European Geriatric Medicine
https://doi.org/10.1007/s41999-020-00326-x

REVIEW

Bilingualism for delaying the onset of Alzheimer's disease: a systematic review and meta-analysis

Andrea M. Paulavicius[1] · Carolina C. Mizzaci[1,2] · Daniela R. B. Tavares[1,3] · Aline P. Rocha[1] · Vinicius T. Civile[1,4] · Rodrigo R. Schultz[5] · Ana Carolina Pereira Nunes Pinto[1,6] · Virginia F. M. Trevisani[7,8]

Received: 3 February 2020 / Accepted: 24 April 2020

Key summary points

Aim To assess the effects of bilingualism compared to monolingualism on the clinical manifestation of Alzheimer's Disease.
Findings Data from meta-analyses suggest that bilingual individuals exhibit Alzheimer's Disease symptoms are diagnosed later than monolingual participants.
Message Bilingualism may delay the manifestation of symptoms and diagnosis of Alzheimer's Disease.

Abstract

Objective To assess the effects of bilingualism compared to monolingualism on the clinical manifestation of Alzheimer's disease.
Methods We searched the databases: MEDLINE, The Cochrane Central Register of Controlled Trials, Embase and LILACS, and searched by hand and in gray literature for studies published before September 2019. The quality of included studies was assessed using the Newcastle–Ottawa Scale. Two reviewers independently searched for studies, extracted data, and performed the quality assessment.
Results Eight studies were included in this review. Data from meta-analyses suggest that bilingual individuals with Alzheimer's disease exhibit symptoms (694 participants; mean difference (MD) (4.05 years; 95% CI: 1.87–6.22 and are diagnosed later (1012 participants; MD 2.0 years; 95% CI: 0.08–3.92) than monolingual participants.
Conclusion Bilingualism may delay the manifestation of symptoms and diagnosis of Alzheimer's disease. Further studies with more rigorous methodology are needed to improve the precision of the results.

Keywords Alzheimer's disease · Systematic review · Bilingualism · Cognitive reserve · Meta-analysis

Introduction

Dementia is a devastating and highly prevalent disease. Worldwide, nearly 50 million people live with dementia [1]. Alzheimer's disease (AD) is the most common cause

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s41999-020-00326-x) contains supplementary material, which is available to authorized users.

✉ Ana Carolina Pereira Nunes Pinto
anacarolinapnp@hotmail.com

1 Department of Evidence-Based Medicine, Brazilian Cochrane Centre, Federal University of São Paulo (UNIFESP), Rua Napoleão de Barros 865, Vila Clementino, São Paulo, SP 04024-002, Brazil

2 Dante Pazzanese Institute of Cardiology, São Paulo, SP, Brazil

3 Department of Geriatrics and Gerontology, Federal University of São Paulo (UNIFESP), São Paulo, SP, Brazil

4 Paulista University (UNIP), São Paulo, SP, Brazil

5 Department of Neurology, Federal University of São Paulo (UNIFESP), São Paulo, SP, Brazil

6 Department of Biological and Health Sciences, Federal University of Amapa (UNIFAP), Macapá, AP, Brazil

7 Brazilian Society of Rheumatology, Discipline of Rheumatology, Federal University of São Paulo (UNIFESP), São Paulo, SP, Brazil

8 Santo Amaro University (UNISA), São Paulo, SP, Brazil

Published online: 04 May 2020

of dementia and may be involved in 80% of the cases [2]. AD is a progressive degenerative brain disease of unknown cause, characterized by gradual decline in cognitive functions, including memory, praxis, executive function, and language [3]. AD causes an expressive effect on the individual's life and generates a huge impact on public health [4]. As the population of older adults rises globally, strategies for delaying or preventing the onset of AD symptoms become increasingly important [5].

Recent studies have indicated that lifelong bilingualism plays an important role on the cognitive reserve (CR) [6, 7]. CR is distinguished by the individual ability to enhance neural networks and maintain cognitive function despite the neural changes associated with age. Physicians frequently observe individuals with relevant level of brain atrophy but with preserved cognitive functioning. The exact mechanism that underlies CR is not well-known [6]. However, the protective effects of bilingualism may be a result of how human brain has adjusted to the additional skill provided by managing two or more languages [8]. Older bilingual adults switch between perceptual tasks significantly faster than their monolingual peers despite requiring less activation in primary task-switching regions as measured by magnetic resonance imagining (MRI) [9]. Furthermore, bilinguals may have increased gray and white matter densities in cerebral regions related to executive control, such as the left prefrontal cortex, anterior cingulated cortex, left inferior parietal lobule, and the left caudate [10, 11].

The idea of bilingualism as an enhancing factor to CR is promising and relatively new, but not completely established. On one hand, preliminary evidence has suggested that bilingualism might delay the onset of dementia symptoms [12, 13]. On the other hand, some studies have failed to find protective effects of bilingualism, showing no significant differences between monolingual and bilingual AD patients in age at the time of AD diagnosis [14, 15]. Therefore, we designed this systematic review to compare the effect of bilingualism versus monolingualism on the onset of AD.

