Trends in Alzheimer’s Disease and Dementia in the Asian-Pacific Region

Guest Editors: Neelum T. Aggarwal, Manjari Tripathi, Hiroko H. Dodge, Suvarna Alladi, and Kaarin J. Anstey
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Editorial
Trends in Alzheimer’s Disease and Dementia in the Asian-Pacific Region

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1. Introduction

Dementia is an age associated illness with a devastating impact on patients and their families. In the USA, the broader society impact of dementia continues to be overwhelming, due largely to the huge health care and economic burden associated with the disease. Although the projected numbers of those affected, the economic, healthcare, and caregiver costs continue to have a place in US public policy, it is only recently that these issues are beginning to take a center stage in other regions in the world with their aging populations. It has been estimated that 35.6 million people are living with dementia worldwide—a number that is projected to increase to 65.7 million by 2030 and 115.4 million by 2050.

Approximately, 60% of the world’s population lives in the Asian Pacific region—a home to many different ethnic groups. This issue of the International Journal of Alzheimer’s Disease is dedicated to dementia in the Asian and Pacific region and discusses from an Asian-Pacific perspective common themes often noted in the literature from Europe and North America. Themes discussed in this special issue include (1) the prevalence and incidence rates of dementia in Asian countries, (2) the role of biological and genetic risk factors to the development of dementia, (3) characterization of dementia in culturally diverse populations, and (4) activities of daily living functioning and its relation to cognitive functioning.

In this issue, two studies examined the prevalence, incidence, and mortality rates of dementia. H. H. Dodge et al. examined changes in dementia prevalence and the relative prevalence of AD compared to VaD over time using eight large Japanese prevalence studies. Unlike past studies on this topic, the authors thoroughly examined diagnostic criteria used in each study (through contacting original investigators of the most studies), changing age structures as well as regional variability as possible explanations of trends in overall prevalence and ratios of AD to VaD. The study suggests that, in contrast to the USA and some European countries, all-cause dementia prevalence is increasing in Japan. It was inconclusive whether the prevalence of AD as opposed to VaD has been increasing or not, because of variability in diagnostic criteria, regional variability, and gender difference in vascular disease prevalence. This study illustrates the complexity of evaluating prevalence rates of dementia and how knowledge of population trends in risk factors and diagnostic methods influences the interpretation of data. In addition, the authors offer useful suggestions for future epidemiological work on dementia prevalence and incidence in Japan which may be applied to other countries.

In another article, the prevalence rates and mortality of dementia was examined in elderly persons living in Hong Kong. This study suggests that within 30 years the number of people in Hong Kong aged 60 and older will be more than triple; thus, the increase of prevalence of dementia cases in this region will prove to be substantial. The authors also
discuss two other important issues related to care for those with dementia: (1) the impact of a declining "oldest old support ratio" and (2) the burden of dementia as measured by the Disability Adjusted Life Years (DALYs) approach. The authors postulate that by using these two metrics, in addition to data regarding the ongoing trends in the region, a successfully long-term care strategy for dementia of the aging population in Hong Kong can be achieved.

2. The Role of Biological and Genetic Risk Factors to Dementia

The article by L. N. Kota et al. examined the role of diabetes, APOE e4 carrier state to dementia in a cohort of elderly persons in Southern India. In India, the latest data suggest that the prevalence of dementia cases, predominantly that of Alzheimer's disease (AD), is estimated to increase from 3.7 million people to 6.35 million people by 2025. This staggering increase is accompanied by an ongoing pandemic rise of diabetes in Indians, with current estimates at 40.9 million persons affected. How these two factors are associated with genetic risk factors, namely, APOEe4 carrier status was the focus of this article. Two important findings were presented in this article: (1) the APOE e4 allele appears to be associated with AD in this population—thus replicating findings from previous studies in this population and (2) persons with AD who have diabetes were more likely to be APOE e4 positive compared to those with normal cognition. The authors conclude that although more work needs to be done in this area, lifestyle modification to prevent diabetes, thereby perhaps slowing the prevalence rate of dementia and AD, should be a major focus on public health initiatives in this region.

3. Characterizing Dementia in Culturally Diverse Populations

The article by G. Nair et al. provides valuable insights into the characteristics of a memory clinic within a public hospital in India, a country that is expected to have more than 150 million older adults by 2025. The authors describe the challenges of establishing a clinical research based facility that provides services for patients with significant linguistic and cultural diversity. This article provides invaluable information on the methods used to establish research facilities in a developing country and documents the practical aspects such as staff training, outreach, and consensus diagnosis. The memory clinic has implemented the National Alzheimer's Coordinating Center (NACC) standardized Uniform Data Set (UDS) evaluation and will provide an invaluable resource for research, both within India and internationally. Although the sample is not representative, presentation of some descriptive data on the rates of diagnosis and demographic characteristics of diagnostic groups shows that dementia diagnosis, particularly Alzheimer's disease, is occurring at relative young ages in this community. Such information over time may provide important insights into culturally specific risk factors.

A second article examined another area of focus in cognitive research in diverse populations—the development and utilization of linguistically and culturally validated, cognitive screening tests. L. Zheng et al. developed a Chinese version of the Montreal Cognitive Assessment (MOCA)—the MOCA-Chinese Los Angeles (MOCA-ChLA)—that can be used with Cantonese or Mandarin speakers. The MOCA was carefully translated and culturally adapted for use in the two languages (as well as in Taiwanese) and administered to over 1,000 ethnic Chinese elderly residing in the Los Angeles area who were taking part in a population-based Chinese-American Eye Study (CHES). The MOCA-ChLA was found to be free of floor and ceiling effects, scores were not influenced by gender, and Mandarin and Cantonese speaking subgroups performed similarly. As the authors noted, further studies are warranted to determine cutpoints for optimal sensitivity, specificity for the diagnosis of MCI and dementia, and refine adjustment scores for individuals with low education; so that the MOCA-ChLA can be used for a screening tool for identifying MCI and dementia in other communities.

4. Activities of Daily Living and Dementia

As dementia becomes more prominent in both Eastern and Western cultures, it is well known that maintaining activities of daily living (ADL) becomes a major focus for care. Past studies have shown that person-centered care, where care is targeted to encourage, support, and maintain patients' hobbies and leisure activities (in addition to supporting medical and basic IADL needs), improves the quality of life (QOL) of patients and reduces behavioral psychological symptoms of dementia (BPSD). Yet, maintaining patients' advanced activities of daily living (AADL: e.g., participation in meetings, socializing with others, taking a walk, reading a newspaper, watching TV, etc.) and leisure activities (e.g., travelling, care of a pet, gardening, etc.) is often ignored in public social services. H. Takechi et al. examined types, frequency, and support needs on AADL and leisure activities by interviewing 39 pairs of early-to-mid stage dementia patients and their family caregivers. This was a time-consuming study because a large variability in patients' leisure activities required in-depth interviews with patients and caregivers, using open-ended questions for some categories. Despite the difficulty, the authors were able to outline potential domains and types of cares required for person-centered care. This type of study provides support for more studies in this area, as it can lead to a better quality of life for those affected by dementia and also their caregivers.

5. Summary

In this special issue, we highlight several important themes emerging from the Asia-Pacific region as they relate to dementia research. The encompassing message is that this region, with its rapidly growing population of persons with dementia, will place a heavy societal and economic burden to all countries in the region. Studies on the possible inter-ethnic differences in prevalence and incidence of dementia,
risk factors and protective factors, and treatment for inter-
vention strategies need to be employed on an international
level.

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Research Article

Trends in Prevalence and Mortality of Dementia in Elderly Hong Kong Population: Projections, Disease Burden, and Implications for Long-Term Care

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Background. We describe the trends in prevalence and mortality of dementia among older people in Hong Kong over time. Projections of the number of older people with dementia through 2039 and estimation of the disease burden are also included.

Methods. Prevalence data were extracted from previous studies in Hong Kong. Mortality data were obtained from the Department of Health of Hong Kong. Projections of the number of people with dementia were calculated by applying the prevalence rates of dementia obtained from previous studies to Hong Kong population projections. The burden of dementia was measured by Disability-Adjusted Life Years (DALYs).

Results. The number of people aged 60 and above with dementia is projected to increase by 222%, from 103,433 in 2009 to 332,688 in 2039, with a large proportion of those living in institutions. The number of deaths due to dementia among people aged 60 and above has more than doubled between 2001 and 2009. Mortality rates for dementia have also risen. In 2006, about 286,313 DALYS were lost due to dementia.

Conclusions. The information presented may be used to formulate a long-term care strategy for dementia of the ageing population in Hong Kong.

1. Introduction

With population ageing all over the world, the impact of dementia is set to accelerate in the coming years [1], in that it is a chronic disease and is one of the major contributors to disability and increases the burdens to caregivers as well as health and social care systems. In Hong Kong special administrative region (Hong Kong), the population is also ageing rapidly, such that the population aged 60 and above nearly doubled during the past two decades, from 531,600 (10.3%) in 1981 to 1,351,000 (19.2%) in 2011 [2]. It is projected that in 2039, there will be nearly three million people aged 60 and above in Hong Kong [3]. Life expectancy at birth in Hong Kong has also been on the rise for two decades, from 72.3 years for men and 78.5 years for women in 1981 to 80.5 years and 86.7 years in 2011 respectively [4].

It is well known that dementia becomes more prevalent with increasing age; hence, the prevalence of dementia is expected to increase significantly, with substantially increasing disability burden and costs of long-term health and social care. Informal caregivers would need to be an integral part of care since the “oldest old support ratio” (ratio of people aged 50–74 years to people aged 85 years and above) has been decreasing as evidenced in the past two decades due to population ageing [5]. The decreasing ratio implies each informal caregiver is caring for more people aged 85 years and above. Given the expanding population with dementia and the shrinking pool of informal caregivers, a question of how to maintain continual care for such patients arises. Comprehensive long-term care for dementia requires accurate and updated information about trends and burden of the disease. In Hong Kong, a number
of studies have investigated the prevalence of dementia [6–8]. However, it remains unclear whether the prevalence of dementia has increased, decreased, or remained stable over time. Furthermore, very few studies examined trends in mortality from dementia in Hong Kong, although it is among the top ten leading causes of death.

In this study we presented trends in prevalence and mortality of dementia among people aged 60 years and above in Hong Kong over a number of years. We projected the number of older people three decades later, as well as estimated the burden of dementia using Disability-Adjusted Life Years (DALYs). We also described the impact of dementia on an ageing population and made recommendations on the health and social care systems for improving long-term care.

2. Data

Previous trends in the percentage of older people with dementia were sourced from a series of three household surveys conducted by Census and Statistics Department of Hong Kong in 2000 [9], 2004 [10], and 2008 [11] and from two community studies conducted by Chiu et al. in 1995 [6] and by Lam et al. in 2005/2006 [7, 8]. The latest available estimates of the percentage of older people with dementia, that is, those obtained from the Census and Statistics Department of Hong Kong in 2008 [11] and from the Lam et al. study in 2005/06 [7, 8], were used for the prevalence projection.

The International Classification of Diseases (ICD) code was used for classifying mortality from dementia in Hong Kong. From 2001, deaths due to dementia were identified by the 10th revision of the ICD codes (ICD-10) F01, F03, G30, and G31. Before 2001, deaths due to dementia were identified by the 9th revision of the ICD codes (ICD-9). However, many deaths due to dementia were not coded accordingly in the ICD-9 system [12]. Hence, we studied all deaths due to dementia that occurred in Hong Kong from 2001 and onwards. Annual data on the deaths due to dementia by age and sex between 2001 and 2009 were obtained from the Department of Health of Hong Kong [13]. The mid-year population estimates between 2001 and 2009 and population projections for the Hong Kong population in 2039 were obtained from the Census and Statistics Department of Hong Kong [2, 3].

3. Method

Age-sex-specific number of people with dementia was estimated for community and institutional populations separately. The total numbers of people with dementia in the community and in institutions in Hong Kong in 2009 and 2039 were estimated by multiplying the age-sex-specific percentage of older people with clinically diagnosed dementia obtained from the Lam et al. study in 2005/06 [7, 8] to the Hong Kong population living in the community; and the percentage of older people with respondent-reported dementia obtained from the Census and Statistics Department of Hong Kong in 2008 [11] to the Hong Kong institutional population. To obtain the population living in the community and institutional population, the proportions of the respective population in Hong Kong were assumed to be constant as those in 2008 [11] and applied to the mid-year population in 2009 and the projected population in 2039 [3]. To assess the trends in mortality, age-adjusted dementia mortality rates were calculated for both sexes. Mortality rates were standardised using the direct method to the Hong Kong population as of mid-2009 as the standard [2].

The burden of dementia for people aged 60 or above in the year 2006 was assessed with the DALYs, a summary measure of the burden from premature mortality in terms of years of life lost (YLLs) and the burden from morbidity in terms of years lost due to disability (YLDs). YLLs were calculated based on the age at which the person dies and the life expectancy for people of that age (as determined by a life table) [14]. YLDs from dementia were calculated by multiplying the number of people with dementia in Hong Kong by the disability weight that applies to them. It is assumed that all people with dementia in 2006 experienced their condition for the entire year. Based on the Dutch weights from the Global Burden of Disease study of WHO [15], disability weights for mild, moderate, and severe dementia were 0.27, 0.63, and 0.94, respectively. Because disability weights for dementia were defined for different levels of severity of dementia, we calculated the average disability weight for the estimation of YLDs. Based on a local study conducted by Chiu et al. [6] the proportions of mild, moderate, and severe dementia were 65.6%, 25.0%, and 9.4%, respectively. Therefore, combined with the disability weights listed above, the average disability weight for dementia was calculated by multiplying the proportion of mild, moderate, and severe dementia with the corresponding disability weight, hence giving an average of 0.42. The YLDs due to dementia was thus calculated by multiplying the number of people with dementia by the disability weight and the life span with dementia.

4. Results

4.1. Trends in Prevalence Rates of Dementia. According to respondent-reported data, the percentage of community-dwelling people aged 60 and above in Hong Kong with dementia increased from 0.6% in 2000 [9] to 1.1% in 2004 [10], and remained stable until 2008 (1.1%) [11]. The percentage of community-dwelling people aged 70 and above with clinically diagnosed dementia also increased from 4.5% in 1995 [6] to 9.3% in 2005-2006 [7, 8]. The percentage of people with clinically diagnosed dementia increased with age and approximately doubled for every five years until around age 90. It was also observed that a higher percentage of females have dementia than males at older ages.

The percentage of people living in institutions with dementia was higher than that people living in the community, with 30.7% of institutionalized people aged 60 and above reported (by proxy respondents) having dementia in 2004 [10] and 2008 [11] and 17.4% aged 70 and above were found to have clinically diagnosed dementia in 1995 [6]. Owing to the limited data, it was unable to test for the trends statistically. However, the estimates suggested a probable increasing trend in prevalence.
4.2. Estimated and Projected Prevalence of Dementia. Having applied the age-sex-specific percentage of older people with dementia to the Hong Kong population, an estimated 85,012 people aged 60 and above living in the community had dementia in 2009 of whom over 30% were aged 85 and above. This number is projected to increase to 271,320 people in 2039 (Figure 1). For the institutional population, an estimated 18,421 people aged 60 and above were living with dementia in 2009. By 2039, this is projected at 61,367 people (Figure 2). Combining the community and institutional populations, the estimated number of people aged 60 and above with dementia would increase from 103,433 in 2009 to 332,688 in 2039, an increase of 222%.

4.3. Trends in Mortality Rates of Dementia. Deaths due to dementia among the people aged 60 and above had more than doubled over the past 9 years, accounting for 2% of all deaths in 2009 compared to 1% of all deaths in 2001. The age-standardized mortality rate among people aged 60 and above remained stable between 2001 and 2007, but increased sharply in 2008 and 2009 (Figure 3). The rates between 2001 and 2009 increased by 103% for males (from 23.3 per 100,000 to 47.3 per 100,000) and 36% for females (from 45.6 per 100,000 to 62.0 per 100,000). The mortality rates increased exponentially with age. In 2009, while males aged 60 to 84 had a higher age-specific mortality rate from dementia than their female counterparts, the reverse was observed for those aged 85 and above.

4.4. Estimated DALYs Lost due to Dementia. The DALYs lost due to dementia for people aged 60 or above in 2006 was 286,313. The majority of burden was due to disability, with YLDs making up 99% of DALYs. The remaining 1% of the burden was due to the YLLs from dementia. The burden of disease from dementia is disproportionately carried by women. While the burden for males was 83,051 DALYs (29% of total), the female burden was 203,262 DALYs (71% in total). Males experienced 839 YLLs and 82,212 YLDs, while females experienced 1,148 YLLs and 202,114 YLDs.

5. Discussion

Several population-based observational studies have reported secular trends in the prevalence of dementia worldwide. However, trends in dementia prevalence vary markedly from
one study to another [16–20], and there have been few data on the trends in prevalence of dementia in Hong Kong. Based on existing local studies, an increasing trend in the percentage of people with dementia was observed in Hong Kong. We also projected that within 30 years, the number of people aged 60 and above with dementia will more than triple, from 103,433 people in 2009 to 332,688 people in 2039. Recent data from the Rotterdam Study revealed that the incidence of dementia is declining, perhaps because of preventive measures and better control and treatment of vascular risk factors [21] and therefore the prevalence of dementia may increase more slowly than expected. However, an increasing trend was observed for the prevalence of hypertension in Hong Kong over the past years, especially in the middle-aged group [22, 23] which may probably lead to an increasing trend in prevalence of vascular dementia in the future. The increasing burden indicates the challenges ahead and more should be done to improve the long-term care for people with dementia and their caregivers.

The increasing prevalence of dementia suggests the need for urgent plans for better long-term institutional care system with dementia-specific services. In Hong Kong, most of the institutions are not geared to meeting the distinct needs of people with dementia and therefore access of people with dementia and their caregivers to adequate services is limited. Quality of care, autonomy, and dignity of institutional care are also important issues that need to be addressed. Periodic reports in the media in the past have emphasized undesirable behavior leading to abuse. The quality of care depends on a large extent on adequate staff numbers [24]. However, there is not sufficient number of staff to meet many of the residents’ needs in Hong Kong and it is recognized that there is a tension between quality and affordability, which is unlikely to be resolved until the financing of long-term care is addressed. There is also a shortage of well-trained staff. Heath care professionals in institutional care were generally inadequately trained in dementia needs. Up to standard training must be developed for all these people to cater for a more effective and high-quality care for people with dementia. The lack of staff continuity is another issue that needs to be resolved. With the increasing prevalence of dementia, more well-trained professionals would be required. Career development, promotion opportunity, training, and recognition should be provided to encourage more new professionals.

