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Midlife use of written Japanese and protection from late life dementia

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Abstract

Background—The cognitive reserve hypothesis would predict that use of written Japanese should confer protection against dementia because of the complexity of its ideograms compared with written English. We sought to test this hypothesis in analyses from a longitudinal study of Japanese-American men.

Methods—Participants were second-generation Japanese-American men (*Nisei*) on the island of Oahu, Hawaii, who were seen in 1965 and in subsequent examinations to detect dementia beginning in 1991-1993. Use of spoken and written Japanese was self-reported in 1965 (Analyses 1 and 2), and mid-life use of written Japanese and written English was self-reported in 1994-1996 (Analysis 3). We analyzed prevalent dementia outcomes in 1991-1993 (Analysis 1, n=3,139) using logistic regression, and incident dementia outcomes in 1994-2002 (Analysis 2, n=2,299) and in 1997-2002 (Analysis 3, n=1,655) using Cox proportional hazards regression. Dementia outcomes included all-cause dementia, probable and possible Alzheimer disease, and probable vascular dementia. We adjusted models for probable and possible confounders.

Results—Participants who reported proficiency with written Japanese were older and had lower incomes. For Analysis 1, there were 154 prevalent cases of dementia, 74 of Alzheimer disease, and 43 of vascular dementia; for Analysis 2, 236 incident cases of dementia, 138 of Alzheimer disease, and 45 of vascular dementia; and for Analysis 3, 125 incident cases of dementia, 80 of Alzheimer disease, and 20 of vascular dementia. There was no relationship in adjusted models between self-reported proficiency with written Japanese and any dementia outcomes.

Conclusions—Proficiency with written Japanese does not appear to be protective for dementia.

One of the prevailing theories of why plaque and tangle burden has an imperfect correlation with Alzheimer disease is referred to as reserve.[1-5] The reserve hypothesis is that either brain reserve (e.g., total brain volume, dendritic/synaptic density—"hardware") or cognitive reserve (e.g., higher educational attainment, cognitively or physically demanding

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occupations or behaviors—"software") buffer the effects of the Alzheimer's disease process or processes, leading to relative protection.

Early studies of elderly Japanese-American individuals found rates of dementia and the proportions of dementia subtypes to be more similar to those found in US white populations than those found in Japan.[6,7] A later study found lower rates of 2-year cognitive decline in those less assimilated to Western culture than in those who were more assimilated.[8] One of the reasons hypothesized for this finding was the more complicated structure of written Japanese compared to written English[8] – facility with written Japanese provided protection because it led to increased reserve. Studies in bilingual individuals suggest that language processing in the two languages involve both shared and separate systems[9] and that, of patients presenting with dementia, bilingual individuals appeared to present later.[10]

There are two distinct sets of characters in written Japanese—the ideographic *Kanji* script and the syllabic *Katakana* script. A third distinct set of characters, the syllabic *Hiragana* script, is used for non-Japanese words. Japanese schooling involves learning more than 1000 *Kanji* characters in elementary and junior high school. *Kanji* is perceptually more complex and demanding than English script because many more than 26 basic perceptual elements are used.[11]

The reserve hypothesis would predict that fluency with *Kanji* should provide protection from dementia. We tested this hypothesis using data from the Honolulu Asia Aging Study. We limited our sample to second-generation offspring of immigrants from Japan (*Nisei*) to eliminate generational effects, and controlled analyses for the number of years of formal schooling. It was not uncommon to send *Nisei* children to Japan for their education; these individuals are called *Kibei*. Years of childhood spent in Japan was previously found to be associated with poorer baseline cognitive functioning in this study population.[12] Not surprisingly, a high proportion of the *Kibei* participants read and wrote Japanese. We excluded *Kibei* participants from our primary analyses because we could not differentiate between written Japanese language use and other environmental exposures in Japan.

Methods

Overview

This paper reports three analyses from a longitudinal epidemiologic study of Japanese-American men (Table 1). In Analyses 1 and 2, midlife self-reported use of spoken and written Japanese is the exposure of interest. In Analysis 3, late-life self-reported use of spoken and written Japanese and English in midlife are the exposures of interest. Outcomes for all analyses include any dementia, Alzheimer disease, and vascular dementia. We analyzed data from Honolulu Heart Program participants for whom dementia status was determined (1) in 1991-1993 and (2) later as part of the Honolulu Asia Aging Study. We controlled for confounding by including age and education in our regression models, and assessing head circumference (an indirect but robust measure of brain reserve[13]) and other factors as additional potential confounders.

