

Apparent Increases in Age-Specific Morbidity and Mortality of Alzheimer's Disease in Japan

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Abstract

Alzheimer's disease occurrence and death rates in Japan are thought to have been rapidly increasing in recent years, as seen from crude patient and mortality data. We analysed these recent trends from 1999 to 2014 using age-specific estimated patient rates (ASPRs) and mortality rates (ASMRs) obtained from E-Stat (the portal site of official statistics of Japan). Both ASPRs and ASMRs increased over time in elderly people according to simple exponential patterns. While ASPRs increased by a factor of less than 5 from 1999 to 2014 (estimated patient rates at age 85 - 89 years increased from 170 to 816 per 100,000), ASMRs increased by a factor of more than 10 (mortality rate at age 85 - 89 years increased from 8.1 to 87.7 per 100,000). Conversely, ASPRs for vascular dementia and unspecified dementia decreased to less than half over the same period (estimated patient rates at age 85 - 89 years decreased from 998 to 322 per 100,000), although mortality rates increased slightly (rates at age 85 - 89 years increased from 55.6 to 91.3). Interestingly, summed ASPRs of Alzheimer's disease and those of vascular and unspecified dementia were almost identical in 1999 and 2014, with estimated patient rates at age 85 - 89 years of 1168 and 1138 per 100,000 in the years 1999 and 2014, respectively. While ASPRs for Alzheimer's disease in females were significantly higher than those in males (at age 85 - 89 years, female-male ratios in 1999 and 2014 were 1.46 and 1.37, respectively), male and female mortality rates were almost identical in 1999 and 2014 (female-male mortality ratios at age 85 - 89 years were 1.01 and 0.97 in 1999 and 2014, respectively). In conclusion, apparent recent increases in morbidity due to Alzheimer's disease in Japan may be due to improvements in diagnostic accuracy, considering that total ASPRs of dementia remained almost unchanged. The apparent heightened morbidity in females may be due to differences in the proportion of each sex attending medical services with relatively mild symptoms because no sex-specific differences in mortality were found. There is no clear explanation for the observed increase in the summed ASMRs of Alzheimer's disease and other dementias, although this might also represent a diagnostic shift from other causes of death.

Keywords: Alzheimer Disease; Age-Specific Morbidity; Age-Specific Mortality; Sex Differences

Abbreviations

ASPR: Age-Specific Estimated Patient Rate; ASMR: Age-Specific Mortality Rate

Introduction

Dementia has a great burden to societies. Many cohort studies have conducted to find the prevalence and causes of the dementia all in the world [1-6] and also in Japan [7-10]. The major type of the dementia was the vascular type, then Alzheimer' type has exceed the vascular type in 1995 [7]. A recent study show Alzheimer' type is twice more than the vascular type [16].

With the increase in mean life expectancy, Alzheimer's disease has become an important contributor to mortality, with a reported attributable risk of 37.0% for ages 75 - 84 years and 35.8% for age \geq 85 years in USA [11].

Among dementias, the proportion of Alzheimer's disease in Japan has been said to be rapidly increasing both in terms of morbidity and mortality. Specifically, the reported mortality has increased by a factor of almost 10 over the past 20 years. This apparent increase in Alzheimer's disease is interesting; however, no obvious increases have been observed in suggestive pathological factors, except increased mean life expectancy.

To elucidate this apparent increase in Alzheimer's disease, we analysed changes in age-dependency of morbidity and mortality of Alzheimer's disease compared with other common neurological and psychological diseases.

Materials and Methods

Data were obtained from the Japanese Government Portal Site E-Stat [12]. Mortality rates were based on death certificates regulated to be written by medical doctors in the Vital Statistics. Patient rates were based on the records of outpatients and hospitalized patients in hospitals and clinics that were randomizedly adopted for every three years in the Patient Survey.

