

# Prevalence of Alzheimer's disease and other dementias in rural India

## The Indo-US study

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**Article abstract**—*Objective:* To determine the prevalence of AD and other dementias in a rural elderly Hindi-speaking population in Ballabgarh in northern India. *Design:* The authors performed a community survey of a cohort of 5,126 individuals aged 55 years and older, 73.3% of whom were illiterate. Hindi cognitive and functional screening instruments, developed for and validated in this population, were used to screen the cohort. A total of 536 subjects (10.5%) who met operational criteria for cognitive and functional impairment and a random sample of 270 unimpaired control subjects (5.3%) underwent standardized clinical assessment for dementia using the *Diagnostic and Statistical Manual of Mental Disorders*—fourth edition diagnostic criteria, the Clinical Dementia Rating Scale (CDR), and National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable and possible AD. *Results:* We found an overall prevalence rate of 0.84% (95% CI, 0.61 to 1.13) for all dementias with a CDR score of at least 0.5 in the population aged 55 years and older, and an overall prevalence rate of 1.36% (95% CI, 0.96 to 1.88) in the population aged 65 years and older. The overall prevalence rate for AD was 0.62% (95% CI, 0.43 to 0.88) in the population aged 55+ and 1.07% (95% CI, 0.72 to 1.53) in the population aged 65+. Greater age was associated significantly with higher prevalence of both AD and all dementias, but neither gender nor literacy was associated with prevalence. *Conclusions:* In this population, the prevalence of AD and other dementias was low, increased with age, and was not associated with gender or literacy. Possible explanations include low overall life expectancy, short survival with the disease, and low age-specific incidence potentially due to differences in the underlying distribution of risk and protective factors compared with populations with higher prevalence.

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The dementias of late life, including AD, have been acknowledged as a major public health problem in Western industrialized countries. A growing number of community studies have reported on the prevalence of AD—and of dementia in general—in North America, Europe, and Australia. In a review of prevalence studies of dementia in western Europe and the United States conducted since 1989, Hendrie found that prevalence rates in those aged 65 years and older ranged from 3.6% to 10.3%.<sup>1</sup> Age-specific prevalence rates for AD and dementia double approximately every 5 years.<sup>1</sup>

However, the majority of the world's elderly do not live in the West. It has been estimated that 59% of the world's population aged 65 years and older in the year 2000 will be in developing countries.<sup>2</sup> Primarily because of lesser emphasis on the health of older adults and lesser resources for health research compared with the industrialized nations, developing countries have not been able to report reliable prevalence data on aging-related disorders such as dementia. Thus, the extent of the public health burden

currently posed by AD and other dementias in developing countries remains an open question. Furthermore, it is possible that different risk and protective factors for and against dementia operate in developed and developing countries. The possibility of discovering new risk factors and formulating new etiologic hypotheses led the National Institute on Aging in 1988 to announce a grant program on cross-national investigations of the epidemiology of dementia.<sup>3</sup> The program required comparisons between the selected overseas population and a reference US population.

We undertook a study of dementia among the elderly in a rural population in Ballabgarh in northern India. The reference population in the United States was that of the rural Monongahela Valley in southwestern Pennsylvania, from which an elderly rural cohort was already participating in a dementia epidemiologic study (described briefly later). We have previously reported<sup>4–6</sup> the instruments developed for the Ballabgarh study and the methodology of the instruments development. We now report the results

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of the Ballabgarh survey for the prevalence of AD and other dementias.

**Methods.** *Background.* The Indo-US Cross-National Dementia Epidemiology Study is a collaborative project of the University of Pittsburgh, PA, and the Centre for Ageing Research, India (CARI) in New Delhi, India, conducted with the cooperation of the Comprehensive Rural Health Services Project (CRHSP) at Ballabgarh (the field practice site of the Centre for Community Medicine, All-India Institute of Medical Sciences, New Delhi). The cross-national study has two major goals. The first is to investigate the epidemiology of dementia in the rural northern Indian population of Ballabgarh. The second is to compare the Ballabgarh results with those obtained in the US reference population in the Monongahela Valley, near Pittsburgh, using comparable methods. This article reports age- and gender-specific prevalence rates of dementia in the Ballabgarh population.

*Study population.* As reported previously,<sup>6,7</sup> the field practice site in the rural area of Ballabgarh in the northern Indian state of Haryana is approximately 35 km from New Delhi. It consists of 28 villages with a total population of 63,237 at the time the current survey began. The majority of the population follows agricultural occupations; the current older generation, particularly the women, have little or no formal education. All older individuals live with family members, usually in the home of a son or other male relative. The CRHSP has, for more than three decades, maintained an up-to-date census of the entire population of the 28 field practice villages in Ballabgarh. We were given access to the census database to allow us to identify the older residents of the area. Because of the lower average life expectancy of the rural Indian population (estimated for the years 1996 to 2001 as 63.5 years at birth),<sup>8</sup> we selected the official retirement age of 55 years as the lower age cutoff for our study, which was a total population survey of those at or above this age.