Study population

The Honolulu Heart Program included Japanese-American men born 1900-1919 living on the island of Oahu in 1965.[14] Three midlife examinations, conducted in 1965-1968, 1968-1970, and 1971-1974, included collection of clinical and demographic information. In the fourth examination in 1991-1993, the Honolulu Asia Aging Study was started as an extension of the Honolulu Heart Program; 3,734 Honolulu Heart Program cohort members (80% of survivors) participated. As shown in Figure 2, we limited our analyses to the 3,139 *Nisei* participants educated in the U.S. We performed sensitivity analyses in which we

included the 596 *Issei* (1st generation immigrants) and *Kibei*. One participant was excluded due to missing exposure data. Subsequent examinations were conducted in 1994-1996 (examination 5), 1997-1999 (examination 6), and 1999-2000 (examination 7). The Honolulu Asia Aging Study was approved by institutional review boards of the Kuakini Medical Center and the Honolulu Department of Veterans Affairs, and all participants gave written informed consent.

Assessment of cognitive function and dementia

Dementia was assessed during examinations 4 (1991-1993; prevalent cases), 5 (1994-1996; incident cases), 6 (1997-1999; incident cases) and 7 (1999-2000; incident cases) by means of a multistep procedure described fully elsewhere.[7,15] The 100-point Cognitive Abilities Screening Instrument was used to screen the entire sample in the participant's choice of either Japanese or English. This instrument was developed as a test of global cognitive functioning for use in comparative studies of dementia in Japan and the United States.[16] At examination 4 (1991-1993), a stratified random sampling scheme was used. A subgroup of participants was identified for full dementia evaluation based on results of cognitive test scores, age, education, and scores from the Informant Questionnaire on Cognitive Decline in the Elderly.[17] At examination 5 (1994-96), those who scored less than an education-adjusted cutpoint (cognitive test scores of 77 for participants with low education and 79 for high education) or who had an absolute drop in cognitive test score of at least 9 points were selected for full dementia evaluation. At examinations 6 (1997-1999) and 7 (1999-2000), those who scored less than 70 points were selected for full dementia evaluation. While in other settings we have found that this instrument may have marked item-level bias (referred to as differential item functioning),[18] similar analyses in the Honolulu Asia Aging Study did not find large amounts of differential item functioning[19]. At all examinations, the dementia evaluation included the Consortium to Establish a Registry for Alzheimer's Disease neuropsychological battery[20] and a neurologic examination. We are unaware of analyses of the neuropsychological battery for differential item functioning. Participants who met the criteria for dementia underwent neuroimaging and blood tests for diagnosis of dementia subtype. A consensus diagnosis was reached by the study neurologist and at least two other physicians with expertise in geriatrics and dementia. The panel used the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*[21] criteria to diagnose dementia, the National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association criteria[22] to diagnose probable or possible Alzheimer disease, and the Alzheimer Disease and Treatment Centers criteria[23] to diagnose probable vascular dementia. Following the cognitive test, interviewers described the language used during interactions with the participant. Options included English with or without problems, mixed Japanese and English, or Japanese exclusively.

Assessment of spoken and written Japanese language proficiency

At Honolulu Heart Program examination 1 in 1965, participants were asked “Do you speak Japanese?” and “Do you read or write Japanese?” (Further description of the questions is provided in the eAppendix; http://links.lww.com.) Response options were no, very little, fair, well, and unknown. Responses to these questions (categorized as no/very little vs. fair/well) informed the exposure variable for Analyses 1 and 2. The reference group was those who said they spoke Japanese at least fairly well but who read or wrote, at most, very little Japanese (“spoke but did not read Japanese”). We compared men who indicated they spoke, at most, very little Japanese (“neither spoke nor read Japanese”), and men who indicated they both spoke and read or wrote Japanese at least fairly well (“both spoke and read Japanese”) to this reference group. One man indicated he spoke very little Japanese but read Japanese fairly well; he was included in the “both spoke and read Japanese” group. The reserve hypothesis would predict that there would be minimal difference in dementia risk

between the "spoke but did not read Japanese" and the "neither spoke nor read Japanese" groups, but that there should be protection for the "both spoke and read Japanese" group.