Age-specific mortality rates (ASMRs) were based on vital statistics. Age-specific (estimated) patient rates (ASPRs) were based on patient surveys. Patient rates are used herein as equivalent indicators of prevalence or morbidity. Data taken at 3-year intervals from 1999 to 2014 were compared. Rates for estimated patients and patient deaths were indicated per 100,000 people. For ASPRs and ASMRs, ages at the start of the study (1999) were grouped in 5-year intervals from age 0 - 4 to age 85 - 89; ages ≥ 90 years were included as a single group. From 2005 to 2014, ages were grouped up to 95 - 99 years; ages ≥ 100 years were included as a single group. Surveyed patients and deaths are assumed to obey a Poisson distribution. The significance level was considered at $p < 0.05$ unless stated otherwise.

Results

Figure 1A shows ASPRs of Alzheimer’s disease from 1999 to 2014. Total patient numbers increase exponentially with age, as seen in most other chronic diseases. The number of patients began to increase past age 60 and rapidly increase past age 70. Patient rates per age group increased every year; at age 85 - 89, the number of patients had increased by more than a factor of 4 from 1999 to 2014 (from 170 to 816 per 100,000). Figure 1B shows ASMRs during the same period. Mortality increased every year much more rapidly; at age 85 - 89, mortality had increased by a factor of more than 10 from 1999 to 2014 (from 8.1 to 87.7 per 100,000).