A total of 5,649 Ballabgarh residents were identified as being age 55 or older in the census database. Each of these individuals was visited at home by a project field worker, who confirmed the subject's age as previously described,<sup>7</sup> as well as ascertained address, next of kin, and other identifying information. Of the 5,649 individuals identified in the census, 242 were found to be younger than 55 years, 114 had died, 92 had relocated outside the study area, and 67 were duplicate listings. The field worker explained the purpose and procedures of the study and attempted to obtain informed consent according to protocols approved by both the University of Pittsburgh Institutional Review Board and the CARI Human Volunteers Protection Committee. Only eight eligible persons and their families refused to participate in the study. The study population described in this paper consists of the remaining 5,126 individuals.

The reference US population is in the rural mid Monongahela Valley near Pittsburgh, in southwestern Pennsylvania. A sample from this population has been involved since 1987 in an ongoing prospective community study of the epidemiology of dementia, known as the Monongahela Valley Independent Elders Survey (MoVIES Project).<sup>9,10</sup> This population is referred to hereafter as the MoVIES cohort.

*Data collection.* After obtaining informed consent, field workers then administered a scripted, completely standardized screening interview with the following components:

- Demographic/identifying information
- Determination of literacy (defined as the ability to read the local newspaper and write a sentence)
- Screening of vision and hearing to determine whether subjects could be cognitively tested
- Blood pressure, height, and weight measurements
- Cognitive screening battery (described later)
- Activities of daily living (ADL; described later)
- Exposure/risk factor profile—a standardized protocol that addresses diet, smoking, alcohol use, history of head trauma, exposure to potential toxins (organic solvents, pesticides, heavy metals found in many indigenous medicines and tonics), history of selected neurologic symptoms, and family history of dementia and neurologic illnesses

The entire screening interview lasted approximately 90 minutes in the majority of subjects.

Cognitive screening was performed by means of a battery of tests developed for this study, descriptions and norms for which have been described previously in detail.<sup>5,6</sup> Briefly, the test battery was designed to be psychometrically sound, reliable and valid, minimally biased by culture and education, optimally sensitive and specific for dementia, and facilitative of judicious comparisons between the Ballabgarh population and the MoVIES cohort. Because of this last requirement, the cognitive screening battery had to be comparable with the battery already in use in the MoVIES Project, which has been described elsewhere in detail.<sup>9-12</sup> The Ballabgarh battery also had to be in the Haryanvi dialect of Hindi, and appropriate for use with elderly, illiterate rural residents. Three years were spent in intensive and systematic instrument development, described previously,<sup>4,6</sup> including translation and backtranslation, cultural modifications, several stages of pretesting on volunteers, pilot testing, and field testing random sample populations. The final battery, used in the prevalence survey, consisted of five elements:

1. The Hindi Mental State Exam<sup>5</sup> (HMSE)—a modified Hindi version of the Mini-Mental State Examination (MMSE)<sup>13</sup>
2. Immediate learning, delayed recall, and delayed recognition of a 10-item word list (adapted from the Consortium to Establish a Registry for Alzheimer's Disease [CERAD] battery used in the MoVIES Project<sup>6,14,15</sup>) using auditory rather than visual presentation of the words for these primarily illiterate subjects
3. Verbal fluency for the names of fruits and animals<sup>6,15,16</sup>
4. The Object Naming Test—a test of confrontation naming adapted from the Boston Naming Test<sup>6,15,17</sup> using three-dimensional objects rather than line drawings
5. Constructional praxis—copying four geometric drawings<sup>6,15,18</sup>

Based on their scores on these tests, subjects were classified as cognitively impaired using the following operational criteria for cognitive impairment: 1) scores at or below the 10th percentile of the population on the HMSE or 2) scores at or below the 10th percentile of the population on at least one memory test and one test of another cognitive domain. All other subjects completing the cognitive tests were classified as cognitively unimpaired. We

have reported previously<sup>10</sup> that similar percentile-based and multiple-domain-based criteria were more sensitive and specific for dementia than the use of the MMSE alone in the MoVIES Project. If a subject did not complete a test for any reason, the "missing" score on this test was treated as if it was an indicator of impairment. All impaired subjects and a 5% sample of unimpaired subjects were selected for the clinical and diagnostic evaluation described later.