There also needs to be an improvement in the end-of-life care for people with dementia. However, palliative and hospice care services are not particularly well developed in Hong Kong, with few comprehensive services provided in hospital settings. A survey in a nonacute hospital in Hong Kong revealed that those with dementia tend to have more nonpalliative interventions compared to patients with cancer [25] as had been noted in a previous study of nursing home residents in the United States [26]. It has been pointed out that palliative and hospice care could greatly improve the care of patients with advanced dementia resulting in better quality of life, greater caregiver satisfaction, and at the same time, reducing hospitalisation [27]. Therefore, there is a need to raise awareness to improve the quality of care for such patients. Recently, a continuous quality improvement initiative aimed at improving the quality of end-of-life care for noncancer patients had been developed and integrated into part of the care plan in a nonacute hospital in Hong Kong [28]. Evaluation of its impact on patients and their caregivers is warranted.

Informal caregivers will also remain a core part of the long-term care for dementia. However, being an informal caregiver can be detrimental to both the physical and psychological health as well as health-related quality of life [29, 30]. Therefore, both practical and psychological support for caregivers of dementia patients would need to be improved. Support and counselling services should be provided from the moment of diagnosis as the financial and emotional impact on people with dementia and their families can be enormous. It has been recognized that enhanced counselling and support treatment may reduce caregivers’ depression [31]. Collaborative care management including education on communication and coping skills, legal and financial advice, patient exercise guidelines, and caregiver guide has also been shown to improve the quality of care and behavioural and psychological symptoms of dementia for both people with dementia and their caregivers [32].

Standardized to the World Health Organization population, the age-adjusted mortality rate for dementia of all ages in Hong Kong in 2008 (3.5 per 100,000 population) was lower than the corresponding rates in the United States (24.8 per 100,000 population), the United Kingdom (17.1 per 100,000 population), and Australia (15.3 per 100,000 population), comparable to China (3.2 per 100,000 population), but higher than Japan (2.5 per 100,000 population) and Singapore (0.02 per 100,000 population) [33]. The increasing trend in age-adjusted dementia mortality rates in Hong Kong since 2007 may be attributed to several factors, including increasing awareness, increased diagnosis, and population ageing. Sharp increase has also been observed in Australia since 2006 [34] where some deaths that were previously coded as cerebrovascular disease were coded as vascular dementia due to change in coding instructions. This change may be explained by the increased awareness of dementia. Perhaps this phenomenon occurred in Hong Kong with some time lag.

The increased mortality rates highlight the importance of early detection and cognitive assessment of the disease. Currently diagnosis tends to be made at a later stage of the disease, with up to 90% of people with mild dementia never receiving a diagnosis. To encourage early detection, competencies of early diagnosis of dementia should be developed and cognitive function should be a regular feature of health assessment for the elderly in primary care. The findings of this study also suggest that dementia is a leading cause of disability in older people in Hong Kong and the burden associated with it is substantial, as with China and other countries [35]. Nevertheless, limited awareness of dementia and/or denial of its existence, and stigma attached to the condition, may lead to excess disability. Therefore public education and training of health-care professionals and caregivers are needed in raising awareness of the disease and its management.
There are limitations in this study. The data in this study were compiled from different sources, some studies reporting rates for Alzheimer’s disease while others reported other forms of dementia. Therefore we have presented the trends for all these categories combined. Trends for the subtypes of dementia could not be investigated. There is a possibility of diagnosis being affected by change in awareness of the disease, such that increasing awareness may partly account for the increasing trend in prevalence. Like other self-reported data, respondent-reported data are subject to reporting error. Nevertheless, it is a commonly used method in household surveys. As for the projections, we used constant age-sex-specific prevalence rates of clinically diagnosed dementia for the projections which reflect the impact of demographic ageing alone. However, percentage of people with dementia appears to have increased and therefore the number of people with dementia is expected to increase even faster. There may be some underreporting of dementia as a cause of death, with many deaths incorrectly attributed to pneumonia or other causes. To tackle this, the attributable risk methodology could be adopted. However, the relative risk of death established by Mathers and Leonardi in 2003 [36] may not apply to the recent deaths with the sharp increase of mortality coded as dementia since 2008. Therefore, mortality statistics need to be interpreted with caution. Finally, we did not have information regarding factors that contributed to trends in the prevalence and mortality of dementia. Efforts need to be made to monitor the secular trends of various predisposing risk factors.

In conclusion, dementia is a significant health and social problem in Hong Kong. The increasing trends in prevalence and mortality of dementia and its high-disability burden have an enormous impact on the health care and social services systems. Therefore the formulation of a dementia care strategy as part of a long-term care strategy for the elderly would be important for Hong Kong.

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Review Article

Trends in the Prevalence of Dementia in Japan

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There is a paucity of data regarding trends in dementia and its subtype prevalence in Japan. Our aims in the current paper are to: (1) summarize epidemiological studies of dementia in Japan including relevant details of study protocol and diagnostic criteria, (2) compare the age-specific prevalence of all-cause dementia among studies, and (3) assess the trends in Alzheimer’s disease (AD) versus vascular dementia (VaD) over time. We reviewed diagnostic criteria, all-cause dementia prevalence, and the AD/VaD ratio from 8 large population studies of dementia in Japan. Compared with the Okinawa 1992 study, studies conducted in 1994, 1998, 2005, and 2008 had a higher prevalence of all-cause dementia using Poisson regression models, after controlling for age and sex. In contrast to the US and some European countries, all-cause dementia prevalence is increasing in Japan. The prevalence of AD as opposed to VaD seems to be increasing over time, but large variability in diagnostic criteria, possible regional variability, and differences in prevalence of subtypes of dementia between men and women make it difficult to draw a conclusion about this trend at the national level. Further studies, for example, comparing the population attributable risk of vascular diseases to the prevalence and incidence of dementia could help to clarify the regional variations in etiological subtypes.

1. Introduction

It has been reported that the prevalence and incidence of dementia in the United States have been either stable or even declining over the last 2 decades of the 1990s [1]. An important question is what the dementia trends are in other countries. This question is particularly relevant to the case of Japan which is an economically advanced country like the US, but is believed to have a different level of vascular disease risk [2]. Studies conducted in the late 1980s and early 1990s reported that vascular dementia (VaD) was more prevalent than Alzheimer’s disease (AD) in Japan, compared with the US and other western countries where AD is more prevalent than VaD [3]. In studies among Japanese Americans conducted in the early 1990s [4, 5], the prevalence ratio of AD to VaD was higher than that reported among Japanese in Japan and more closely resembled that found in the Caucasian population. This suggests that there might have been environmental factors that changed the risks of developing subtypes of dementia after Japanese immigrated to the US. On the other hand, more recent studies conducted in the late 1990s suggest that the cross-national differences found in the past may have been due to differences in the diagnostic methods used [6, 7]. Standardization of diagnosis is one of the challenges of cross-national comparisons of dementia prevalence. There is an ongoing debate as to whether: (1) the higher proportion of VaD found in the past studies in Japan could be due to differences in diagnostic criteria used in Japan and the US, (2) the similar AD/VaD ratio with that of the US found in recent Japanese studies.
could be due to decreased cerebrovascular disease incidence over the past decades in Japan, or (3) there is no systematic time trend in AD/VaD ratio in Japan and the observed variation is due to regional differences within Japan. Despite a growing interest in the influence of vascular disease and its risk factors on Alzheimer’s disease (AD) [8–12], there is a paucity of data regarding dementia prevalence trends in Japan. Our aims in the current study are to: (1) summarize epidemiological studies of dementia in Japan including relevant details of study protocols and diagnostic criteria, (2) compare age-specific prevalence of all-cause dementia among studies, and (3) assess the trends in AD versus VaD over time. Previous studies which concluded an increase in dementia prevalence were targeted for the dementia prevalence study [6, 20].

2. Methods

2.1. Study Design and Sample. We selected dementia prevalence studies in Japan that were designed to be representative of specific communities or prefectures with at least 500 study participants aged 65 and older, and whose age-specific prevalence for either 5- or 10-year age intervals for AD and VaD was published between 1990 and 2009 in international journals, using MEDLINE with the search words “Japan,” “dementia,” and “prevalence.” We used the former criterion (n ≥ 500) in order to have a large enough sample size to allow meaningful between-cohort comparisons of dementia prevalence. Eight studies met these criteria: the Hisayama study [16, 17] conducted at four time points, the Okinawa study [18], the Radiation Effect Research Foundation Adult Health Survey (RERF-AHS, a.k.a Hiroshima study) [7], the Tajiri Project [6], and the Ama-cho study [14]. Brief descriptions of each study cohort follow (See also Table 1 for further summary).

2.1.1. Hisayama Study. Hisayama is a rural community adjacent to the city of Fukuoka, a major city of Kyushu Island. An epidemiological study of stroke has been carried out prospectively there since 1961. Cross-sectional dementia prevalence was estimated 4 times, in 1985, 1992, 1998, and 2005 [16, 17].

2.1.2. Okinawa Study. Okinawa is the southernmost island in Japan. Random sampling was conducted to recruit study participants in the selected sites between 1991 and 1992 [18].

2.1.3. Radiation Effect Research Foundation Adult Health Survey (RERF-AHS) (Hiroshima Study). In 1958, the Atomic Bomb Casualty Commission began the Adult Health Study (AHS) to survey the occurrence of illnesses and changes in physiological and biochemical function resulting from exposure to atomic bomb radiation. The original AHS cohort consisted of atomic bomb survivors and their controls, selected from residents in Hiroshima and Nagasaki. Between 1992 and 1996, those aged 60 and older who were residents of Hiroshima and members of the AHS were examined [7].

2.1.4. Tajiri Project. The Tajiri project is a community-based study started in 1988 for the prevention of stroke, dementia, and bed-confinement in Tajiri, an agricultural area in northern Japan. In 1998, all residents 65 years and older were targeted for the dementia prevalence study [6, 20].

2.1.5. Ama-cho Study. This study was conducted in the municipality of Ama-cho, a rural island town in the northwestern part of Japan. All residents as of the prevalence day of March 1, 2008 were requested to participate in the dementia prevalence study [14].

2.2. Statistical Analysis. Differences in overall dementia prevalence among 8 studies were examined using Poisson regression models based on the number of dementia cases (weighted numbers of cases for Okinawa studies) and the number of participants by 10-year age groups (except the youngest age group where 5-year ages were used: 65–69, 70–79, 80–89, and 90+) to provide large enough sample sizes in each group for meaningful statistical comparisons, yet controlling for changing age composition over time. The Okinawa 1992 study sample was used as a reference group because it was the largest and was conducted at the mid-point of assessment years among the 8 studies.

3. Results

3.1. Diagnostic Criteria. Table 1 gives a brief description of each study and the criteria used to define dementia and dementia subtypes. All assessments, except in the Tajiri study, were based on multistage assessments, during which all participants were screened in Phase 1 (screening phase), and selected participants and controls from Phase 1 received final diagnoses from physicians in Phase 2 (clinical assessment phase). The Tajiri study determined dementia diagnoses for all participants. The dementia diagnostic criteria used in Japanese studies were either DSM-III [21], DSM-III-R [22], or DSM-IV [23]. The diagnostic criteria used to define subtypes of dementia varied among the studies in Japan. The following criteria were used to define VaD: Hachinski ischemic scores [24], NINDS-AIREN [25], DSM-IV [23], and the Alzheimer’s Disease Diagnostic and Treatment Centers (ADDTC) [26] criteria. For AD, DSM-III-R [22], DSM-IV [23], and NINCDS-ADRDA [27] were used.

3.2. Comparisons of Prevalence of Dementia among Studies. The overall prevalence of dementia among those aged 65 and older ranged from 5.6% (Hisayama 1992) to 11.3% (Ama-cho 2008) (Table 1). Poisson regression models for dementia prevalence showed that compared with the Okinawa 1992 study, Hiroshima 1996 (P = 0.0002), Tajiri 1998 (P < 0.0001), Hisayama 2005 (P < 0.0001), and Ama-cho 2008 (P = 0.007) had a higher prevalence of all-cause dementia, controlling for sex and age groups (Table 2). There were no differences between the Okinawa 1992 study and Hisayama studies conducted in 1985, 1992, and 1998. No difference was found between men and women.
| Study name/site (study years) | Sampling frame | Assessment protocol | Prevalence of all-cause dementia among those aged 65 and older: |
|------------------------------|----------------|---------------------|-------------------------------------------------------------|
|                              |                | Phase 1             | (1) Prevalence in percentage (95% CI)                      |
|                              |                | Phase 2             | (2) Number of cases (all subtypes combined/AD/VaD)         |
|                              |                |                     | (3) AD percentage out of all dementia                       |
|                              |                |                     | (4) AD/VaD ratio                                            |

**Hisayama (1985, 1992, 1998, and 2005)**

- Total residents aged ≥ 65 in the area:
  - Year 1985: \( N = 938 \)
  - Year 1992: \( N = 1231 \)
  - Year 1998: \( N = 1442 \)
  - Year 2005: \( N = 1711 \)
- Study participants at Phase 1 (participation rates):
  - Year 1985: \( N = 887 \) (94.6%)
  - Year 1992: \( N = 1189 \) (96.6%)
  - Year 1998: \( N = 1437 \) (99.7%)
  - Year 2005: \( N = 1566 \) (91.5%)
- Sampling weights used to reflect prevalence of population at large? (Yes/No): No

- Phase 1
  - Suspected dementia cases selected using Hasegawa dementia scale, neuropsychological tests, and ADL
- Year 1985
  - (1) 6.7 (5.0–8.3)
  - (2) 59/12/21
  - (3) 20.3%
  - (4) 0.57
- Year 1992
  - (1) 5.6 (4.4–7.1)
  - (2) 68/21/22
  - (3) 30.8%
  - (4) 0.95
- Year 1998
  - (1) 7.1 (5.7–8.5)
  - (2) 102/49/28
  - (3) 48.0%
  - (4) 1.96
- Year 2005
  - (1) 12.5 (10.7–14.2)
  - (2) 195/96/51
  - (3) 49.2%
  - (4) 1.89

**Okinawa (1991-1992)**

- Randomly sampled one city from the urban districts and one town/village from the rural districts from each of 5 regions covering the entire Okinawa prefecture. Randomly selected approximately 17% of the residents from the selected cities and towns/villages in each region.
- Pilot study was conducted \( (N = 789) \) to examine the best MMSE cut-point for screening. MMSE score of 16 had the maximum combination of sensitivity and specificity to identify the demented in the community.
- Selected those with MMSE ≤ 16 \( (N = 482) \)

- Phase 1
  - Pilot study was conducted \( (N = 789) \)
  - (1) 6.7 (3.6–7.8)
  - (2) 170/80/55
  - (3) 47.1%
  - (4) 1.51
| Study name/site (study years) | Sampling frame | Assessment protocol | Prevalence of all-cause dementia among those aged 65 and older: |
|------------------------------|----------------|---------------------|------------------------------------------------------------|
|                             |                |                     | (1) Prevalence in percentage (95% CI)                      |
|                             |                |                     | (2) Number of cases (all subtypes combined/AD/VaD)         |
|                             |                |                     | (3) AD percentage out of all dementia                      |
|                             |                |                     | (4) AD/VaD ratio                                           |

### Hiroshima (Radiation effect research foundation Adult Health Survey ((RERF-AHS)) (1992–1996)

- **Study participants at Phase 1:**
  - Phase 1: $N = 3524$
  - Sampling weights used to reflect prevalence of population at large? (Yes/No): Yes

- **Sampling frame**
  - Residents in Hiroshima among the Original AHA cohort (atomic bomb survivors in Hiroshima and Nagasaki and their controls followed since 1958) evaluated by biennial physical exams between 1992 and 1996. Targeted $N = 2934$

- **Assessment protocol**
  - Phase 2 ($N = 482$)
    - DSM-III-R for dementia, NINCDS-ADRDA for AD, and Hachinski’s ischemic score as a guideline for VaD

- **Prevalence**
  - (1) $8.5$ (7.2–9.8)
  - (2) $25.8$ (17.4–36.3)
  - (3) $47.4$
  - (4) $1.85$

### Tajiri Project (1998)

- **Study participants at Phase 1:**
  - Phase 1: $N = 2222$
  - Sampling weights used to reflect prevalence of population at large? (Yes/No): No

- **Sampling frame**
  - All residents in Tajiri town aged ≥ 65, targeted $N = 3207$
  - Study participants $N = 1654$
  - Subsample selected for dementia subtype identification study, targeted $N = 564$
  - Sampling weights used to reflect prevalence of population at large? (Yes/No): No

- **Assessment protocol**
  - All ($N = 1654$) were evaluated by CDR & DSM-IV (not multistage sampling)
    - MRI study: 564 selected randomly from 1654 above, of whom 497 participated in MRI study (dementia subtype identification study). Comparisons of prevalence of VaD using 3 different criteria: (1) DSM-IV for AD and VaD, (2) NINCDS-ADRDA for probable AD, NINDS-AIREN for possible AD with CVD and probable VaD; (3) ADDTC for probable ischemic vascular dementia

- **Prevalence**
  - (1) $8.5$ (7.2–9.9)
  - Based on subtype analysis with MRI
    - (I) Using NINCDS-ADRDA, NINDS-AIREN
      - (2) $3.2/0.6/0.6$
      - (3a) $62.5$
      - (4a) $3.33$
    - (II) Using DSM-IV for AD and VaD
      - (2a) $32/0.32/0.32$ (2b) $32/0.18/0.18$
      - (3a) $40.6$
      - (3b) $56.2$
      - (4a) $1.00$ (4b) $2.25$

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The difference between (a) and (b) above is due to diagnostic differences between assessors.
| Study name/site (study years) | Sampling frame | Assessment protocol | Prevalence of all-cause dementia among those aged 65 and older: |
|------------------------------|----------------|---------------------|-------------------------------------------------------------|
| Ama-cho (2008)               | All residents in Ama-cho aged ≥ 65, targeted N = 943 | Phase 1 (N = 917) | (1) Prevalence in percentage (95% CI) |
|                              | Study participants N = 917 (after excluding 23 subjects out of 943 subjects who resided out of town at the time of phase 1 interview) | Suspected dementia cases selected through interviews with subjects and their informants, which assessed cognitive changes, psychiatric symptoms, personality changes, problem behaviors, activities of daily living, psychological and medical symptoms, and through assessments of the subjects’ medical history offered by the home doctors of the subjects | (2) Number of cases (all subtypes combined/AD/VaD) |
|                              | Sampling weights used to reflect prevalence of population at large? (Yes/No): No | Phase 2 (N = 120) DSM-IV for dementia, NINCDS-ADRDA for AD, and NINDS-AIREN for VaD | (3) AD percentage out of all dementia |
|                              |                                                             |                     | (4) AD/VaD ratio |

(1) 11.3 (9.1–13.2)  
(2) 104/66/16  
(3) 63.5%  
(4) 4.12  

*CASI: The Cognitive Abilities Screening Instrument [19].
we list age-specific prevalence of dementia and AD/VaD
sample sizes (\(n\) DSM-IV criteria. = largely depending on the criteria used: 62.5% (AD/VaD = included in one model, with the Okinawa study being a reference.

