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THEORETICAL REVIEW

Does bilingualism protect against dementia? A meta-analysis

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Abstract

Evidence suggests that bilingualism may contribute to neuroplasticity and cognitive reserve, allowing individuals to resist cognitive decline associated with Alzheimer's disease progression, although the idea remains controversial. Here, we argue that the reason for the discrepancy stems from conflating incidence rates of dementia and the age at which the symptoms first appear, as well as statistical and methodological issues in the study designs. To clarify the issues, we conducted a comprehensive meta-analysis on the available literature regarding bilingualism and Alzheimer's disease, including both retrospective and prospective studies, as well as age of onset and incidence rates. Results revealed a moderate effect size for the protective effect of bilingualism on age of onset of symptoms of Alzheimer's disease (Cohen's $d = 0.32$), and weaker evidence that bilingualism prevents the occurrence of disease incidence itself (Cohen's $d = 0.10$). Moreover, our results cannot be explained by SES, education, or publication bias. We conclude with a discussion on how bilingualism contributes to cognitive reserve and protects against Alzheimer's disease and recommend that future studies report both age of onset as well as incidence rates when possible.

Keywords Alzheimer's disease · Bilingualism · Dementia · Meta-analysis

As adults age, cognitive functions decline due to loss of gray matter (Thompson et al., 2003), white matter (de Mooij, Henson, Waldorp, & Kievit, 2018; Ge et al., 2002), brain signal complexity (Dauwels, Vialatte, & Cichocki, 2010; Fernández et al., 2010), and functional connectivity between brain regions (Brier et al., 2012). These losses affect language (Weiler et al., 2014), memory (Nyberg, Lövdén, Riklund, Lindenberger, & Bäckman, 2012), motor control (Seidler et al., 2010), and higher-order executive processes (Borghesani et al., 2013) across the population. According to the World Health Organization (2019), age is the single strongest risk factor for dementia, and dementia currently affects more than 50 million people worldwide. This number is projected to continue doubling approximately every 20 years (Prince, 2015; Prince et al., 2013) and in 2015 alone cost approximately US$818 billion (Wimo et al., 2017). By the time people reach 85 years or older, as many as 1 in 4 people are diagnosed with dementia (Prince, 2015; Prince et al., 2013). Given the numerous advances in the medical field leading to increased longevity of life, it is imperative to identify factors that might help to delay symptoms of dementia.

Currently, the most common form of dementia is Alzheimer's disease (S. Bennett, Grant, & Aldred, 2009), and there is no known cure for this ailment (Cummings, Tong, & Ballard, 2019; Pohanka, 2013). Some studies have suggested a causal link between Alzheimer's pathology and beta-amyloid proteins (Hardy & Higgins, 1992; Sadigh-Eteghad et al., 2015), but others have suggested that these proteins are a by-product of the disease rather than the cause itself (Kepp, 2016). Regardless, it is clear that we are far from understanding how to prevent the pathology from progressing with increasing age (Kepp, 2016). Fortunately, there are things that we can do to prevent the onset of *symptoms* of Alzheimer's disease and other dementias (Alladi et al., 2017; Bak & Alladi, 2014; Stern et al., 2018). These cognitive reserve factors include increasing the amount of physical activity in our daily lives (Sofi et al., 2011), achieving higher levels of education (Stern, Albert, Tang, & Tsai, 1999), improving our social networks (D. A. Bennett, Schneider, Tang, Arnold,

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& Wilson, 2006), and taking on more challenging jobs (Alvarado, Zunzunegui, Del Ser, & Béland, 2002). By incorporating these factors into our daily lives, the brain is able to reorganize itself in a way that allows us to deal with brain pathology for longer periods of time before showing signs of cognitive decline (Stern, 2009). Bilingualism has been reported as one such cognitive reserve factor that can delay the onset of symptoms of dementia by about 4–5 years compared with monolinguals (Bialystok, Craik, & Freedman, 2007; Craik, Bialystok, & Freedman, 2010; Zheng et al., 2018). However, some have contested the idea that bilingualism protects against dementia (Mukadam, Sommerlad, & Livingston, 2017; van den Noort et al., 2019), and so the present study was conducted to evaluate the evidence for these effects.

Bialystok et al. (2007) were the first to examine the effect of bilingualism on the progression of Alzheimer's symptoms. They examined the records of 184 patients (51% bilingual) diagnosed with dementia in Toronto, Canada, and demonstrated that bilinguals showed symptoms of dementia approximately 4 years later than comparable monolinguals, despite equivalent progression of Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) scores prior to diagnosis. The authors concluded that a lifetime of experience managing two languages that compete for selection contributes to cognitive reserve (Stern, 2009) and protects against cognitive decline in older age. These findings have since been replicated several times with different populations while controlling for potentially confounding variables including socioeconomic status, education, occupational level, and immigration status. For example, Craik et al. (2010) examined 102 bilinguals and 109 monolinguals and found that bilinguals were on average 5.1 years older than monolinguals at age of onset of symptoms of dementia, independent of education, occupational status, and gender; all factors that contribute to cognitive reserve. Alladi et al. (2013) further expanded these findings by ruling out immigration status as a contributor to potential group differences. This last point is of particular importance as bilinguals in North America are often recent immigrants, and differences between monolinguals and bilinguals might be due to the increased cognitive demands for bilinguals having to navigate new cultural environments rather than second-language experience itself. Similarly, perhaps only those with greater access to resources allowed them to immigrate in the first place. Alladi et al. (2013) circumvented this issue by examining 257 monolinguals and 391 bilinguals in India who had been in the country for several generations. In these samples, bilinguals still showed a 4-year delay in the age at which symptoms first appeared, independent of education, gender, occupation, and whether individuals lived in rural versus urban settings. These studies support the claim that bilingualism constitutes an important protective factor in delaying the onset of symptoms of dementia.