**Functional impairment (ADL) scale.** The *Diagnostic and Statistical Manual of Mental Disorders*—fourth edition (DSM-IV)<sup>19</sup> diagnostic criteria for dementia require that cognitive impairment be accompanied by impairment in social and occupational functioning. Particularly in this illiterate population we were concerned that the cognitive tests might be insufficiently specific for dementia (i.e., subjects might perform poorly on cognitive tests without concomitant functional impairment). ADL/instrumental ADL (IADL) scales used in the West did not appear to be suitable for the rural environment and societal expectations of Ballabgarh elderly. For example, these elderly rural individuals do not perform routinely, and therefore cannot be assessed on, instrumental ADLs (such as use of checkbooks or household appliances), as expected of their Western counterparts. However, until they suffer deficits in their own daily functioning, they cannot be said to be functionally impaired. We therefore developed de novo for this study an 11-item ADL scale, described in detail elsewhere,<sup>20</sup> to assess the regular activities and functions performed by and expected of this population, with a particular view to capturing those activities likely to be most affected by cognitive impairment. Nine of the 11 items were designated as potentially relevant to dementia. We have shown scores on this scale to be associated with scores on the HMSE.<sup>20</sup> The scale was administered to a responsible household member of each subject, who was asked whether the subject performed each listed activity regularly and adequately. ADL screening by informant report was obtained for 316 subjects who did not or could not complete the cognitive screening, usually because of severe sensory impairment or physical illness. For this study, inability to perform any three or more of the nine items designated the subject as functionally impaired. Subjects meeting this designation were also asked to undergo the clinical and diagnostic evaluation.

**Clinical and diagnostic evaluation.** Clinical evaluation was conducted using a standardized diagnostic protocol on all selected subjects who consented to be examined. The protocol was based on the MoVIES diagnostic protocol,<sup>10,12</sup> which itself was a field-use version of the clinical assessment protocols of CERAD<sup>15</sup> and the University of Pittsburgh Alzheimer's Disease Research Center (ADRC), with further modifications for the rural Indian setting. The clinical diagnostic protocol for the current study included a general medical history and physical examination, a detailed neurologic examination and mental status examination,<sup>7,21</sup> subject history obtained from a responsible family member, a family history, appropriate laboratory investigations, and a diagnostic algorithm allowing the diagnosis of dementia according to the DSM-IV,<sup>19</sup> the stage of dementia on the Clinical Dementia Rating Scale (CDR),<sup>22</sup> and the diagnosis of probable and possible AD according to National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related

Disorders Association (NINCDS-ADRDA) criteria.<sup>23</sup> These categories and ratings were applied to be comparable with the MoVIES Project and are the focus of this article. The algorithm also includes additional steps to make the diagnosis of dementia according to the International Classification of Diseases (ICD)-10 for future comparison to other international studies.

The clinical evaluations, which lasted 2 to 3 hours, were performed by the project medical officer (R.P.) and neurologist (V.C.) in the subjects' homes or other familiar and accessible location within each village. The examiners were blind to the reason for the subjects' selection for clinical evaluation (i.e., whether they had been classified as cognitively impaired, functionally impaired, or unimpaired control subjects), and they did not examine screening data before evaluating the subject. All evaluations were performed by the same US-trained and board-certified clinically experienced neurologist who had previously established reliability with the Pittsburgh-based investigators (M.G. or S.T.D.) by examining patients and subjects together at the University of Pittsburgh ADRC, the community-based MoVIES Project; at an urban clinical center in New Delhi; and in the field for the Ballabgarh project. In patients diagnosed with dementia, as detailed later, laboratory investigations were performed to assist with differential diagnosis of the dementia. Blood tests included chemistry (glucose, albumin and total protein, direct and total bilirubin and liver enzymes, blood urea nitrogen, creatinine, uric acid, electrolytes, triglycerides, and cholesterol [total, high-density lipoprotein, low-density lipoprotein, and very low density lipoprotein]), hematology (hemoglobin, erythrocyte sedimentation rate, total and differential leukocyte count), thyroid function tests (T3, T4, and thyroid-stimulating hormone), and syphilis serology. MRI scans of the head were read independently by the neuroradiologist and neurologist (V.C.). Interrater reliability in MRI interpretation was established between the Pittsburgh-based (S.T.D.) and the New Delhi-based (V.C.) neurologists.

In the event that subjects died between screening and clinical evaluation, an intensive interview of family household members was conducted (similar to the family interview, which was conducted with respect to living subjects) to determine whether the subject met DSM-IV criteria for dementia (cognitive and functional decline sufficient to interfere with social and occupational functioning) before death, and other relevant information.

**Determination of prevalence.** Using all the previously described information, the presence of prevalent dementia was determined according to a diagnosis of dementia (according to DSM-IV<sup>19</sup>) and the stage of dementia (according to the CDR<sup>22</sup>): 0, no dementia; 0.5, possible dementia; 1, mild dementia; 2, moderate dementia; 3, severe dementia; 4, profound dementia; and 5, terminal dementia. We calculated prevalence in two ways based on CDR stage: 1) prevalence of individuals with a CDR score >0 (i.e., possible dementia or higher) or 2) prevalence of individuals with a CDR score  $\geq$ 1 (i.e., mild dementia or higher).