A limitation of the Honolulu Heart Program examination 1 questions is that specific forms of written Japanese (*Kanji*, *Katakana*, or *Hiragana*) are not specified. At examination 5, additional questions were asked regarding languages spoken and how well participants could read and write in Japanese and English in the middle years of their lives (ages 40-50). Responses to these questions informed the exposure variables for Analyses 3a (written and spoken Japanese), 3b (written and spoken English), and 3c (written Japanese and written English). One question addressed how well the participant could read Japanese. We dichotomized responses to this question to identify participants who indicated they "could read most Japanese magazines, books and newspapers" compared with participants who, at most, "could read simple Japanese magazines, books, and newspapers." A second question asked participants how well they could write Japanese. We dichotomized responses to this question to identify participants who indicated they "could write well in Japanese in any form" compared with participants who, at most, "could write in *Hiragana* or *Katakana* but not *Kanji*." We combined responses to identify participants who indicated they could read Japanese at this level, write Japanese at this level, or both ("highly literate in Japanese") compared with participants who could neither read nor write Japanese at this level ("not highly literate in Japanese"). We combined this categorization with responses to the question about languages spoken in midlife to identify 3 groups: (1) participants who did not speak Japanese and were not highly literate in Japanese (n=502); (2) participants who spoke at least some Japanese but who were not highly literate in Japanese (n=1024, reference category); and (3) participants who were highly literate in Japanese (n=129; all but 14 spoke at least some Japanese). The reserve hypothesis would predict that there would be minimal difference in dementia risk between groups 1 and 2, but that mastery of *Kanji* script by group 3 should provide protection.

Two similar questions were asked about literacy in English. We dichotomized the reading question to differentiate participants who indicated they had "no difficulty reading English" from those who indicated that, at most, they "could read simple books, magazines, or newspapers," and the writing question to differentiate participants who "could print or write with no difficulty" from those who indicated that, at most, they "could print or write simple sentences." We specified no difficulty with reading or writing English to identify those who were "highly literate in English" (n=1540) compared with those who were "not highly literate in English" (n=115) for Analysis 3b.

Finally, we combined the English and Japanese literacy variables together for Analysis 3c. Our reference category was participants who were highly literate in English but not in Japanese (n=1,437). Other groups were (1) the 89 participants who were not highly literate in either English or Japanese; (2) the 26 participants who were highly literate in Japanese but not in English; and (3) the 103 participants who were highly literate in both Japanese and English.

Assessment of covariates

We controlled for a number of factors that could be related to dementia and proficiency with language. Age (as the time scale for the Cox model and as a covariate) and educational level (1-8, 9-11, 12, and 13 or more years) were assessed by questionnaire. Apolipoprotein E (ApoE) genotype was characterized as the presence of at least one vs. zero ε4 alleles. We measured head circumference using a flexible tape. Income was assessed using the response scale shown in Table 2. Body mass index was assessed using measured height and weight. We categorized smoking behavior as current, prior, and never. Hypertension was defined using measured blood pressure and antihypertensive medication use. Diabetes and family

history of Alzheimer disease were assessed using self-report. We assessed stroke using self-report and then confirmed with medical record surveillance. Parkinsonism was assessed by physical examination.

Analytic samples

Specific samples are summarized in Figure 1. We performed sensitivity analyses in which we included *Kibei* and *Issei* participants.

Data analysis

Analysis 1 evaluated prevalent dementia outcomes at the time of examination 4. In Analysis 2, participants were considered at risk if they did not have dementia at examination 4. We then assessed risk of incident dementia outcomes at examination 5, 6, or 7. In Analysis 3, participants were considered at risk if they did not have dementia at examination 5, and subsequent risk of incident dementia diagnoses at examination 6 or 7 was assessed (see Figure 1). Participants were censored at the time of any dementia diagnosis, drop out, or death in Analyses 2 and 3.

Statistical Analysis

We used logistic regression for Analysis 1. Since stratification was used to determine who was further evaluated to identify prevalent cases of dementia, we weighted these analyses based on the probability of being selected. (Results without weighting were similar.)