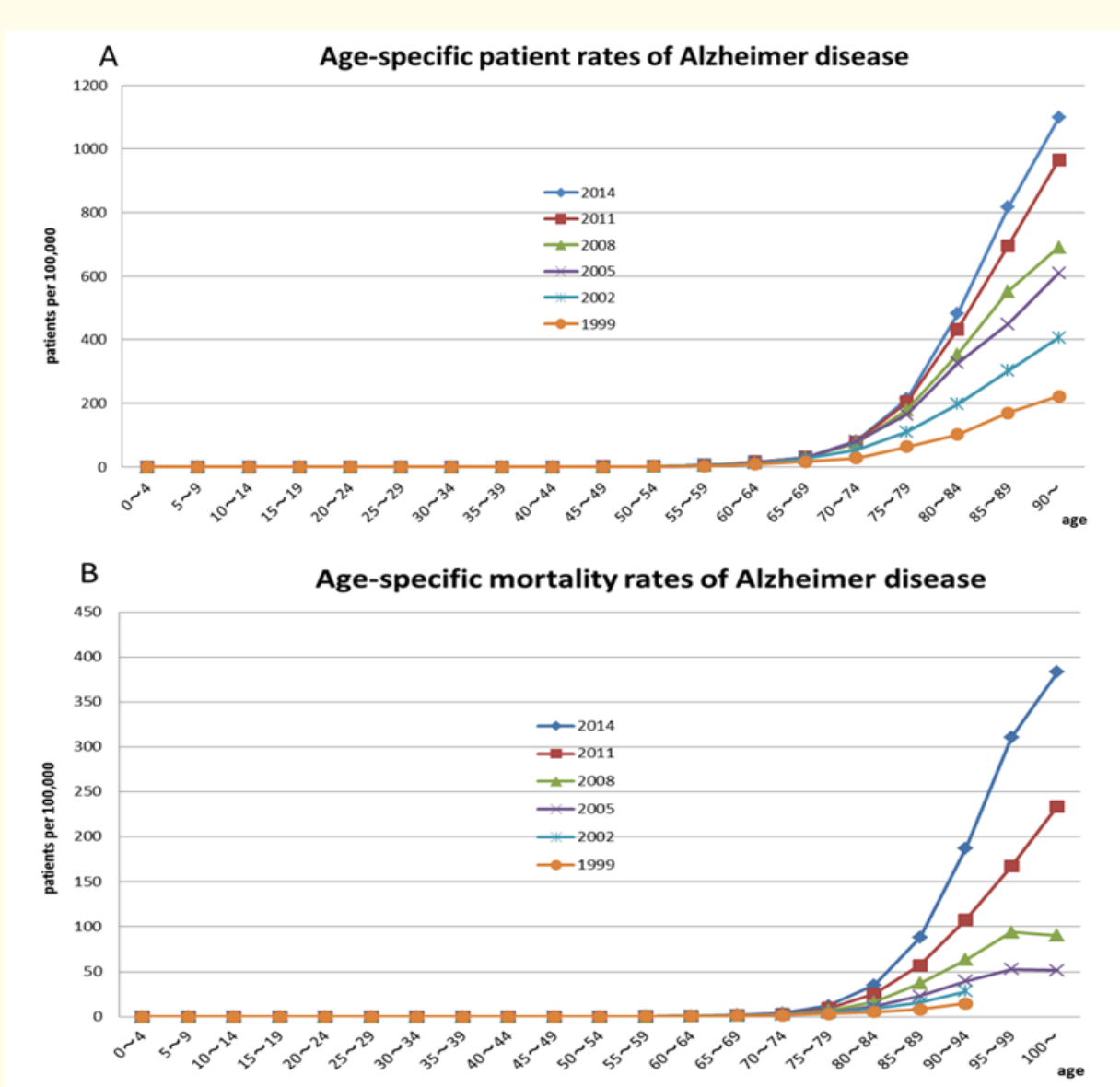


Figure 1: Age-specific estimated patient rates and mortality rates of Alzheimer’s disease.

A. Age-specific estimated patient rates of Alzheimer’s disease at 3-year intervals from 1999 to 2014 obtained from the Japanese Patient Survey. B. Age-specific mortality rates of Alzheimer’s disease at 3-year intervals from 1999 to 2014 obtained from Japanese Vital Statistics. For years 1999 and 2002, dots plotted at 90 - 94 reflect mortality rates for patients aged over 90 years old.

Figure 2 shows ASPRs and ASMRs of vascular and other dementias; ASPRs for these conditions gradually decreased every year, in contrast to the increase observed with Alzheimer’s disease. ASMRs for vascular and other dementias gradually increased every year, although much more slowly than in Alzheimer’s disease.