With regard to the subtype of dementia, the presence of clinically diagnosable AD was determined according to the NINCDS-ADRDA criteria<sup>22</sup> in subjects with a CDR score  $\geq$ 0.5. These subjects were designated as probable AD, possible AD, or other (non-AD) dementia. For the AD preva-

**Table 1** Study sample demographics: Age, sex, and literacy

Age group, y	Men			Women			Total,* n (%)
	Illiterate, n (%)	Literate, n (%)	All men, n (%)	Illiterate, n (%)	Literate, n (%)	All women, n (%)	
55–64	523 (45.3)	623 (54.7)	1,155 (100)	1,199 (95.5)	57 (4.5)	1,256 (100)	2,411 (47.0)
65–74	641 (58.0)	464 (42.0)	1,105 (100)	845 (95.6)	39 (4.4)	884 (100)	1,989 (38.8)
75–84	235 (63.2)	137 (36.8)	372 (100)	210 (94.6)	12 (5.4)	222 (100)	594 (11.6)
85+	66 (74.2)	23 (25.8)	89 (100)	40 (93.0)	3 (7.0)	43 (100)	132 (2.6)
Total	1,465 (53.8)	1,256 (46.2)	2,721 (100)	2,294 (95.4)	111 (4.6)	2,405 (100)	5,126 (100)

\* This column includes column percentages indicating the percent of the entire study population in each age group.

lence data reported in this article, we grouped probable and possible AD.

**Statistical analysis.** Bivariate relations among demographic variables (age, gender, and literacy) were examined using the Mantel-Haenszel chi-square test for trend, treating age as a categorical variable (four 10-year age intervals).

Prevalent dementia and AD were defined as reported earlier. Age-specific prevalence rates within 10-year age intervals, and 95% CIs about these rates (assuming a Poisson distribution), were calculated separately for the entire population, for men and women, and for literate and illiterate subjects. Logistic regression models were used to explore the associations of age, gender, and literacy with prevalent dementia. Three age group variables were used to compare each of the older groups (65 to 74 years, 75 to 84 years, and >85 years) with the youngest group (55 to 64 years).

**Results.** Of the 5,649 subjects identified as age 55 years or older in the CRHSP census database, 5,126 were alive and residing in the Ballabgarh area, age confirmed, and willing to participate. The mean age of the study population was  $66.5 \pm 7.6$  years (SD) with a median of 65 years. Men comprised 53.1% and women comprised 46.9% of the population. Illiteracy, defined as the inability to read and write, was reported by 73.3% of the total cohort. One to 10 years of education were reported by 4.2% of women and 43.3% of men, whereas 1.2% of men and 0% of the women had more than 10 years of education, reflecting the perceived value in the community of education for women of this generation.

Table 1 shows the breakdown of the population by age, gender, and literacy. Women were more likely to be illiterate than men (Mantel-Haenszel chi-square ( $Q_{MH}$ ) = 9.1,  $p$  = 0.003). Illiteracy was associated with older age in the entire study population ( $Q_{MH}$  = 1126.6,  $p$  = 0.001) and in men ( $Q_{MH}$  = 66.3,  $p$  = 0.001) but not in women ( $Q_{MH}$  = 0.4,  $p$  = 0.526).

Of the 5,126 individuals who were screened, 536 (10.5%) were selected for clinical evaluation on the basis of cognitive or functional impairment, and 270 (5.3%) were selected as unimpaired control subjects. Of these 806 subjects who were selected for clinical evaluation, 627 were evaluated in person, 12 of whom had aphasia or hearing loss such that history had to be obtained from the family, and the mental status examination was limited by these deficits. Thirty-two died before clinical evaluation could be

conducted and had to be diagnosed based solely on information obtained from the family. Seven had permanently relocated outside the study area since the screening.

Clinical evaluation was not done in 147 subjects who had been selected for this evaluation. A total of 104 of them had been selected on the basis of cognitive impairment, missing cognitive data, or functional impairment, and 28 had been selected as unimpaired control subjects. Seven had migrated out of the area since the screening. A total of 105 subjects or their families refused clinical evaluation and an additional 28 subjects were unavailable at home for evaluation after multiple attempts to visit them. In each of these cases, the neurologist and medical officer interviewed the family to determine the reason for refusal or unavailability and whether dementia might be present. Of those who refused, 43 were described by the family as still employed or too busy with housework and family matters; 37 were described as medically ill, blind, or severely hearing impaired but with no cognitive limitations; and 25 refused to be examined but were described by their families as in good health with no cognitive limitations. Of those who were unavailable, all were described as healthy and highly functional. Some were working or taking care of family during the day, and others were on extended trips outside the area (e.g., to visit relatives elsewhere or on religious pilgrimages).

Forty-three individuals were found to meet criteria for dementia, with a CDR score of at least 0.5. Of these 43 subjects, seven had a CDR score of 0.5, 14 had a CDR score of 1, and 22 had a CDR score from 2 to 5. Of the 43 subjects, 36 were diagnosed as having probable or possible AD. Of the 43, one subject had been selected for clinical evaluation as an unimpaired control and was determined to have suffered cognitive and functional decline following a stroke that occurred between screening and clinical evaluation. Of the 43, eight were deceased and had to be diagnosed based on information from the family.