We used Cox proportional hazards regression for Analyses 2 and 3. We estimated time of dementia diagnosis halfway between the last visit free of dementia and the visit at which dementia was diagnosed. Age served as the time scale for all Cox models.[24]

For all analyses, we used separate models for each outcome (any dementia, Alzheimer disease, and vascular dementia). We initially fit unadjusted models, and then adjusted for age and education. We screened for additional confounding by adding ApoE ε4, income, and health variables one at a time to the age- and education-adjusted models. A potential confounder was retained in the model if it met two criteria. First, the difference in the value of the β coefficient corresponding to language group membership for models including and excluding the potential confounder had to differ by at least 15%. Second, if the change was greater than 15%, the absolute value of the β coefficient in the model including the potential confounder had to be at least 0.1 (so adjusted odds or hazard ratios had to be less than 0.90 or greater than 1.11). The rationale for this compound criterion for confounding was that even large percentage differences in β coefficients close to zero could nevertheless still result in very small (and clinically insignificant) overall effects. We attempted a model including all possible confounders but this proved unstable because of small cell sizes. We did not look for interactions between possible confounding variables; we only examined their main effects. We tested the assumption of proportional hazards for the final adjusted models using Schoenfeld residuals; these assumptions were tenable for all models. All statistical analyses were carried out using Stata software, version 9.2.[25]

We used R[26] to construct a plot of the point estimates and 95% confidence intervals (CIs) for the primary exposure of interest, “both spoke and read Japanese” vs. “spoke but did not read Japanese” for Analyses 1, 2, and 3a.

Results

Of the 3,139 participants in Analysis 1, 561 (18%) neither spoke nor read Japanese, 1,847 (59%) spoke but did not read Japanese, and 731 (23%) both spoke and read Japanese.

Demographic characteristics, health risk factors, and health conditions are shown in Table 2. On average, those who both spoke and read Japanese were older and had lower household incomes; were more likely to have spoken Japanese as their first language and to have had trouble with English during the exam; were less likely to have ever smoked; and were shorter, with smaller head circumference. BMI categories, ApoE ε4 allele frequencies, and medical conditions were similar across groups. Rates of medical conditions were similar across language exposure groups even after adjusting for education and age (eTable 1; http://links.lww.com). The distribution of education across exposure groups is shown in eTable 2, interviewer descriptions of language use across exposure groups are shown in eTable 3, and the distribution of baseline cognitive test scores across exposure groups is shown in the eFigure.

The distributions of baseline cognitive test scores were similar across the three groups, though mean baseline scores were lower in those who both spoke and read Japanese (Table 2). There were 154 prevalent cases of dementia, 74 of Alzheimer disease, and 43 of vascular dementia for Analysis 1. There were 236 incident cases of dementia, 138 of Alzheimer disease, and 45 of vascular dementia over 13,838 person-years of follow-up for Analysis 2. For Analysis 3, there were 125 incident cases of dementia, 80 of Alzheimer disease, and 20 of vascular dementia over 7,178 person-years of follow-up. The number of dementia evaluations, dementia outcome prevalence rates, and weighted adjusted odds ratios (ORs) of prevalent dementia outcomes at the time of examination 4 are shown in Table 3. The point estimates for odds ratios for dementia outcomes associated with reading Japanese were all greater than 1.0; all confidence intervals included 1.0. The number of dementia evaluations, rates and adjusted hazard ratios (HRs) of incident dementia outcomes at examinations 5-7 (Analysis 2) are shown in the middle section of Table 3. The point estimate for Alzheimer disease was slightly less than 1.0 (adjusted HR 0.84 [95% CI = 0.56 - 1.28]). The reduced hazard for Alzheimer disease for the “both spoke and read Japanese” group was of similar magnitude as that for the “neither spoke nor read Japanese” group (0.79 [0.48 - 1.69]).

We compared self-reports of Japanese language proficiency at Honolulu Asia Aging Study examination 5 with those of the same participants at Honolulu Heart Program examination 1 (eTable 4). Overall there was consistency in self-reporting of language proficiency across the life span, though a sizable proportion of participants had different assessments in late life than they had in mid-life of their ability to speak and read Japanese.

Rates and adjusted HRs of incident dementia outcomes at examinations 6-7 associated with self-reported language use in midlife (Analysis 3) are shown in the bottom section of Table 3. As in Analysis 2, the point estimate for the adjusted HR for Alzheimer disease for the group that was highly literate in Japanese was less than 1.0 (0.86 [0.38 - 1.93]), of similar magnitude as for the group that neither spoke nor read Japanese (0.73 [0.43 - 1.26]). Less than high degrees of literacy in English were associated with increased risk of dementia outcomes, though confidence intervals included 1.0. When combined in the same analysis, no consistent pattern emerged for literacy in Japanese and English. As indicated in Table 3, only a single covariate—height—met our criteria for confounding, and in only a few analyses. Models that included and excluded height were very similar. Models including and excluding income were also very similar (eTable 5).

