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#### Japan-US Comparisons of the Prevalence of Dementia

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Both Japan and the United States are facing a sharp increase in the elderly population; for example, the proportion of those aged 65 and older among the total population is projected to increase from 23% in 2010 to 36% in 2050 in Japan and from 13% in 2010 to 21% in 2050 in the US. Cognitive impairment and dementia are strong predictors of incident disability (e.g., 1-4). For the improved well-being of the elderly and the reduction of overall societal burden caring for the elderly, it is critical to find effective means to treat dementia or delay the progression of the disease.

Cross-national comparisons on the disease prevalence, incidence and trajectories of health related outcomes often shed light on potential risk and protective factors associated with various diseases. Cross-national comparisons also serve as validation of the associations found in other populations. Currently Japan holds the highest life expectancy in the world, but whether the Japanese elderly have better cognitive health compared with the elderly in the US is unknown. The reported prevalence of dementia among those aged 65 and older in Japan ranges from 5.3% to 7.2% (5-9), which is within the range reported in the US. One of difficulties, especially in cross-national comparisons, is how to standardize diagnostic methods. The most commonly used dementia diagnostic criterion is either DSM-III-R (10) or DSM-IV (11), which requires cognitive impairment severe enough to interfere with social or occupational functioning. However, social and occupational functioning expected for age groups/generations could vary considerably across cultures. The diagnosis and etiology of dementia also varies among countries; for example, it was thought that vascular dementia (VaD), rather than Alzheimer's Disease (AD), was more prevalent in Japan compared with the US and other western countries. However, more recent studies suggest that the previous findings in Japan might be due to the differences in diagnostic methods (9).

In this study, we systematically reviewed the literature on the prevalence of dementia in Japan and compared them with the prevalence representative of the US population reported by the Aging, Demographics, and Memory Study (ADAMS)(12). Our aims are to: 1) summarize diagnostic criteria used in epidemiological studies of dementia in Japan, 2) compare age-specific prevalence of dementia between the US and Japan, and 3) examine whether any systematic differences exist in the proportion of VaD vs. AD among Japanese studies, and between the US and Japanese studies.

## Study design and sample

We selected dementia prevalence studies in Japan which are representative (or aimed to be representative) of specific communities or a prefecture with at least 500 study participants aged 65 and older. We selected the latter criterion (n>=500) in order to have a large enough sample size to allow meaningful between-group comparisons on dementia prevalence. Four studies met these criteria: the Hisayama study, the Okinawa study, the Radiation Effect Research Foundation Adult Health Survey (RERF-AHS), and the Osaki-Tajiri Skip Study (aka Tajiri project). Brief descriptions of each study cohort follow. **Hisayama study**: Hisayama is a Japanese rural community adjacent the city of Fukuoka, a major city of Kyushu Island. An epidemiological study of cerebral stroke has been carried out prospectively there since 1961. A dementia prevalence study was conducted twice, in 1985 and again in1992. At the time of the national census in 1985, there were 938 Hisayama residents aged 65 years and older. A total of 887 subjects from this population were examined to identify cases of dementia, with a screening rate of 94.6%, as described previously (13). Out of 887 subjects, 59 cases of dementia were detected (6.65%). All patients with dementia were followed up by the usual surveillance methods of the Hisayama study and when patients died, autopsies were performed. The assessment was repeated in 1992. As of April 1, 1992, there were 1231 residents aged 65 years or older in the town. A total of 1189 residents (96.9%) was interviewed in the same way as in the survey conducted in 1985. Dementia was diagnosed in 68 patients (5.72%) (7,11).

**Okinawa study**: Okinawa is the most southern island in Japan. The prefecture is divided into five regions under the prefectural public health system. One city from the urban districts and one town/village from the rural districts of each region (i.e., 10 study sites) were selected and from each selected sites, random sampling was conducted to recruit study participants. Out of 3524 subjects aged 65 and older identified, 3312 (94%) underwent the dementia screening. Dementia was diagnosed in 172 patients (crude 5.19%; 7.27% with sample weight adjustment) (5).

**Radiation Effect Research Foundation Adult Health Survey (RERF-AHS):** In 1958, the Atomic Bomb Casualty Commission, later succeeded by the Radiation Effects Research Foundation, 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. Members of the AHS are invited to participate in biennial health examinations that include clinical evaluations and routine laboratory assessments. Between 1992 and 1996, 2934 men and women aged 60 and older who resided in Hiroshima were examined in the AHS. After excluding those who refused the dementia screening test at the time of the biennial health examination, 2222 subjects among the AHS (75.7%) were screened for dementia. Of these, 2052 completed the dementia screening assessment (69.9% of the eligible AHS member) with 7 subjects from nursing homes. Dementia was diagnosed in 160 patients (7.2%) (8).

**Tajiri Study**: The Tajiri project is a community-based study started in 1988 on 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 (N=3207) were targeted for the dementia prevalence study with1654 participants (51.6%) participating in the study and 1501 subjects completing the assessment. Of those assessed, 80 subjects were rated as Clinical Dementia Rating Scale (CDR)>=1.0 (5.3%) (9, 14)

For US figures, we used the results from the Aging, Demographics, and Memory Study (ADAMS) (15), the first prevalence study that calculated the nationally representative dementia prevalence. Briefly, the ADAMS sample was drawn from the larger Health and Retirement Study (HRS), an ongoing nationally representative cohort study of individuals born prior to 1954. The ADAMS assessments occurred between 2001 and 2003. All participants were >=71 years old and a total of 856 individuals participated. Full details of the ADAMS sample design and selection procedures are described elsewhere (16).

### Methods

All age-specific prevalence rates, and their 95% confidence intervals were provided by either published articles or were directly obtained from study groups upon our request. To create comparison tables with US figures and allow a large enough sample size for the comparison among studies, we used 10 year age intervals starting at age 70 (the starting age of US figures are 71) in this study.

### Results

Preliminary results include the following: 1) Dementia diagnostic criteria used in Japanese studies were DSM-III or DSM-III-R in all studies. Diagnostic criteria to define sub-types of dementia varied among studies in Japan and included Hachinski scores, NINCDS-AIREN, and ADDTC for VaD, and DSM-III-R and NINCDS-ADRDA for AD. 2) A significantly lower prevalence of overall dementia compared with the US figures was observed for women in their 80's in Okinawa. Interestingly, the prevalence of dementia among women aged 90 and older in Okinawa was somewhat higher than that of the US. This could be due to Okinawan women's longevity, that is, more Okinawan women aged 95 and older were

included in the study causing a higher prevalence rate compared with the US samples. Alternatively, Okinawan elderly, especially women, might have the similar lifetime risk of dementia as with the US elderly. Therefore, their prevalence rate "catches up" at a later stage of their life, before death. 3) Despite the differences in diagnostic criteria, among the youngest age group examined here (age 70-79), the prevalence of VaD was consistently higher than that of AD in Japan. As age increases, the proportion of AD among the total dementia cases increases and among those aged 90 and older, the proportion of AD among the total dementia cases could even surpass the proportion observed in the US. In the US, the prevalence of AD is consistently higher than that of VaD across all age groups. 4) There is a debate whether the higher prevalence of VaD than AD reported in the studies conducted in 1980s was due to the differences in diagnostic criteria used between the US and Japan. However, the Hisayama study which conducted the assessment at two points using the same diagnostic criteria showed that the proportion of AD vs. VaD increased sharply in 1992 compared with the result reported in 1985. Most of the changes in AD/VaD ratio over time observed in Japan could be due to the decline in stroke incidence in Japan, rather than the difference in diagnostic criteria

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