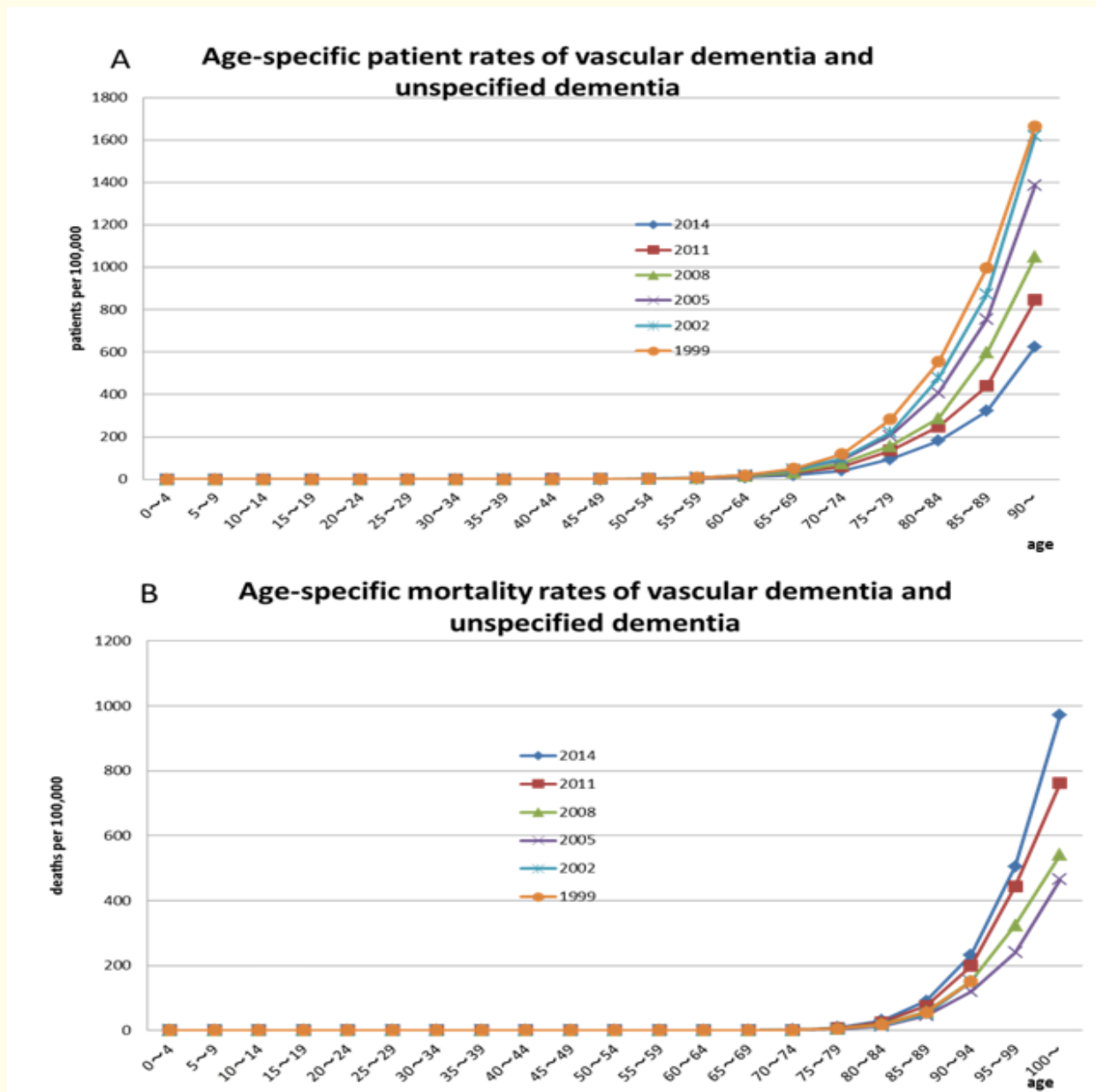


Figure 2: Age-specific estimated patient rates of vascular dementia and unspecified dementia. A. Age-specific estimated patient rates of vascular dementia and unspecified dementia. B. Age-Specific mortality rates of vascular and unspecified dementia. For years 1999 and 2002, final dots are mortality rates of patients aged over 90 years old.

Figure 3A shows the summed ASPRs of Alzheimer’s disease and vascular and other dementias. Only very small changes, if any, were observed across the 15 years. Conversely, summed ASMRs (in figure 3B) increased gradually every year, as expected from figure 1B and figure 2B.

Estimated male and female patient rates and mortality rates for Alzheimer’s disease at age 85-89 are shown in figure 4. While estimated patient rates for both males and females increased by more than a factor of 4 from 1999 to 2014, estimated female patient rates were about 1.4 times greater than for males in any given year (Figure 4A). In contrast, male and female mortality rates of ages 85-89 years were almost identical in both 1999 and 2014 (Figure 4B).