There were 335 *Kibei* participants, most of whom read and wrote Japanese. Odds and hazard ratios were essentially unchanged when we included the *Kibei*.

Figure 2 provides a graphical display of our primary results. All 95% CI regions include the null. With two exceptions, the point estimates are at least 1.0, contrary to the relationship expected based on the cognitive reserve hypothesis.

Discussion

Self-reported use of written Japanese did not appear to be protective for dementia, Alzheimer disease, or vascular dementia. Arguably, in two analyses, use of written Japanese was associated with a barely reduced risk for Alzheimer disease (adjusted HR <1.0 in Analyses 2 and 3a; both 95% CI's include 1.0). However, in those same analyses, use of neither spoken nor written Japanese was associated with similar protection (Table 3). This pattern of findings is more consistent with random variation than with neuroprotection garnered from richly developed neural circuitry required to process the numerous pictograms and ideographs involved with *Kanji* script.

There are many potential explanations for a negative result. These include a true negative finding and several different types of error. In general, the point estimates associated with use of written Japanese suggest harm rather than protection, which does not seem biologically plausible (Figure 2). Recall bias is always a concern in studies of dementia. Here, exposure data were collected in midlife for Analyses 1 and 2, decades before dementia onset. In Analysis 3 we excluded individuals found to be demented at the time of exposure ascertainment. Some of these individuals may have had milder forms of cognitive deficits that were not diagnosed. Recall bias that was non-differential between exposure groups would produce bias towards the null, decreasing our ability to find an effect. Furthermore, findings from Analysis 2 –not subject to recall bias – were similar to those from Analysis 3.

Confounding is an important issue in observational studies. We adjusted models for age and education, and considered confounding related to ApoE genotype, self-reported income, and numerous health factors. In this population, Japanese speakers and those with proficiency with written Japanese were older and had lower incomes in late life than those who did not have proficiency with written Japanese (Table 2). This fact permits us to disentangle proficiency with written Japanese from socio-economic status (SES) in this study; similar studies in Japan would not be able to separate the effects of these factors. Height was the only covariate that met our criteria for confounding, for some analyses, despite our use of fairly liberal criteria for confounding. Models that included and excluded height produced essentially the same results. We specifically assessed head circumference as a potential confounder and did not find confounding related to this variable. Nevertheless, it is theoretically possible that some additional unmeasured confounder could exist, and that adjustment for that confounder would show protection from dementia outcomes associated with spoken or written Japanese.

We limited these analyses to 2nd generation sons of Japanese immigrants (*Nisei*). We obtained similar results when we included 1st generation immigrants (*Issei*). Our rationale for excluding the *Issei* was that their life experiences were very different from the *Nisei*, and factors relating to proficiency with Japanese written language could be very different for the two generations of participants. Similarly, in our primary analyses, we excluded *Kibei* participants who received some of their education in Japan. Our rationale was that we would be unable to exclude written Japanese use (expected to be much more common among participants with some education in Japan) from other exposures in Japan. A secondary rationale was that an earlier study found an inverse relationship between childhood years spent in Japan and cross-sectional cognitive performance in the Honolulu Asia Aging Study.[12] If this finding represented higher proportions with current or developing dementia, including these participants in our primary analyses would be expected to show less protection from dementia outcomes associated with written Japanese use. In any case, results when including and excluding the *Kibei* were essentially unchanged. Among the *Nisei*, we found an inverse relationship between years of (Western) formal schooling and written Japanese language proficiency. This may be due to different priorities for families

who chose to enroll their sons in special Japanese language schools. These data provide us with the opportunity to determine whether the choice to study Japanese language among children of Japanese immigrants might have a relationship with risk of dementia decades later. We found no evidence that this choice had any impact on dementia outcomes. There are many reasons one might choose to learn the language of one's ancestors, or any second language. These data suggest that prevention of dementia should not be part of the rationale for encouraging second language acquisition.