Results are based on a Poisson regression model where all study data are
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results showed that compared with the all-cause dementia
models using only the Hisayama studies (4 time points). The
95% CI: 0.01–0.64, \(P < 0.0001\) controlling for sex and age
groups (not shown in Table 1).

### 3.3. AD/VaD Ratios
AD/VaD ratios among those aged 65
and older are listed in the last column of Table 1. The
Okinawa (1992), Hiroshima (1996), Tajiri (1998), and Ama-
cho (2008) studies used the same criteria for diagnoses of
AD (NINCDS-ADRDA) and the AD/VaD ratio among those
aged 65 and older was 1.85, 1.85, 3.33, and 4.12 for the above
studies, respectively. The Hisayama studies which conducted
4 cross-sectional studies using the same diagnostic criteria
for subtypes of dementia also showed the increasing trend in
the ratio of AD/VaD, ranging from 0.52 in 1985 to 1.96 in
1998, and 1.92 in 2005. The Tajiri project, which conducted
an MRI substudy to identify dementia etiologies, showed that
the proportion of AD among total dementia cases differed
largely depending on the criteria used: 62.5% (AD/VaD = 3.3) using NINDS-AIREN criteria, and 40.6% (AD/VaD = 1.0) or 56.2% (AD/VaD = 2.3) depending on assessors using DSM-IV criteria.

Even though we selected studies with relatively large
sample sizes (\(n \geq 500\)), the number of cases was too small
to conduct meaningful comparisons of age-specific AD/VaD
dratios for the age group 65–70 (<5 for each case). Therefore,
we list age-specific prevalence of dementia and AD/VaD
dratios for the age groups 70–79, 80–89, and 90 and older
in Table 3. The youngest age group examined here (age 70–79) had a prevalence of VaD that was consistently higher
than that of AD in Japan (i.e., AD/VaD < 1) except in more recent studies conducted in 2005 (Hisayama) and 2008
(Ama-cho). Except for these two recent studies (Hisayama
2005 and Ama-cho 2008), as age increased, the proportion of
AD among the total dementia cases increased.

### 4. Discussion

#### 4.1. Overall Dementia
Eight major prevalence studies conducted in Japan were reviewed in an attempt to identify trends in prevalence of all-cause dementia and subtypes of
dementia, paying careful attention to diagnostic protocols.
We found that compared with the Okinawa 1992 study, studies conducted in later years (1994 (Hiroshima), 1998
(Tajiri), 2005 (Hisayama), and 2008 (Ama-cho)) had a
higher prevalence of all-cause dementia, after controlling
for age groups and sex. Within 4 studies conducted in
Hisayama (1985, 1992, 1998, and 2005), we also found that
the prevalence in 2005 was higher than that in 1985, after
controlling for age groups and sex. Thus, the dementia
prevalence seems to be increasing in Japan, in contrast to
the US where decreasing or stable prevalence of all-cause
dementia has been reported [1].

A number of reasons may explain the observed trends.
Two diseases that could have high impact on the prevalence of
dementia at national levels are cerebrovascular disease
and type 2 diabetes, as shown by their relatively high
population attributable risk % (PAR%) of dementia in the
United States [12, 28]. According to the National Nutrition
Survey in Japan, those with hemoglobin A1C values ≥ 6.0%
(possible type 2 diabetes) were estimated to be 22.8%, 37.4%,
and 40.9% among men aged 70 and older in year 1997,
2002 and 2007, respectively, and the comparative figures
among women were 27.2%, 28.2%, and 34.6% [29]. On
the other hand, the decline in stroke incidence reached
plateaus around the late 1990s after a continuous sharp
decline beginning in 1960 [30], thus further declines in
dementia due to stroke would not be expected after the
1990s. However, it is possible that the prevalence of small
vessel cerebrovascular disease with resultant microinfarcts
that would not be accounted for in these vascular disease
statistics could play a latent or underappreciated role in
causing or contributing to dementia. The increase in type 2
diabetes, the metabolic syndrome and its associated vascular
complications (risk factors for AD [31]), with a plateau in
decreasing trends in major stroke incidence, could have lead
to an increase in dementia prevalence in recent years in
Japan. It is also possible that increasing public awareness of
dementia in recent years is resulting in enhanced recognition
of functional and cognitive declines that might previously
have been dismissed as “normal aging.” Longer survival of
those who suffered from stroke/TIA due to advanced medical
treatment could also increase the prevalence of dementia
to some extent. Unfortunately, autopsy confirmation in
large proportions of the participants in these epidemiologic
studies is not available, thus limiting conclusions as to more
specific underlying etiologies.

| Table 2: Factors associated with all-cause dementia prevalence. |
|----------------------------------|-----------------|-----------------|
| Age group | Coefficient (\(P\) value) | 95% confidence interval |
| 65–69 (reference) | 0 | |
| 70–79 | 1.24 (<0.0001) | 1.14–1.34** |
| 80–89 | 2.62 (<0.0001) | 2.52–2.71** |
| 90 and + | 3.51 (<0.0001) | 3.41–3.62** |
| Sex | |
| Women (reference) | 0 | |
| Men | −0.01 (0.50) | −0.06–0.03 |
| Study name (year) | |
| Hisayama 1985 | 0.16 (0.25) | −0.11–0.43 |
| Hisayama 1992 | −0.02 (0.85) | −0.26–0.21 |
| Okinawa 1992 (reference) | 0 | |
| Hiroshima 1996 | 0.30 (0.0002) | 0.14–0.46** |
| Hisayama 1998 | 0.08 (0.39) | −0.11–0.28 |
| Tajiri 1998 | 0.37 (<0.0001) | 0.19–0.55** |
| Hisayama 2005 | 0.49 (<0.0001) | 0.35–0.64** |
| Ama-cho 2008 | 0.27 (0.007) | 0.07–0.47** |

Results are based on a Poisson regression model where all study data are
included in one model, with the Okinawa study being a reference.
** Significant at \(P < 0.01\).

As a post hoc analysis, we also ran Poisson regression
models using only the Hisayama studies (4 time points). The
results showed that compared with the all-cause dementia
prevalence in 1985, that of 2005 was higher (coefficient: 0.32,
95% CI: 0.01–0.64, \(P = 0.04\) controlling for sex and age
groups (not shown in Table 1).
Table 3: Prevalence of dementia (%) and its subtype by 10 years age group and by study site.

| Study name/site (Study years) | Age 70–79 | | | Age 80–89 | | | Age 90 and older | |
|------------------------------|-----------|---|---|-----------|---|---|-----------|---|
|                              | Prevalence in percentage (95% CI) | AD/VaD ratio | Number of cases: all subtypes combined/AD/VaD | Prevalence in percentage (95% CI) | AD/VaD ratio | Number of cases: all subtypes combined/AD/VaD | Prevalence in percentage (95% CI) | AD/VaD ratio | Number of cases: all subtypes combined/AD/VaD |
| Hisayama (1985)              | 3.41 (1.92–5.56) (440) | AD/VaD = 0.13 | 15/1/8 | 19.50 (13.65–26.52) (159) | AD/VaD = 0.75 | 3/1/6/8 | 57.14 (28.86–82.34) (14) | AD/VaD = 2.50 | 8/5/2 |
| Hisayama (1992)              | 3.35 (2.00–5.25) (537) | AD/VaD = 0.22 | 18/2/9 | 13.39 (9.34–18.37) (239) | AD/VaD = 1.44 | 32/13/9 | 46.43 (27.51–66.13) (28) | AD/VaD = 6.00 | 13/6/1 |
| Okinawa (1991-1992)          | 3.67 (2.32–5.02) (1481) * | AD/VaD = 0.59 | 45/16/27 | 14.93 (10.97–18.89) (619) * | AD/VaD = 2.10 | 81/42/20 | 36.83 (28.08–45.58) (117) * | AD/VaD = 3.66 | 37/22/6 |
| Hiroshima (1992–1996)        | 5.67 (4.09–7.66) (741) | AD/VaD = 0.93 | 42/13/14 | 19.04 (14.97–23.87) (394) | AD/VaD = 2.64 | 75/45/17 | 41.67 (26.97–61.50) (60) | AD/VaD = 4.66 | 25/14/3 |
| Hisayama (1998)              | 3.99 (2.65–5.76) (676) | AD/VaD = 1.71 | 27/12/7 | 16.84 (12.76–21.59) (297) | AD/VaD = 1.92 | 50/25/13 | 35.59 (23.55–49.13) (59) | AD/VaD = 3.33 | 21/10/3 |
| Tajiri (1998)                | 5.18 (3.80–6.93) (908) | AD/VaD = N/A | 7/3/0* | 22.33 (17.37–28.26) (309) | AD/VaD = 1.50 | 22/12/8* | 51.52 (30.00–82.51) (33) | AD/VaD = N/A | N/A |
| Hisayama (2005)              | 6.86 (5.13–8.94) (729) | AD/VaD = 2.40 | 50/24/10 | 27.74 (20.50–29.37) (384) | AD/VaD = 1.84 | 95/46/25 | 53.49 (42.41–64.32) (86) | AD/VaD = 1.71 | 46/24/14 |
| Ama-cho study (2008)         | 6.7 (4.12–9.02) (432) | AD/VaD = 1.75 | 29/14/8 | 17.8 (14.81–26.41) (275) | AD/VaD = 11.33 | 49/34/3 | 41.3 (26.51–61.52) (58) | AD/VaD = 4.50 | 24/18/4 |

AD/VaD: the number of AD cases/the number of VaD cases.
*Based on subsample analysis with MRI results.
N/A: sample size is too small to perform the calculation (AD + VaD cases < 5).
Random sampling was used for screening. N reported is not weighted. Prevalence, proportions of subtypes of dementia, and AD/VaD ratio used weighted frequencies to show those of the population at large.
Our finding could be also partly due to regional variability in prevalence of dementia. We found that Okinawa had a lower overall prevalence of dementia compared with other cohorts except Hisayama studies in 1985, 1992, and 1998. These two regions (Okinawa and Hisayama) have had lower incidence of cerebrovascular diseases in comparison with other regions studied here. For example, the rate of cerebrovascular mortality, as a proxy of cerebrovascular disease incidence, declined sharply between 1975 and 2000 by over 65% in all regions and declined further between 2000 and 2005 by over 10% in all regions (Table 4), with the above two regions constantly having lower rates than other regions. Historically, salt consumption has been high in the northern part of Japan because vegetables and marine products are cured with salt to preserve them during the longer winter months and consumed with processed white rice. This dietary pattern is believed to be one of the reasons of the higher prevalence of hypertension and large vessel cerebrovascular disease in the northern prefectures in Japan [32]. The low dementia prevalence in Okinawa and Hisayama (except 2008), which is located in the southern part of Japan, could not only be due to a lower rate of VaD resulting from lower cerebrovascular disease incidence, but also due to lower AD prevalence resulting from reduced vascular injuries [8, 12, 33, 34].

4.2. AD versus VaD. Vascular dementia (VaD) was believed to be more prevalent than Alzheimer’s disease (AD) in Japan in the 1980s, in contrast to the US or other western countries, but studies conducted in the late 1990s and after showed patterns that were more similar to the US [13, 15, 35]. This “westernization” of the dementia prevalence pattern could be partly due to the declining stroke incidence observed during the 1980s as described above. However, it could also be due to changes in diagnostic criteria used in Japan. For example, in the Tajiri study, patients received a diagnosis of “possible AD with CVD” by means of the NINDS-AIREN criteria, provided that the vascular effect on dementia was considered to be too ambiguous to diagnose as VaD [6], which lead to relatively high proportion of AD out of all dementia cases (over 62%). The study also demonstrated the difficulty of obtaining consensus on the definition of VaD, even for experienced neurologists using the same criteria; two neurologists blinded to each other’s diagnosis did not agree when diagnosing VaD versus AD under DSM-IV criteria: the proportion of VaD out of total dementia cases ranged from 40.6% to 56.2%, depending on assessors. We expect that lack of imaging data may result in underdiagnosis of subcortical vascular brain injury (e.g., white matter hyperintensity, and silent brain infarcts, etc.) and thus lead to underestimation of VaD. However, more recent studies including the Tajiri, Hisayama (1998; 2005), Hiroshima and Ama-cho studies used imaging data, and these tend to show higher AD/VaD ratios (i.e., not higher VaD prevalence) compared with earlier studies. Therefore, it is likely that changes in diagnostic criteria at least partly explain the higher proportion of diagnosed AD in recent years.

In all studies except more recent studies conducted after 2000, as age increased, the proportion of AD among the total dementia cases increased: the youngest age group examined (age 70–79) had a prevalence of VaD that was consistently higher than that of AD in Japan (i.e., AD/VaD < 1). On the other hand, among the older age groups, AD had been more prevalent. In fact, among the oldest age group (age ≥ 90), AD/VaD ratios in Japan were not necessarily lower than the US figures even among studies conducted in the early 1990s, ranging from 2.5 (Hisayama 1985) to 6.0 (Hisayama 1992). In the Aging, Demographics, and Memory Study (ADAMS) [36, 37], which is the first study in the US to calculate a nationally representative dementia prevalence, the age-specific AD/VaD ratios were found to be 2.36, 4.43, and 4.79 for age group 71–79, 80–89, 90 and older, respectively, using DSM-III-R [22] and DSM-IV [23] criteria for dementia and NINCDS-ADRDA criteria for AD, that is, the age-associated increase in AD prevalence seems to be more evident in Japan than in the US. This could be partly due to the fact that the gender gap in life expectancy is larger in Japan compared with US and the proportion of women increases more steeply as age increases in Japan. For example, in 1990, the life expectancy at age 65 was 18.9 years for women and 15.1 years for men in the US, that is, a gender gap of 3.8 years, while the comparative figure in Japan was 20.0 years and 16.2 years, with the gender gap of 4.8 years. Similarly, in 2008, the life expectancy at age 65 was 19.8 years for women and 17.1 years for men in the US, with the gender gap of 2.7 years, while the comparative figure in Japan was 23.6 years and 18.6 years, with the gender gap of 5.0 years. Cerebrovascular disease is more common among men than women, and we expect a higher proportion of VaD among men than women. A steeper age-associated increase in AD prevalence found in Japan, therefore, could be due to a higher proportion of women among the older old age groups in Japan. Comparisons of age-specific AD/VaD ratios between men and women could clarify this issue, but we were unable to do so due to the small sample size once we stratify prevalence by sex and age groups, especially among those aged 90 and older. However, at least among the younger two age groups (ages 70–79; 80–89), we see an increasing trend in the proportion of AD cases as age group goes up in both men and women (data not shown). These results also suggest that it is important to consider the age/sex structure of samples when we compare the AD/VaD ratio among different cohorts. The comparison of aggregated ratios could be misleading.

4.3. Incidence of Dementia. Although incidence of dementia and its subtype would give a more accurate picture regarding the trend, there is a paucity of dementia incidence studies in Japan. To our knowledge, only three incidence studies have been reported thus far: (1) the Hisayama cohort, following their 1985 cohort for 7 years [38]; (2) the Tajiri project, following a sub-sample of their 1998 cohort [39] for up to 7 years; (3) the Hiroshima study (Radiation Effects Research Foundation adult health study), following their 1992–1996 prevalence cohort until the year 2003 [40]. The incidence of all-cause dementia was 19.3 per 1000 person-years for men and 20.9 for women in the Hisayama study, 33.9 for men and 44.0 for women in the Tajiri study, and 12.0 for men and
16.6 for women in the Hiroshima study. The Hisayama and Hisorhisma studies reported significant gender differences in subtypes of dementia incidence: Hisayama reported that the incidence of VaD increased with age and was consistently higher than that of AD for men, while the incidence of AD was higher than that of VaD for women age 75 years or older. The incidence of AD markedly increased after the age of 80 in either sex, but overall, VaD was more common in the Hiroshima study. The Hiroshima study also reported that probable AD showed the most remarkable increase with age, and probable VaD was significantly lower among women. Overall, AD was more common in this study, possibly because the Hiroshima study was conducted later than the Hisayama study, after a further decline in stroke incidence had occurred. In all 3 incidence studies, NINCDS-ADRDA criteria were used for AD and NINDS-AIREN for VaD. In Japan, AD incidence and prevalence tend to increase with age more than VaD and older old women predominantly have AD rather than VaD. Therefore, when aggregated, the overall prevalence of AD may become higher as more women survive in the oldest old age group. As we mentioned earlier, it is important to consider the age/sex structure of samples when examining trends in the AD/VaD ratio.

4.4. Conclusion. In conclusion, our systematic review shows that (1) there is an increasing trend in overall dementia in Japan. Although we cannot confirm definitively from the current study, the possible explanation of the increase could be a shift in health conditions among the elderly in Japan, including the increase in diabetes mellitus in more recent years despite the plateau in decline in stroke incidence during the late 1990s; (2) the similar AD/VaD ratio found in recent studies in Japan with that of the US could be due to a combination of at least 3 factors: (a) shifting diagnostic criteria (more in line with US consensus diagnosis), (b) possible shifting in health conditions among the elderly in Japan (decline in stroke incidence, but increase in metabolic disease e.g., type 2 diabetes, hyperlipidemia, and atherosclerosis), (c) an increase in the proportion of the oldest old who had an historically higher prevalence of AD (as opposed to VaD) in Japan, and (d) regional variations (i.e., a north-to-south gradient in VaD) possibly due to large difference in dietary patterns.