One compelling study demonstrating bilingualism as a form of cognitive reserve was conducted by Perani et al. (2017). Forty-five bilinguals and 40 monolinguals with probable Alzheimer's disease, matched for symptom duration, underwent positron emission tomography (PET). Results revealed that bilinguals were on average 5 years older than their monolingual peers, and PET scans revealed that the bilingual brains had greater cerebral *hypometabolism*—an index of Alzheimer's progression. In other words, bilinguals were able to withstand the effects of deteriorating brains without showing signs of dementia for several years longer than monolinguals. This suggests that bilingualism rewires the brain in a fashion that allows them to deal with increasing levels of neuropathology before showing symptoms. Critically, this does not mean that bilinguals do not develop the disease, but rather that they are able to cope for longer than monolinguals once they get the disease. It is important to reiterate that these studies do not claim that bilingualism protects against neuropathology; bilinguals and monolinguals both develop the disease (incidence), but bilinguals last for longer before showing symptoms (age of onset). This is an important distinction, and researchers often mistakenly conflate the two concepts. A further nuance to this distinction is that bilinguals with cognitive reserve are more likely to have undetected Alzheimer's disease burden than do monolinguals as their reserve masks the disease, and thus may escape detection by the medical system.

Mukadam, Sommerlad, and Livingston (2017) recently published a meta-analysis on the available literature concluding that they "did not find evidence that bilingualism, when appropriately adjusted for education, protects from cognitive decline or dementia. Public health policy should, therefore, remove recommendations regarding bilingualism [3] as a strategy to delay dementia" (pg. 53). This study has received widespread media attention and has already received 37 citations since its publication in 2017. To put this in context, if all articles published in a particular journal received this many citations in the span of 2 years, then the journal's impact factor would be 37. Mukadam et al.'s claim that bilingualism should be removed from public policy recommendations, therefore, needs to be carefully examined. Their conclusion was based on a meta-analysis of only four empirical studies that examined *incidence rates* of dementia rather than the age of onset. Unfortunately, the authors dismissed all age-of-onset studies and did not include them in their analyses on the grounds that they were of "lower quality" because they were retrospective rather than prospective and did not control for cultural background and education levels. However, as mentioned above, incidence rates of Alzheimer's disease and age of onset of the disease are two conceptually different constructs and should not be conflated. There is no reason that we are aware of that one should expect bilingualism to *prevent* Alzheimer's neuropathology. Rather, in a similar fashion to other forms of cognitive reserve, brain reorganization allows bilinguals to stave off *symptoms* of the pathology for longer periods of time. Thus, Mukadam et al.'s (2017) conclusion that bilingualism does not protect from cognitive decline or dementia is premature.

Two commentaries were published in response to the Mukadam et al. (2017) meta-analysis that highlight other issues that warrant a reevaluation of the findings. E. Woumans, Versijpt, Sieben, Santens, and Duyck (2017) argued that most of the retrospective studies, which had been dismissed for not controlling for education and cultural background *did*, in fact, control for these variables and still found a protective effect of bilingualism. This is exemplified by the studies of Craik et al. (2010), Alladi et al. (2013), and Perani et al. (2017), discussed above, who all controlled for these variables and still showed that the age at which symptoms appeared was 4–5 years later for bilinguals than monolinguals. E. Woumans et al. also point out that two additional incidence studies favoring bilingualism as a protective factor were not included in the meta-analysis conducted by Mukadam et al. (2017). Grundy and Anderson (2017) further pointed out that the authors eliminated one of the incidence studies on the grounds that it was of "lower quality," yet *two* of the four studies included in their final analysis were given the same quality score. A second issue is that while prospective studies usually focus on incidence rates, many prospective studies also include age of onset of the symptoms in their descriptive statistics, making it possible to examine age of onset of Alzheimer's disease in prospective and retrospective studies within the same model. Including retrospective and prospective studies in a single meta-analysis would allow for the examination of whether the type of study (retrospective vs. prospective) moderated the overall effect (Grundy & Anderson, 2017).

It is important to clarify that the terms *retrospective* and *prospective* should not be conflated with age of onset and incidence rate. While the focus of prospective studies examining the effects of bilingualism on Alzheimer's disease to date has been on the incidence rate of Alzheimer's (i.e., how many people get the disease), prospective studies could just as easily examine the age at which symptoms first appear. On the other hand, retrospective studies focus almost exclusively on the age of onset of symptoms. This is because the samples examined in retrospective studies are usually from a population of patients who already have Alzheimer's disease. Nonetheless, evidence from at least one retrospective study at the population level suggests that incidence rates of Alzheimer's disease are lower in bilingual than monolingual countries (Klein, Christie, & Parkvall, 2016). This is in contrast to Mukadam et al.'s (2017) findings that bilingualism does not affect incidence rates of Alzheimer's disease.

The present study was designed to address conflicting findings in the literature and to empirically determine whether bilingualism is protective against incidence rates and/or age of onset of Alzheimer's symptoms. We thus conducted the first comprehensive meta-analysis on the available literature regarding bilingualism and Alzheimer's disease including both retrospective and prospective studies, as well as age of onset and incidence rates, to examine the strength and reality of any effects.

Method

A search of the literature was conducted between 2017 and December 2018 using the following terms: "AD onset bilingualism," "AD bilingualism," "Alzheimer's bilinguals," and "dementia bilingualism" using the PsycInfo and Microsoft Academic search engines. An initial search yielded 73 unique records, of which 21 studies were deemed to be eligible for further analysis. Our criteria for subsequent inclusion was (a) the study must report either mean age of onset or incidence for both bilingual and monolingual samples, and (b) the study should be about Alzheimer's disease, including amnestic mild cognitive impairment (MCI), the direct precursor to Alzheimer's, or at least include information about this dementia variant. Fifty-four studies were removed for not meeting these criteria. Of the 21 studies we selected for inclusion, three reported incidence statistics, while 15 reported age of onset. Additionally, three studies reported both the incidence and age of onset. For each study, a single effect size, Cohen's d, was calculated using the Campbell collaboration online effect size calculator (http://www.campbellcollaboration.org). Where means and standard deviations for each group were available, these were preferentially used; otherwise, effect sizes were calculated from the available statistics. We used the same method to derive Cohen's d measures of mean difference for education and socioeconomic status (SES) between monolinguals and bilinguals for every study reporting these measures separately by group (n = 19 for education, n = 9 for SES).

Results

Table 1 provides background information for all included studies.