Several limitations should be considered for these analyses. Proficiency with spoken and written languages was assessed only through self-report. We found some consistency across decades in self-reporting of use of written Japanese, but less consistency for proficiency with spoken Japanese (eTable 4). We excluded people with prevalent dementia at the time of Honolulu Asia Aging Study examination 5 from Analysis 3, but the accuracy of self-reported exposures could have been affected by undetected mental problems. The power to detect a beneficial effect of proficiency with written Japanese for vascular dementia was somewhat limited. Cross-sectional studies of dementia can be biased if the level of participation varies across exposure groups, because lack of participation is strongly associated with the presence of dementia. While in theory this could lead to bias in the prevalent dementia cases analyzed in Analysis 1, it should not interfere with the incident cases analyzed in Analyses 2 and 3, where we found similar results. Test bias related to language may lead to biased results from the neuropsychological battery used to evaluate cognitive ability in participants with low cognitive test scores. We did not have additional data on acculturation, vocabulary, or reading level.[27] We limited our analyses to dementia, though we found similar results when we analyzed rates of change in cognition. The cognitive test has insufficient coverage to address changes in specific cognitive domains. While we used two complementary exposure definitions, a more robust measure of exposure – such as measured written and spoken Japanese skill in midlife – would have strengthened our confidence in our findings. We do not have measures of frequency of exposure to written Japanese. These analyses should thus be considered exploratory.

In summary, we did not find evidence to support the cognitive reserve hypothesis. Proficiency with written Japanese language was not associated with reduced risk for dementia outcomes. Our data provide no support for the hypothesis that acquisition of a second language might help to prevent dementia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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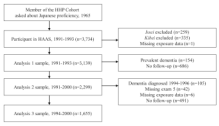

Figure 1.

Flow chart summarizing analytic samples. HHP indicates Honolulu Heart Program; HAAS, Honolulu Asia Aging Study.

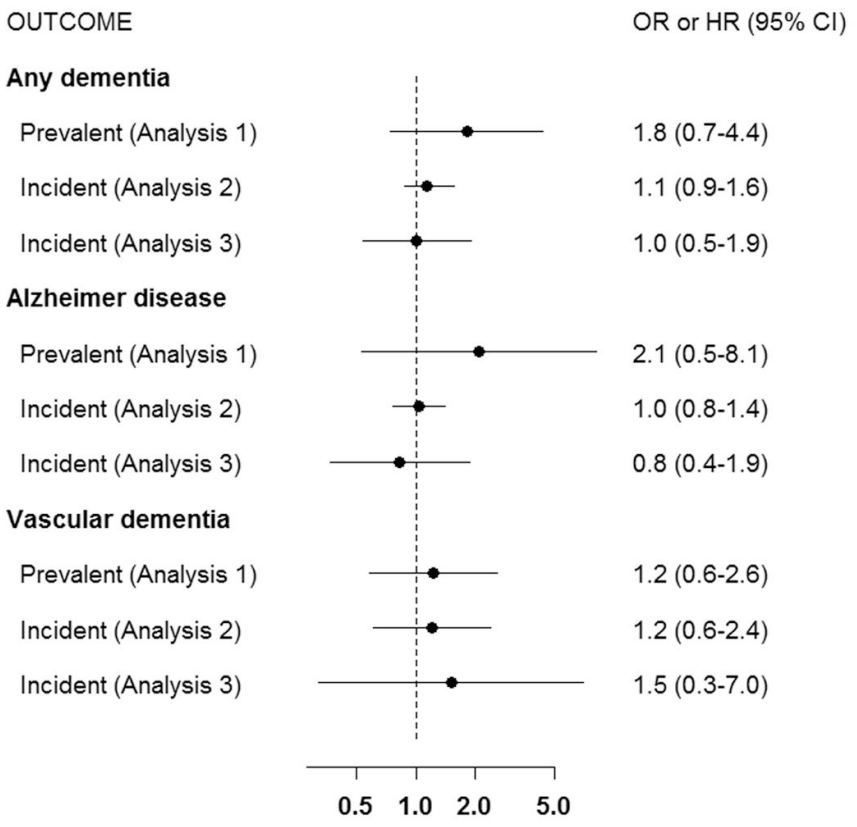

Figure 2.
Association between use of written Japanese language with dementia outcomes adjusted odds ratios (Analysis 1) and hazard ratios (Analyses 2 and 3), with 95% confidence intervals.