The study limitations include relatively small sample sizes, especially for the oldest old group. The Okinawa study took into account the potential dementia cases among those who were screened at Phase 1 (screening phase), but did not participate in Phase 2 (clinical assessment phase), using weights generated from Phase 1. However, as with most other epidemiological studies of dementia, there was no way of precisely estimating the frequency of dementia among those who did not participate in the screening phase. Future studies could aid in monitoring changing prevalence patterns and their causes by including some of the following elements. First, as with Hisayama studies, it would be ideal for studies to examine the prevalence of dementia and its subtypes repeatedly at the same locations using the same criteria. Second, it would be helpful if future epidemiology studies would recruit more participants aged 90 and older (e.g., through aggressive age-stratified sampling protocols) to improve estimates of prevalence in this age group. Third, more comprehensive diagnostic criteria should be used for inter-cohort comparisons: as suggested by Viswanathan and colleagues [8], AD and VaD exist in a continuum of disease. It might be more meaningful if we could apply, for example, more specific clinicopathological criteria for mixed dementia [44–50] than those currently used. Increased use of standardized neuroimaging such as the Alzheimer’s Disease Neuroimaging Initiative (ADNI) [51] might aid in the development of more specific and comparable criteria for the diagnosis of VaD. Finally, autopsy confirmation of the underlying potential causes of dementia in epidemiological studies would go a long way to help resolve these important uncertainties in the shifting patterns over time of the dementias.


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Research Article

Chinese-Language Montreal Cognitive Assessment for Cantonese or Mandarin Speakers: Age, Education, and Gender Effects

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The Montreal Cognitive Assessment Chinese-Language Los Angeles version (MoCA-ChLA) was developed and administered during an in-home interview to 1,192 participants (mean age 62.5 years, mean education 11.6 years) in a population-based Chinese American Eye Study (CHES) in Los Angeles. The MoCA-ChLA score (mean ± SD) was 23.8 ± 4.2 with little ceiling and no floor effects. The score increased with higher education, decreased with advancing age, and was not related to gender. Compared to the education 1–6 years group, the mean MoCA-ChLA score was 2.6 and 4.6 higher in the education 7–11 and 12–20 years groups, respectively. The Mandarin- (n = 612) and Cantonese- (n = 612) speaking subgroups performed comparably; Cronbach’s alpha of the MoCA-ChLA score was 0.78 and 0.79 for these two groups, respectively. Item response theory analysis showed good discriminating power for executive function and memory. These properties support the MoCA-ChLA as a useful screening tool for aging and dementia studies for Mandarin or Cantonese speakers.

1. Introduction

The Chinese American population is one of the most rapidly growing minorities in the United States [1, 2]. According to the USA Bureau of the Census (2010), the number of Chinese Americans increased 229% from 1.62 to 3.8 million from 1990 to 2010 [2]. One-third of Chinese Americans (1.25 million) reside in California, and the number of Chinese Americans with dementia is expected to more than triple in the next 30 years [3]. However, few studies have focused on the screening for cognitive impairment among Chinese-Americans. Linguistically and culturally appropriate cognitive screening tests to detect and stage cognitive impairment are needed to facilitate early detection and intervention. The lack of such instruments also limits the participation of Chinese Americans in cognitive and aging research.

The Montreal Cognitive Assessment (MoCA) is a brief cognitive screening test designed to distinguish individuals with mild cognitive impairment (MCI) who perform in the normal range of the Mini-Mental State Examination (MMSE) from cognitively normal elderly [4]. Since Chinese Americans migrated primarily from Mainland China, Hong Kong, Macau, and Taiwan, the Chinese-speaking population in the USA consists of three major cultural subgroups whose primary dialect is Mandarin (Putonghua), Cantonese, or Taiwanese [5]. These three groups may use different words or expressions for some concepts and may differ in level of education.

We therefore translated and adapted the MoCA for Mandarin-, Cantonese-, and Taiwanese-speaking Chinese Americans with one common written version named the MoCA Chinese Los Angeles version (MoCA-ChLA). The MoCA-ChLA was administered to 1,192 Chinese residents in Monterey Park, California, as part of a population-based study. The City of Monterey Park in Los Angeles County, the first suburban Chinatown in the USA [6], has the highest
Table 1: MoCA-ChLA domains and subitems.

| Primary domain                  | Test Subitem                                      | Score range |
|--------------------------------|---------------------------------------------------|-------------|
| Short-term memory              | Recall 5 words after 5 min.                       | 0–5         |
| Visuospatial construction      | Clock drawing                                    | 0–3         |
|                               | Copying a cube                                   | 0–1         |
|                               | Alternating trail making                         | 0–1         |
| Executive function             | Generating animal names                          | 0–1         |
|                               | Similarities                                     | 0–2         |
|                               | Digit spans (forward & backward)                  | 0–2         |
| Attention and concentration    | Target detection                                 | 0–1         |
|                               | Five serial subtractions of 7                     | 0–3         |
| Language                       | Naming 3 animals                                  | 0–3         |
|                               | Repeating 2 sentences                            | 0–2         |
| Temporal and spatial orientation| To time and place                                | 0–6         |
| Total                          |                                                   | 0–30        |

percentage of Chinese Americans of any USA municipality, at 43.7% of its population (60,269) in 2010 [2]. The goal of this study was to characterize the effects of preferred language, age, education, and gender on the performance of the MoCA-ChLA in this minority population.

2. Methods

2.1. Contents of the MoCA. The MoCA was specifically developed as a screening tool for mild cognitive impairment and early dementia [4]. Compared to the MMSE, it includes more memory items and assesses key aspects of executive function. The MoCA has 12 items that assess 6 cognitive domains including short-term memory, visuospatial construction, executive functions, attention and concentration, language, and temporal and spatial orientation (Table 1). The MoCA is scored on a 30-point scale and takes about 10 minutes to administer and 1 minute to score. In the original study, the MoCA was administered to 277 English- or French-speaking Canadians, aged 65 years or older, with mean education of 11.9 years (averaged over normal, MCI, and Dementia groups). One point was added for persons with education of less than 12 years. In terms of identifying MCI, a MoCA score of ≤26 showed a sensitivity of 90% and a specificity of 87% in the original study [4]. Later, a study in the UK found sensitivity of 83% and much lower specificity of 50% [7]; a Korean study reported a sensitivity of 89% and a specificity of 84% [8]; a recent study in Japan reported a sensitivity of 93% and a specificity of 87% in screening for MCI [9]. These studies all added 1 point for education <12 years with the exception of the Korean study, where 1 point adjustment was made for education <6 years.

2.2. Development of MoCA-ChLA. As of April 2010, the MoCA has been translated independently into Mandarin, Cantonese, and Taiwanese versions (http://www.mocatest.org/). We carefully reviewed the instrument and instruction manual of the original MoCA in English, as well as the three Chinese versions developed separately in Beijing, Hong Kong, and Taiwan. The written words in the three Chinese versions are not identical and in some instances misinterpreted the intention of the original MoCA test item. For example, in the Hong Kong version, sentence repetition seems to assess articulation more than attention, as the subject is asked to repeat something like “Sasha age sixty six” [10]. In addition, all 3 Chinese versions tend to follow a literal translation of the English instructions, such that the resulting Chinese sentences sound unnatural and are difficult to comprehend, especially to individuals with little or no formal education.

In developing the MoCA-ChLA, we attempted to maintain the neuropsychological intention of the original MoCA instrument. We incorporated appropriate parts of the existing Chinese versions, made modifications of other parts, and ensured that the spoken instructions would be easily understood by Mandarin, Cantonese, and Taiwanese-speakers. In the 5-word learning test, we changed “face” to “hair” and “velvet” to “teacup.” “Face” is a single character word in Chinese that could mean the physical face or the social face. “Velvet” can be either a 2-character or a 3-character word depending on the dialect, and could be unfamiliar to older and low-educated Chinese. In contrast, the words “hair” and “teacup,” like “church,” “daisy,” and “red” are all unambiguous 2-character words in Chinese and familiar to all. We changed the phonemic fluency task (generating words beginning with letter F within 60 seconds) to a semantic fluency task (generating names of 4-legged animals) because Chinese is a monosyllabic language and each phoneme has multiple ambiguous meanings, which undermines the meaningfulness of phonemic fluency in Chinese. Generating animal names has shown good validity as a measure of verbal fluency among Chinese elderly [11, 12].

The development of the MoCA-ChLA was an iterative process. First, the MoCA-ChLA items were adapted jointly by a bilingual neuropsychologist (ELT) and a bilingual epidemiologist (LZ). Subsequently, they were back translated into English by a bilingual psychologist (PL) without knowledge of the original MoCA items. Successive versions were reviewed for clarity by focus groups of native Mandarin,
Cantonese, or Taiwanese speakers in the lay community. Wording was adjusted where necessary, and the process was repeated until the final MoCA-ChLA was considered by the two bilingual psychologists (ELT and PL) to be linguistically and semantically equivalent to the original MoCA, unambiguous, and easily comprehensible. The final version of MoCA-ChLA items is shown in Figure S1, see Supplementary Materials online at doi:10.1155/2012/204623.

An instruction manual for the administration and scoring of the MoCA-ChLA was developed and used to train 15 Mandarin, Cantonese, or Taiwanese-speaking interviewers. Subtle flaws in the manual were corrected after feedback and field testing of 178 subjects. Subsequently, all interviewers underwent rigorous rater training: received a copy of the final Record Form (Figure S1) and Manual to study, participated in two in-person training sessions, and passed a 12-item multiple-choice quiz on the administration and scoring of the MoCA-ChLA, before starting formal field testing.

2.3. Study Population. The MoCA-ChLA was administered as part of the Chinese American Eye Study (CHES) during an in-home interview. The CHES is a population-based study designed to estimate the prevalence of visual impairment and major eye diseases among Chinese Americans aged at least 50 years residing in 9 census tracts in Monterey Park, Los Angeles County. We interviewed 2,837 eligible participants at home as of October 18, 2011 (Figure 1). Of these, 764 refused MoCA-ChLA screening, 274 could not be tested due to self-reported decreased hearing, and 441 could not be tested due to self-reported vision problems. Among 1,358 persons tested with the MoCA-ChLA, complete test forms were obtained for 1,240. All participants were tested in their preferred language; 575 were tested in Cantonese, 612 in Mandarin, 5 in Taiwanese, 4 in Vietnamese, and 44 in English. The latter two subgroups were excluded, resulting in a total of 1,192 participants in our analyses.

We subdivided the sample by age and education. The median education of 12 years was used to divide the sample into high-(12–20 years) and low-(1–11 years) education groups. The low-education group was further subdivided into mid-low (7–11 years) and low-low (1–6 years) groups. The median age of 60 years was used to divide the sample into middle-age (50–59 years) and older age (60–100 years) groups. The older age group was further subdivided into young-old (60–74 years) and old-old (75–100 years) groups. The definition of these subgroups is somewhat arbitrary; however, these divisions allow sufficient sample size in each category and are comparable with groupings reported in the literature.

2.4. Statistical Analysis. The MoCA-ChLA total score equals the sum of all its subitems unadjusted for years of education. The distribution of the MoCA-ChLA total score and demographic variables was examined and nonparametric
analyses were performed where appropriate. Demographic characteristics, MoCA-ChLA total score, and subitem scores were compared between the Cantonese- and Mandarin-speaking groups among the 3 education groups (1–6, 7–11, and 12–20 years) and among the 3 age groups (50–59, 60–74, 75–100 years) using Wilcoxon rank sum tests and chi-square tests. Due to very small sample size (n = 5), individuals who preferred to be tested in Taiwanese were not included as a separate dialect comparison group. Cronbach’s coefficient alpha was used to estimate the internal consistency of the MoCA-ChLA for the total sample and for the Mandarin-speaking and the Cantonese-speaking subgroups separately.

Nonparametric analysis of covariance (rank ANCOVA) was used to compare MoCA-ChLA total score and its subitem scores between the two dialect groups adjusting for age and education (gender was not included as a covariate as the gender distribution did not differ between the 2 dialect groups). In order to clarify the relationships between MoCA-ChLA score and age, education, and gender, rank ANCOVA was performed to compare MoCA-ChLA total score (1) among the 3 education groups controlling for age, gender, and testing dialect; (2) among the 3 age groups controlling for education, gender, and testing dialect; (3) between men and women controlling for age and education (testing language was not included as a covariate as it did not differ between men and women).

For each education group, we determined the 15th percentile of the MoCA-ChLA score in the middle-age group (MP15) to explore how age relates to possible cognitive impairment. The MP15 scores were 18 in the low-low (1–6 years), 20 in the mid-low (7–11 years), and 22 in the high-(12–20 years) education groups. The Cochran-Mantel-Haenszel test was used to test whether the percent of participants at or below MP15 score differs as a function of advancing age controlling for level of education.

Item response theory (IRT) methods [13] were used to evaluate the test characteristic curves (TCCs) and test information curves (TICs) of the MoCA ChLA total score and 6 cognitive domain scores (Table 1 shows items comprising each domain). A TCC represents a nonlinear regression of the total or domain scores on ability. It can be a very useful tool for evaluating the range of measurement and the degree of discrimination at different points of the ability continuum. In addition, the degree to which the TCC is linear provides an indication of the extent to which the measure provides interval scale or linear measurement [14]. A TIC relates latent ability in SD unit to the information (precision of measurement) for the total or domain scores. The information on the y-axis is the reciprocal of the variance of measurement. The TIC provides a means to ascertain what range of ability levels a test is optimally suited to measure [15]. A graded response model [16] was implemented using the R package ltm (http://www.r-project.org/). All statistical testing except IRT analysis was performed at a two-sided 5% level of significance and used Statistical Analysis System version 9.2 software (SAS Institute, Cary, NC, USA).

3. Results

3.1. Demographic Characteristics. We administered the MoCA-ChLA to 1,192 (61.6% female) Chinese Americans living in the city of Monterey Park, Los Angeles County, California. Their mean age at testing was 62.5 years (median 60 years, range 50 to 100 years) and mean level of education was 11.6 years (median 12 years, range 1 to 20 years). Their mean MoCA-ChLA score was 23.8 (SD 4.2, median 25, range 6 to 30). Only 3% of participants received a perfect score of 30. The 5th, 50th, and 95th percentiles were 16, 25, and 29, respectively, (Figure 2).

3.2. Comparisons by Preferred Dialect. Compared to Cantonese-speaking participants, Mandarin-speaking participants on average were 3 years older, had 3 more years of education, and had 1 point higher MoCA-ChLA scores (Table 2). The gender distribution did not differ between the 2 groups. After adjustment for age and education, the two dialect groups did not differ in MoCA-ChLA total and item scores, except on sentence repetition, where Mandarin speakers scored significantly better. 64.1% of Mandarin (versus 49.6% of Cantonese speakers) received a full score on sentence repetition (P = 0.003) (data not shown).

The Cronbach’s coefficient alpha of MoCA-ChLA as an index of internal consistency was 0.79, 0.78, and 0.79, respectively, for the whole sample (n = 1,192) and for the Mandarin (n = 612) and Cantonese (n = 575) speakers. In the total sample, the standardized scores of Cronbach’s coefficient alpha ranged from 0.77 to 0.79 for all 12 items of the MoCA-ChLA.

3.3. Effect of Education. Females were disproportionately represented in the low-low education group: 72%, 61%, 59% in the low-low-, mid-low-, and high-education groups, respectively (P = 0.01) (Table 3). The low-low education group was significantly older than the higher education groups (P = 0.01). Significantly more participants (75.3%) were tested in Cantonese in the low-low education group while more participants (61.9%) were tested in Mandarin in the high-education group (P < 0.0001). Lower education
Table 2: Comparisons of age, gender, education, and MoCA-ChLA scores between Cantonese and Mandarin speakers.

| Characteristics          | Cantonese speaking (n = 575) | Mandarin speaking (n = 612) | P value1 | Adjusted P-value2 |
|--------------------------|-------------------------------|----------------------------|----------|-------------------|
| Age in years, mean ± SD  | 61 ± 8.5                      | 63.9 ± 11                  | <0.0001  |                   |
| Women, no. (%)           | 363 (63.1)                    | 367 (60.0)                 | 0.26     |                   |
| Years of education, mean ± SD | 10.3 ± 3.8              | 12.9 ± 3.7                 | <0.0001  |                   |
| Unadjusted MoCA, mean ± SD | 23.3 ± 4.2               | 24.4 ± 4.1                 | <0.0001  |                   |
| Adjusted MoCA2, lsmean ± SE | 23.7 ± 0.16            | 23.9 ± 0.15                | 0.36     |                   |

1From Wilcoxon rank sum test for continuous variables and chi-square for gender.
2Adjusted P-value obtained from nonparametric analysis of covariance with adjustment for age and education.

Table 3: Comparison of age, gender, test language, and MoCA-ChLA score among the three education groups.

| Variables                  | Education 1–6 years (n = 178) | Education 7–11 years (n = 282) | Education 12–20 years (n = 732) | P value1 | Adjusted P-value2 |
|---------------------------|-------------------------------|-------------------------------|--------------------------------|----------|-------------------|
| Age in years, mean ± SD   | 63.6 ± 9.7                    | 61.1 ± 8.8                    | 62.8 ± 10.4                     | 0.01     |                   |
| Female, no. (%)           | 128 (71.9)                    | 172 (61.0)                    | 434 (59.3)                      | 0.01     |                   |
| Testing language, no. (%) |                               |                               |                                |          |                   |
| Cantonese                 | 134 (75.3)                    | 167 (59.2)                    | 274 (37.4)                      | <0.0001  |                   |
| Mandarin                  | 44 (24.7)                     | 115 (40.8)                    | 453 (61.9)                      |          |                   |
| Taiwanese                 | 0 (0)                         | 0 (0)                         | 5 (0.7)                         |          |                   |
| Unadjusted MoCA, mean ± SD| 20.2 ± 4.7                    | 23.1 ± 3.9                    | 25.0 ± 3.6                      | <0.0001  |                   |
| Adjusted MoCA2, lsmean ± SE| 19.7 ± 0.6                | 22.3 ± 0.6                    | 24.3 ± 0.6                      | <0.0001  |                   |

1P value obtained from Kruskal-Wallis test for continuous variables, from Chi-square test for gender, from Fisher exact test for testing language.
2Adjusted P-value obtained from nonparametric analysis of covariance with adjustment for age, gender, and testing language.

Figure 3: The 25th, 50th, and the 75th percentile of MoCA-ChLA score by age and education groups.

The middle-age (50–59) group and old-old (75–100) group shows that, for the P25 scores, there were approximately 4, 4, and 6 points of difference for the high-, middle-low-, and low-low-education groups. The corresponding numbers for the P50 scores were 3, 2, 6, and those for the P75 scores were 2, 3, and 1. In other words, in general age-related differences were greatest for the P25 scores, less so for the P50 scores, and least for the P75 scores. Even for the low-low-education group age-related differences in P25 and P50 score were prominent but minimal for the P75 score.