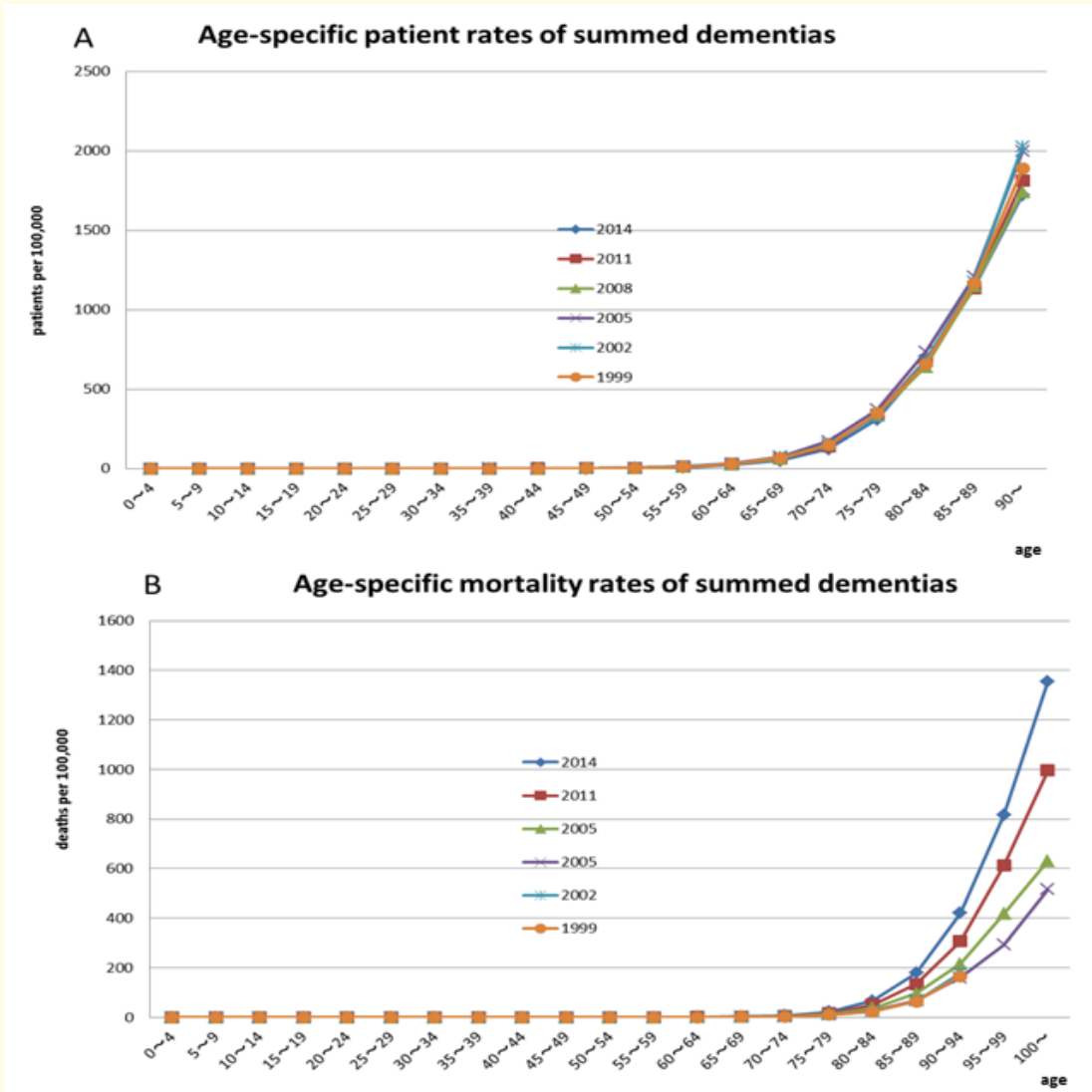
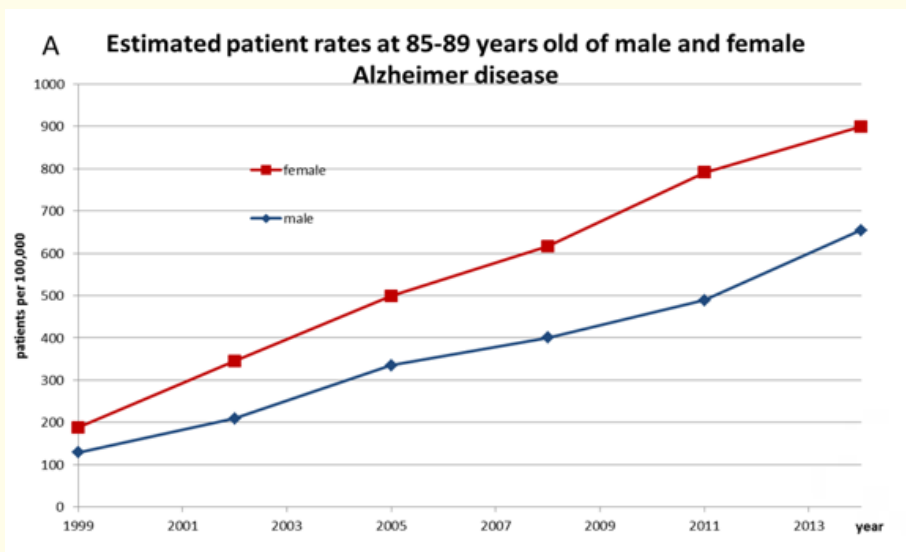


Figure 3: Age-specific estimated patient rates and mortality rates of summed dementias. A. Age-specific estimated patient rates of summed dementias. Summed values of estimated patient rates of Alzheimer’s disease (Figure 1A) and vascular dementia and unspecified dementia (Figure 2A) from 1999 to 2014 are plotted. B. Age-specific mortality rates of summed dementias. Summed values of mortality rates of Alzheimer’s disease (Figure 1B) and vascular dementia and unspecified dementia (Figure 2B) from 1999 to 2014. For years 1999 and 2002, final points reflect mortality rates of patients aged over 90 years old.