The positive predictive value of the 10th percentile screening criteria for CDR score  $\geq 0.5$  was 8.4% and the negative predictive value of the 10th percentile screening criteria for CDR score  $\geq 0.5$  was 97.4%. The comparable figures in the MoVIES cohort were 53.3% and 90.9% respectively.<sup>10</sup> These values depend both on the prevalence of the disorder and on the sensitivity and specificity of the screening tests. Because we anticipated that prevalence would be low, our goal was total ascertainment of subjects. We therefore made an a priori decision to maximize sensitivity (i.e., tolerate a large proportion of false positives to

**Table 2** Age-specific prevalence by gender

		All dementias (DSM-IV <sup>19</sup> ), CDR ≥ 0.5		All dementias (DSM-IV <sup>19</sup> ), CDR ≥ 1.0		Probable and possible AD (NINCDS-ADRDA), CDR ≥ 0.5	
Age, y	No. at risk	n	Rate, % (95% CI)	n	Rate, % (95% CI)	n	Rate, % (95% CI)
Men							
55–64	1,155	3	0.26 (0.05–0.76)	3	0.26 (0.05–0.76)	1	0.09 (0.00–0.48)
65–74	1,105	10	0.90 (0.43–1.66)	7	0.63 (0.25–1.30)	7	0.63 (0.25–1.30)
75–84	372	5	1.34 (0.44–3.14)	4	1.08 (0.29–2.75)	4	1.08 (0.29–2.75)
85+	89	9	10.11 (4.63–19.19)	8	8.99 (3.88–17.71)	9	10.11 (4.63–19.19)
Total	2,721	27	0.99 (0.65–1.44)	22	0.81 (0.51–1.22)	21	0.77 (0.48–1.18)
Women							
55–64	1,256	3	0.24 (0.05–0.70)	2	0.16 (0.02–0.57)	2	0.16 (0.02–0.57)
65–74	884	4	0.45 (0.12–1.16)	4	0.45 (0.12–1.16)	3	0.34 (0.07–0.99)
75–84	222	5	2.25 (0.73–5.26)	4	1.80 (0.49–4.61)	2	0.90 (0.11–3.25)
85+	43	4	9.30 (2.53–23.81)	4	9.30 (2.53–23.81)	4	9.30 (2.53–23.81)
Total	2,405	16	0.67 (0.38–1.08)	14	0.58 (0.32–0.98)	11	0.46 (0.23–0.82)
Both sexes							
55–64	2,411	6	0.25 (0.09–0.54)	5	0.21 (0.07–0.48)	3	0.12 (0.03–0.36)
65–74	1,989	14	0.70 (0.38–1.18)	11	0.55 (0.28–0.99)	10	0.50 (0.24–0.92)
75–84	594	10	1.68 (0.81–3.10)	8	1.32 (0.58–2.65)	6	1.01 (0.37–2.20)
85+	132	13	9.85 (5.24–16.84)	12	9.09 (4.70–15.88)	13	9.85 (5.24–16.84)
Grand total	5,126	43	0.84 (0.61–1.13)	36	0.70 (0.49–0.97)	32	0.62 (0.43–0.88)

NINCDS-ADRDA = National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association; CDR = Clinical Dementia Rating Scale.

minimize false negatives); thus the low yield of the clinical evaluations was not unexpected.

Based on these 43 subjects, the overall prevalence of all dementias with CDR  $\geq 0.5$  was 0.84% (95% CI, 0.61 to 1.13) for the age group 55+ years, and was 1.36% (95% CI, 0.96 to 1.88) in the age group 65+ years. Based on the 36 subjects with probable and possible AD, the overall prevalence of AD was 0.62% (95% CI, 0.43 to 0.88) in the age group 55+ years, and 1.07% (95% CI, 0.72 to 1.52) in the age group 65+ years.

Table 2 shows age-specific prevalence rates in men, women, and the total sample for three different categories of dementia diagnoses: all dementias, with CDR scores of at least 0.5; all dementias, with CDR scores of at least 1; and probable and possible AD, with CDR scores of at least 0.5.

Table 3 shows age-specific prevalence rates in the literate versus the illiterate members of the cohort for the same three categories of dementia diagnosis.

In the total study population as well as in both genders and literacy groups (see tables 2 and 3), it can be seen that the prevalence rates appear substantially higher in the oldest age group (85+ years). Caution is urged in interpreting these results because the total sample size is very small ( $n = 132$ ) in this age group, and the 95% CIs about the rates are extremely wide.

Table 4 summarizes the results of logistic regression

modeling to explore associations among age, gender, literacy, and AD and other dementias.

In bivariate analyses, when including those with CDR  $\geq 0.5$ , greater age is associated significantly both with AD and with all dementias in all age categories. When restricting the analyses to demented subjects with CDR  $\geq 1$ , the association is slightly less than significant for the 65 to 74 years age group but highly significant for the other age groups. There were no significant associations of either gender or literacy with all dementias. With respect to AD, although gender showed no association, there was a trend toward literacy being protective against AD ( $p = 0.07$  when CDR  $\geq 0.5$ , and  $p = 0.1$  when CDR  $\geq 1$ ).

In multiple logistic regression models adjusting for age, neither gender nor literacy was associated with either all dementias or AD. There was also no significant gender-literacy interaction effect on either dementia or AD. Potentially, lack of power due to the small overall number of prevalent subjects may have prevented these associations from being detected, but this seems unlikely because the odds ratio estimates were close to one.