3.4. Effect of Age. Females were disproportionately represented in the middle-age group: 65.8%, 60.0%, and 49.6% in the middle-age, young-old, and old-old age groups, respectively (P = 0.001) (Table 4). Advanced age was associated with higher education with borderline significance (P = 0.06). Significantly more participants (70.2%) were tested in Mandarin in the old-old group than the other 2 age groups (48.5% in the middle-age group, 49.3% in the young-old group) (P < 0.0001). Advanced age was significantly associated with lower MoCA-ChLA scores with or without adjustment for education, gender, and testing dialect (P < 0.0001).

The percentage of participants who were at or below the MP15 score increased with age, especially among the young-old and old-old groups across all three education groups (Figure 4). In each education group, multiple participants achieved the exact MP15 score. Therefore the percentage of participants who were at or below the MP15 score in each education group was greater than 15%. The association...
Table 4: Comparison of education, gender, test language, and MoCA-ChLA score among the three age groups.

| Variables                  | Age 50–59 years | Age 60–74 years | Age 75–100 years | P value1 | Adjusted P value2 |
|----------------------------|-----------------|-----------------|-----------------|----------|-------------------|
| Education in years, mean ± SD | 11.4 ± 3.6     | 11.9 ± 4.2      | 12 ± 4.4        | 0.06     |                   |
| Female, no. (%)            | 384 (65.8)      | 280 (60.0)      | 70 (49.6)       |          |                   |
| Cantonese, no. (%)         | 301 (51.5)      | 233 (49.9)      | 41 (29.1)       | <0.0001  |                   |
| Mandarin, no. (%)          | 283 (48.5)      | 230 (49.3)      | 99 (70.2)       |          |                   |
| Taiwanese, no. (%)         | 0 (0)           | 4 (0.9)         | 1 (0.7)         |          |                   |
| Unadjusted MoCA, mean ± SD | 24.4 ± 3.8      | 23.9 ± 4.2      | 21.3 ± 5.1      | <0.0001  |                   |
| Adjusted MoCA2, lsmean ± SE| 23.6 ± 0.6      | 22.8 ± 0.6      | 20.1 ± 0.6      | <0.0001  |                   |

1 P value obtained from Kruskal-Wallis test for continuous variables, from Chi-square test for gender, from Fisher exact test for testing language.
2 P value obtained from nonparametric analysis of covariance with adjustment for education, gender, and testing language.

Figure 4: Percent of participants at or below the MP15 (the 15th percentile of the MoCA-ChLA score in the 50–59 age group).

between MP15 and age remained strong after adjusting for education (P < 0.0001 from the Cochran-Mantel-Haenszel test).

3.5. Effect of Gender. Men were on average 2 years older and had 1 more year of education than women (Table 5). Fifty percent of women versus 53.5% men were tested in Mandarin (P = 0.39). The mean MoCA-ChLA score did not differ between men and women (P = 0.52). The association remained nonsignificant after adjustment for age and education (P = 0.59).

3.6. IRT Results. TCCs for the MoCA ChLA score in the total sample, Cantonese-, and Mandarin-speaking groups are shown in Figure 5. These curves relate latent ability/cognitive function in SD units to the expected total score. The MoCA-ChLA test demonstrated similar measurement properties in the total sample and the 2 testing dialect groups. Nonlinearity was apparent for the high-functioning individuals. A 2-SD change in ability from 3 to 1 corresponded to an approximate 3 point loss in MoCA-ChLA score, while a 2-SD change in ability from −3 to −1 corresponded to an approximate 10 point loss in MoCA-ChLA score. This indicated very little floor effect and some ceiling effect of the MoCA-ChLA. The TICs relate latent ability in SD unit to the precision of measurement for domain scores. The TIC of the MoCA ChLA for the total sample peaked around −1, indicating that the MoCA ChLA mainly provides information for respondents with low to average ability (−4 to 1). Similar patterns of discrimination ability and measurement precision were observed for the 2 testing dialect groups.

TCCs for the 6 cognitive domain scores are shown in Figure 6. The TCCs relate latent ability in SD units to the expected total domain score (% of maximum score, for comparability across domains). All 6 domain scores showed reduced discrimination at high-ability levels. The temporal and spatial orientation domains, attention and concentration domains, and the language domain showed lower discrimination and some ceiling effect in the ability range of 1 to 3. The executive function and memory domains demonstrated high-discrimination ability for the ability range of −2 to 2. Similar patterns of domain discrimination were observed among the total sample and the 2 testing dialect groups (figures not shown).

TICs for the 6 cognitive domain scores are shown in Figure 7. The level of information provided by each of the 6 domains varied, with the executive function domain providing the highest precision. The TICs for the executive function domain and the memory domain peaked in the ability range of −2 to 2. For the language domain and the visual spatial domain, most test information was contained in the ability range of −3 to 1. The attention domain and the orientation domain provided little information for ability level of 0 or above.

4. Discussion
We administered the MoCA-ChLA to 1,192 (61.6% female) Chinese-speaking community residents in Monterey Park,
Figure 5: Test characteristic curves and test information curves of the MoCA ChLA total score. The upper figures are for the total sample ($n = 1192$); the middle figures are for the Cantonese speakers ($n = 575$); the lower figures are for the Mandarin speakers ($n = 612$).
Table 5: Comparisons of age, education, testing language, and MoCA-ChLA scores between men and women.

| Characteristics         | Men (n = 458) | Women (n = 734) | P value$^1$ | Adjusted P value$^2$ |
|-------------------------|---------------|-----------------|-------------|----------------------|
| Age in years, mean ± SD | 63.8 ± 10.4   | 61.7 ± 9.6      | 0.0003      |                      |
| Years of education, mean ± SD | 12.2 ± 3.9   | 11.3 ± 3.9      | 0.0002      |                      |
| Testing language, no. (%) |               |                 |             |                      |
| Cantonese               | 212 (46.3)    | 363 (49.5)      | 0.39        |                      |
| Mandarin                | 245 (53.5)    | 367 (50)        |             |                      |
| Taiwanese               | 1 (0.2)       | 4 (0.5)         |             |                      |
| Unadjusted MoCA, mean ± SD | 23.9 ± 4     | 23.8 ± 4.3      | 0.52        |                      |
| Adjusted MoCA$^2$, lsmean ± SE | 23.8 ± 0.1  | 23.8 ± 0.2      | 0.59        |                      |

$^1$From Wilcoxon rank sum test for continuous variables and Fisher exact test for testing language.

$^2$P value obtained from nonparametric analysis of covariance with adjustment for age and education.

Los Angeles County, California. The MoCa-ChLA had small ceiling effect and no floor effect and good internal consistency regardless of whether the participants spoke Mandarin or Cantonese. Similar to other cognitive screening instruments [17], the MoCa-ChLA score increased with more years of education, decreased with age, and was not related to gender. Compared to the education 1–6 years group, the mean MoCa-ChLA score was 2.6 and 4.6 higher in the education 7–11 and 12–20 years groups, respectively. We did not interview a collateral informant regarding possible dementia or cognitive decline and could not determine whether prevalence of dementia might have differed by educational group. Therefore, it would be premature to recommend adjustments in the MoCa score based on level of education, especially in the old-old groups. Compared to other cognitive domain scores, IRT analysis showed that the executive function domain demonstrated the best discriminating power and precision in measurement for participants in the cognitive function range of ±2SD. These properties support the MoCa-ChLA as a useful screening tool, with appropriate adjustments for education level, for studies of aging and dementia among individuals speaking the two major Chinese dialects of Mandarin and Cantonese.

A major strength of our study is the large sample size of Cantonese or Mandarin speakers that were tested using one common written version MoCa-ChLA. Nunnally and Bernstein suggested 0.70 as an acceptable value for the Cronbach's coefficient alpha [18]. In our study, the MoCa-ChLA total score, as well as all the subitems score, demonstrated reasonable internal consistency. This is one of
the first studies to demonstrate comparability of a cognitive impairment screening tool in these two dialects. Significantly more participants (75.3%) were tested in Cantonese in the low-low-education group while more participants (61.9%) were tested in Mandarin in the high-education group \( (P < 0.0001) \), which may reflect historically earlier immigration of blue collar workers from Canton province in southern China. Although the Mandarin speakers scored points higher than the Cantonese speakers, these differences were no longer significant after correcting for education.

There may be two likely reasons for the small number \( (n = 5) \) of participants who expressed a preference to be tested in Taiwanese: (1) In the 20th century, the population living in Taiwan comprised 2 major groups: mainlanders who migrated from mainland China to Taiwan in 1949 and native Taiwanese. In the 1970s and 1980s, the majority of immigrants from Taiwan who settled in Monterey Park were mainland Chinese \( [6, 19] \), whose mother language is Mandarin rather than Taiwanese dialect. (2) Since 1949, Mandarin has been the language taught in all schools and used as the official language throughout Taiwan; native Taiwanese may prefer Mandarin when taking a test even if they use Taiwanese dialect in their daily lives.

Another strength of our study is a sizable number of participants with less than 12 years of education \( (n = 181 \text{ for } 1–6 \text{ years of education}, n = 282 \text{ for } 7–11 \text{ years of education}) \). The effects of age and education are in the expected directions, as we observed higher MoCA-ChLA scores among younger and higher educated participants. Our data indicate that education is a more potent variable than age in predicting the performance on MoCA-ChLA. After adjusting for age, the mean MoCA-ChLA scores were, respectively, 2.0 and 4.6 points lower in the mid-low-(7–11 years) and low-low-(1–6 years) education groups in comparison to that of the high-education \( (12–20 \text{ years}) \) group \( (n = 277) \). Our recommendations of adding 2 points for persons with 7–11 years of education and 5 points for 1–6 years of education are significantly larger than the 1 point addition recommended in the original MoCA publication for persons with less than 12 years of education. In the latter study, the sample size was modest \( (n = 277) \), and the proportion of participants with less than 6 years of education was not specified. Caution should be exercised in adopting the same rule in other studies. In epidemiologic studies where a significant proportion of participants are poorly educated, the prevalence of cognitive impairment may be overestimated by following the limited education adjustment recommended by the original MoCA paper. For example, in a Korean study, more than 50% of the participants completed 6 years of education or less, but only 1 point was added to the MoCA score for this education group \( [8] \).

We found a significant association between MoCA-ChLA and age after controlling for the level of education. Moreover, scoring at or below the 15th percentile of the middle-age group, used as a surrogate marker for cognitive impairment, was most prevalent in participants aged 75 or older with less than 7 years of formal schooling \( (n = 277) \). The significance of these findings in this cross-sectional study is not clear and could result from several factors: (1) low-education is a vulnerability factor for normal cognitive aging, (2) low education is an independent risk factor for MCI or dementia, or (3) birth cohort effect may differentially affect the old-old group.

Women were disproportionately represented in the low-low education group. This is not surprising, given the cultural deemphasis on education of women in China prior to the second half of the 20th century. Men were on average 2 years older and had 1 more year of education than women. Gender did not affect MoCA-ChLA score before and after controlling for age and education.

IRT analysis suggested that the executive function domain had the best discriminating power and highest precision in measurement for participants in the cognitive function range of \( \pm 2 \text{SD} \). The memory domain also demonstrated high-discrimination ability although the level of precision is not as high as the executive domain. The executive function domain included the items of alternating trail making, generation of animal names, and verbal abstraction/similarities. Our finding supported the MoCA-ChLA in screening both executive and memory dysfunction in Chinese speaking Cantonese or Mandarin. These domains are particularly important when screening for cognitive impairment related to cerebrovascular and Alzheimer diseases.

Several limitations of our study should be considered. Although the MoCA-ChLA was administered by trained interviewers, data from a collateral informant regarding the participants’ cognitive, affective, and physical conditions or functional decline were not obtained. Further characterization of the sample will be needed to (1) provide normative data, (2) identify cases of MCI and dementia, (3) determine cut points for optimal sensitivity and specificity for the diagnosis of MCI, (4) refine adjustment scores for individuals with low education, and (5) verify the hypotheses regarding age-related cognitive decline.

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Research Article

Relative Preservation of Advanced Activities in Daily Living among Patients with Mild-to-Moderate Dementia in the Community and Overview of Support Provided by Family Caregivers

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Little is known about the extent to which advanced activities of daily living among patients with dementia are preserved and how family caregivers of these patients support them in the community. In this cross-sectional assessment of pairs of patients with dementia and their family caregivers, we evaluated basic, instrumental, and advanced activities of daily living by comparing past and present status observed by caregivers with subjective estimations by patients with dementia. We also asked about ways in which support was provided by family caregivers. Thirty-nine pairs of patients with dementia and caregivers who presented to our memory clinic were interviewed. The mean age of patients with dementia was 75.3 ± 7.0 years, and Mini-Mental State Examination scores were 22.3 ± 3.4. We found relative preservation of advanced activities of daily living compared with instrumental activities of daily living. Caregivers provided instrumental, informational, and reminding support to patients with dementia. These findings may reinforce the concept of person-centered support of patients with dementia in the community.

1. Introduction

As the number of patients with Alzheimer’s disease (AD) increase, social care costs that patients, their families, and society pay are expected to increase [1]. Although Banerjee and Wittenberg report various advantages of early diagnosis of dementia [2], including social cost reductions, the effects of pharmacological therapy are limited, as drug therapy induces only slight improvements in patients and caregivers’ daily lives. In addition, caregivers often have limited social support [3].

Patients with AD are often unable to complete activities of daily living (ADL). This inability spans from basic ADL (BADL), such as clothing and bathing to instrumental ADL (IADL), such as shopping and food preparation, and advanced ADL (AADL), such as hobbies and working. The preservation of advanced activities is important to help people maintain their self-identity. Support and intervention for patients such as person-centered care and dementia care mapping, which includes understanding the patient’s life history, individuality, and perspectives, are being widely accepted as an approach to deliver high-quality dementia care [4]. With this style of support, care workers recognize that the personality of the patients with dementia is concealed rather than lost, personalize the person’s care and environment, offer shared decision-making, interpret behaviors from the viewpoint of the person, and prioritize the relationship with the patients as much as the care tasks [5]. This approach may reduce agitation and result in use of significantly fewer neuroleptic medications in nursing home residents [6, 7]. In addition, before a diagnosis is given and until family caregivers find formal support after a diagnosis is made, family members can provide the so-called person-centered care by themselves during daily caregiving because they know the patients well.
Compared with the late stage of dementia, patients and family tend to experience more difficulties in early- to middle-stage dementia with behavioral psychological symptoms of dementia (BPSD). Lövheim et al. revealed a higher prevalence of BPSD such as aggressiveness, wandering, restless behavior, hallucinatory symptoms, and depressive symptoms in middle-stage dementia and showed that persistent symptoms of passiveness, including apathy, often are more prominent in the later stage [8]. Maslow suggested a theory of human motivation from basic physical needs to self-actualization [9], and Buron recommended analyzing support needs of patients with AD along with Maslow’s model to provide person-centered care [10]. When basic physical needs are satisfied, patients tend to have psychological needs, especially when the care is focused on the body or care tasks [11, 12]. Although support for patients in BADL and IADL to maintain minimal requirements of their daily lives has been discussed and is being developed, studies on support in early- to middle-stage dementia, and in particular in AADL, are scarce.

To provide better person-centered care from the early stage of dementia, person-centered support in AADL should be developed. In addition, this care should be given by formal caregivers, volunteers, and/or mutual aids in addition to family caregivers to reduce the burden of family caregivers in an ageing society and the rapid increase of patients. The aim of this study was to analyze declines in different types of ADL (BADL, IADL, and AADL) by comparing current and previous (around but before family noticed first symptoms of dementia) support needs in ADL retrospectively in community dwelling patients and to examine what kind of support family caregivers provided, especially in the early stages of dementia.

2. Methods

2.1. Participants. Community dwelling peoples with mild-to-moderate dementia and their family caregivers who regularly visited the memory clinic in Kyoto University Hospital for more than 6 months were invited to participate. To be included, the patient’s Mini-Mental State Examination (MMSE) score had to be greater than 15, and they had to have a family caregiver, regardless of whether they were living together or not.

All participants were informed about the aim, risks, and benefits of the study, and consented to be included. This study was approved by the ethical committee of Kyoto University Hospital.

A total of 39 patients with AD (18 males and 21 females; mean age, 75.3 ± 7.0 years; mean MMSE score, 22.3 ± 3.4) and their family caregivers (12 males and 27 females) were included. The mean duration from the first visit at our hospital to the interview was 2.1 ± 1.4 months. The mean age of caregivers was 63.1 ± 13.8 years. The relationships to the patient were spouse, 23 (59.0%); child, 11 (28.2%); spouse of patient’s child, 3 (7.7%); and other, 2 (5.1%). The diagnosis of AD was made according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer’s Disease and Related Disorders Association [13, 14].

2.2. Survey Questions and Statistical Analysis. Interviews took place from September 2004 to October 2005 by clinical psychologists and a speech therapist who are skilled at dementia care. During an interview, all participants (39 pairs of patients and their family caregiver) were asked how much support the patient needed in ADLs at the time of the interview and in the past (around but before the onset of symptoms of dementia), and what kind of assistance family caregivers provided in daily lives. Patient’s support needs in AADL and IADL were evaluated by the patient and caregiver separately. Also, patient’s levels of BADL (toilet, feeding, dressing, grooming, physical ambulation, and bathing) were rated by caregivers using a 5-point scale from 0 (fully dependent) to 4 (independent) based on the Lawton scale [15]. Lawton’s IADL (responsibility for own medications, ability to handle finances, mode of transportation, food preparation, shopping, ability to use telephone, housekeeping, and laundry) were rated by patients and caregivers on a 4-point scale (0, does not do spontaneously; 1, needs extreme assistance and support; 2, needs a little assistance and reminding or does it imperfectly; 3, fully independent). Although Lawton and Brody developed a 2-point scale for these variables, we evaluated patient’s IADL using a 4-point scale in this study to evaluate support needs more precisely.

