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Non-Native Language Use and Risk of Incident Dementia in the Elderly

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Abstract

Cognitive reserve is invoked to explain the protective effects of education and cognitivelystimulating activities against all-cause dementia and Alzheimer's disease (AD). For non-native English speakers (n-NES), speaking English may be a cognitive activity associated with lower dementia risk. We hypothesized that n-NES have lower risk of incident dementia/AD and that educational level might modify this relationship. Participants took part in the Einstein Aging Study (Bronx, NY), a longitudinal study of aging and dementia. All (n = 1779) spoke fluent English and self-reported birthplace and whether English was their first language. n-NES additionally reported mother tongue, age of English acquisition, and current percentile-use of a non-English language. Nested Cox proportional hazards models progressively adjusted for gender, race, education, and immigrant and marital status estimated hazard ratios (HR) for incident dementia/AD as a function of n-NES status. 390 (22%) participants were n-NES. 126 incident dementia cases occurred during 4174 person-years of follow-up (median 1.44; range 0–16); 101 individuals met criteria for probable/possible AD. There was no statistically-significant association between n-NES status and incident dementia in the fully-adjusted model (HR 1.26; 95% CI 0.76–2.09; p = 0.36). Results were similar for AD. Stratification of education into three groups revealed increased risk of dementia for n-NES with ≥ 16 years of education (HR 3.97; 95%) CI 1.62–9.75; p = 0.003). We conclude that n-NES status does not appear to have an independent protective effect against incident dementia/AD, and that n-NES status may contribute to risk of dementia in an education-dependent manner.

Keywords

Cohort studies; dementia; incidence; multilingualism

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INTRODUCTION

Broadly defined, bilingualism is the ability to communicate in more than one language [1]. Bilingualism necessitates development of cognitive systems for differential access to and manipulation of multiple languages. In children, bilingualism has been associated with a relative cognitive processing advantage, attributed to enhanced selective attention arising from the constant need to suppress the non-active language [2]. From a cognitive aging perspective, it is unknown whether bilingualism is more likely to be beneficial or burdensome. In language tasks, older bilinguals may have higher rates of 'tip of the tongue' word retrieval failures, less proficiency in confrontational naming, and generation of shorter word lists in verbal fluency tasks [3, 4]. However, bilingualism may also attenuate decline in executive function tasks, leading some to characterize it as a cognitively-stimulating activity that bolsters 'cognitive reserve,' the brain's ability to compensate for accumulating neurodegenerative pathology [5, 6]. Several recent case-control studies have reported that speaking more than one language may delay the onset of Alzheimer's disease (AD) [3, 7–9], although longitudinal studies have been less promising [4, 10].

Using longitudinal data from the Einstein Aging Study, we investigated whether language use affects risk for incident dementia and AD. We tested the hypothesis that non-native speakers of English (n-NES) have lower risk for incident dementia/AD than native English speakers (NES). Because cognitive reserve is associated with experiential factors such as education [11] and these factors have been linked to dementia risk [12], we also investigated whether educational attainment modifies the association between n-NES and risk of dementia, hypothesizing that the two factors would be synergistically related.

MATERIALS AND METHODS

Study population

The Einstein Aging Study (EAS) is a community-based longitudinal study of cognitive aging and dementia located in the Bronx, NY. Study design and methods for recruitment and annual assessment have been previously described [13–15]. Briefly, population lists of Medicare recipients (1993–2004) or Bronx County registered voters (2004–2010) were used to generate sampling frames for participant recruitment. Telephone-based screening interviews were used to establish preliminary eligibility, which included age ≥ 70 years, Bronx residence, and sufficient English fluency for neuropsychological testing. Individuals with audiovisual impairment precluding neuropsychological assessment or inability to ambulate were excluded. Since 1993, 1944 individuals have been enrolled. Enrolled individuals made annual in-person study visits at the EAS Aging Research Center at the Albert Einstein College of Medicine (Einstein). Written informed consent was obtained from all participants at study entry. Study protocols were approved by the Einstein institutional review board. The analytic sample included here consists of the 1779 participants (92% of the total EAS cohort) assessed between October 1993 and September 2010 who were non-demented at baseline and for whom demographic information about native language and birthplace was available.

Clinical information and ascertainment of language use

Trained research staff used structured interviews and questionnaires to collect sociodemographic data (e.g., age, gender, self-reported race/ethnicity, and years of education) and self-reported medical history. All participants self-reported birthplace, permitting ascertainment of immigration status. At baseline, all participants were asked whether English was the first language they learned. n-NES were further asked to define

their mother tongue, the age at which they learned English, and the percentage of time they currently spoke English.