We also examined survival (duration) from the roughly estimated onset of disease (as reported by the family) until death, or until the end of the prevalence survey (for the demented subjects who were still alive as of January 15, 1998). Five subjects in whom date at onset could not be

**Table 3** Age-specific prevalence by literacy

		All dementias (DSM-IV <sup>19</sup> ), CDR ≥ 0.5		All dementias (DSM-IV <sup>19</sup> ), CDR ≥ 1.0		Probable and possible AD (NINCDS-ADRDA), CDR ≥ 0.5	
Age, y	No. at risk	n	Rate, % (95% CI)	n	Rate, % (95% CI)	n	Rate, % (95% CI)
Literate							
55–64	689	4	0.58 (0.16–1.49)	3	0.44 (0.09–1.27)	2	0.29 (0.04–1.05)
65–74	503	2	0.40 (0.05–1.44)	2	0.40 (0.05–1.44)	0	0.00 (0.00–0.73)
75–84	149	2	1.34 (0.16–4.85)	2	1.34 (0.16–4.85)	1	0.67 (0.02–3.74)
85+	26	1	3.85 (0.10–21.42)	1	3.85 (0.10–21.42)	1	3.85 (0.10–21.42)
Total	1,367	9	0.66 (0.30–1.25)	8	0.59 (0.25–1.15)	4	0.29 (0.08–0.75)
Illiterate							
55–64	1,722	2	0.12 (0.01–0.42)	2	0.12 (0.01–0.42)	1	0.06 (0.00–0.32)
65–74	1,486	12	0.81 (0.42–1.41)	9	0.61 (0.28–1.15)	10	0.67 (0.32–1.24)
75–84	445	8	1.80 (0.78–3.54)	6	1.35 (0.49–2.93)	5	1.12 (0.36–2.62)
85+	106	12	11.32 (5.85–19.77)	11	10.38 (5.18–18.57)	12	11.32 (5.85–19.77)
Total	3,759	34	0.90 (0.63–1.26)	28	0.74 (0.50–1.08)	28	0.74 (0.50–1.08)
Grand total	5,126	43	0.84 (0.61–1.13)	36	0.70 (0.49–0.97)	32	0.62 (0.43–0.88)

NINCDS-ADRD = National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association; CDR = Clinical Dementia Rating Scale.

estimated were excluded. Among all remaining demented subjects (CDR  $\geq$ 0.5), the median survival was 3.3 years. Among subjects with any dementia and CDR  $\geq$ 1.0, median survival was 3.3 years. Among subjects with AD and CDR  $\geq$ 1.0, median survival was 2.7 years. However, some of these subjects are still alive and their total duration of illness is not yet known. Restricting these calculations to the 20 demented subjects who are deceased, median survival was 2.7 years in all three groups. Given the overall small number of subjects and the uncertainty of their disease onset, these duration data should be interpreted with caution.

**Discussion.** We have reported on the results of a major prevalence survey of the total population age 55 years and older in a well-defined community-dwelling population in rural northern India. The

study has several relatively unique features. It is the first reported major study of a Hindi-speaking population, two-thirds of whom are illiterate. A major component of the study was the development of a standardized methodology for screening and a diagnosis suitable for illiterate Hindi-speaking subjects. Our approach to screening involved tests of several cognitive domains, as well as functional impairment, and the use of a population percentile on each test to select subjects for more detailed clinical evaluation. The size of the cohort was considerably larger than those of previous studies from India.

Our major finding from this population was that overall population prevalence, both of probable and possible AD, and of overall dementia, was low. As reported consistently in the world literature,<sup>1</sup> the

**Table 4** Associations of AD and overall dementia with age, gender, and literacy

Dementia stage (Clinical Dementia Rating)	Dementia type	Unadjusted odds ratios (95% CIs)					Odds ratios (95% CIs) adjusted for age	
		Age, y*			Gender†	Literacy‡	Gender†	Literacy‡
		65–74	75–84	85+				
CDR $\geq$ 0.5	Overall dementia	2.8 (1.1–7.4)	6.9 (2.5–19.0)	43.8 (16.4–117.2)	0.7 (0.4–1.2)	0.7 (0.3–1.5)	0.9 (0.5–1.6)	0.8 (0.4–1.8)
	AD	4.1 (1.1–14.8)	8.2 (2.0–32.8)	87.7 (24.7–311.8)	0.6 (0.3–1.2)	0.4 (0.1–1.1)	0.8 (0.4–1.7)	0.5 (0.2–1.3)
CDR $\geq$ 1.0	Overall dementia	2.7 (0.9–7.7)	6.6 (2.1–20.2)	48.1 (16.7–138.8)	0.7 (0.4–1.4)	0.8 (0.4–1.7)	1.0 (0.5–1.9)	0.9 (0.4–2.0)
	AD	4.3 (0.9–20.5)	8.2 (1.5–44.7)	120.5 (26.7–544.2)	0.6 (0.3–1.4)	0.4 (0.1–1.3)	0.9 (0.4–2.1)	0.4 (0.1–1.5)

\* Each age group is compared with the reference (youngest) age group, 55–64 years.