We chose AADL items referring to Koyano’s paper validating Tokyo Metropolitan Institute of Gerontology (TMIG) index where the highest two sublevels of competence among Lawton’s seven sublevels are regarded as AADL [16]. We also chose items from leisure activities described by Baltes et al. where the activities of elderly was divided into obligatory activities (BALD/IADL) and leisure activities [17]. The 8 common AADL items interviewed in this study were selected two from TMIG index (reading a newspaper, giving advice to family), four from the study by Baltes (watching TV, taking a walk, care of a grandchild, socializing with others) and two activities (shopping on special occasions, participating in a meeting) were subjectively selected taking urban environment of the survey area and typical ability of old people there into consideration. We asked carefully to avoid patient’s passive behavior in AADL, asking caregivers, for example, “Does he/she actively watch TV programs which he/she is interested in?” We divided AADLs into two categories: common AADLs that include intellectual and social activities common to many people, and leisure activities, which can vary in individuals depending on the person’s character, interests, and routines. Leisure activities included those suggested by Baltes et al., such as gardening and reading [17]. In addition, patients and caregivers were asked to list as many activities and interests of patients as possible. For example, based on Baltes et al., interviewers asked “what has the patient been interested or stuck on these days?” Support needs for common AADLs were rated using the same 4-point scale used for IADL. Activities that the patient has not done since he/she was healthy were not taken into account in the analysis. In addition, caregivers provided concrete examples in which they provided daily
The mean number of support categories for each activity was more than one type of support for a single activity, and the using the paired ADL evaluations and patient’s self-evaluation were analyzed. In addition, “reminding support” such as reminding the patient beside the patient were classified as “emotional support.” In “appraisal support,” and listening to the patient and staying port. “ Praising or encouraging the patient was classified as informational support. Giving specific advice to the patient was categorized as “instrumental support.” Taking the patient to the place he/she needs to go, doing activities with the patient, and preparing for the activity were categorized as “instrumental support.” Giving specific advice to the patient was classified as “instrumental support.” Giving specific advice to the patient was categorized as “instrumental support.”

Patient’s declines in different types of ADL (BADL, IADL, and AADL) in addition to differences between caregiver’s ADL evaluations and patient’s self-evaluation were analyzed using the paired t-test. Caregivers were allowed to describe more than one type of support for a single activity, and the mean number of support categories for each activity was calculated. All data were analyzed using SPSS version 17.0. P values less than 0.05 were considered as significant.

| Table 1: Demographics of patients and caregivers. |
|-----------------------------------------------|
| Patients (n = 39) | Caregivers (n = 39) |
|-------------------|---------------------|
| Age (y) | 75.3 ± 3.4 | 63.1 ± 13.8 |
| Female (%) | 53.8 | 69.2 |
| MMSE score | 22.3 ± 3.4 |
| Family relationship |
| Spouse | 23 |
| Children | 11 |
| Daughter-in-law | 3 |
| Other | 2 |
| MMSE: Mini-Mental State Examination. |

3. Results

Table 1 shows background characteristics of participants. Compared to previous levels (before the symptom onset), BAdL declined by 11.3% (±8.7), IADL declined by 57.4% (±19.5), and AADL declined by 46.4% (±20.0) based on caregiver’s assessment. There was remarkable deterioration in IADL and AADL compared with BADL (P < 0.01, BADL versus IADL; P < 0.01, BADL versus AADL). The difference in decline between IADL and AADL was not significant. Among BADL, significant declines (P < 0.05) were observed in toileting, bathing, dressing, and grooming; no significant changes were seen in physical ambulation and feeding (Table 2).

There were significant declines in all IADL (P < 0.01) based on caregiver’s assessment. Remarkable declines were observed in responsibility for own medications and handling finances. There was a wide range of decreases in previous IADL scores depending on the activities, because original levels largely varied depending on individuals; however, all changes were significant. In addition, significant declines were shown in IADL.

Patient’s self-evaluation of current ADL levels was compared with caregivers’ evaluation (Table 3). Although patients recognized their functional declines, they generally estimated their activity levels as much higher than objective observations provided by family caregivers. In IADLs, significant differences between patient’s self-evaluation and caregiver’s objective evaluations were shown in all eight activities. On the other hand, there were no significant differences between patient’s self-evaluation and caregiver evaluations for the AADLs of taking a walk, watching TV, shopping on special occasions, and taking care of grandchildren. The level of inconsistency between the patient and caregiver was calculated for each IADL and AADL by the dividing patient’s self-evaluation score by the caregiver score. Levels of inconsistency were larger for IADLs (1.98 ± 0.42) than for AADLs (1.38 ± 0.34, P < 0.05).

When focusing on the average number of activities that patients had continued and those that patients had quit since symptom onset, it was revealed that most patients could continue watching TV (89.8%) and shopping on special occasions (89.1%) as common AADLs. However, a remarkable number of patients quit reading newspapers (28.9%), participating in meetings (50%), and giving advice to the family (43.2%). Patients tended to cite traveling, gardening, hobby classes, and going to theaters as their leisure activities, although there were wide variations in activities. Patients seemed to be able to continue two leisure activities on average.

Table 4 shows how many types of support caregivers provided for each common AADL at the time of the interview. Most support was categorized as instrumental support (34.6% of total supports) and reminding support (38.0%). Caregivers sometimes provided emotional support (16.7%) and informational support (10.2%). In general, there was less appraisal support compared with other types of support. Instrumental, informational, and reminding support tended to be provided when patients went out such as for shopping and meetings. In addition, among leisure activities, caregivers were more likely to provide support for going out such as travelling and going to theaters. On the other hand, patients seemed to enjoy some activities (playing music, singing, taking care of pets, and gardening) without support.

4. Discussion

Although patients’ BADL declined gradually, greater deteriorations were observed in AADL and IADL. We expected larger declines in AADL compared with IADL based on Maslow’s hierarchy of motivations [9]. However, there was no significant difference between declines in AADL and those in IADL. There were significant gaps between patient’s self-evaluation of ADLs and caregiver’s evaluations. Reminding support, which seems to play an important role in encouraging patients in activities, instrumental support, and informational support, made up a large percentage of total support for AADL and leisure activities. Most support in AADL and leisure activities was provided for patient’s going out.

From the viewpoint of complexity of activities and Maslow’s hierarchical model, we hypothesized that AADL would be more damaged rather than IADL in dementia patients. In fact, Vriendt et al. describe that detecting subtle
### Table 2: Differences in ADL activities of patients; past and present, based on caregiver’s assessment.

| Activities                  | Present     | Past      | Percent decrease | Number | P value |
|-----------------------------|-------------|-----------|------------------|--------|---------|
| **Basic ADL**               |             |           |                  |        |         |
| Dressing                    | 3.05 ± 0.83 | 4.00      | 23.7             | 39     | P < 0.01|
| Bathing                     | 3.28 ± 1.00 | 4.00      | 17.9             | 39     | P < 0.01|
| Grooming                    | 3.51 ± 0.68 | 4.00      | 12.2             | 39     | P < 0.01|
| Toilet                      | 3.59 ± 0.82 | 4.00      | 10.3             | 39     | P < 0.01|
| Feeding                     | 3.92 ± 0.27 | 4.00      | 1.9              | 39     | ns      |
| Physical ambulation         | 3.92 ± 0.27 | 4.00      | 1.9              | 39     | ns      |
| **Instrumental ADL**        |             |           |                  |        |         |
| Responsibility for own medications | 0.58 ± 0.76 | 3.00      | 80.7             | 38     | P < 0.01|
| Ability to handle finances  | 0.59 ± 0.93 | 2.92 ± 0.36 | 79.6         | 37     | P < 0.01|
| Mode of transportation      | 0.92 ± 1.14 | 2.97 ± 0.16 | 69.1         | 37     | P < 0.01|
| Food preparation            | 0.86 ± 0.85 | 2.39 ± 0.96 | 64.2         | 28     | P < 0.01|
| Shopping                    | 1.09 ± 0.71 | 2.62 ± 0.78 | 58.4         | 34     | P < 0.01|
| Ability to use telephone    | 1.85 ± 1.04 | 2.97 ± 0.16 | 37.9         | 39     | P < 0.01|
| Housekeeping                | 1.35 ± 0.85 | 2.15 ± 1.13 | 37.0         | 34     | P < 0.01|
| Laundry                     | 1.74 ± 1.02 | 2.56 ± 0.89 | 31.9         | 27     | P < 0.01|
| **Advanced ADL (common AADL)** |          |           |                  |        |         |
| Participation in a meeting  | 0.84 ± 0.99 | 3.00      | 71.9             | 32     | P < 0.01|
| Giving advice to family     | 0.92 ± 0.95 | 2.89 ± 0.46 | 68.2         | 37     | P < 0.01|
| Reading a newspaper         | 1.32 ± 1.14 | 3.00      | 56.1             | 38     | P < 0.01|
| Shopping on special occasions | 1.38 ± 0.86 | 2.78 ± 0.63 | 50.5         | 37     | P < 0.01|
| Socializing with others     | 1.54 ± 0.98 | 3.00      | 48.6             | 35     | P < 0.01|
| Watching TV                 | 1.82 ± 1.05 | 3.00      | 39.3             | 39     | P < 0.01|
| Taking a walk               | 2.26 ± 0.92 | 3.00      | 24.6             | 23     | P < 0.01|
| Care of a grandchild        | 2.64 ± 0.50 | 3.00      | 12.1             | 11     | P < 0.05|

### Table 3: Difference of present activities of daily living (ADL) evaluated by patients and caregivers.

| Activity                  | Caregiver evaluation | Self-evaluation | Level of inconsistency* | Number | P value |
|---------------------------|----------------------|-----------------|-------------------------|--------|---------|
| **Instrumental ADL**      |                      |                 |                         |        |         |
| Responsibility for own medications | 0.58 ± 0.76 | 1.75 ± 1.17 | 3.02                     | 31     | P < 0.01|
| Ability to handle finances | 0.59 ± 0.93 | 1.73 ± 1.07 | 2.93                     | 31     | P < 0.01|
| Mode of transportation    | 0.92 ± 1.14 | 1.72 ± 1.23 | 1.87                     | 35     | P < 0.01|
| Food preparation          | 0.86 ± 0.85 | 1.65 ± 1.13 | 1.92                     | 24     | P < 0.01|
| Shopping                  | 1.09 ± 0.71 | 1.81 ± 1.11 | 1.66                     | 26     | P < 0.01|
| Ability to use telephone  | 1.85 ± 1.04 | 2.59 ± 0.55 | 1.40                     | 37     | P < 0.01|
| Housekeeping              | 1.35 ± 0.85 | 2.19 ± 1.11 | 1.62                     | 26     | P < 0.01|
| Laundry                   | 1.74 ± 1.02 | 2.42 ± 0.93 | 1.39                     | 23     | P < 0.01|
| **Advanced ADL (common AADL)** |              |                 |                         |        |         |
| Participation in a meeting | 0.84 ± 0.99 | 1.52 ± 1.33 | 1.81                     | 25     | P < 0.01|
| Giving advice to family   | 0.92 ± 0.95 | 1.38 ± 1.06 | 1.50                     | 24     | P < 0.05|
| Reading a newspaper       | 1.32 ± 1.14 | 2.37 ± 1.02 | 1.80                     | 37     | P < 0.05|
| Shopping on special occasions | 1.38 ± 0.86 | 1.26 ± 1.03 | 0.91                     | 29     | ns      |
| Socializing with others   | 1.54 ± 0.98 | 2.06 ± 1.24 | 1.34                     | 29     | P < 0.05|
| Watching TV               | 1.82 ± 1.05 | 2.26 ± 0.92 | 1.24                     | 38     | ns      |
| Taking a walk             | 2.26 ± 0.92 | 2.42 ± 0.90 | 1.07                     | 19     | ns      |
| Care of a grandchild      | 2.64 ± 0.50 | 2.75 ± 0.50 | 1.04                     | 4      | ns      |

*Level of inconsistency was calculated by dividing the patient’s self-evaluation score by caregivers evaluation score.*
Table 4: Support provided by family caregivers to maintain advanced activities of daily living (AADL) of patients.

| Activities                               | Number of activities | Number of support | Rate of support (mean ± SD) | Classification of support (number for each category) |
|------------------------------------------|----------------------|-------------------|----------------------------|---------------------------------------------------|
| **Common AADL**                          |                      |                   |                            | Instrumental Informational Appraisal Emotional Reminding |
| Shopping in special occasions            | 33                   | 68                | 2.03 ± 0.92                | 28 11 1 5 23                                        |
| Participation in a meeting               | 16                   | 31                | 1.94 ± 1.00                | 12 3 0 4 12                                        |
| Socializing with others                  | 29                   | 31                | 1.07 ± 0.88                | 8 1 0 4 18                                         |
| Taking a walk                            | 21                   | 20                | 0.95 ± 0.86                | 7 1 0 5 7                                          |
| Reading a newspaper                      | 27                   | 14                | 0.52 ± 0.80                | 2 2 0 6 4                                          |
| Watching TV                              | 35                   | 17                | 0.49 ± 0.85                | 2 3 0 7 5                                          |
| Care of a grandchild                     | 11                   | 2                 | 0.18 ± 0.60                | 1 0 0 0 1                                          |
| Giving advice to family                  | 21                   | 0                 | 0.0                         | 0 0 0 0 0                                          |
| **Subtotal common ADLs**                 | 193                  | 183               | 0.90 ± 0.74                | 60 21 1 31 70                                       |
| **Leisure activities**                   |                      |                   |                            |                                                   |
| Going to watch a movie and/or a concert  | 13                   | 32                | 2.46 ± 0.52                | 13 1 0 7 11                                        |
| Making a trip                            | 15                   | 35                | 2.33 ± 0.72                | 14 1 1 6 13                                        |
| Sports                                   | 4                    | 9                 | 2.25 ± 1.50                | 3 1 0 2 3                                          |
| Going for a calligraphy lesson, and so forth | 13               | 26                | 2.00 ± 0.71                | 10 3 0 1 12                                         |
| Continuation of work                     | 4                    | 7                 | 1.75 ± 0.96                | 2 3 0 0 2                                          |
| Playing games                            | 8                    | 9                 | 1.13 ± 0.99                | 3 0 0 2 4                                          |
| Playing a musical instrument, singing    | 4                    | 4                 | 1.00 ± 0.82                | 1 0 0 1 2                                          |
| Care of a pet                            | 3                    | 2                 | 0.67 ± 1.15                | 1 0 0 0 1                                          |
| Gardening                                | 11                   | 4                 | 0.36 ± 0.92                | 1 1 0 1 1                                          |
| Other                                    | 5                    | 13                | 2.60 ± 0.89                | 4 2 0 3 4                                          |
| **Subtotal of leisure activities**       | 80                   | 141               | 1.66 ± 0.92                | 52 12 1 23 53                                       |
| **Total**                                | 273                  | 324               | 1.31 ± 0.84                | 112 33 2 54 123                                    |

Changes in AADL in addition to IADL can be more useful to detect early symptoms of dementia [19]. However, our study showed no significant difference between IADL decline and AADL decline. The reason why AADL decline was similar to that of IADL could be firstly because of the difficulty of capturing the levels of AADL in the manner to compare it accurately with IADL. Secondly, caregivers might tend to underestimate decline of patients’ AADL, since it is assumed that patient’s AADL could be maintained with little help such as reminding compared to IADL support. Thirdly, their leisure activities could be necessarily maintained because enjoying leisure activities is deeply connected to their character and self-identity, and no one can enjoy instead of the patient. Fourthly, we could not easily hypothesize that AADL would be damaged earlier compared to IADL in persons with dementia, because ability to perform AADL can be affected by not only cognitive function but also social and emotional factors which are deeply affected by patient’s self-identities.

It seems to be easier to arrange support for BADL and IADL rather than AADL in patients, because there are less individual variations in how to provide this support. However, the importance of support in AADL and leisure activities cannot be overemphasized from a viewpoint of person-centered care [4, 5]. Cohen-Mansfield et al. suggested that hobbies/leisure activities can be one of four important domains of self-identity (hobby/leisure activities, professional role, family role, and personal attributes) [20] and showed that encouraging activities that stimulate patients’ identity roles could increase their interest, pleasure, and activity involvement, as well as reduce their agitation in residential care settings [21].

Unfortunately, support in AADL and leisure activities is often overlooked or omitted from public social services, because lack of support in AADL or leisure activities is not life threatening, whereas patients cannot survive without support for eating or toileting. In fact, support covered by Japanese Long-Term Care Insurance (LTCI) is limited to essential housekeeping and physical care. The system does not allow home helpers to support patient’s leisure activities or AADL [22].

This study revealed that family caregivers often provide instrumental support, such as taking a patient to shopping or to activities, in addition to reminding support, including informing patient of events and activities. These kinds of support could help patients maintain independence and autonomy and should be included as part of dementia care. Providing these types of support is not time consuming if the caregiver knows the patient's lifestyle and interests.
However, this is not usually the case for outside caregivers, and thus providing this type of support is not easy for several reasons. First, caregivers need to learn additional skills to help them gain information about the patient’s life history and individuality. Second, learning about individual patients can be time consuming and it is difficult for service providers to charge for this seemingly “non-medical” service such as reminding, which can be finished within minutes.

Activities for patients with dementia in formal care settings, including day care and short-term care, should be person-centered as well. Activities should be beneficial to patients and suited to individual interests and preferences. However, activities for patients with dementia in formal care settings and the efficacy of these activities have not been well studied, because these short-term care services were originally started primarily to provide relief for family caregivers. In fact, uniform exercise and recreation activities are often offered during formal care, and the effects of institutional respite on care recipients, including ADLs, BPSD, and cognitive function are still inconclusive [23–25].

To improve person-centered dementia care in the community, it is important for care providers to reconsider care skills and service provision by knowing what kind of support family caregivers provide in daily care. Furthermore, person-centered care can be strengthened by supporting family caregivers, who know the person’s life history and preferences. In a longitudinal study, Burgener and Twigg showed that care recipient’s quality of life (QOL) can be affected by caregiver factors such as caregiver distress [26]. Family caregivers of patients should be supported socially, psychologically, and economically by society and the community, although differences in attitudes to family caregiving may vary by culture.

Gaps between patient’s self-evaluation and caregiver evaluation in ADLs (especially IADL and AADL) indicate the need to ask caregivers as well as patients about declines in ADL, because patients might not be aware of small declines or pathological changes. Service and care providers should listen to caregiver’s evaluations along with patient’s self-evaluation when arranging support, so that the patient’s activity levels are evaluated appropriately, and they can be supported in activities that stimulate their sense of identity. As Cohen-Mansfield et al. suggested, the goal of support should be individual patient’s self-actualization and maintaining identity, not only supporting them in essential BADL [21]. Regarding relative preservation of evaluated status of AADL by patients compared to that of IADL, we guess that the patients could be psychologically reluctant or shameful to admit their loss of IADL functions by themselves compared to AADL, because IADL may require more functional element obligatory to daily life than AADL, resulting in denial of the present real IADL status of them. Another reason may come from caregivers’ support for AADL below the surface which could maintain the patients’ AADL without their awareness.