Cognitive evaluation

Trained neuropsychological assistants administered a battery of cognitive performance tests at baseline and each successive annual evaluation. The Blessed Information-Memory-Concentration test (BIMC) was used to establish global cognitive status [16]. Pre-morbid intelligence was evaluated by the Wide Ranging Achievement Test (WRAT-reading portion) [17], and by the Vocabulary and Information subtests of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) through 2004 and the WAIS-III thereafter [18, 19]. Domain-specific cognitive tests assessing attention, episodic memory, executive function, visuospatial ability, and language comprised the remainder of the battery; each domain was evaluated by at least two tests. Attention was assessed using WAIS-R/III Digit Span and the Trail-Making Test (Part A). Memory was evaluated with the Free and Cued Selective Reminding Test (FCSRT) and Wechsler Memory Scale-Revised Logical Memory I [20-22]. The Controlled Oral Word Association test ("F/A/S") and the Trail-Making Test (Part B) were used to assess executive function [23, 24]. Visuospatial ability was assessed by the WAIS-R/III Block Design and Digit-Symbol Substitution subtests and the Clock Drawing Test. The Category Fluency (animals/fruit/vegetables) and 15-item Boston Naming tests evaluated language [25, 26]. Participants and/or their informants completed standardized questionnaires about cognitive and functional status (e.g., the Lawton-Brody Activities of Daily Living Scale and the CERAD C1A for participants; the CERAD C2A and IQ-Code by informants) [27–29]. Depressive symptoms were assessed by the 15-item Geriatric Depression Scale [30].

Dementia diagnosis

A diagnosis of dementia was based on standardized criteria from the Diagnostic and Statistical Manual, fourth edition (DSM-IV) and required impairment in memory plus at least one additional cognitive domain, accompanied by evidence of decline from a previous level of functioning [31]. A licensed neuropsychologist used a combination of internallyand externally-validated norms to determine whether impairment existed in any of the five cognitive domains [32]. A board-certified neurologist independently interviewed and examined each participant, then assigned a Hachinski Ischemic Score, completed a Clinical Dementia Rating scale, and documented a clinical impression of whether dementia was present [33-35]. Final diagnostic determination was made at consensus case conferences attended by the neuropsychologist, the neurologist and a geriatric social worker. Memory impairment was defined by FCSRT ('free recall'≤24) or WMS-R Logical Memory (≤1.5 standard deviations below the age-adjusted mean) [36]. Functional status was determined by responses on participant scales and informant questionnaires, and clinical evaluation. AD was diagnosed in demented participants who met clinical criteria for probable or possible disease established by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer Disease and Related Disorders Association [37].

Statistical methods

We classified participants dichotomously based on whether English was their first language. We modeled the relationship between n-NES and risk of incident dementia/AD with a series of nested Cox proportional hazards regression models to obtain hazard ratios (HRs) and 95% confidence intervals (CIs). NES served as the reference group and outcomes (any dementia or AD) were modeled separately. Chronological age was used as the time scale in all models [38]. Time of dementia/AD diagnosis was assigned the visit date immediately preceding the consensus conference making the diagnosis. Covariates were pre-specified on the basis of plausible relationships to dementia and language use. Gender, race, and years of education

(entered as a continuous variable) were included as standard demographic variables. Immigrant and marital status were selected as life experience variables with the potential to confound associations between language use and dementia risk. We initially fit an unadjusted model, then adjusted progressively for gender, race, and years of education (Model 2), and immigration and marital status (Model 3). Self-reported history of hypertension, diabetes, myocardial infarction, and stroke were separately added to the final model as potentially confounding cardiovascular risk factors. They neither changed the results nor improved fit of the full model that is presented. Results were also unchanged when we substituted WRAT-derived English reading proficiency for years of education, to account for potential regional and national variation in methods and quality of available education [40]. Similarly, inclusion of both education and reading level did not improve model fit (LR 0.04; p = 0.85) or meaningfully change the results. Education and reading proficiency were moderately correlated (pairwise r = 0.48; p < 0.0001), so only education was retained in the full model.

To explore whether educational attainment modified the relationship between n-NES and risk of dementia, we added a multiplicative interaction term (e.g., n-NES \times years of education) to the full model. We retained the lower order terms in addition to the interaction term and used the likelihood ratio statistic (LR) to evaluate the interaction term for statistical significance. Potential interactions between n-NES and immigration and marital status were each independently assessed in a similar manner. Stratified results are reported in the case of statistically-significant interaction. Scaled Schoenfeld residuals demonstrated that the proportional hazards assumption for the full multivariate model was tenable [39].

In a subgroup analysis, we examined active use of the non-English language as the exposure of interest in the n-NES group. We selected a 50% language-usage threshold to model 'balanced' bilingual use between English and the native language and ran a series of nested models, comparing n-NES with non-English usage of at least 50% to all non-users (NES plus n-NES with <50% usage). To look for a usage-dose effect, we then reran the models with any ongoing use of the non-English native language as the exposure group.

STATA/IC version 10.1 (StataCorp LP, College Station, TX) was used for all analyses. Two-sided probability values <0.05 were considered statistically significant for all tests except interaction terms, where an alpha <0.10 was used to account for diminished power.

RESULTS

Sample characteristics

Over 4174 person-years of follow-up (median 1.4; range 0–16 years) there were 126 cases of incident dementia; 101 cases met criteria for probable or possible incident AD. During follow-up, 594 (33%) individuals died and 150 (8%) were lost to follow-up. At baseline, compared to individuals who did not develop dementia, those who later became demented were older and performed worse on tests of global cognition and episodic memory (Table 1), although test scores were within the normal range. Educational attainment was similar in the two groups.