Each of the analyses were conducted in R using the metafor package (Viechtbauer, 2010) using the Hunter–Schmidt method of pooling variance. Forest plots were generated using the "meta" package (Schwarzer, 2007). We conducted five analyses: The first analysis examined the impact of incidence versus age-of-onset studies; the second analysis was a sensitivity analysis and included only a single contribution per study; the third analysis examined prospective studies only. Two final analyses used meta-regression to examine how education and SES interacted with bilingualism to affect Alzheimer's age (combined incidence and onset).

Table 1. Background information for studies included in the meta-analyses

Author	Year	Title	Age of onset		Incidence	Cognitive measures	Language background
			ML	BL			
Alladi et al.	2013	Bilingualism delays age at onset of dementia, independent of education and immigration status	61.1	65.6		Better cognitive scores for bilinguals. MMSE: M = 16.7, B = 18.9 Addenbrooke's Cognitive Examination–Revised: M = 48.6, B = 55.5	Bilingualism was defined as "ability to meet the communicative demands of the self and the society in their normal functioning in two or more languages in their interaction with the other speakers of any or all of these languages." Most monolinguals only knew Telugu, and most bilinguals knew Telugu and English or Hindi or Dakkhini.
Alladi et al.	2017	Bilingualism delays the onset of behavioral, but not aphasic forms of frontotemporal dementia	58.4	61.7		No difference. MMSE: M = 15.9, B = 18.1 Addenbrooke's Cognitive Examination–Revised: M = 48.0, B = 53.7	Bilingualism was defined as "ability to meet the communicative demands of the self and the society in their normal functioning in two or more languages in their interaction with the other speakers of any or all of these languages."
Bialystok et al.	2007	Bilingualism as a protection against the onset of symptoms of dementia	71.4	75.5		No difference. MMSE: M = 21.3, B = 20.1	Bilinguals were defined as those who had spent the majority of their lives, beginning in early adulthood, speaking at least two or more languages fluently—ideally daily, but at least weekly.
Bialystok et al.	2014	Effects of bilingualism on the age of onset and progression of MCI and AD: Evidence from executive function tests	70.9	78.2		Marginally worse scores for bilinguals. MMSE: M = 23.4, B = 22.3 (p = .05) Behavioral Neurology Assessment: M = 72.7, B = 63.8 (p = .07)	Bilinguals were defined as those who had spent the majority of their lives, beginning in early adulthood, speaking at least two or more languages fluently—ideally daily, but at least weekly
Chertkow et al.	2010	Multilingualism (but not always bilingualism) delays the onset of Alzheimer's disease: evidence from a bilingual community	76.7	77.6		No difference. MMSE: M = 23.1, B = 22.8	Bilinguals were defined as those who spoke both French and English from youth. Monolinguals spoke either only French or only English.
Clare et al.	2016	Bilingualism, executive control, and age at diagnosis among people with early-stage Alzheimer's disease in Wales	76.23	79.27		No difference. MMSE: M = 23.9, B = 22.8	"Monolingual was defined as speaking English for all or most of one's life and being fluent in English, but not in any other language, and 'bilingual' was defined pragmatically in terms of speaking both Welsh and English for all or most of one's life and being fluent in both languages, but not in any other languages."
Craik et al.	2010	Delaying the onset of Alzheimer's disease Bilingualism as a form of cognitive reserve	72.6	77.7		No difference. MMSE: M = 21.5, B = 20.4	Bilinguals were defined as those who had spent the majority of their lives, beginning in early adulthood, speaking at least two or more languages fluently—ideally daily, but at least weekly.

Table 1. (continued)

Author	Year	Title	Age of onset		Incidence	Cognitive measures	Language background
			ML	BL			
Duncan et al.	2018	Structural brain differences between monolingual and multilingual patients with mild cognitive impairment and Alzheimer's disease: Evidence for cognitive reserve	77.1	76.7		No difference. MMSE: *M* = 22.5, *B* = 22.5	Bilinguals were defined as those who had spent the majority of their lives, beginning in early adulthood, speaking at least two or more languages fluently—ideally daily, but at least weekly.
Iyer et al.	2014	Dementia in developing countries: Does education play the same role in India as in the West?	Bilinguals showed later age of onset. Age of onset effect size determined from test statistics			Cognitive measures not reported by group.	Bilingualism was defined as "ability to meet the communicative demands of the self, and the society in their normal functioning in two or more languages in their interaction with the other speakers of any or all of these languages."
Kowoll et al.	2016	Bilingualism as a contributor to cognitive reserve? Evidence from cerebral glucose metabolism in mild cognitive impairment and Alzheimer's disease	71.6	74.6		No difference. MMSE: *M* = 23.9, *B* = 24.9	Bilinguals were defined as those who had spent the majority of their lives, beginning in early adulthood, speaking at least two or more languages fluently—ideally daily, but at least weekly. Bilinguals spoke nine different first languages, the most common were German and Hungarian. Seven different second languages were spoken, the most common being German and English.
Lawton et al.	2015	Age of dementia diagnosis in community dwelling bilingual and monolingual Hispanic Americans	81.1	79.3	No difference statistically	No difference. Modified MMSE (/100): *M* = 78.9 (9.9), *B* = 79.6 (15.6)	Participants came from the Sacramento Area Latino Study on Aging. Items "Do you speak English" and "Do you speak Spanish" on a 4-point scale (from 0–3) from *not at all* to *almost always* were used to define groups. Bilinguals were identified as those who responded 2 (*very often*) or 3 (*almost always*) to both questions. Monolinguals were identified as those who responded 0 (**not at all**) or 1 (*not very often*) to either question.
Nebreda et al.	2011	A short-form version of the Boston Naming Test for language screening in dementia in a bilingual rural community in Galicia (Spain)			Higher incidence rate for monolinguals	No difference. Spanish MMSE: *M* = 24.5, *B* = 24.8	"Bilingualism was assessed following a modification of the questionnaire of bilingualism included in the Spanish-Galician version of the Bilingual Aphasia Battery (BAT; Paradis, 2011)
Ossher et al.	2013	The effect of bilingualism on amnestic mild cognitive impairment	73.75	77.3		No difference. MMSE: *M* = 27.8, *B* = 27.7	Bilinguals were defined as those who had spent the majority of their lives, beginning in early adulthood, speaking at least two or more languages fluently—ideally daily, but at least weekly.