Methods

This systematic review evaluated the effect of bilingualism on the onset of clinical manifestations of AD. The recommendations proposed by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [16] and Cochrane Collaboration Handbook [17] were followed.

Search method

We searched Cochrane Central Register of Controlled Trials (CENTRAL) MEDLINE (OVID), EMBASE, and LILACS using relevant descriptors and synonyms, adapting the search to the specifications of each database (Supplementary Figs. 1, 2, 3, and 4). We used the technique of snowballing, searching the lists of references of the included studies. All studies published before September 2019 were included, and no language restrictions were used in the selection.

Data collection and analysis

Primary studies that compared participants diagnosed with AD who spoke two or more languages with participants who spoke only one language were included. We included cohort, cross-sectional, and case–control studies. Case series, case reports, narrative reviews, and editorials were excluded. In this review, the main outcomes were age at AD diagnosis; time of clinical AD manifestation; and incidence of AD. Studies including patients with other types of dementia were included only if AD patients' data were presented separately.

Study quality was evaluated using the Newcastle Ottawa Scale (NOS), a validated scale for the assessment of observational studies [18]. It was developed to assess the quality of nonrandomized studies directed to the task of incorporating the quality assessments in the interpretation of meta-analytic results [18]. A 'star system' is used in which a study is assessed in three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case–control or cohort studies, respectively [18]. A study can be awarded maximum nine stars [18]. We used a predefined form to extract data from included studies. The authors of relevant studies were contacted in the case of missing study details.

Study selection, data extraction, and assessment of risk of bias were performed by two review authors independently. All disagreements in selection, data extraction, or risk of bias assessment were solved through discussion or, if required, by consulting with a third author. After extraction, data were analyzed using Review Manager 5.3 (RevMan) software. Continuous data were pooled using DerSimonian–Laird random-effects model. The results were presented as mean difference (MD) with 95% confidence interval (CI) [17].

Results

The database search yielded a total of 248 records. After removing duplicated records, we examined 202 titles and abstracts and excluded those clearly not related to the review question. We retrieved 17 full-text articles for further scrutiny. We finally selected 8 studies for inclusion in this systematic review [12–15, 19–22]. PRISMA flow chart shows the study retrieval and selection process (Fig. 1). None of the included studies were prospective. The study details are summarized in Table 1.

Six studies recruited only AD participants. Two of them included participants with other types of dementia but provided data for AD patients separately and were included in this review. The spoken languages varied substantially across the studies. Some studies, such as the one from India [12], included a bilingual population containing a lot of different language combinations. Four of the studies included both immigrant and non-immigrant individuals [13, 15, 19, 22]. The other studies recruited completely non-immigrant samples [12, 14, 20, 21].

All studies were evaluated using the domains of the NOS; the results of NOS evaluation are shown in Supplementary Table 1. Two studies received four stars [19, 22], and six of them received five stars [12–15, 20, 21].

Quantitative syntheses

Age at onset of AD symptoms

We pooled data from four studies [12, 19–21] that had evaluated the age at onset of AD symptoms in bilinguals compared to monolinguals. This first analysis, shown in Fig. 2, included 694 participants. We found that bilingual patients exhibit AD symptoms later (MD 4.05 years; 95% CI: 1.87–6.22) than monolingual patients.

Age at AD diagnosis

Five studies [14, 15, 19, 20, 22] evaluated the age at AD diagnosis. Pooled data from 1012 participants, shown in Fig. 3, indicate that bilingual patients are diagnosed with AD later (MD 2.0 years; 95% CI: 0.08–3.92) than monolinguals.

Incidence of AD

The incidence of AD could not be evaluated, since none of the included studies were prospective.