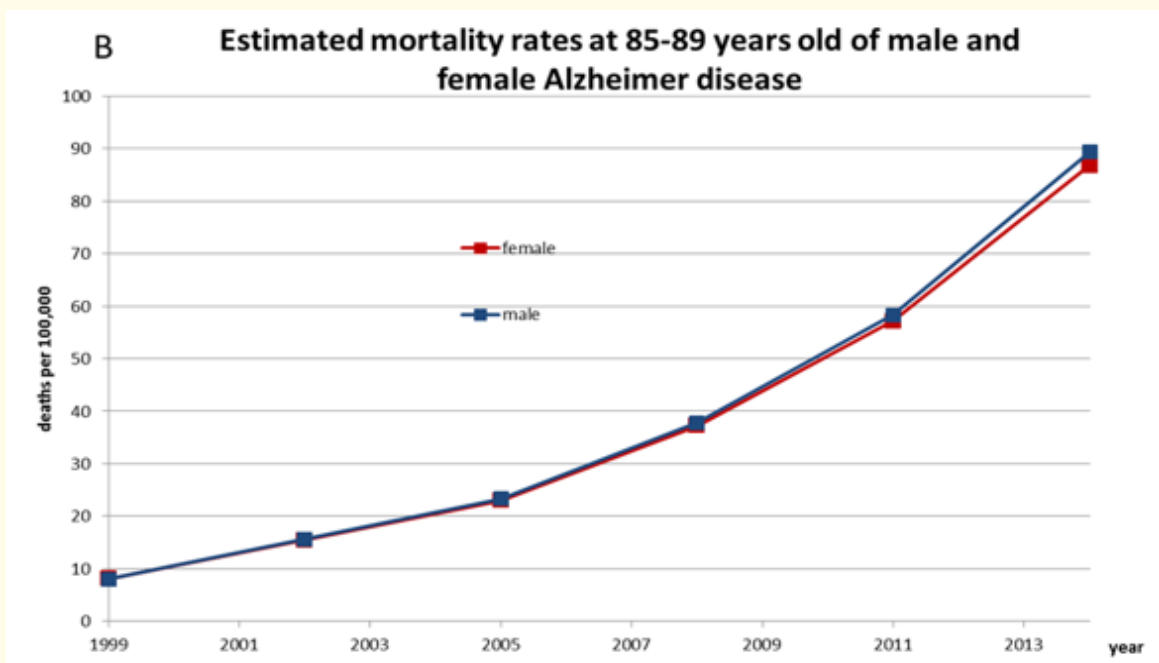
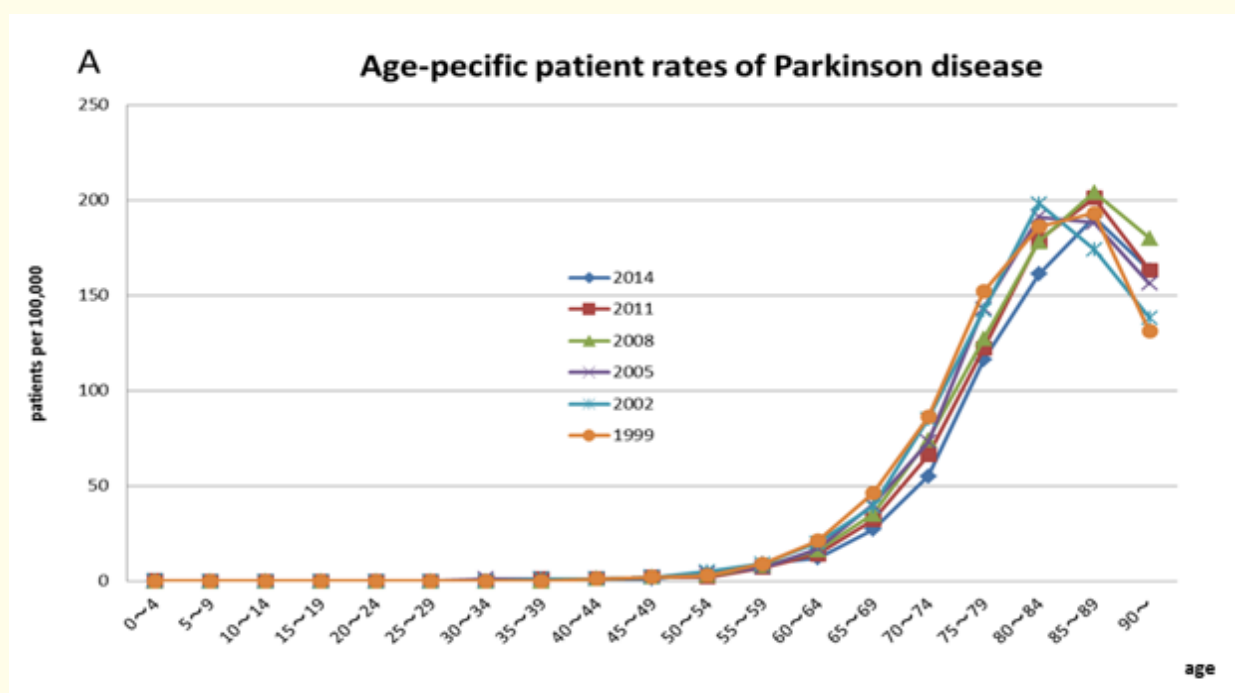