A non-English first language was self-reported by 390 (22%) participants; 123 of whom reported ongoing use of the non-English language. Median (IQR) age of English acquisition in n-NES was 7 (5–15) years. Of 25 languages reported, the most common 'mother tongues' were Yiddish (n = 94; 24%), Italian (n = 82; 21%), Spanish (n = 61; 16%), and German (n = 49; 13%). At study entry, n-NES were slightly older than NES and were more likely to be white and to be married (Table 2). n-NES had significantly fewer years of education than NES, although WRAT-derived reading grade level was similar, indicating that n-NES had

attained English proficiency comparable to NES. Baseline performance on neuropsychological tests of global cognitive status (BIMC) and episodic memory (FCSRT) was similar between the two groups. Self-reported history of hypertension was less frequent in n-NES than NES. Neither group demonstrated depressive symptomatology. Median CDR scores were zero (indicating 'no dementia') in both groups. Within n-NES only (Table 3), those reporting any current use of the non-English language (active users) were younger, more likely to be white, and more likely to be immigrants than those exclusively using English (nonusers). English reading proficiency was similar for the two groups but active users had greater variability. Active users also had higher frequency of self-reported diabetes and performed slightly worse on the BIMC, although test scores remained well within normal limits. Median (IQR) percent-usage of English in active users was 50% (20–90%); age of English acquisition in active users was double that of nonusers.

A birthplace outside of the United States was reported by 398 (22%) individuals; 243 of whom were n-NES. Compared to non-immigrants (11% n-NES), non-native English was significantly more common among immigrants ($X^2 = 460.2$, p < 0.0001). In n-NES immigrants, median English acquisition age was 13 (8–20) years and at study entry median (IQR) percentile-use was 100 (65–100%); 24% reported any current use of their native language. The median WRAT-derived reading grade level was 12 for both immigrants and non-immigrants, but the IQR was broader in immigrants (9–13) than in non-immigrants (11–13) and there was a statistically-significant group difference (Wilcoxon rank sum z = 2.57; p = 0.01). Immigrants also had fewer years of education than individuals born in the US (11.8 versus 13.5 years; 2-tailed t = 8.06, p < 0.0001); mean educational attainment in the immigrant group was lower than in the n-NES group. Immigrants were predominantly Caucasian (60%; $X^2 = 27.2$, p < 0.0001). Median baseline GDS scores were similar for immigrant and US-born groups (Wilcoxon rank-sum z = 0.22; p = 0.83).

Relationship between language use and incident dementia and AD

Mean (SD) age of dementia diagnosis in n-NES was 82.3 (5.8) years, compared to 81.2 (5.6) years in NES (2-tailed t = -3.54; p = 0.0004). Results were similar for age at AD diagnosis. In the primary Cox proportional hazards models for any dementia and AD (Table 4), the point estimates for risk associated with n-NES were not different than 1.0. None of the covariates were statistically-significant independent predictors of risk for any dementia or AD. Additional adjustment for baseline percentage-use of English did not significantly change the HR for n-NES. This result should be interpreted cautiously, as it likely underestimates non-English use in NES, for whom we imputed 100% English (NES were not asked about non-English language use).

Addition of the multiplicative interaction term of n-NES and educational attainment significantly improved the final Cox regression model (LR 4.11; p = 0.04). After stratification at the median of educational attainment (12 years), n-NES status was found to be associated with increased risk (HR > 1.0) in the more educated group and relative protection (HR < 1.0) in the less educated, although neither HR was statistically significant. To explore this qualitative interaction, we divided education into three groups (Low: 0–11 years; Intermediate: 12–15 years; and High: \geq 16 years), calculated absolute dementia incidence rates by education level in n-NES and NES groups, and re-ran the final Cox models for each education group (Table 5). Within NES only, absolute incidence of dementia was highest in the Low group and declined with increasing educational attainment. In n-NES, absolute incidence was high in both Low and High groups, indicating a U-shaped relationship between n-NES and education. In the stratified full models for any dementia, n-NES in the Low and Intermediate groups had non-significantly lower dementia risk than NES. In the High group, risk for incident dementia was significantly increased by a factor of four for n-NES compared to NES. Additionally adjusting for reading level in the stratified

models did not alter the results as presented. Interactions between n-NES and immigration and marital status were non-significant.

We found no effect of bilingualism in the subgroup analysis, either when modeled as any reported use of the non-English native language (HR = 1.26, 95% CI 0.65–2.44, p = 0.49) or at 50% active usage (HR = 1.59, 95% CI 0.72–3.54, p = 0.25). Although the HR for those in the more active group (n = 64) was higher, all CI once again included 1.0.

DISCUSSION

Our findings contribute to the literature on patterns of language use and their relationship to risk for incident dementia and AD. Compared to a reference group of native English speakers, n-NES status was associated with a small non-significant increase in risk for both any dementia and AD in both unadjusted and adjusted main effects models (all HR exceeded 1.0). We therefore conclude that non-native use of English does not appear to be an independent predictor of risk (or protection) for either dementia or AD. However, we did detect an education-dependent association between n-NES status and risk of dementia. Specifically, n-NES with at least 16 years of education had a four-fold increased risk for dementia compared to those with less education.