Table 1. (continued)

Author	Year	Title	Age of onset ML	Age of onset BL	Incidence	Cognitive measures	Language background
Perani et al.	2017	The impact of bilingualism on brain reserve and metabolic connectivity in Alzheimer's dementia	71.42	77.13		No difference. MMSE: $M = 22.4$, $B = 21.1$	German Italian bilinguals were compared with Italian monolinguals. Bilinguals scored a 0.74 on the following scale: BI = 1 − |%L1 use − %L2 use|, where 0 is completely monolingual and 1 is perfectly balanced bilingual.
Ramakrishnan et al.	2017	Comparative effects of education and bilingualism on the onset of mild cognitive impairment	55.8	63.2		Better cognitive scores for bilinguals. Addenbrooke's Cognitive Examination–Revised: $M = 86.2$, $B = 89.3$	Bilingualism was defined as "ability to meet the communicative demands of the self, and the society in their normal functioning in two or more languages in their interaction with the other speakers of any or all of these languages."
Sanders et al.	2012	Nonnative language use and risk of incident dementia in the elderly			No difference statistically	No difference. Blessed Information-Memory-Concentration test: $M = 2$, $B = 2$ Free and Cued Selective Reminding test: $M = 29.9$, $B = 30.1$	Participants came from Einstein Aging Study in the Bronx, NY. Nonnative English speakers were compared to native English speakers.
Wilson et al.	2015	Early life instruction in foreign language and music and incidence of mild cognitive impairment	Bilinguals showed later age of onset. Age of onset effect size determined from test statistics		Higher incidence rate for monolinguals	Cognitive measures not reported by group.	Participants came from the Rush Memory and Aging Project. Participants were asked whether they had any foreign language training by the age of 18, and if so, how many years. Individuals were classified as having no foreign language training, 0–4 years, and more than 4 years of foreign language training. The latter two groups were average together for the present meta-analysis.
E. V. Y. Woumans et al.	2015	Bilingualism delays clinical manifestation of Alzheimer's disease	73.8	75.5		No difference. MMSE: $M = 24.2$, $B = 23.8$	Bilingualism was determined on the basis of L2 proficiency and frequency of use on a scale from *perfect/native language*, *very good*, *good*, *moderate*, *poor*, and *nonexisting*. A patient was considered bilingual if he/she rated him/herself as *good* or higher for all four L2 skills AND spoke this L2 at least weekly before and now. Bilinguals consisted mostly of Dutch L1 and French L2 individuals. All monolinguals, with the exception of one French-speaking, were Dutch-speaking individuals.
Yeung et al.	2014	Is bilingualism associated with a lower risk of dementia in community-living older adults? Cross-sectional and prospective analyses			No difference statistically	No difference. MMSE: $M = 91.2$, $B = 89.3$	English monolinguals were compared with both English bilinguals and English as a second language (ESL) individuals. English bilinguals were those participants who spoke

Table 1. (continued)

Author	Year	Title	Age of onset ML	Age of onset BL	Incidence	Cognitive measures	Language background
							English as a first language and who could speak a second language (mostly French). ESL individuals were those who were bilingual but who listed their first language as any language other than English.
Zahodne et al.	2014	Bilingualism does not alter cognitive decline or dementia risk among Spanish-speaking immigrants			No difference statistically	Better cognitive scores for bilinguals on an executive function composite	All participants listed Spanish as their first language. Monolinguals were those who indicated on a 4-point scale that they spoke English *not at all*, and bilinguals were defined as those who indicated that they spoke English *not well*, *well*, or *very well*.
Zheng et al.	2018	The protective effect of Cantonese/Mandarin bilingualism on the onset of Alzheimer's disease	63.65	70.93		Better MMSE scores for Cantonese/Mandarin bilinguals and Mandarin monolinguals than Cantonese monolinguals. MMSE scores collapsed across the monolingual groups: *M* = 14.0, *B* = 16.4	Bilinguals were defined as those who had spent the majority of their lives, beginning at least in early adulthood, speaking two languages fluently—ideally daily, but at least weekly.

Note. ML = monolingual; BL = bilingual; MMSE = Modified Mini-Mental State Examination; MCI = mild cognitive impairment; AD = Alzheimer's disease

Incidence versus age of onset

In this initial approach, effects from 21 studies were converted into d' (positive values indicate bilinguals were older) and entered separately for incidence and age of onset measures. Three studies reported both incidence and age of onset and were thus entered twice.

This initial analysis revealed a moderate overall effect of bilingualism, standardized mean difference (SMD) = 0.32, CI [0.22, 0.42] (see Fig. 1). The effect was stronger for studies examining age of onset, SMD = 0.40, CI [0.29, 0.51], than those which examined incidence, SMD = 0.10, CI [−0.08, 0.28], and the test for subgroup differences was significant. The confidence intervals for the incidence studies included zero and therefore did not reach statistical significance. A trim-and-fill analysis was then used to test for publication bias and recompute a corrected effect size (see Fig. 1b). The trim-and-fill procedure identified six "missing" studies (indicated by the hollow points in the funnel plot), and computed effect sizes for hypothetical studies that would normalize the distribution of effect sizes. Recomputing the meta-analysis led to an overall SMD of 0.22, CI [0.11, 0.33], which was still significant, $Z = 3.98$, $p < .0001$, suggesting that even after accounting for publication bias, bilinguals are older on average when they encounter Alzheimer's disease than are monolinguals.

Sensitivity analysis

A sensitivity analysis was conducted to limit each study to a single contribution, and thus the three studies with more than one effect (e.g., incidental and age-of-onset) were averaged prior to analysis (see Fig. 2). The sensitivity analysis yielded an overall SMD of 0.35, CI [0.24, 0.47], which was comparable to the uncorrected initial model. Trim-and-fill analysis also yielded a similar result, SMD = 0.25, CI [0.13, 0.37], suggesting that the initial analysis was not badly affected by the inclusion of separate effects for the three studies in question. Thus, although the first analysis did not reveal that incidence rates were reliably lower for bilinguals than for monolinguals, combining the effect sizes for incidence rates and age of onset in studies that report both (i.e. in prospective studies) leads to an overall reliable effect size. This suggests that even prospective studies may provide a protective effect of bilingualism on Alzheimer's disease.