Figure 4: Estimated patient rates and mortality rates for 85 - 89-age group for male and female Alzheimer’s disease patients. A. Estimated patient rates for 85 - 89-age group for male and female Alzheimer’s disease patients, comparing rates from 1999 to 2014. B. Mortality rates for 85 - 89-age group for male and female Alzheimer’s disease patients, comparing mortality rates from 1999 to 2014.

In figure 5, ASPRs and ASMRs for Parkinson’s disease, another important neurological cause of death, are shown for comparison. Patient and mortality rates for Parkinson’s disease increased with age but began to decrease again with age. The peak age for patient rates was about 90 years and that for mortality rates was about 95 years. From 1999 to 2014, ASPR changed only slightly, whereas the mortality rate almost doubled for the 85 - 89-age group.



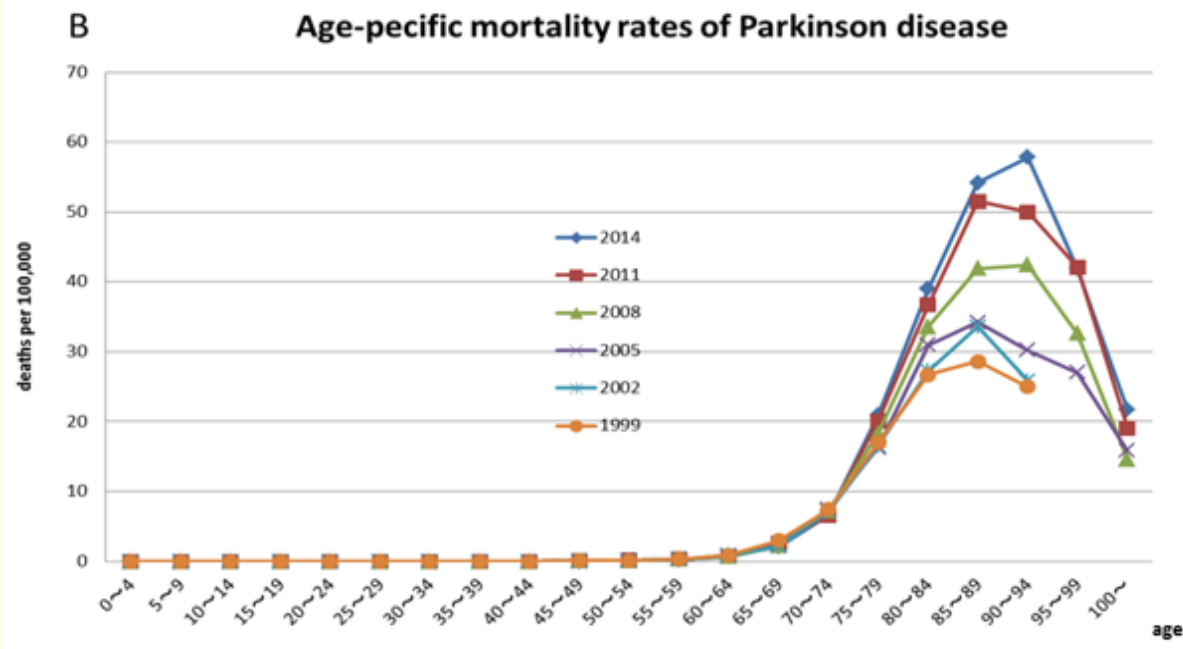


Figure 5: Age-specific estimated patient rates and mortality rate of Parkinson's disease.