TABLE 1
Summary of Exposures and Outcomes Used in Analyses

Analysis	Exposure	Outcome
Analysis 1	Based on questions asked in 1965 (at ages 46-65) on whether participants spoke and read Japanese	Any dementia, Alzheimer disease, or vascular dementia prevalent in 1991-1993 (ages 72-91)
Analysis 2	Based on questions asked in 1965 (at ages 46-65) on whether participants spoke and read Japanese	Any dementia, Alzheimer disease, or vascular dementia incident in 1994-1996 (ages 75-94), 1997-1999 (ages 78-97), or 1999-2000 (ages 81-100)
Analysis 3	Based on questions asked in 1994-1996 (at ages 75-94) on whether in midlife (age 40-50) participants spoke and read Japanese (Analysis 3a), English (Analysis 3b), and both Japanese and English (Analysis 3c)	Any dementia, Alzheimer disease, or vascular dementia incident in 1997-1999 (ages 78-97) or 1999-2000 (ages 81-100)

TABLE 2

Selected Demographic Characteristics by Midlife Self-Reported History of Spoken and Written Japanese

	Neither spoke nor read Japanese, No. (%)	Spoke but did not read Japanese, No. (%)	Both spoke and read Japanese, No. (%)
Age category at examination 4 (years)			
71-75	283 (50)	793 (43)	265 (36)
76-80	209 (37)	734 (40)	242 (33)
81-93	69 (12)	320 (17)	224 (31)
Formal schooling (years)			
1-8	148 (26)	548 (30)	230 (31)
9-11	126 (22)	418 (23)	122 (17)
12	182 (32)	584 (32)	181 (25)
13+	105 (19)	297 (16)	198 (27)
ApoE ε4 alleles (number)			
0	444 (79)	1467 (79)	583 (80)
1 or 2	101 (18)	332 (18)	131 (18)
Missing	16 (3)	48 (3)	17 (2)
CASI score at examination 4			
< 74	41 (7)	218 (12)	127 (17)
74 to <82	65 (12)	282 (15)	125 (17)
82 – 100	455 (81)	1347 (73)	479 (66)
Self-reported yearly income at examination 4			
< $15,000	95 (17)	364 (20)	153 (21)
$15,000-19,999	87 (16)	363 (20)	113 (15)
$20,000-29,999	135 (24)	401 (22)	123 (17)
≥$30,000	174 (31)	479 (26)	228 (31)
Missing	70 (12)	240 (13)	114 (16)
Self-reported first language at examination 1			
Japanese	213 (38)	803 (43)	350 (48)
English	159 (28)	421 (23)	131 (18)
Both	160 (29)	514 (28)	187 (26)
Other	0 (0)	1 (0)	2 (0)
Missing	29 (5)	108 (6)	61 (8)
Language of testing at examination 4			
English only	430 (77)	1444 (78)	515 (70)
Trouble with English/ any Japanese	10 (2)	71 (4)	63 (9)
Missing	121 (22)	332 (18)	153 (21)
Body mass index (kg / m^2) at examination 4			
<20 (underweight)	68 (12)	206 (11)	105 (14)
20-25 (normal weight)	311 (55)	1023 (55)	386 (53)
25.1-30 (overweight)	155 (28)	528 (29)	189 (26)

	Neither spoke nor read Japanese, No. (%)	Spoke but did not read Japanese, No. (%)	Both spoke and read Japanese, No. (%)
>30 (obese)	12 (2)	32 (2)	17 (2)
Missing	15 (3)	58 (3)	34 (5)
Smoking status at examination 4			
Never	176 (31)	625 (34)	293 (40)
Past	317 (57)	982 (53)	330 (45)
Current	37 (7)	124 (7)	46 (6)
Missing	31 (6)	116 (6)	62 (8)
Height (inches) at examination 4			
Lowest third (54.5 – 63)	153 (27)	514 (28)	283 (39)
Middle third (63.5 – 65)	198 (35)	654 (35)	233 (32)
Highest third (65.5 – 71.5)	210 (37)	679 (37)	214 (29)
Missing	0 (0)	0 (0)	1 (0)
Head circumference (cm) at examination 5			
Lowest third (45.9 – 55.0)	138 (25)	447 (24)	184 (25)
Middle third (55.1 – 56.3)	145 (26)	432 (23)	177 (24)
Highest third (56.4 – 60.8)	148 (26)	502 (27)	138 (19)
Missing	130 (23)	466	232 (32)
Hypertension (BP≥140/90 OR on antihypertensive medication) at examination 4			
No	143 (26)	502 (27)	177 (24)
Yes	418 (75)	1345 (73)	554 (76)
Hypertension (BP≥160/95 on antihypertensive medication) at examination 4			
No	257 (46)	859 (46)	334 (46)
Yes	304 (54)	988 (54)	397 (54)
Diabetes at examination 4			
No	437 (84)	1455 (84)	585 (85)
Yes	80 (16)	285 (16)	104 (15)
Parkinsonism at examination 4			
No	484 (96)	1549 (97)	581 (96)
Possible	14 (3)	32 (2)	14 (2)
Yes	4 (1)	13 (1)	11 (2)
History of stroke at examination 4			
No	505 (90)	1629 (88)	647 (88)
Self-report only; unconfirmed stroke	35 (6)	138 (8)	58 (8)
Self-report plus confirmed by surveillance	21 (4)	80 (4)	26 (4)

