contrast, subjects for clinical evaluation in the present study were selected from all strata of memory performance on the population survey. Previous studies have also varied in such features as participation rate, blinding of evaluators to screening test results, the degree to which examination procedures are specified, the comprehensiveness of the clinical examination, and the assumption that certain diagnoses are mutually exclusive. Further, some apparent differences are likely due, at least in part, to chance, especially because of the small sample sizes of some studies.

The present study also provides a higher estimate of the proportion of individuals with cognitive impairment due to Alzheimer's disease rather than other causes than have some previous studies. This may well be due to differences in the populations studied. Studies based on hospitalized or outpatient populations are more likely to include individuals with unusual findings or those for whom currently available therapies might be useful, leading to the inclusion of fewer persons with Alzheimer's disease. With regard to studies based on community populations, two[25,27] of the three previous US studies that provided clinical diagnoses included larger proportions of black participants than did our study. Higher rates of stroke among blacks[49] may account, at least in part, for larger proportions of dementia due to stroke in those studies than in the present one. In the present study, 35% of those selected for clinical evaluation either declined evaluation or died before being invited to participate. Since data for all those invited to participate were available from the population survey, we were able to examine whether a bias against selection of those at high risk of dementing illnesses other than Alzheimer's disease (especially stroke) might have influenced our findings. The information on possible risk factors for stroke provides some indirect evidence against this possible bias. Subjects undergoing clinical evaluation were similar to those selected but not evaluated because of death or refusal in all characteristics examined, including age; sex; systolic and diastolic blood pressure; history of previous stroke, heart attack, or diabetes; and previous or current cigarette smoking.

The National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria used in this study consider absence of other diagnoses of dementing illness in determining probability of Alzheimer's disease. Our estimates of disease prevalence in the population are, to some degree, underestimates since those with another, coexisting, cause of dementia are excluded. Therefore, we also calculated prevalence estimates without the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association restriction that any other disease that could account for dementia be absent for the diagnosis of probable Alzheimer's disease. The prevalence rates for probable Alzheimer's disease among estimates without this restriction are slightly higher. For the community population over the age of 65 years the prevalence rate for probable Alzheimer's disease was 11.6% (CL, 9.4 and 13.7). For those 65 to 74 years old it was 4.1% (CL, 1.9 and 6.2). For those 75 to 84 years of age, it was 20.9% (CL, 15.4 and 26.3), and among those 85 years or older, 47.8% (CL, 38.1 and 57.5).

Several limitations of the present study should be noted. Only retrospective information is available regarding duration and previous course of disease. Further, since the selection for clinical evaluation was based on a single prevalence survey in the community, it is possible that disease with a rapidly progressive course is underrepresented due to selective removal by death or institutionalization. Our population survey included only noninstitutionalized individuals. If institutionalized persons had been included, it is likely that our prevalence estimates for both cognitive impairment and Alzheimer's disease would have been higher. This reason for underestimation may be somewhat less important in East Boston, however, because the presence of an active home-care program[50] may enable some individuals to remain in the community who might otherwise enter institutions. Al-

though a high proportion (80.8%) of age-eligible residents underwent memory testing, those not tested, especially those represented by proxy respondents, may have had a higher risk of dementing illness. To the extent this is the case, our results will underestimate the true prevalence of disease. Finally, the generalizability of the findings of this study of a single, defined community population cannot yet be fully judged. This will depend on reports from other community-based studies with adequate sample sizes and appropriate diagnostic methods.

Despite these limitations, we believe the most plausible interpretation of the data to be that Alzheimer's disease is a common condition in this community population of persons over the age of 65 years, that Alzheimer's disease (or conditions that cannot be separated from it by present clinical criteria) is the most common diagnosis accounting for cognitive impairment in this population, and that its prevalence increases markedly with age. These findings suggest that the public health impact of Alzheimer's disease will increase with the continuing growth of the oldest population groups in the United States[51] and other developed countries[52] and emphasize the need to define potentially modifiable causal factors.

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