A. Age-specific estimated patient rates of Parkinson's disease. B. Age-specific mortality rate of Parkinson's disease. For years 1999 and 2002, final points reflect mortality rates of patients aged over 90 years old.

Discussion

The apparent rapid increase in Alzheimer's disease patients in recent years seems to be due to a shift within dementia diagnoses and potentially improved diagnostic accuracy, considering summed dementias (Alzheimer's disease and vascular and unspecified dementias) remained almost constant in ASPRs from 1999 to 2014, as seen in figure 5.

However, ASMR of total summed dementias has increased over these 15 years (Figure 5). This seems a little peculiar considering that medical progress over these years would be expected to contribute to decreased mortality rates in most causes of death. In reality, the total mortality rate at age 85 - 89 years did decrease significantly over this time (from 10,498.6 to 8,177.0 per 100,000 in 1999 and 2014, respectively). One possible explanation is a diagnostic shift of the cause of death from other fatal diseases of elderly people to Alzheimer's disease or other dementias. The occurrence of death due to pneumonia associated with dementia, for instance, was reported to be quite common [13]; shifts in the cause of death from pneumonia to dementia might, therefore, contribute to increased dementia mortality.

Although the crude female mortality rate from Alzheimer's disease in Japan is known to be significantly higher than the male mortality rate [14], comparison of the 85 - 89-age group showed no noticeable differences from 1999 to 2014. However, the estimate patient rates for females from the same age group were significantly higher than the male rates. Deaths from Alzheimer's disease are thought to occur mainly during the severe stage of the disease [15]. These findings might indicate that the male-female difference in patient rates is due to the relative abundance of female patients with mild symptoms attending medical facilities compared to males, while the rates of severe patients show no difference between males and females. A suggested reason for the relative scarcity of mild-symptom male patients is that, in Japan, elderly men often live without active social or domestic roles, while elderly women are expected to do most of the domestic work alone; therefore, the slightly abnormal behaviour is soon noticed, leading to clinical diagnosis and treatment.

Many studies on Japanese populations, including 'Hisayama Studies', have suggested increasing tendencies both in the prevalence and mortality of Alzheimer's disease [7,8,16-18]. However, as indicated by Wu., et al. [Wu], the methods and characteristics of study population in these studies over time seem to have not been fully controlled.

It has been previously demonstrated that among clinically diagnosed cases of vascular dementia, there is considerable involvement in Alzheimer's disease [19]. The apparent increases in morbidity of Alzheimer's disease might, therefore, indicate an improved accuracy of clinical diagnosis. This study would demonstrate that sustainable health policy against the apparent increase of Alzheimer' disease is required as for anticipating increasing medical and welfare expenditure

Limitations of the Study

- The first, this study is a ecologic study.
- The second, the case definition of dementias are not unified among death and patient records although the case definitions are steady in cohort studies.
- The third, the number of patients are likely to be underestimated in the patient surveys when patients do not consult doctors for medical costs, accessibility to medical facilities, or lack of insight into diseases. However, public health insurance system and Livelihood Protection Act cover the elderly and the poor. And in emergency, emergency medical services are financed by taxes, and completely free access to EMS is guaranteed. Then we think that the rates of patients are less underestimated in this study.

Conclusion

An apparent increase in Alzheimer's disease patients and deaths in Japan was observed, even regarding age-specific rates. However, summed ASPRs of Alzheimer's disease and vascular and unspecified dementia are almost unchanged across the same period, indicating the possibility of diagnostic reclassification from other dementias to Alzheimer's disease, contributing at least to the increase in patient numbers. The abundance of female Alzheimer's disease patients without associated increases in mortality suggests that females account for more mild-symptom patients than males.

Acknowledgements

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Conflict of Interest

We declare that no conflict of interests exists.

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