Prospective Studies

We next restricted the analysis to prospective studies only to examine how this type of design affected reported effect sizes for incidence and age of onset. Only six studies met this criterion, including the three which had both incidental and age-

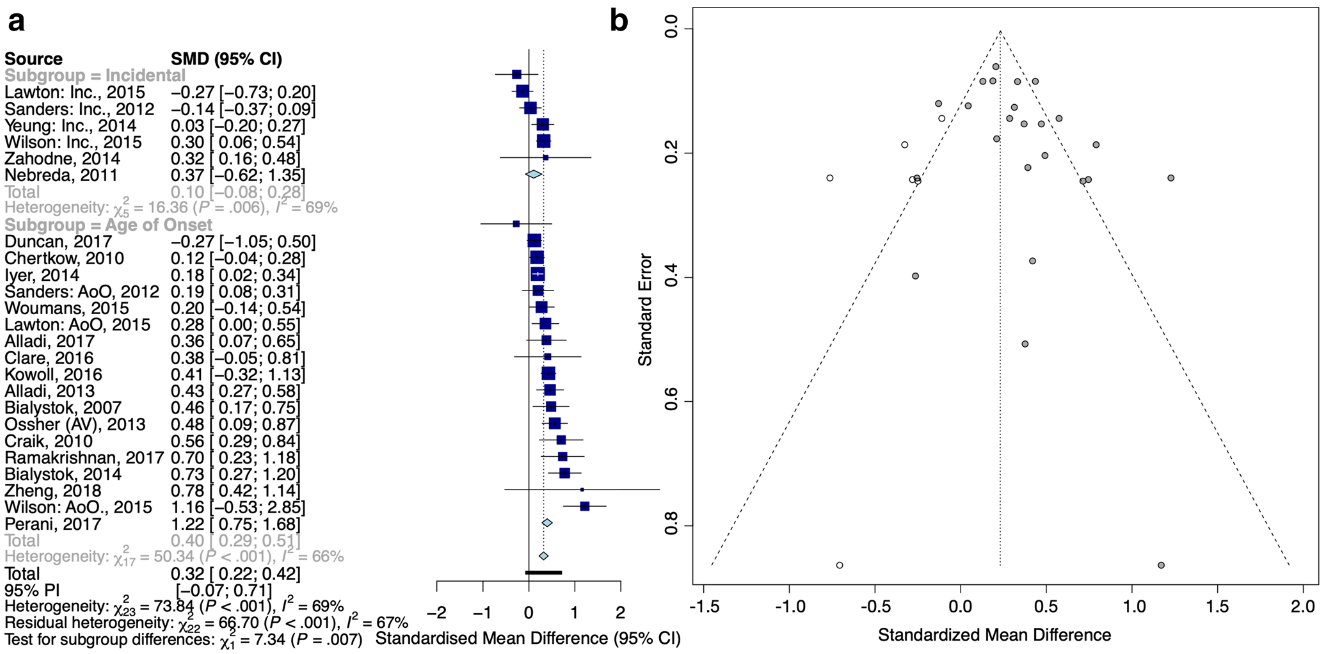

Fig. 1 Effect of bilingualism in incidental and age of onset studies on Alzheimer's. **a** A forest plot with subgroupings by study type. **b** A trim-and-fill funnel plot for the same data

of-onset measures (see Fig. 3). Here, effect sizes were more moderate, SMD = 0.16, CI [0.04, 0.028], but were still reliably different from zero. Importantly, the test for subgroup differences was *not significant*, χ^2 = 1.00, p = .32, suggesting that bilingualism was indiscriminately associated with fewer incidents of Alzheimer's disease and later age of onset of Alzheimer's symptoms. The trim-and-fill analysis did not reveal any evidence of publication bias.

Sensitivity analysis for prospective studies

Once again, a sensitivity analysis was conducted to limit each prospective study to a single contribution, and again the three studies with two contributions were averaged prior to analysis (see Fig. 4). The sensitivity analysis yielded an overall SMD of 0.14, CI [0.00, 0.28], which, again, was similar to the initial model. Figure 5.