Our findings indicate that educational attainment modifies the relationship between n-NES and risk of incident dementia/AD. A substantial body of previously-published work suggests that higher educational attainment lowers dementia risk. Although mechanisms are not yet fully understood, this phenomenon may result from direct protection against neurodegenerative pathology, or effects could be indirect, operating through a compensatory 'cognitive reserve' that buffers the brain from encroaching pathology [5, 41]. In our sample, only in NES did absolute dementia incidence rates demonstrate the expected decline as the level of education increased. In n-NES, absolute dementia incidence was high in the Low education group, as expected, but also high in the High education group. While unusual, our finding of increased dementia risk in the most highly educated group is not unprecedented [42]. How n-NES status might have attenuated the expected protective effect of education in our sample is unclear. One possibility is diagnostic misclassification, although English reading ability was similar between n-NES and NES, making it less likely that poor knowledge of English or poorer education reduced performance on the cognitive tests or influenced the results of the consensus diagnosis. Our use of well-established procedures and standardized criteria for the diagnosis of dementia further mitigates this possibility, particularly since information about native language was not a standard datum reviewed in diagnostic consensus case conferences. Another possibility is that informative censoring in our participants differed by language group. To test this possibility, we compared follow-up time between n-NES and NES and found no statistically-significant group difference, indicating that results were unlikely to have been biased by differential selective attrition or informative censoring based on follow-up time. A third possibility, more theoretical and therefore speculative, is that the result was caused by the presence of unmeasured confounders in the highly educated n-NES, such as personality traits or stressful life events, or to level of participation in other cognitively-stimulating activities that offset the expected protective effect of education [43]. Finally, it is possible that in n-NES the cognitive reserve benefits accrued from high educational attainment were offset by speaking a non-native language. In the calculus of cognitive reserve, our findings suggest that the relationship between language use and education is one of antagonism rather than synergy, and would support the idea that bilingual activity is more burdensome than beneficial in cognitive aging. These obviously preliminary observations merit further investigation.

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We are aware of only one previous longitudinal study of dementia incidence associated with patterns of language use. Crane et al. studied Japanese-American men in the Honolulu Heart Program who were assessed for use of spoken and written Japanese at midlife and during old age [10]. Their study, like ours, found that the predominant main effect of self-reported written Japanese proficiency on risk of any dementia, AD, or vascular dementia was to increase rather than diminish risk, without reaching statistical significance. Crane et al. restricted their analyses to main effects; a strength of our analysis is that we also examined effect modification. Most published studies on the relationship between language use and dementia have focused on cross-sectional age at diagnosis. In a retrospective study from a memory disorders clinic in Toronto, Bialystok et al. reported that self- or informant-reported symptoms of memory loss in bilingual individuals with AD began approximately four years later than in monolinguals [7, 8]. Chertkow et al. failed to confirm this finding in a study from a Montreal-based memory disorders clinic. However, after stratifying by immigrant status (inferred from native language and site of primary/secondary schooling), they report that speaking more than two languages was associated with a nearly five-year delay in diagnosis of AD [9]. Compared to native speakers, in our study n-NES were about one year older at the time of dementia diagnosis, however, they were also older at enrollment and had roughly equivalent follow-up time, so it is unsurprising that they were older at diagnosis in the absence of an association between n-NES status and dementia. Immigration, which we ascertained directly from participants, did not appear to confound, predict, or modify the effect of language use on dementia risk.

There are several limitations associated with this study, which could account for the unexpected findings and the lack of statistical significance in some analyses. Stratifying by education constrained power, and this may account for the lack of statistical significance in two of our three educational groupings. Our choice of language use comparison groups was largely dictated by the nature of the EAS' sample population. In EAS, categories of language use were operationalized for identification of potential confounders in the analysis of neuropsychological data and cognitive outcomes and not primarily to assess bi- or multilingualism. Consequently, only n-NES individuals were asked about their use of additional languages. This likely underestimated the degree of bilingualism in our data, as we could not capture native English speakers who subsequently learned one or more additional languages. We did not have additional data on acculturation, the number of non-English languages spoken, proficiency, or the setting in which additional languages were learned. Notably, although n-NES were more likely than NES to be married, two-thirds were nonetheless widowed, divorced, or never married. This may have influenced their access to other individuals who spoke their native language by the time they enrolled in our study.

Our results are strengthened by the fact that our data were longitudinal, which reduced recall bias and permitted analysis of incident dementia. Also, our sample comprised older adults who were community-residing and relatively healthy at baseline, which may have reduced our vulnerability to selection bias. Obtaining information about birthplace directly from EAS participants allowed us to assess the potential role of immigrant status as independent predictor, confounder, and effect modifier of the relationships between n-NES and outcomes related to dementia.