† Women compared with men.

‡ Literate subjects (can read and write) compared with illiterate subjects.

prevalence of both AD and of overall dementia increased with age in Ballabgarh; however, we did not find associations with either gender or literacy. It should be recognized that we selected an age cutoff of 55+ years, rather than 60+ or 65+ years as is usually the case for studies of dementia prevalence, because of the lower average life expectancy of the population. Because approximately half of our study population was younger than 65 years of age, we have reported prevalence rates both for the 55+ group and for the 65+ group.

Previous clinical and pathologic studies of dementia in India suggest that AD is rare or unrecognized in most clinical populations. Shankar et al.,<sup>24</sup> from the National Institute of Mental Health and Neurosciences in Bangalore in southern India, reported the first autopsy-confirmed case of AD from India in a man with disease onset at age 73 and no family history of dementia. This article also noted that although there was a general belief that AD was rare in the Indian subcontinent, this impression might have resulted from a lack of objective evaluation and autopsy confirmation. From the same institution, Satishchandra et al.<sup>25</sup> reported a histologically confirmed familial case of AD in a woman with onset at age 47. Barodawala and Ghadi<sup>26</sup> noted that typical AD pathology was present but rare in an autopsy series of 100 patients age 60+ years from Bombay, acknowledging that the sample was small and biased. In a review of literature on dementing disorders in India, Wadia<sup>27</sup> noted that there were few systematic studies of adequate size and representation to provide good estimates of prevalence in India. However, he observed that in the Zoroastrian community (primarily in Bombay), where average survival had reached the eighth decade of life, AD had become quite frequent. Thus the clinical literature seems to suggest that regional and ethnic differences in prevalence are found within India.

As expected, the prevalence rates found in our study in Ballabgarh in northern India are considerably lower than those reported from the MoVIES Project<sup>28</sup> using comparable methodology, and other Western countries.<sup>1</sup> However, comparisons should also be made with other epidemiologic studies reported from India. Previous dementia prevalence studies were conducted in the two southern states of Tamilnadu<sup>29,30</sup> and Kerala.<sup>31</sup> Two of these studies were conducted in rural areas,<sup>30,31</sup> and one was conducted in an urban area.<sup>29</sup> All three southern studies reported higher total and age-specific prevalence rates than those found in Ballabgarh. Overall dementia prevalence was 2.7% in the urban Madras sample,<sup>29</sup> which was 53.5% illiterate; 3.5% in the rural Thiruporur sample,<sup>30</sup> which was 91.2% illiterate; and 3.4% in the rural Thiruvaniyoor sample.<sup>31</sup> Literacy rates were not reported from the latter community, but it is located in the state of Kerala, which is known to have the highest literacy rates and life expectancy in the country. In sharp contrast, a prevalence study of major neurologic disorders in the far

northern Indian state of Kashmir<sup>32</sup> found no subjects with AD; however, 42% of the population of that region was younger than 14 years, and the Kashmir survey<sup>32</sup> only included 31 subjects age 60+ years.

All these studies were based on stratified random or cluster samples from the target population, whereas we surveyed the entire population age 55+ years in our target area. The other studies were conducted on smaller samples than ours, used age cutoffs of 60 or 65 years, and did not use cognitive screening instruments specifically designed for illiterate populations. They reported overall and age-specific prevalence rates, as we have done, but did not provide CIs. Thus, differences between our prevalence rates and those of other studies in India may partly reflect methodological differences and may partly be a function of true regional differences. India is an ethnically heterogeneous country with marked regional differences in physiognomy, culture, language, education, diet, health practices, life expectancy, and possibly risk gene frequencies. It would be entirely plausible to find interregional variations in the distribution of both disease and risk factors. Multicenter surveys with comparable methodology within India are needed to determine the nature and extent of regional variation, and prospective studies are needed to help determine the risk or protective factors that may underlie differences in disease distribution.

Other prevalence studies in developing countries and nonindustrialized societies included an urban study in Ibadan, Nigeria<sup>33</sup>; a study of native Canadians (Cree) on a reservation in Manitoba, Canada<sup>34</sup>; and an urban study in Shanghai, China.<sup>35</sup> In the Nigerian study, age-adjusted prevalence rates of both dementia and AD were lower than that seen in blacks in their reference US population in Indianapolis, IN.<sup>33</sup> The Cree study<sup>34</sup> also found low rates compared with white Canadians in the same Canadian province, but both Cree and Nigerian prevalence rates were higher than the Ballabgarh rates. It should be noted that both the Nigerian and the Cree prevalence rates were based on relatively small numbers of subjects, as were ours. By contrast, the Shanghai study found rates comparable with those of Western studies, based on a large sample and a substantial number of subjects.<sup>35</sup>

Overall and age-specific prevalence rates for dementia and AD in Ballabgarh appear to be the lowest reported in the world literature thus far. Potential explanations for this are discussed next.