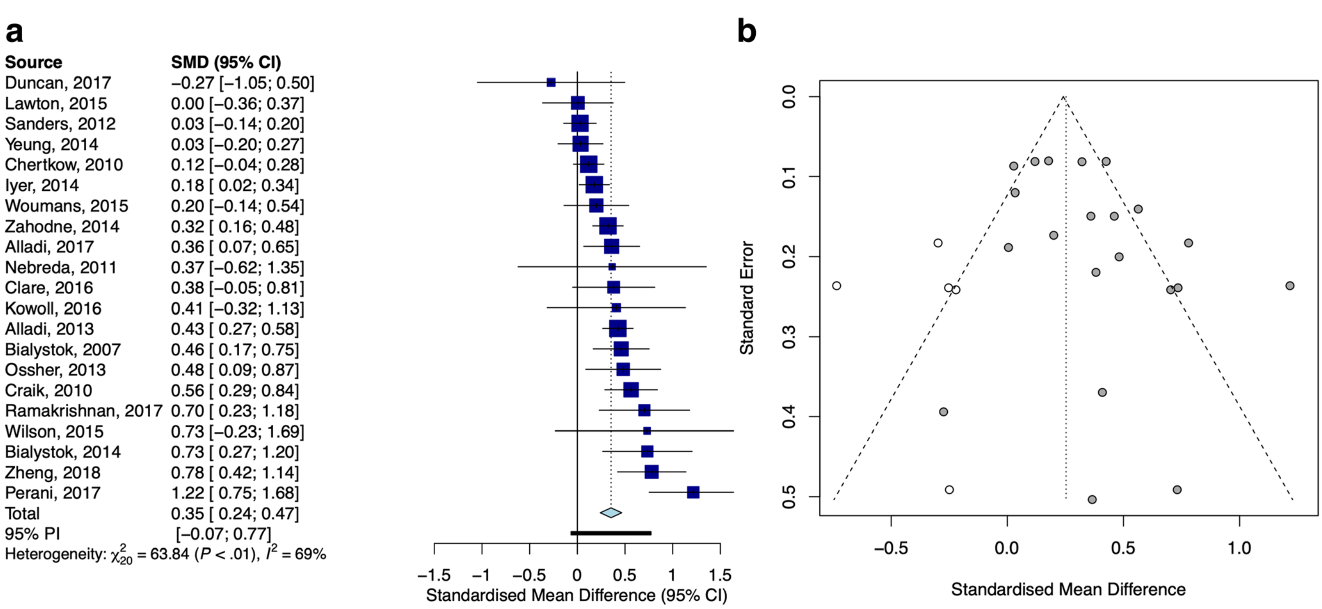

Fig. 2 Sensitivity analysis results. **a** A forest plot of the results. **b** A trim-and-fill funnel plot for the same data

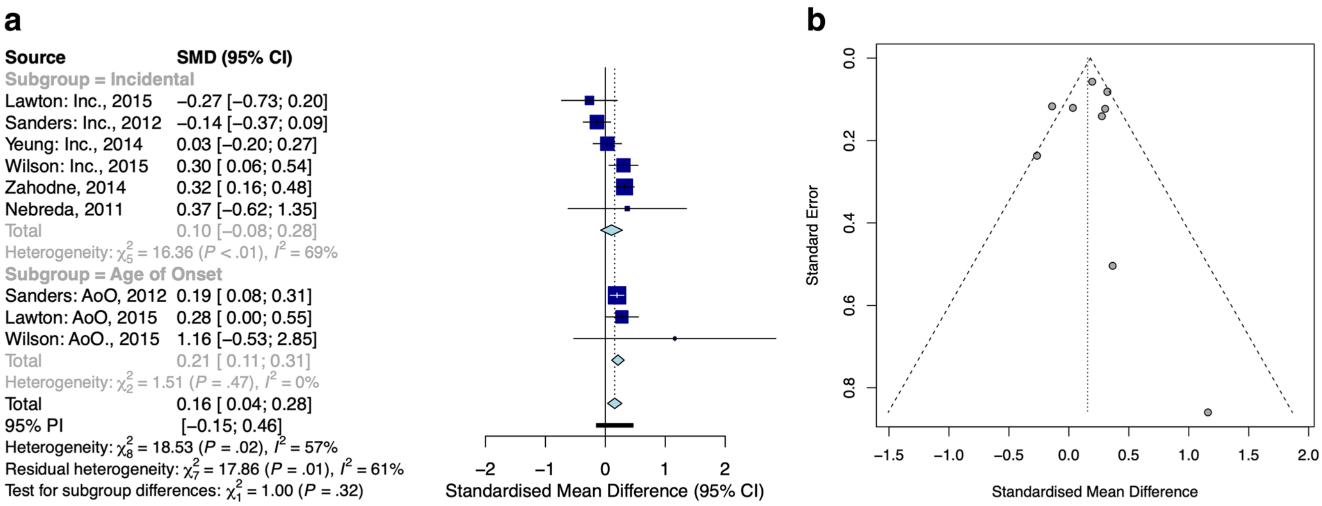

Fig. 3 Prospective studies. **a** The forest plot results. **b** The trim-and-fill funnel plot

Meta-regression: Effects of education and socioeconomic status

For studies reporting education and SES or a close proxy such as level of occupational attainment, separate meta-analytic regressions were fit with age of onset/incidence between groups as the predicted outcome, and the difference between bilinguals and monolinguals on education and SES measures converted to d' as the predictor. Once again, higher values indicate that bilinguals had higher scores. Both findings are represented in Fig. 4. Briefly, the meta-analytic effect of education differences between bilinguals and monolinguals on Alzheimer's age was 0.013, CI [−0.15, 0.18], while the meta-analytic effect of SES differences between bilinguals and monolinguals on Alzheimer's age was −0.1016, CI [−0.58, 0.38]. In short, while it is possible that each of these effects is predictive of Alzheimer's on their own, differences between bilinguals and monolinguals on SES or education were not predictive of differences in age of onset or incidence of Alzheimer's.

Effect of lab

Finally, given the recent trend among meta-analyses in the field of bilingualism attempting to disentangle potential laboratory biases from outcome measures, we also conducted a subgroup meta-analysis for age of onset by laboratory. We did not conduct a subgroup analysis for incidence studies as no lab produced more than one study of this type, and the results would not differ from those presented earlier.

We coded each lab numerically and ran a subgroup analysis as described above using "Lab" as the grouping variable (see Fig. 6). We grouped studies from labs reporting only a single result into an "Others" category. Figure 6a shows that there was a significant effect of subgroup, $\chi^2 = 14.6$, $p = .002$; however, this was driven entirely by Lab 3, which provided lower estimates of age of onset than average, and once they were removed (see Fig. 6b), there were no longer any significant differences between research groups, $\chi^2 = 2.48$, $p = .29$. This suggests that on the whole, the effect sizes being reported across research groups for age of onset is consistent.

Discussion

The present study provides an updated perspective on bilingualism and solidifies its position as a contributor to cognitive reserve. Our study uniquely reintegrates two different approaches to addressing bilingualism's role in Alzheimer's dementia: namely *when* symptoms manifest (age of onset) and *if*