CASI indicates Cognitive Abilities Screening Instrument; BP, blood pressure

TABLE 3

Associations of Self-reported Use of Spoken and Written Japanese and English with Dementia Outcomes

	All-cause dementia		Probable or possible Alzheimer disease		Probable Vascular dementia	
Language use group (number evaluated for dementia)	**Cases/total no. or cases/person years**	**Adjusted[a] OR or HR (95% CI)**	**Cases/total no. or cases/person years**	**Adjusted[a] OR or HR (95% CI)**	**Cases/total no. or cases/person years**	**Adjusted[a] OR or HR (95% CI)**
Analysis 1: Prevalent outcomes at Examination 4 (cases/total; odds ratio)						
Neither spoke nor read Japanese (n = 29)	18/561	0.78 (0.45-1.35)	5/561	0.48 (0.17-1.33)	6/561	0.96 (0.38-2.40)
Spoke but did not read Japanese[b] (n = 168)	91/1,847	1.0	48/1,847	1.0	23/1,847	1.0
Both spoke and read Japanese (n = 91)	45/731	1.80 (0.74-4.39)	21/731	2.07 (0.53-8.13)	14/731	1.22 (0.58-2.56)
Analysis 2: Incident outcomes at Examinations 5-7 (cases/ person years; hazard ratio)						
Neither spoke nor read Japanese (n = 116)	29/2,631	0.68 (0.46-1.02)	20/2,631	0.79 (0.48-1.29)	4/2,631	0.47 (0.17-1.35)
Spoke but did not read Japanese[b] (n = 460)	144/8,232	1.0	86/8,232	1.0	28/8,232	1.0
Both spoke and read Japanese (n = 194)	63/2,975	1.03 (0.76-1.40)	32/2,975	0.84 (0.56-1.28)	13/2,975	1.22 (0.62-2.40)
Analysis 3: Incident outcomes at Examinations 6-7 (cases/ person years; hazard ratio).						
Analysis 3a: Japanese.						
Neither spoke nor read Japanese (n = 83)	32/2,180	0.88 (0.58-1.32)[‡]	18/2,180	0.74(0.43-1.26)[‡]	8/2,180	1.66 (0.65-4.23)[‡]
Spoke but did not read Japanese[b] (n = 188)[c]	81/4,440	1.0	55/4,440	1.0	10/4,440	1.0
Both spoke and read Japanese (n = 28)[c]	12/558	1.01 (0.54-1.89)	7/558	0.86 (0.38-1.93)	2/558	1.47 (0.31-6.99)
Analysis 3b: English.						
Not highly literate in English (n = 47)	14/484	1.49 (0.82-2.70)	10/484	1.63 (0.80-3.33)	3/484	2.10 (0.56-7.90)
Highly literate in English[b] (n = 252)	111/6,694	1.0	70/6,694	1.0	17/6,694	1.0
Analysis 3c: both Japanese and English						

	Probable or possible					
	All-cause dementia		Alzheimer disease		Probable Vascular dementia	
Language use group (number evaluated for dementia)	**Cases/total no. or cases/person years**	**Adjusted[a] OR or HR (95% CI)**	**Cases/total no. or cases/person years**	**Adjusted[a] OR or HR (95% CI)**	**Cases/total no. or cases/person years**	**Adjusted[a] OR or HR (95% CI)**
Highly literate in neither Japanese nor English (n = 35)	11/373	1.62 (0.83-3.12)	8/373	1.81 (0.83-3.97)	3/373	n/a
Highly literate in English but not Japanese[b] (n = 236)	102/6,247	1.0	65/6,247	1.0	15/6,4247	n/a
Highly literate in Japanese but not English (n = 12)	3/112	1.17 (0.36-3.80)	2/112	1.16 (0.27-4.91)	0/112	n/a
Highly literate in both Japanese and English (n = 16)	9/447	1.08 (0.54-2.18)	5/447	0.95 (0.38-2.41)	2/447	n/a

[a] Adjusted for age and education only unless indicated

[b] Reference category

[c] Models also adjusted for height

"n/a" indicates too few cases of incident vascular dementia were available for these analyses