**False negatives.** We first considered the possibility that we "missed" patients with dementia because our screening and diagnostic methods were insufficiently sensitive. This possibility seems unlikely because we used the distributions of cognitive and functional scores in the same population to develop the instruments and cut points, and also because none of the identified demented subjects (except for the one who had a stroke subsequent to screening) were found in the screen-negative category. Further-

more, information from the families of those who refused or were unavailable for detailed clinical evaluation did not suggest that these subjects were demented. Standardized diagnostic evaluation was carried out by a neurologist (V.C.) with considerable experience in both the United States and India, and who sees a large number of demented patients in his urban practice in New Delhi, the metropolitan area closest to Ballabgarh. Because all subjects lived with their extended families, it is likely that cognitive and functional deficits would have been noticed by a household member. However, potential functional impairment may have been missed because the lifestyles of these rural elderly illiterate subjects do not require them to perform instrumental ADLs comparable with those in Western industrialized societies or even urban Indian society. Finally, respect for the elderly and misattribution of mild impairment to "normal aging" may also have contributed to underreporting by family members. It remains possible that some subjects with incipient or early dementia had not yet crossed the threshold into impairment that would be recognized by themselves or their families, who therefore denied any disability. These subjects would be expected to continue to decline over time and should therefore be detected during the follow-up phase of the study, which is in progress.

Because we screened subjects using cognitive tests developed specifically not to require literacy, we were perhaps less likely than other groups to have overestimated the prevalence of cognitive impairment because of confounding by education and literacy (i.e., we may have had fewer false positives than other studies). Finally, given the cooperation of the population and the low screening refusal rate in our total population survey, it appears reasonable to state that our sample would be affected little, if at all, by response or selection bias.

*Low life expectancy.* Average life expectancy in India is lower than in the West, just as the less socioeconomically developed regions of India have shorter average life expectancies than others. If fewer subjects live into the age of risk, overall incidence (and therefore overall prevalence) will be lower than in areas with longer life expectancy. Selective survival of those not at risk for dementia might further compound such a trend. These hypotheses can only be explored through prospective study.

*Shorter survival with duration of disease.* Prevalence is a function not just of incidence but also of duration or survival with the disease. In a region or society where demented individuals do not live very long with their disease, prevalence will be low even if incidence is not. Although the survival estimates in our survey are also low compared with current Western clinical experience, it should be noted that they are based on estimates of onset as reported by the family, and may be underestimates if the manifestations of dementia were detected late or were attributed, in earlier stages, to normal aging. The number of deceased demented subjects is too small to war-

rant further survival analysis at this stage; additional follow-up of the population may help to clarify this issue. However, knowledge of the area and the community allows us to speculate about potential reasons for shortened survival with dementia. One possibility is that there is a particularly rapid and malignant form of dementia and AD in this area, but the clinical characteristics of these subjects did not appear atypical. Another possibility is some degree of benign neglect and fatalism. Families care for these patients at home in a nurturing environment, but have neither the means nor the inclination to provide technologically advanced medical care or life support. Because the traditional attitude toward the elderly is one of respect, family members will not force medical care or even food on an older relative who takes to his or her bed and refuses to eat. Declines in interest and functioning with age are perceived as normal and acceptable, and death as inevitable. All these factors may serve to shorten the duration of disease, and thus lower prevalence of disease, in this population.

*Low age-specific incidence.* Finally, it is possible that age-specific incidence is low in this population because of the presence of underlying protective factors, or the absence of underlying risk factors, compared with other populations. Again, prospective follow-up of a disease-free cohort is required to determine age-specific incidence rates, and also to identify the presence of such risk or protective factors. Genotyping of the Ballabgarh cohort, which is underway, may reveal the underlying distribution of known risk genes for AD (such as the  $\epsilon 4$  allele of the apolipoprotein E gene) to be different from those reported from other populations, including the MoVIES cohort. Other environmental risk or protective factors, or gene-environment interactions, in the Indian population may be related to diet, comorbid chronic or infectious diseases, and so forth, as we have hypothesized before.<sup>7,36,37</sup> Given the current interest in education as a protective factor against AD,<sup>35</sup> it might have been expected that prevalence of dementia or AD would have been high in this largely illiterate population, but we did not find this to be the case. Comparison of prevalence and risk factor distributions among different regions, and among different socioeconomic strata within India and other countries, may help to shed more light on this issue.

*Implications.* Our finding of low dementia and AD prevalence in a rural northern Indian population is of interest primarily because it suggests a variety of explanations with different implications, as outlined earlier. It is clear that there are regional differences in prevalence within India. It remains to be determined whether these differences are a function of differential incidence, differential survival, or both. If prospective studies show age-specific incidence to be different across populations, this finding will promote the search for new risk and protective factors. If the main explanation is revealed to be differential overall life expectancy or differential sur-

vival with dementia, the implication will be that, as average life expectancy and standards of living improve, the societal and public health burden of dementia will increase concomitantly.

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