In summary, our data do not support our hypothesis that n-NES have lower risk of incident dementia or AD. We conclude that n-NES status does not appear to have an independent protective effect against incident dementia/AD, and that n-NES status may contribute to risk of dementia in an education-dependent manner. Future studies should consider exploring the role of education as an effect modifier of the relationship between patterns of language use and risk for dementia, AD, and cognitive decline.

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References

- 1. Francis WS. Cognitive integration of language and memory in bilinguals: Semantic representation. Psychol Bull. 1999; 125:193–222. [PubMed: 10087936]
- Bialystok, E. Bilingualism in Development: Language, Literacy, and Cognition. Cambridge University Press; Cambridge, UK: 2001.
- Kave G, Eyal N, Shorek A, Cohen-Mansfield J. Multilingualism and cognitive state in the oldest old. Psychol Aging. 2008; 23:70–78. [PubMed: 18361656]
- Crane PK, Gruhl JC, Erosheva EA, Gibbons LE, McCurry SM, Rhoads K, Nguyen V, Arani K, Masaki K, White L. Use of spoken and written Japanese did not protect Japanese-American men from cognitive decline in late life. J Gerontol B Psychol Sci Soc Sci. 2010; 65:654–666. [PubMed: 20639282]
- Stern Y. What is cognitive reserve? Theory and research application of the reserve concept. J Int Neuropsychol Soc. 2002; 8:448–460. [PubMed: 11939702]
- Bialystok E, Craik FI, Klein R, Viswanathan M. Bilingualism, aging, and cognitive control: Evidence from the Simon task. Psychol Aging. 2004; 19:290–303. [PubMed: 15222822]
- Bialystok E, Craik FI, Freedman M. Bilingualism as a protection against the onset of symptoms of dementia. Neuropsychologia. 2007; 45:459–464. [PubMed: 17125807]
- Craik FI, Bialystok E, Freedman M. Delaying the onset of Alzheimer disease: Bilingualism as a form of cognitive reserve. Neurology. 2010; 75:1726–1729. [PubMed: 21060095]
- Chertkow H, Whitehead V, Phillips N, Wolfson C, Atherton J, Bergman H. Multilingualism (but not always bilingualism) delays the onset of Alzheimer disease: Evidence from a bilingual community. Alzheimer Dis Assoc Disord. 2010; 24:118–125. [PubMed: 20505429]
- Crane PK, Gibbons LE, Arani K, Nguyen V, Rhoads K, McCurry SM, Launer L, Masaki K, White L. Midlife use of written Japanese and protection from late life dementia. Epidemiology. 2009; 20:766–774. [PubMed: 19593152]
- Manly JJ, Schupf N, Tang MX, Stern Y. Cognitive decline and literacy among ethnically diverse elders. J Geriatr Psychiatry Neurol. 2005; 18:213–217. [PubMed: 16306242]
- Brayne C, Ince PG, Keage HA, McKeith IG, Matthews FE, Polvikoski T, Sulkava R. Education, the brain and dementia: Neuroprotection or compensation? Brain. 2010; 133:2210–2216. [PubMed: 20826429]
- Sanders AE, Wang C, Katz M, Derby CA, Barzilai N, Ozelius L, Lipton RB. Association of a functional polymorphism in the cholesteryl ester transfer protein (CETP) gene with memory decline and incidence of dementia. JAMA. 2010; 303:150–158. [PubMed: 20068209]
- Verghese J, LeValley A, Hall CB, Katz MJ, Ambrose AF, Lipton RB. Epidemiology of gait disorders in community-residing older adults. J Am Geriatr Soc. 2006; 54:255–261. [PubMed: 16460376]
- 15. Ray L, Lipton RB, Zimmerman ME, Katz MJ, Derby CA. Mechanisms of association between obesity and chronic pain in the elderly. Pain. 2011; 152:53–59. [PubMed: 20926190]
- Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and of senile change in the cerebral gray matter of elderly subjects. Brit J Psychiatry. 1968; 114:797–811. [PubMed: 5662937]
- 17. Wilkinson, GS. WRAT 3: The Wide Range Achievement Test 3 administration model. Wide Range, Inc; Wilmington, DE: 1993.