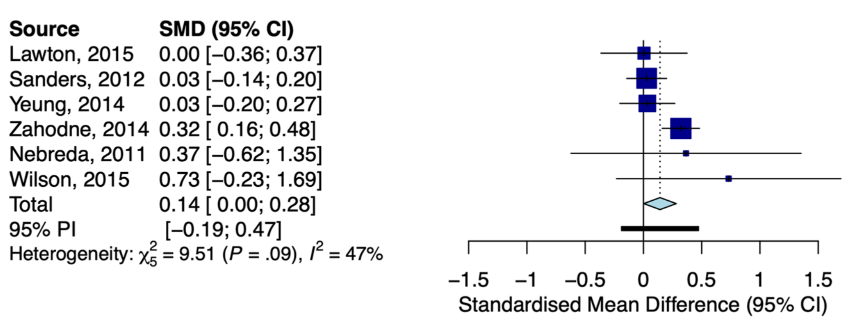

Fig. 4 Prospective studies sensitivity analysis

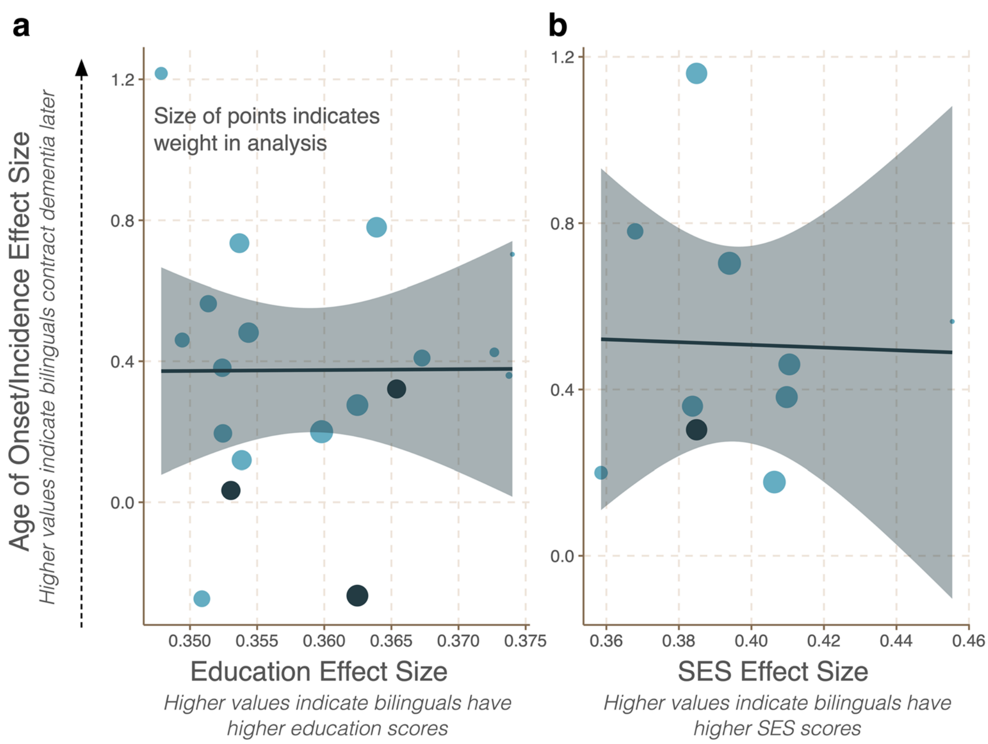

Fig. 5 Metaregression analyses between the age of onset/incidence and (**a**) education and (**b**) socioeconomic status (SES). All values are effect sizes (e.g., the difference in average education between monolinguals and bilinguals). Studies are weighted by their contribution, and this is represented by the size of each point on the plot

symptoms manifest at all (incidence). We note that integration and comparison of effect sizes across similar yet not necessarily identical study types is a strength of meta-analysis, which we capitalize on in this work. Our approach also allows us to directly compare the effect sizes associated with each of these study types with the use of "subgroup" analysis (Borenstein &

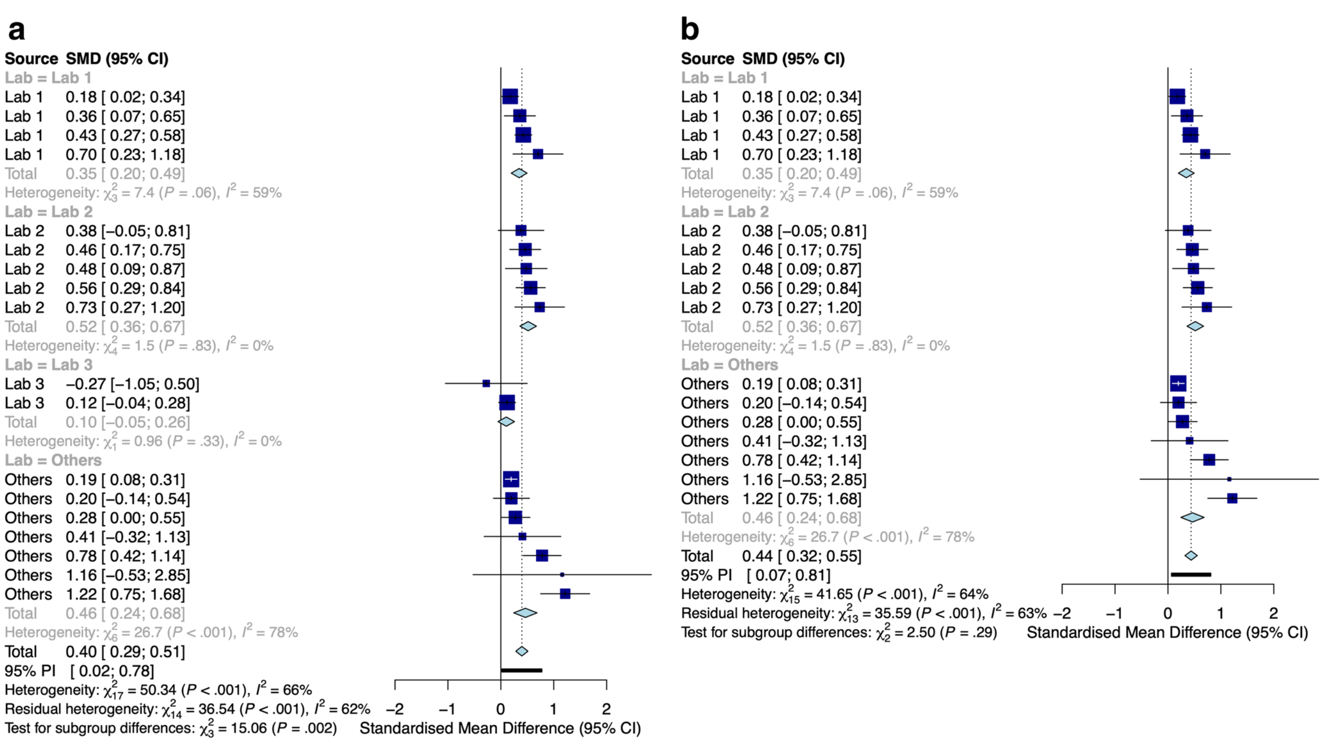

Fig. 6 Analysis of age of onset by lab group. **a** All the lab groups. **b** The subset of homogeneous groups