Limitations of this study include sampling bias and recall bias: participants were recruited in only one clinic in one university hospital in Japan, and data (previous levels of ADL) were collected retrospectively at one interview. Longitudinal observation studies are needed to reveal if family support in AADL can be helpful in maintaining patient’s QOL. In addition, similar studies should be undertaken worldwide to reveal regional differences and cultural differences in family caregiving and support for patients with dementia. Another limitation is that we could not show the evidence of the benefit of caregiver’s support on patient’s QOL in this study. We asked about it in our interview using a visual analogue scale. The analysis did not show any significant associations between them even after controlling for care recipients’ age and dependencies in BADL/IADL, possibly because there are a large number of factors which can affect patient’s QOL: patient’s dependency level and severity of dementia, amount of caregiver support, patient’s lack of awareness of being helped, relationships between patient and caregiver, and so on (data not shown).

5. Conclusion

This study revealed that family caregivers of patients with AD provide various supports in patient’s AADL and leisure activities, which could play an important role in maintaining the identities of patients. It is difficult to assess levels of AADL in patients with dementia because there are individual variations in preferred activities and daily routines. However, knowing the type of support provided by family caregivers may be helpful when support for the patients with dementia is going to be provided by mutual aids in communities, volunteers, or additional care workers in the future.

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Research Article

Characterizing Cognitive Deficits and Dementia in an Aging Urban Population in India

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Rapid rise in the population of older adults in India will lead to the need for increased health care services related to diagnosis, management, and long-term care for those with dementia and cognitive impairment. A direct approach for service provision through memory clinics can be an effective, successful, and sustaining means of delivering specialized health care services. We have established a memory clinic in Mumbai, India by employing the diverse clinical skills available in Indian academic institutions, diagnostic and research expertise of clinicians and psychologists, and the support of the U.S. National Institutes of Health. Our project involved recruitment of patients, clinical and neuropsychological assessment, and standardized diagnostic procedures, demonstrating the feasibility of using research methods to develop a memory clinic. In this paper, we describe the development of a community-based memory clinic in urban India, including linguistic and cultural factors and present detailed results, including diagnostic characterization, on 194 subjects with various stages of cognitive deficits. Our findings support the feasibility of developing a memory clinic in a public hospital and successful use of research diagnostic criteria to categorize cognitive deficits observed in this population, which may be used to inform the development of other such clinics.

1. Introduction

The mental health of aging persons in India is receiving growing attention as the country is projected to be the home of one of the world’s largest populations of elders [1]. By 2025, the number of persons in India over 60 is projected to reach over 150 million [2]. In light of this rapidly increasing population, dementia and cognitive impairment are expected to increase as well. A comprehensive review of mental health conditions in India across the lifespan summarizes the growing problem of dementia [3]. Prevalence rates of dementia in India over the past two decades ranged from approximately 1.4% among those 65 years and older [4] to 3.5% among those 60 years and older [5] in rural settings; in urban settings, prevalence rates were reported as 2.44% among those 65 years and older [6]. Recently, however, crude prevalence rates of dementia in India have been reported as high as 10.6% in persons 65 and older living in rural areas and 7.5% for those in urban areas [7].

Early detection of cognitive impairment and dementia is critical to its management and will require developing the capacity to efficiently evaluate and manage occurrence of disease [8]. The establishment of specialized memory clinics can provide the capacity to identify and treat dementia in the population and can also act as a resource from which information about disease and its management can be shared with other practitioners and throughout the community. Evaluations must be able to provide differential diagnoses of specific subtypes of dementia and impairment and be sensitive enough to capture staging of disease severity in...
order to direct appropriate interventions. Among developing countries, as elsewhere, Alzheimer’s disease and vascular dementia are the two most common types of dementia observed [9]. The assessment of mild cognitive impairment (MCI) may be more challenging in these populations due to the lack of normative data across the breadth of socio-economic strata that exists in a country as large as India. Several research efforts have reported assessing dementia subtypes in India with commonly used measures. The 10/66 Dementia Research Group has successfully employed dementia evaluations including neuropsychological tests in cross cultural contexts in order to inform diagnoses of Alzheimer’s type dementia based on DSM-IV criteria [10]. In addition, standardized measures have been used to characterize Alzheimer’s disease, vascular dementia, and dementia with Lewy bodies [11, 12]. Neuropsychological evaluations in this population have been used to diagnose mild cognitive impairment [13] in some settings. These are encouraging efforts for the utility of commonly used dementia assessment methods in developing countries such as India and support the development of standardized dementia assessments in memory clinics to evaluate and characterize cognitive impairment.

Nonetheless, there are few reports of memory clinics in India, particularly in public hospitals in medical school settings where the patient population is diverse, and models of clinical services need to accommodate the challenges of multiple linguistic and cultural factors as well as educational and economic extremes. In this paper, we report the results of integrating commonly used research methods in dementia evaluation with a diverse sample of older adults seen at a public hospital. We also provide our experiences in dealing with the challenges faced in assessing cognitive disorders in this population.

Our research team established a memory clinic under the Cognitive Disorders in the Elderly Joint Indo-US Dementia Research Project in Mumbai, funded by an NIH/NIA/FIC grant. This clinic was designed to facilitate clinical and neuropsychological dementia evaluations and offer participants treatment options, as well as house dementia studies and clinical trials. Clinical researchers from Mount Sinai School of Medicine’s Alzheimer Disease Research Center (MSSM ADRC) collaborated with clinicians in the Topiwala National Medical College/Nair Charitable Hospital, a state-run public hospital in Mumbai, India, in order to plan, coordinate, and execute the establishment of the clinic in the hospital. The purpose of this preliminary paper is to describe the development of a memory clinic in Nair Charitable Hospital, including the outreach process, the evaluation methods including linguistic and cultural considerations, training the clinical team, and developing consensus diagnostic procedures, and describe the clinical population seen at the clinic.

2. Methods

2.1. Outreach Process. The clinic was established as a center for individuals with memory and cognitive problems, which offered evaluation, treatment, and management including education for families and caregivers. In order to raise awareness about the utility of the services offered at the memory clinic, outreach efforts focused on education about dementia and cognitive disorders and included description of the possible personal and social impact of these disorders. The initial outreach for the clinic was made through the departments of Psychiatry and Neurology at Nair Hospital which are the home departments of the local Principal Investigators of the research project. The broader medical community was then engaged and informed of the clinic through special lectures, seminars, and workshops sponsored by Nair and open to the medical and aging care communities throughout Mumbai.

2.2. Evaluations. The data reported here was collected from patients seen in the memory clinic who underwent the informed consent process for research as approved by the Nair Charitable Hospital and Topiwala National Medical College Ethics Committee. Informed consent procedures for those who may not have been able to give consent followed the ethical guidelines of the Nair Hospital Ethics Committee, including obtaining a signature from a proxy. While the clinic would provide the clinical evaluation without consent, the consent allowed for summarizing and reporting data from the clinical evaluation. Virtually all who were asked to participate agreed to consent. Participants were then administered a standardized clinical evaluation and battery of neuropsychological tests. These instruments were modeled after the National Alzheimer’s Coordinating Center (NACC) standardized Uniform Data Set (UDS) evaluation [14] (which is available at the following URL http://www.alz.washington.edu/WEB/forms-uds.html) and the MSSM ADRC’s clinical core assessment (available upon request from the author, M. Sano).

The evaluation included a semistructured interview with both the patient and an informant in order to provide an accurate and comprehensive account of symptoms. In addition to basic demographic information, a semistructured assessment of the presenting cognitive complaints, a history of symptoms, a quantified functional assessment, and measure of instrumental and basic activities of daily living are collected. Psychiatric, medical, and family history of dementia and cognitive loss were recorded. Laboratory tests were ordered to rule out medical illnesses such as B12 deficiency, thyroid illness, and acute infection when needed. Medical comorbidities were recorded including diabetes, hypertension, thyroid dysfunction, and coronary and pulmonary disease. Global mental status and disease severity were assessed using the Mini-Mental State Examination (MMSE) [15] or Hindi version of the MMSE [16] and clinical dementia rating scale (CDR) [17]. Mood and psychiatric disorders were assessed by patient and informant (usually family)—reported history and with psychiatric and behavioral symptom scales (Neuropsychiatric Inventory [18] and Geriatric Depression Scale [19]). An adapted blessed functional activity scale [20] assessed activities of daily living. Neurological examination included the clinician assessment of cognition, motor, and sensory function and a standardized...
assessment of extrapyramidal symptoms (EPS), based on the UPDRS [21]. All participants were advised to undergo clinical imaging (CT or MRI) however, since the procedure was not included in this study, it is not available for all cases. When available, scans were reviewed by the clinic’s neurologist, and imaging results were recorded and discussed during diagnostic consensus conferences.

2.3. Training the Clinical Team. The clinical team included local neurologists, psychologists, and a social worker. A study neurologist conducted the semi-structured clinical interviews and physical examinations. Study neurologists were trained in administering the semi-structured interview through tutorial and observation of experienced ADRC dementia clinicians. Master’s level psychologists (the minimum educational level required to practice psychology in India) administered a neuropsychological assessment (results not reported here). Standardized training procedures for conducting the neuropsychological assessment included viewing a standardized training DVD, observing neuropsychological assessments performed by the senior psychologist at the memory clinic, and administering neuropsychological assessments under the supervision of a neuropsychologist. Deidentified copies of the neuropsychological scoring protocols were sent to the MSSM ADRC psychometrician who reviewed them for administration and scoring errors and provided feedback. All staff received training and certification where available to conduct standardized measures such as mental status (MMSE [15] or HMSE [16]) and disease severity (CDR) [17]. We used standardized training techniques which have been demonstrated to yield reliable results [22]. A social worker facilitated clinical visits and clinical followup, including visiting the home as needed.

2.4. Diagnosis. Research diagnostic categories and methods of assignment were modeled after the NACC Uniform Data Set [14] and the MSSM ADRC. Diagnostic worksheets, designed to be completed by a clinician, were created to ensure classification was made according to published criteria. All cases received a consensus diagnosis either at an internal (Nair Hospital clinicians and staff only) or joint (Nair Hospital and MSSM clinicians and staff) consensus conference. Joint conferences were held during site visits and over Skype conference calls, and all consensus conferences were attended by at least one clinician and one psychologist. Specific diagnostic categories were based on standard research criteria: dementia of the Alzheimer’s type, as outlined in the DSM-IV [23]; probable and possible Alzheimer’s disease (AD) [24]; probable and possible Ischemic Vascular Dementia (VaD) [25]; mixed dementia, defined as the presence of ischemic vascular dementia and another systemic or brain disorder causing dementia [25]; dementia with Lewy bodies (DLBs) [26–28]; frontotemporal dementia (FTD) [29]; mild cognitive impairment (MCI) both amnestic and nonamnestic types [30]; other disorders, such as psychiatric disorders, were diagnosed when standard criteria was available.

2.5. Linguistic and Cultural Factors. Careful consideration of linguistic and cultural factors was required prior to applying the clinical research and assessment methodology described above in this population. One of the first challenges was identifying age or date of birth. Since some participants, particularly those of low literacy, were not able to specifically identify their age or date of birth, methods of approximation were used. Such methodology included first asking the participant or informant to spontaneously recall major historical events and temporally relate them to personal milestones during childhood and adulthood. A prepared list of historical events was then reviewed with the participant or informant who was asked again to relate them to personal milestones. Similar methodology has been previously described [31].

Interview and assessment were completed in one of four languages, English, Hindi, Marathi, and Gujarati (among the most common languages spoken in Mumbai) depending on the language the patient was proficient in. All examiners were proficient in all four languages. However, some cases required use of an interpreter (other clinical staff in the hospital). Separate interviews were offered with individual informants or family members in order eliminate possible discomfort from discussing the patient’s cognitive or functional difficulties in the presence of the patient. Additionally, staff members of both genders were available to discuss what may be viewed as socially inappropriate behaviors with informants and family members.

The high rate of illiteracy and low education in this population required consideration and adaptation of evaluation methods. The HMSE was used for those who were of low literacy as items were adapted for illiterate rural Indian populations [16]. Several assessment items required further explanation (e.g., providing an example of what sentence is) or concrete, real-world framing (e.g., subtracting rupees for serial subtractions). Additionally, demonstrations were offered for alternating movement instructions during the neurological exam.

2.6. Data Analysis. This paper summarizes demographic and clinical features using descriptive statistics (mean, SD, range, and frequency) for the cohort recruited between the years 2006 and 2010. Diagnostic categories were enumerated and demographics and medical history are provided for major diagnostic groups. The HMSE has a maximum score of 31, whereas the maximum MMSE is 30. In order to combine scores across participants into one variable, the HMSE was converted to a percent correct which was then calculated out of 30 and was combined with MMSE scores into one adjusted MMSE variable (this method has not been validated). Demographic and medical comorbidity variables were examined with one-way ANOVA (age and years of education) or chi-square or Fisher’s exact test (gender, medical comorbidities) to compare differences among the three most common major diagnostic groups, AD, VaD, and MCI. For the purposes of these analyses, MCI amnestic and nonamnestic groups were combined into one MCI group.
3. Results

During the recruitment period, 212 participants were evaluated for cognitive complaint by Nair Hospital’s memory clinic. The majority of these cases were referred by clinicians from the Nair Neurology or Psychiatry Departments. Among those who came to the clinic with a cognitive complaint, 18 did not receive a diagnosis: four were evaluated too soon after acquiring an ischemic stroke to make an accurate diagnosis; the clinical evaluation was not able to be completed for 13 cases; and in one case, the data was deemed insufficient to make a diagnosis. Therefore, this paper is based on data from 194 clinical cases. CT or MRI imaging results were available on 135 of these 194 cases and available to the members of the consensus conference when these cases were reviewed. Of the 194 cases, date of birth was approximated in 103 cases.

3.1. Demographics and Medical Conditions. Demographic features and medical conditions of the sample are summarized in Table 1. Notably, there is a high percentage of males (64.4%) in this group. The medical conditions assessed are also outlined in Table 1 (data on history of hypertension and diabetes was not available on 3 of the clinical cases, and data on the rest of the conditions was not available on 4 clinical cases; percents are of cases for which data was available). Hypertension was the most common medical condition in the sample, observed in 45.9% of cases. Diabetes and stroke were also present in approximately 20% of cases. A high number (35.3%) of the clinical samples with completed neurological exams (n = 187) were observed to have at least one extrapyramidal symptom (e.g., resting tremor or rigidity). Primary language was available for 192 cases, of these Marathi was the most common (52.1%), followed by Hindi (17.7%), Gujarati (10.4%), and others (19.8%).

3.2. Presenting Complaint. Among those cases seen in the clinic, memory change was the most common presenting complaint and was present in 66.5% of cases. The next two most common presenting complaints were personality change (13.5%) and change in behavior (12.4%). Few participants complained of change in performance (8.3%), language, (6.7%), disorientation (5.2%), depressed mood (2.1%), or psychosis (5.2%). In twenty five clinical cases, more than one presenting complaint was recorded.

3.3. Diagnostic Assignment. Of the 194 cases that were referred to the clinic for a cognitive complaint and received a diagnosis, 65.5% had a diagnosis of dementia (see Table 2). Among those with dementia, 45.7% had AD (probable or possible), 22% had VaD (probable or possible), 15% had mixed dementia (coincident with VaD), progressive dementias in this group included AD, DLB, and Parkinson’s disease-related dementia), and 11% had FTD. The remaining approximately 6% of dementia cases had other diagnoses including dementia due to alcohol abuse or neurotrauma, dementia with Lewy bodies, vitamin B-12 deficiency, or Parkinson’s disease-related dementia.

Of the nondementia clinical cases, approximately 64.2% were diagnosed as MCI (amnestic n = 33, and nonamnestic n = 10), 28.3% had a primary psychiatric disorder (e.g., depression, schizophrenia, psychosis, etc.), and 7.5% were not impaired.

3.4. Dementia Diagnoses. The three most common dementia diagnoses were Alzheimer’s disease, vascular dementia,
and mixed dementia. Significant differences ($F(2, 102) = 5.16, P < .01$) in age were found between the VaD ($\bar{x} = 60.21 \pm 10.97$) and AD ($\bar{x} = 67.64 \pm 9.56$) groups, but not between the mixed dementia group ($\bar{x} = 65.05 \pm 10.01$) and either other group. In addition, there was a significantly higher frequency of females in the AD group (50%) and mixed dementia groups (36.8%) than the VaD group (7.1%; $P < .001$; and $P = .02$, resp.) however, no differences were observed between the AD and mixed dementia groups ($P = .42$). Hypertension was reported more frequently in the VaD group (74.1%; data unavailable for one case) than in the AD group (41.4%; $P < .01$) however, no differences were found between the mixed dementia group (68.4%) and AD or VaD groups. The groups did not differ on any other demographic (i.e., years of education, percent illiterate) variables.

### 3.5. MCI, AD, and VaD

AD and MCI participants were found to be of similar age however, the VaD group was significantly younger than both the AD and MCI groups (see Table 3). Performance was compared on global measures of cognition, function, and psychiatric symptoms between the AD, MCI, and VaD groups (complete data for each measure was unavailable for some cases in each of the diagnostic groups). While there were no significant differences observed between the AD and VaD groups on these measures, overall significant differences were observed between both dementia groups, AD and VaD, and the MCI group on all measures, indicating worse cognition, worse functioning, and more psychiatric symptoms in the dementia groups. There were no differences observed on the geriatric depression scale between any groups.

### 4. Discussion

This work described the challenges of establishing a memory clinic in an urban Indian community and provides evidence of the feasibility of evaluating a diverse patient population. Key elements of the clinic that contributed to its success included organized outreach efforts, standardized evaluations, training for the clinical team, and consensus-based diagnostic processes.

While outreach efforts were comprehensive, the majority of referrals were from knowledgeable neurologists or psychiatrists seeking a comprehensive dementia evaluation for an existing cognitive complaint. It was also likely that in most cases the cognitive complaint was brought to the clinician only after there was interference with activities of daily living. Additionally, patients and family members who came to the memory clinic displayed little knowledge or understanding of dementia or cognitive impairment as a medical entity. This highlights several important issues in this population: first, despite receiving referrals predominantly from specialized clinicians with expertise in dementia, there was considerable uptake of the memory clinic’s services indicating the substantial need for such memory clinics in this community. Second, there remains a great need for education about dementia and cognitive symptoms among general medical settings, communities, and the public at large, beginning with raising awareness about dementia as a distinct medical entity.