- Wechsler, D. Wechsler Adult Intelligence Scale -Revised. The Psychological Corporation; New York: 1981.
- 19. Wechsler, D. Adult Intelligence Scale-III. Psychological Corporation; San Antonio, TX: 1997.
- 20. Buschke H. Cued recall in amnesia. J Clin Neuropsychol. 1984; 6:433-440. [PubMed: 6501581]
- Grober E, Buschke H, Crystal H, Bang S, Dresner R. Screening for dementia by memory testing. Neurology. 1988; 38:900–903. [PubMed: 3368071]
- 22. Wechsler, D. Wechsler Memory Scale Revised. The Psychological Corporation; San Antonio: 1987.
- 23. Benton, AL.; Hamsher, KdeS. Multilingual Aphasia Examination. AJA Associates; Iowa City, IA: 1989.
- Reitan R. Validity of the trail making test as an indicator of organic brain damage. J Comp Physiological Psychol. 1958; 48:474–477.
- Monsch AU, Bondi MW, Butters N, Salmon DP, Katzman R, Thal LJ. Comparisons of verbal fluency tasks in the detection of dementia of the Alzheimer type. Arch Neurol. 1992; 49:1253– 1258. [PubMed: 1449404]
- 26. Kaplan, EF.; Goodglass, H.; Weintraub, S. The Boston Naming Test. Lea & Febiger; Philadelphia: 1983.
- 27. Morris JC, Heyman A, Mohs RC, Hughes JP, van Belle G, Fillenbaum G, Mellits ED, Clark C. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part I. Clinical and neuropsychological assessment of Alzheimer's disease. Neurology. 1989; 39:1159–1165. [PubMed: 2771064]
- Jorm AF, Jacomb PA. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): Socio-demographic correlates, reliability, validity and some norms. Psychol Med. 1989; 19:1015–1022. [PubMed: 2594878]
- 29. Lawton MP, Brody EM. Assessment of older people: Self-maintaining and instrumental activities of daily living. Gerontologist. 1969; 9:179–186. [PubMed: 5349366]
- Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. Clin Gerontol. 1986; 5:165–173.
- Diagnostic and Statistical Manual of Mental Disorders. DSM-IV American Psychiatric Association; Washington, DC: 1994. p. 133
- Holtzer R, Goldin Y, Zimmerman M, Katz M, Buschke H, Lipton RB. Robust norms for selected neuropsychological tests in older adults. Arch Clin Neuropsychol. 2008; 23:531–541. [PubMed: 18572380]
- Hachinski VC, Lassen NA, Marshall J. Multi-infarct dementia. A cause of mental deterioration in the elderly. Lancet. 1974; 2:207–210. [PubMed: 4135618]
- Rosen WG, Terry RD, Fuld PA, Katzman R, Peck A. Pathological verification of ischemic score in differentiation of dementias. Ann Neurol. 1980; 7:486–488. [PubMed: 7396427]
- 35. Morris JC. The Clinical Dementia Rating (CDR): Current version and scoring rules. Neurology. 1993; 43:2412–2414. [PubMed: 8232972]
- Grober E, Lipton RB, Hall C, Crystal H. Memory impairment on free and cued selective reminding predicts dementia. Neurology. 2000; 54:827–832. [PubMed: 10690971]
- 37. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: Report of the NINDS-ADRDA Work group under the auspices of department of health and human services task force on Alzheimer's Disease. Neurology. 1984; 34:939–944. [PubMed: 6610841]
- Thiebaut AC, Benichou J. Choice of time-scale in Cox's model analysis of epidemiologic cohort data: A simulation study. Stat Med. 2004; 23:3803–3820. [PubMed: 15580597]
- Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. Biometrika. 1994; 81:515–526.
- Manly JJ, Jacobs DM, Touradji P, Small SA, Stern Y. Reading level attenuates differences in neuropsychological test performance between African American and White elders. J Int Neuropsychol Soc. 2002; 8:341–348. [PubMed: 11939693]

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- 41. Katzman R, Terry R, DeTeresa R, Brown T, Davies P, Fuld P, Renbing X, Peck A. Clinical, pathological, and neurochemical changes in dementia: A subgroup with preserved mental status and numerous neocortical plaques. Ann Neurol. 1988; 23:138–144. [PubMed: 2897823]
- 42. Duberstein PR, Chapman BP, Tindle HA, Sink KM, Bamonti P, Robbins J, Jerant AF, Franks P. Personality and risk for Alzheimer's disease in adults 72 years of age and older: A 6-year follow-up. Psychol Aging. 2011; 26:351–362. [PubMed: 20973606]
- Hall CB, Lipton MB, Sliwinski M, Katz M, Derby CA, Verghese J. Cognitive activities delay onset of memory decline in persons who develop dementia. Neurology. 2009; 73:356–361. [PubMed: 19652139]

Baseline characteristics of study population by dementia status at followup. Values are mean (SD) unless otherwise noted. Percentages are by column

Variable ^a	All (<i>n</i> = 1779)	Without incident dementia $(n = 1653)$	With incident dementia (<i>n</i> = 126)	<i>p</i> -value ^b
Non-native english speakers (n-nes), n (%)	390 (21.9)	357 (21.6)	33 (26.2)	0.22
Age, years [range]	78.6 (5.3) [70–100]	78.4 (5.3) [70–100]	80.7 (5.4) [70–97]	< 0.0001
Gender, n (% women)	1081 (60.8)	998 (60.4)	83 (65.9)	0.22
Race, <i>n</i> (% white)	1245 (70.3)	1160 (70.5)	85 (67.5)	0.46
Education, years [range]	13.1 (3.6) [0–25]	13.1 (3.6) [5–25]	12.8 (3.6) [5–20]	0.31
Reading grade level ^C (median) [IQR]	12 (10–13) [2–13]	12 (10–13) [2–13]	12 (10–13) [4–13]	0.26
Immigrated to united states, n (%)	398 (22.5)	365 (22.2)	32 (25.4)	0.40
Married, n (%)	707 (39.9)	665 (40.4)	42 (33.6)	0.13
BIMC ^d (median) [IQR]	2 (1-4) [0-13]	2 (1-4) [0-13]	4 (2–6) [0–13]	< 0.0001
FCSRT ^e (free recall) [range]	29.9 (6.3) [13-48]	30.3 (6.0) [14-48]	24.6 (7.3) [9–45]	< 0.0001
15-item GDS ^f (median) [IQR]	2 (1-4) [0-14]	2 (1-4) [0-14]	2 (1-4) [0-12]	0.22
Self-reported diabetes, n (%)	296 (16.6)	280 (16.9)	16 (12.7)	0.22
Self-reported hypertension, n (%)	1021 (57.4)	949 (57.4)	72 (57.1)	0.95
Self-reported stroke, <i>n</i> (%)	163 (9.2)	154 (9.3)	9 (7.1)	0.42
Self-reported MI, n (%)	178 (10.0)	163 (9.9)	15 (11.9)	0.46