Higgins, 2013; Higgins & Thompson, 2004; Smith & Egger, 2008). This method is preferable to simply examining either incidence or age-of-onset studies, as each makes similar, but distinct, claims which often become conflated. Our results support two major findings: First, including incidence studies in a larger framework with age-of-onset studies yields a protective effect of bilingualism overall, and second, while incidence studies have significantly smaller effect sizes than age-of-onset studies, the trend still favors bilinguals (effect size of 0.1). This latter finding is consistent with the recent finding by Klein et al. (2016), who examined the protective effect of bilingualism by country.

We noted earlier that one should not expect bilingualism to *prevent* or reverse Alzheimer's pathology. Rather, bilingualism, like most other forms of cognitive reserve, including higher education and demanding occupation, likely strengthens alternative functional circuits, which may be recruited to allow individuals with increasing amounts of Alzheimer's pathology to present as cognitively normal (Stern, 2002; Stern et al., 2018). Grundy, Anderson, and Bialystok (2017) argued that bilinguals rely more on posterior and subcortical regions than monolinguals do, who shift towards vulnerable frontal circuits with aging. Similarly, Pliatsikas (2019) argues in a recent theoretical paper that bilingualism may increase synaptic density and coupling—especially during the early stages of language learning. Later, as the individual becomes more proficient with the second language, unneeded connections are pruned. This theory is supported by neuroimaging evidence showing bilingualism selectively increases gray-matter volume in subcortical structures early in second-language acquisition, and that these changes subside with time (Burgaleta, Sanjuán, Ventura-Campos, Sebastian-Galles, & Ávila, 2016; Grundy et al., 2017; Pliatsikas, 2019; Pliatsikas, DeLuca, Moschopoulou, & Saddy, 2017). What is left is a highly efficient new circuit optimized for second-language processing, but which may be co-opted to executive function and preventing cognitive decline. Thus, we suspect that bilinguals circumvent damaged structures as they accrue Alzheimer's pathology. These theories are supported by neuroimaging evidence showing that bilingual older adults tend to have greater Alzheimer's related atrophy than monolingual peers who have been matched for symptom severity (Gold, Kim, Johnson, Kryscio, & Smith, 2013; e.g., Kowoll et al., 2016; Perani et al., 2017; Schweizer, Ware, Fischer, Craik, & Bialystok, 2012).

Most investigations examining the incidence of Alzheimer's in bilingual and monolingual older adults examine the number of conversions to dementia during the course of the study and compare the groups (Kawas, Gray, Brookmeyer, Fozard, & Zonderman, 2000; Scarmeas, Levy, Tang, Manly, & Stern, 2001; Stern et al., 1994), but there are limitations to this approach. First, the number of individuals who do end up converting to dementia is comparatively small relative to those who age normally, particularly once subgroups such as monolinguals and bilinguals are included, and thus there is an issue of power (e.g., Zahodne, Schofield, Farrell, Stern, & Manly, 2014). Second, studies of this type collapse time to the duration of the study. Postmortem or archival studies have the advantage here because the individual has lived long enough to have contracted the disease and require the intervention of the medical system. Nevertheless, we note that in the restricted analysis of prospective studies, effect sizes for age-of-onset and incidence rate converged and were not statistically differentiable. Furthermore, there was no detectable publication bias, perhaps due to the enormous investment of resources represented by conducting prospective studies. Thus, we suggest that more prospective studies be conducted over the longer term and that they report *both* age of onset of symptoms *and* incidence.

Many studies examining the effects of bilingualism on cognitive reserve, or cognition more generally, have argued that the effects may be explained by other factors, including education or socioeconomic status. This does not appear to be the case for the studies included in our analyses. Two separate meta-analytic regression analyses using combined age of onset and incidence, as the outcome with the difference in education or SES between monolingual and bilingual participants as predictors failed to yield any effects. Thus, differences in education or SES between monolinguals and bilinguals cannot explain the outcomes we observe in the age of onset or incidence of Alzheimer's disease. That said, we are not arguing that education and SES do not act as reserve factors, or do not interact with bilingualism in specific circumstances (e.g., Gollan, Salmon, Montoya, & Galasko, 2011)—there is ample evidence that they do. Instead, we argue that group differences in SES and education appear unrelated to group difference effect sizes for Alzheimer's incidence or the age of onset. Relatedly, many studies attempt to measure the effect of bilingualism or another factor while statistically "controlling" for the effects of other variables. Miller and Chapman (2001) convincingly argue that using analyses of covariance and multiple regression techniques as a means of "controlling" for confounding variables is ineffective if the study is not a randomized control design, and further introduce the issue of how to interpret the residual variance.

Another issue to consider is the effect of the research group on the outcome measure. Three research groups had conducted more than one age-of-onset study, all other groups reported a single study each. The latter groups were collapsed into a single category, and the four research groups were compared using subgroup meta-analysis. One group significantly underestimated the effect of age of onset compared with all others, and after removing this group none of the remaining groups differed.

We have demonstrated converging evidence that bilingualism is indeed a protective factor against the symptoms of

Alzheimer's dementia. We further demonstrated that while incidence studies had significantly smaller effect sizes than the age-of-onset studies, the average effects converge particularly when examining prospective studies. Theories are now emerging that postulate *mechanisms* for how exercising a second language microstructural brain changes that enable older adults to resist dementia symptoms for longer. This new avenue suggests an exciting opportunity for future cognitive reserve studies to incorporate neuroimaging over a longer period, thus uniting the incidence/age-of-onset studies with the neuroimaging literature.

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Open practices statement To facilitate transparency and reproducibility, all data used for analyses will be available at the following link: (https://figshare.com/articles/Does_bilingualism_protect_against_dementia_A_meta-analysis/12047415)

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