Cultural considerations were key to engaging the community. Since this is a culture that holds high respect for elders, discussing what may be viewed as shortcomings (i.e., cognitive symptoms) can be viewed as a sign of disrespect. Thus, separate, private interviews with individual informants and family members were an important provision in order to collect unhindered information about true deficits. Additionally, same-gendered interviewers also facilitated more forthcoming discussion of behavioral symptoms that may be viewed as socially inappropriate (e.g., hypersexuality, abusive behaviors). In addition, some of the items of the basic and instrumental activities of daily living were not culturally relevant measures of functioning. For example, the item that measures the participant’s ability to eat rates eating with
one’s hands as impaired, but among this population eating with one’s hands is quite common and culturally normal. In such cases, the physician assessing the participant used other items to determine a change from a previous level of functioning. The spoken version of many Indian languages lacks a term for dementia, and “memory impairment” is frequently used to describe a wide range of deficits; thus, exhaustive interviews with informants were often required to obtain a clear understanding of the presentation. The very low literacy of our sample also presented a challenge. While illiteracy in India is high [33], our sample had higher rate of illiteracy than the city of Mumbai [34], which may be a result of recruitment through a state-run hospital.

The distribution of our dementia diagnoses is similar to other reports from India [6, 11, 35] and reports of memory clinics from other developing countries [36, 37], with the most common diagnosis of Alzheimer’s disease, followed by vascular dementia. Alzheimer’s disease is recognized as the most common type of dementia in both developed [38] as well as in developing countries [9]. This complements the known neuropathology which is similar in urban Indian samples and urban samples from the US [39].

As a whole, there were more males than females in this sample. However, the gender distribution is similar to that of western cohorts when diagnostic category is taken into account [40]. In particular, the high proportion of males in the MCI group is comparable to that seen in western samples [41], and a similar pattern in the VaD group has been observed in other reports from memory clinics in India [12]. It is unclear if this represents a difference in medical use pattern or differential awareness or sensitivity to cognitive complaints by gender.

Among the comorbidities assessed in this population, hypertension surfaced as the most common medical comorbidity in both the clinical and comparison groups. Detected hypertension is generally treated in this cohort; however, this data was not available for this publication since initial evaluations often depended on report of medication use without confirmation from other service providers or from more knowledgeable family members. The prevalence of hypertension in the Indian population is receiving increased attention, as it may become a serious health concern among the nation’s population of older adults [42, 43]. Hypertension has been found to be a significantly higher risk factor for vascular dementia than AD in other urban Indian samples [13]; in our sample, hypertension was more frequently found in the VaD and mixed dementia groups than in the AD group. In light of the high frequency of hypertension observed here and in other studies, and of the known contribution to vascular disease, future studies might determine its contribution to the rate of cognitive decline in neurodegenerative illness.

As expected, the cognitive, functional, and psychiatric measures successfully characterized the dementia, AD and VaD, and MCI groups. The AD and VaD groups were observed to be more cognitively and functionally impaired than the MCI group, and the AD and VaD groups also had more neuropsychiatric symptoms than the MCI group. All groups endorsed a comparable, subthreshold number of items on a depression scale.

We note that the age of this cohort is younger than many identified in western countries. Yet it is not dissimilar from ages reported from other clinical cohorts in India with dementia [11, 12]. This is probably not surprising in a setting where illiteracy is high and education is low [35]. Educational achievement is rapidly changing in India as is life expectancy, and with this, we may expect to see a shift in the demographic characteristics of the clinical population. Additionally, in our sample, the MCI group was found to be more highly educated than the AD and VaD groups. This discrepancy may reflect a higher self-awareness in the MCI group, prompting them to be clinically examined at an early indication of some impairment. These findings highlight the need to include sensitive measures to capture the sometimes subtle cognitive and functional changes in MCI across educational levels. In addition, clinical outreach and educational efforts should be attentive to the wide range of education in this older population and how that may impact initial cognitive complaint.

Our sample is one of convenience and may not represent the population as a whole, but it may be representative of those who seek treatment at a public hospital. However, an advantage of assessing a clinical population is that the cases are referred with clear complaint and often functional deficits. When clinical history can document decline in cognition and function, the need to depend solely on normative neuropsychological testing is mitigated. In the clinical setting, the demand for normative data to characterize subtle deficits may be greatest within the average educational spectrum and across many cultural factors. Future studies that hope to capture the earliest cognitive changes in healthy populations should be mindful of the high rate of illiteracy in India, and prepare a diverse battery of neuropsychological measures accordingly taking into account the education, language, and concepts within the culture to truly make the evaluation bias free.

In several cases, participants had never encountered a testing situation before, a limitation commonly observed in developing countries [44], and while great care was taken to provide adequate explanation and comfort in the testing environment, performance may have been affected by the novelty of the situation. Future research studies and memory clinics should explain the nature of the tests and address any anxiety related to assessment prior to the testing. Among several participants, exact birthdates were unknown but estimated by the participant and his or her family, and in some cases, age was also estimated. Such a limitation has been found in other studies conducted in India, as well [45].

In summary, this paper demonstrates the feasibility of developing a memory clinic as described here and the value of using global measures of cognition and measures of functioning and psychiatric symptoms to characterize cognitive impairment in an urban memory clinic in India. As other memory clinics in India have also successfully used the CDR, NPI, and MMSE to inform dementia diagnosis [12], taken together the application of these measures may support their use as best clinical practices in this population. Further,
our results also support the utility of applying research diagnostic criteria to diagnose different dementia types and MCI in this population.

Developing memory clinics and integrating research evaluation methods can lead to early detection of impairment and dementia and also facilitates the development of clinical trials and other research protocols in this population. Based on our experience, what is critical to the development of a memory clinic are devoted offices and treatment rooms, standardized assessment methods, a clinical team with clearly defined roles, standardized diagnostic procedures, and regular consensus conferences. It is likely that most of the resources needed to develop a memory clinic are already present in hospital settings. Hospitals may be able to allocate offices and treatment rooms for this purpose, and existing staff may be able to fill the roles of the clinical team through a training program that promotes capacity building. As the population of older adults in India grows, it will be necessary to prepare to meet the needs of this population, through the continued development of clinical research and memory clinics such as the one reported here.

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Research Article

Dementia and Diabetes Mellitus: Association with Apolipoprotein E4 Polymorphism from a Hospital in Southern India

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Objective. To evaluate the association of Apolipoprotein E4 (ApoE4) in Alzheimer’s dementia (AD) with comorbid diabetes mellitus (DM).

Methods. The study included subjects with Alzheimer’s dementia (AD) (n = 209), individuals with non-Alzheimer’s dementia (nAD) (n = 122), individuals with parental history of AD (f/hAD) (n = 70), and control individuals who had normal cognitive functions and no parental history of dementia (NC) (n = 193). Dementia was diagnosed using International Classification of Diseases-10 revision (ICD-10) criteria. DM was assessed on the basis of self-report and/or use of antidiabetic medications. ApoE genotyping was done using sequence-specific primer polymerase chain reaction.

Results. Apo E4 allele frequencies were highest among AD with comorbid DM (0.35) followed by AD without DM (0.25), nAD with DM (0.13), nAD without comorbid DM (0.12), and NC (0.08). Frequency of ApoE4 in persons with f/hAD was 0.13. The association of AD with co-morbid DM in ApoE4 carriers was more in comparison to NC with DM (OR = 5.68, P = 0.04).

Conclusion. There is a significant association between AD with co-morbid DM and ApoE4 genotype.

1. Introduction

With the rapid change in the demographic profile of India, the prevalence of chronic diseases of the elderly like dementia and DM type 2 is increasing. In India, over 3.7 million people aged 60 years and above suffer from dementia, predominantly of Alzheimer’s type. Assuming that the current prevalence rate remains stable, these numbers are projected to increase to 6.35 million by 2025 [1]. Studies from India indicate that ApoE4 allele is significantly associated with AD, and it is a risk factor [2–5].

There has been a pandemic rise of DM especially among Asian Indians. Currently 40.9 million Indians suffer from DM, and this is projected to increase to 69.9 million by 2025 [6]. Genetic predisposition and environmental factors interact to increase the risk of DM among Asian Indians. DM type 2 which accounts for 90% of DM is predominantly a polygenic disease with various loci identified at PGC-1α, PC-1 (K121Q), IRS-2, MODY, and so forth [7]. Many population-based cross-sectional studies [8] and prospective studies [9–13] have indicated that DM or abnormal glucose tolerance doubled the risk of AD (RR 1.37–2.27); though others have not confirmed this link [14]. Tripathi et al. [15], in a study from Northern India, reported DM as a risk factor for dementia; 33.3% of their sample with dementia had diabetes compared to 9% of the controls (P < 0.001). Other reports from Asia confirm the association between DM and AD in ApoE4 carriers. Peila et al. [16] in a large population-based study of Japanese American men found a significant association between DM, AD, and ApoE4 carriers; subjects with ApoE4 allele and DM had a relative risk of 5.5 for AD. Matsuzaki et al. [17] in a retrospective analysis
of autopsies found a very significant positive association between hyperglycaemia, AD neuropathology, and ApoE4 status (OR 38.9).

We conducted a hospital-based cross-sectional study of dementia, to evaluate the interaction between AD and diabetes, as a function of the ApoE4 allele status.

2. Methods

2.1. Sample. Consecutive persons with dementia attending the Geriatric Clinic of the Department of Psychiatry in National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, and their consenting offspring were invited to participate in this study. This sample is part of a larger study of genetic and clinical correlates in dementia, and details about evaluation have been reported earlier [2]. In this paper, the study sample (n = 594) included AD (n = 209), nAD (n = 122), f/hAD (n = 70), and NC (n = 193). The nAD group consisted of vascular and mixed dementia (n = 46), frontotemporal dementia (n = 30), Lewy body dementia (n = 10), and other dementias (n = 36). Control subjects included genetically unrelated and cognitively intact age-matched subjects. The study was approved by the Ethics Committee of NIMHANS, and informed consent was collected prior to participation. All the subjects were evaluated using a standard protocol including general clinical evaluation, functional assessment (Everyday Abilities Scale for India, EASI [18]), neuropsychology testing (Hindi Mental Status Examination, HMSE [19]), laboratory investigations (haemogram, blood glucose levels), and genotyping and imaging (MRI scans using a 1.5 or 3 Tesla machine; or CT scan) whenever possible. Clinical evaluation was done by trained psychiatric residents and the diagnosis of dementia established using ICD-10 criteria. Further sub-typing was done by a psychiatric/neurology consultant. Their comorbid DM was recorded based on laboratory results or self-reports, being on antidiabetic medication. Other participants were assessed using the same methodology and protocol.

Ten millilitres of venous blood was collected, and DNA was extracted using salting out method [20]. Polymerase chain reaction (PCR) was performed using sequence-specific primer PCR methodology [21]. The presence of 173-bp band was indicative of the specific ApoE haplotype. The results were corroborated with real-time PCR results for 10% of the samples in every experiment.

2.2. Statistical Methods. We compared ApoE4 frequency and DM status in AD, nAD, f/hAD, and NC. Statistical analysis was done using R software [22]. Comparisons between variables were done using chi-square test for categorical variables and unpaired t-test for continuous variables. Fisher’s exact test was used when any of the values in the contingency table was less than 10. Odds ratios and P values were computed, and statistical significance was inferred if P < 0.05.

3. Results

Based on the sample selection, AD, nAD, and the NC were older than 60 years (61.14 ± 11.40 years; 61.73 ± 12.41 years; 60.35 ± 15.65 years, resp.). The AD, nAD, and NC group had crossed the age at risk for onset of DM. Results show that on average, 11.6% of our study group had developed DM. However, the prevalence of DM differed between the various groups, being—17.7% of the AD, 13.9% of the nAD, 6.2% of the NC, and 4.3% of the f/hAD (Table 1).

ApoE4 carrier rates in AD (n = 98/209) were higher than age-matched NC (n = 32/193) (P < 0.0001, Table 1). The difference in ApoE4 carrier status between AD with comorbid DM and NC was significant (P = 0.0001). ApoE4 allele frequencies were highest among AD with co-morbid DM (0.35) followed by AD without DM (0.25), nAD with DM (0.13), nAD without co-morbid DM (0.12), and NC (0.08). The association of AD with co-morbid DM in ApoE4 carriers was more in comparison to NC with DM (OR = 5.68, P = 0.04, Figure 1).

There were 17 individuals in this study who were ApoE4 homozygotes—14 AD, 2 nAD, and one f/hAD. Among the 14 AD with homozygous ApoE4, 6 (42.8%) individuals were receiving treatment for DM. In comparison, there were 84 AD who were ApoE4 heterozygotes, of whom only 14 had DM (16.6%). Homozygous ApoE4 carriers had significantly greater comorbidity of DM and AD (P = 0.035).

4. Discussion

The present cross-sectional study evaluates the relationship between ApoE4 status, AD and DM in a sample from southern India. The study also confirms the significant association between ApoE4 allele and AD in the Indian population [2–5]. The ApoE4 frequency however was not associated with the age of onset of AD, or the degree of cognitive and functional ability as assessed by HMSE and EASI.

The study also reiterates the increased association of AD and DM (P = 0.0004) established by other studies [8–13, 15]. Interestingly, AD individuals with DM were more likely to be ApoE4 carriers compared to NC with DM (OR 5.68). The ApoE4 allele frequency was also significantly high in this group (0.35). The current study indicates a need to evaluate the role of ApoE4 as a risk factor for DM in future. Earlier research of ApoE4 as a risk factor for DM has yielded inconsistent results. Study in Mexican Americans [23] did not find any difference in ApoE4 frequency between diabetics and nondiabetics. It is interesting to note that Xu et al. [10] found a significant association between borderline DM and AD only in non-ApoE4 carriers. Assessment of the ApoE4 status in DM without AD in the Indian population would be able to provide some clarity towards this. Individuals with ApoE4 allele if found to have an increased risk to DM in their middle age, the combined presence of ApoE4 and DM might further increase the risk of AD later. Testing of this hypothesis was not feasible in the present study as it was a cross-sectional one from a Geriatric Clinic which caters to the needs of elderly with dementia. A prospective controlled followup study of the individuals with DM with and without ApoE4 allele into old age is needed to establish the implications of this association of ApoE4, AD and DM.
Table 1: Clinical profile and ApoE polymorphism in the study population.

|                          | Alzheimer’s dementia (AD) \(n = 209\) | Non-Alzheimer’s dementia (nAD) \(n = 122\) | Individuals with parental history of AD \(\text{f/hAD}) \(n = 70\) | Control individuals with no parental history of dementia (NC) \(n = 193\) | \(P\) value \(\text{comparing AD and NC}\) | \(P\) value \(\text{comparing nAD and NC}\) |
|-------------------------|--------------------------------------|------------------------------------------|-----------------------------------------------|-----------------------------------------------|--------------------------------|--------------------------------|
| Mean age in years       | 61.14 ± 11.40                        | 61.73 ± 12.41                           | 37.27 ± 8.87                                  | 60.35 ± 15.65                                | 0.56**                          | 0.41**                        |
| M:F                    | 105:104                              | 75:47                                    | 51:19                                         | 114:79                                       | 0.076*                          | 0.67*                          |
| DM, \(n\) (%)          | 37 (17.7)                            | 17 (13.9)                               | 3 (4.3)                                       | 12 (6.2)                                     | 0.0004*                          | 0.02*                          |
| HMSE                   | 12.71 ± 7.60                        | 14.19 ± 8.19                            | 30 ± 1                                        | 30 ± 1                                       | <0.0001**                        | <0.0001**                      |
| EASI                   | 8.41 ± 2.76                          | 8.19 ± 3.03                             | 0                                              | 0                                            | <0.0001**                        | <0.0001**                      |
| E2E2, \(n\) (%)        | 0 (0)                                | 1 (0.8)                                  | 0 (0)                                         | 0 (0)                                        | 1*                              | 0.39*                          |
| E2E3, \(n\) (%)        | 11 (5.3)                             | 11 (9)                                  | 5 (7.1)                                       | 23 (11.9)                                    | 0.017*                          | 0.42*                          |
| E3E3, \(n\) (%)        | 100 (47.8)                           | 82 (67.2)                               | 48 (68.6)                                     | 138 (71.5)                                   | <0.0001*                         | 0.42*                          |
| E2E4, \(n\) (%)        | 13 (6.2)                             | 4 (3.3)                                 | 0 (0)                                         | 2 (1)                                        | 0.007*                          | 0.21*                          |
| E3E4, \(n\) (%)        | 71 (34)                              | 22 (18)                                 | 16 (22.9)                                     | 30 (15.5)                                    | <0.0001*                         | 0.56*                          |
| E4E4, \(n\) (%)        | 14 (6.7)                             | 2 (1.6)                                 | 1 (1.4)                                       | 0 (0)                                        | 0.0001*                          | 0.15*                          |
| Total ApoE4 carrier, \(n\) (%) | 98 (46.9)                       | 28 (23)                                 | 17 (24.3)                                     | 32 (16.6)                                    | <0.0001*                         | 0.16*                          |
| ApoE4 carrier with DM, \(n\) (%) | 20 (9.6)                       | 4 (3.3)                                 | 0 (0)                                         | 2 (1)                                        | 0.0001*                          | 0.21*                          |

HMSE: Hindi Mental Status Examination (indicates level of cognitive function; highest score possible = 31).
EASI: Everyday Abilities Scale for India (indicates level of functional disability, highest score possible = 12).
\(P\) values calculated by unpaired \(t\)-test**, chi-square test*, and Fisher’s exact test*.

Figure 1: Venn diagram representation of AD and controls with their component distribution. Odds ratio comparing DM occurrence in ApoE4 carriers between AD and controls is 3.85 (\(P = 0.1^*\)). Odds ratio comparing ApoE4-positive DM subjects between AD and controls is 5.68 (\(P = 0.04^{**}\)).

Lack of prospective design, detailed assessment of DM and other validating phenotypes of AD like neuropsychological assessment, and imaging techniques for all the subjects are the limitations of the study. Reasonable sample size, methodological rigor in diagnostic assessment, and an attempt to correlate two conditions of increasing concern in India, that is, diabetes and AD in the context of ApoE4 allele are the strengths of the work.

Translational aspect of this association if proven is very important. In the Indian context, prevalence of diabetes is on the rise. Lifestyle and diet control measures to prevent DM in ApoE4-positive individuals especially with homozygosity
in middle age may modify/reduce the risk of Alzheimer’s dementia.

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