Percentages might not equal 100, due to rounding.

^aAbbreviations: BIMC, Blessed Information-Memory-Concentration test; FCSRT, Free and Cued Selective Reminding test; GDS, Geriatric Depression Scale; IQR, interquartile range; MI, myocardial infarction.

 ${}^{b}p$ -values for comparison of the with and without dementia groups. For continuous variables, group means (Student's *t*-tests) or medians (Wilcoxon rank-sum test) were compared as appropriate; X^2 or Fisher's exact test were used to compare proportions for categorical variables.

^CFrom Wide Ranging Achievement Test, Reading Portion (English proficiency).

^dScores range from 0 to 33 with higher scores indicating worse performance; scores ≥ 8 indicate impairment.

^eScores range from 0 to 48 with higher scores indicating better memory performance. Scores ≤ 24 indicate impaired memory.

 $f_{\text{Scores higher than 6 on the 15-item test indicate significant depressive symptoms.}$

Baseline characteristics of study population by language usage. Values are mean (SD) unless otherwise noted. Percentages are by column

Variable ^a	All (<i>n</i> = 1779)	Native english speakers (<i>n</i> = 1389)	Non-native english speakers $(n = 390)$	<i>p</i> -value ^b
Follow-Up Time (median) [IQR], years	1.44 (0–3.6) [0–16.3]	1.40 (0.0–3.6) [0–16.3]	1.52 (0.0–3.6) [0–11.6]	0.68
Absolute dementia incidence rate (100/ PY)	3.02 (2.54–3.60)	2.87 (2.34–3.52)	3.54 (2.51–4.97)	0.31
Age, years [range]	78.6 (5.3) [70–100]	78.3 (5.2) [70–100]	79.4 (5.6) [70–100]	0.0003
Gender, n (% women)	1081 (60.8)	845 (60.8)	236 (60.5)	0.91
Race, <i>n</i> (% white)	1245 (70.3)	928 (67.2)	317 (81.5)	< 0.0001
Education, years [range]	13.1 (3.6) [0–25]	13.3 (3.4) [2–25]	12.5 (4.2) [0–24]	0.0006
Reading grade level ^C (median) [IQR]	12 (10–13) [2–13]	12 (10–13) [2–13]	12 (10–13) [2–13]	0.78
Immigrated to united states, n (%)	398 (22.5)	155 (11.2)	243 (62.6)	< 0.0001
Married, n (%)	707 (39.9)	531 (38.4)	176 (45.2)	< 0.01
BIMC ^d (median) [IQR]	2 (1-4) [0-13]	2 (1-4) [0-13]	2 (1-4) [0-13]	0.23
FCSRT ^e (free recall) [range]	29.9 (6.3) [13-48]	29.9 (6.3) [13-46]	30.1 (6.4) [11–48]	0.51
15-item GDS ^f (median) [IQR]	2 (1-4) [0-14]	2 (1-4) [0-14]	2 (1-4) [0-14]	0.30
Self-reported diabetes, n (%)	296 (16.6)	233 (16.8)	63 (16.2)	0.77
Self-reported hypertension, n (%)	1021 (57.4)	825 (59.4)	196 (50.3)	0.001
Self-reported stroke, n (%)	163 (9.2)	132 (9.5%)	31 (8%)	0.35
Self-reported MI, n (%)	178 (10.0)	133 (9.6)	45 (11.5)	0.25

Percentages might not equal 100, due to rounding.

^aAbbreviations: BIMC, Blessed Information-Memory-Concentration test; FCSRT, Free and Cued Selective Reminding test; GDS, Geriatric Depression Scale; IQR, interquartile range; myocardial infarction.

 ${}^{b}_{p}$ -values for comparison of n-NES to native speakers. For continuous variables, group means (Student's *t*-tests) or medians (Wilcoxon rank-sum test) were compared as appropriate; X^2 or Fisher's exact test were used to compare proportions for categorical variables.

^cFrom Wide Ranging Achievement Test, Reading Portion (English proficiency).

^dScores range from 0 to 33 with higher scores indicating worse performance; scores ≥ 8 indicate impairment.

^eScores range from 0 to 48 with higher scores indicating better memory performance. Scores ≤ 24 indicate impaired memory.

^fScores higher than 6 on the 15-item test indicate significant depressive symptoms.

Baseline characteristics of n-NES according to use of non-english mother tongue at EAS baseline. Values are mean (SD) unless otherwise noted. Percentages are by column

Variable ^a	No use (<i>n</i> = 267)	Any use (<i>n</i> = 123)	<i>p</i> -value ^b
Age of english acquisition (median) [IQR], years	6 (5–12) [2.41]	14 (6–22) [3–55]	< 0.0001
Follow-up time (median) [IQR], years	1.55 (0.0–3.6) [0.0–11.55]	1.17 (0.0–3.4) [0.0–10.38]	0.60
Age [range]	80.1 (5.7) [70–96]	78.0 (5.0) [70–88]	0.0005
Gender, <i>n</i> (% women)	171 (63.1)	65 (54.6)	0.11
Race, n (% white)	242 (89.3)	75 (63.6)	< 0.0001
Education, years [range]	12.7 (4.0) [5–24]	12.0 (4.8) [1–23]	0.22
Reading grade level ^C (median) [IQR]	12 (11–13) [2–13]	12 (9–13) [2–13]	0.04
Immigrated to United States, n (%)	147 (54.4)	96 (81.4)	< 0.0001
Married, n (%)	118 (43.7)	58 (48.7)	0.36
BIMC ^d (median) [IQR]	2 (1-4) [0-11]	3 (1–5) [0–13]	0.001
FCSRT ^e (free recall) [range]	30.0 (6.3) [11–43]	30.3 (6.6) [15-48]	0.75
15-item GDS ^f (median) [IQR]	2 (1-4) [0-12]	2 (1-4) [0-14]	0.17
Self-reported diabetes, n (%)	34 (12.6)	29 (24.4)	0.004
Self-reported hypertension, n (%)	136 (50.2)	60 (50.4)	0.97
Self-reported Stroke, <i>n</i> (%)	23 (8.5)	8 (6.7)	0.55
Self-reported MI, <i>n</i> (%)	31 (11.4)	14 (11.8)	0.93

Percentages might not equal 100, due to rounding.

^aAbbreviations: BIMC, Blessed Information-Memory-Concentration test; FCSRT, Free and Cued Selective Reminding test; GDS, Geriatric Depression Scale; IQR, interquartile range; MI, myocardial infarction.

 b_{p} -values are from comparison of means using Student's *t*-tests or comparison of medians using the Wilcoxon rank-sum test; X^2 or Fisher's exact test were used as appropriate for comparison of proportions.

^cFrom Wide Ranging Achievement Test, Reading Portion.

 d Scores range from 0 to 33 with higher scores indicating worse performance; scores ≥ 8 indicate impairment.

^eScores range from 0 to 48 with higher scores indicating better memory performance. Scores ≤ 24 indicate impaired memory.

 $f_{\text{Scores higher than 6 on the 15-item test indicate significant depressive symptoms.}$

Non-native speakers of english and risk of any dementia and AD

	Risk for any dementia for n-NES versus NES Hazard ratio (95% CI) <i>p</i> value ^{<i>a</i>}	Risk for Alzheimer's disease for n-NES versus NES Hazard Ratio (95% CI) <i>p</i> value ^{<i>a</i>}
# cases/# censored	126/980	101/1005
Model 1 ^b	1.23 (0.83–1.83) 0.31	1.24 (0.80–1.92) 0.34
Model 2 ^C	1.16 (0.77–1.76) 0.48	1.18 (0.74–1.86) 0.49
Model 3 ^d	1.26 (0.76–2.09) 0.36	1.21 (0.69–2.11) 0.52

Abbreviation: CI, confidence interval.

^aNative English speakers were used as the reference group for n-NES. In the n-NES group there were 33 incident cases of dementia and 27 incident cases of Alzheimer's disease.

 $^{b}\ensuremath{\mathsf{Model}}$ 1: Age used as time scale, but otherwise unadjusted.

^cModel 2: Adjusted for Gender and Race/Ethnicity (male and white race as referents), and years of education.

^dModel 3: additional adjustment for Immigrant Status (born in US as referent) and Marital Status (currently married as referent).

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Table 5

Absolute incidence rates and hazard ratios for dementia risk stratified by educational level

	Nati	Native speakers		n-NES	Absolute incidence (# events/person-years) Hazard ratio (95% CI) p value ^{<i>a</i>}	nts/person-years)	Hazard ratio (95% CI) <i>p</i> value ^{<i>a</i>}
Educational attainment (years)	Events	Person-years	Events	cears) Events Person-years Events Person-years	Native speakers	n-NES	
Low (0-11 years)	31	563	13	292	5.5	4.5	$0.75 \ (0.32 - 1.76) \\ 0.51$
Intermediate (12–15 years)	45	1702	٢	368	2.6	1.9	$0.57 (0.22 - 1.45) \\ 0.24$
High (16–25 years)	17	969	13	271	1.8	4.8	3.97 (1.62–9.75) 0.003

^aResults are from the full Cox proportional hazards model (Model 3); separate models were run for each education group. Native English speakers were used as the reference group for n-NES.