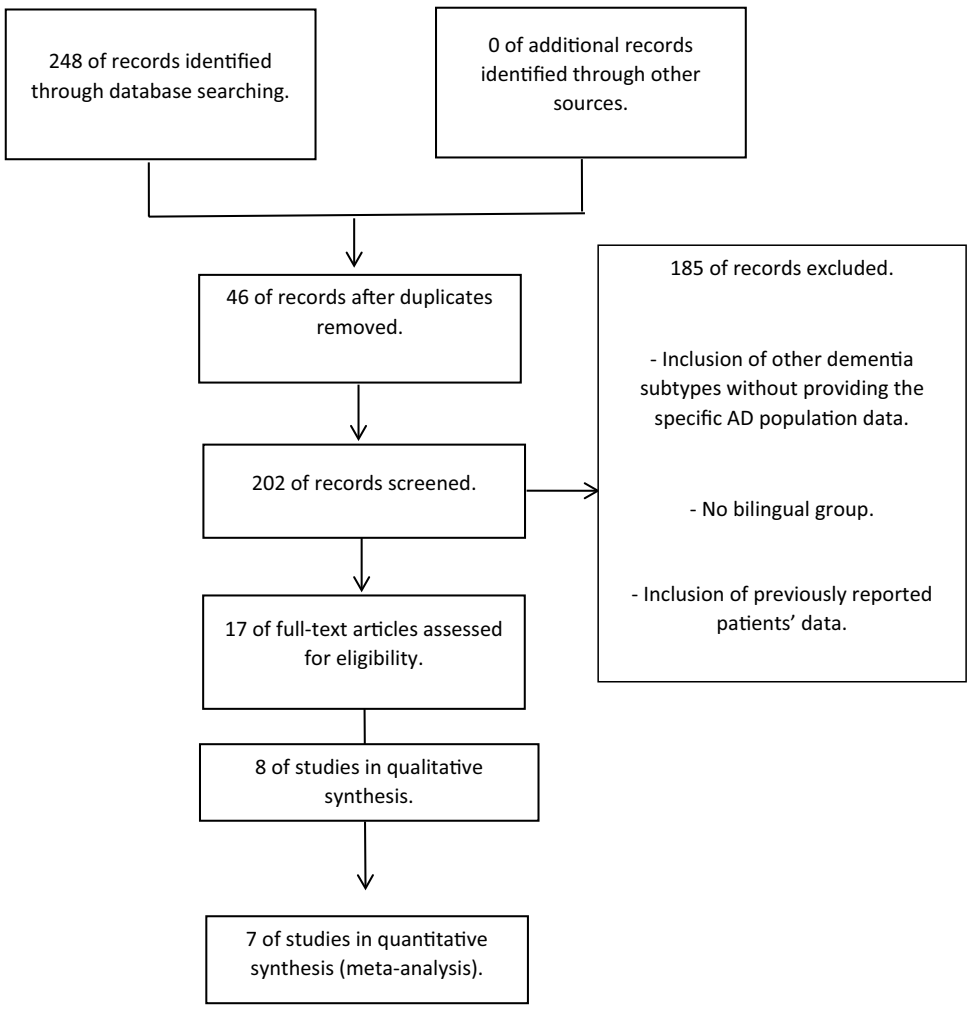

Fig. 1 Study flow diagram

Table 1 Study characteristics

Study	Quality score	Setting/Country	Inclusion criteria	N (B/M)	Age (years, mean ± DP)	Years of schooling mean (SD)	Objective	Results
Alladi et al. [12]	5 stars	Memory Clinic/ India	Dementia (including AD, FTD, VaD and DLB)	240 (142/98)[b]	Not provided for AD patients	Not provided for AD patients	Determine the association between bilingualism and age at onset of dementia and its subtypes	Delay of 3.2 years in the onset of AD symptoms in bilinguals compared to monolinguals (p 0.013)[a]
Bialystok et al. [8]	5 stars	Memory Clinic/ Canada	Dementia (regardless of diagnosis)	132 (not provided)[b]	Not provided for AD patients	Not provided for AD patients	Examine the effect of bilingualism on cognitive functioning and onset of symptoms of dementia	Delay of 4.3 years in the onset of AD symptoms in bilinguals compared to monolinguals ($p < 0.009$)[a]
Chertkow et al. [22]	4 stars	Memory Clinic/ Canada	AD	547 (168/379)	B: 76.7 (7.8) M: 76.7 (7.8)	B: 10.7 (3.7) M:10.9 (3.5)	Assess the age at the time of their AD diagnosis and the age at AD symptom onset	Small protective effect of multilingualism but no effect of bilingualism in the age at diagnosis or age at symptom onset compared to monolinguals
Clare et al. [14]	5 stars	Part of a cohort (BANC) study/ Wales	Early stage AD	86 (37/49)	B: 80.8 (6.9) M: 78.8 (8.0)	B: 11.8 (2.5) M: 12.3 (3.0)	Compare age at AD diagnosis and performance on a range of executive control tasks in bilinguals and monolinguals	No significant differences between groups in performance on executive function tests and age at diagnosis
Craik et al. [19]	4 stars	Memory Clinic/ Canada	AD	211 (102/109)[b]	B: 80.8 (7.7) M: 76.5 (10.0)	B: 10.6 (5.1) M: 12.6 (4.1)	Investigate if bilingualism is a further factor contributing to CR	Bilingualism appears to contribute to CR. Bilinguals had diagnosis 4.3 years later ($p < 0.0006$) and onset of symptoms 5.1 years later ($p < 0.0001$) than monolinguals

Table 1 (continued)

Study	Quality score	Setting/Country	Inclusion criteria	N (B/M)	Age (years, mean ± DP)	Years of schooling mean (SD)	Objective	Results
Schweizer et al. [15]	5 stars	Memory Clinic/ Canada	AD	40 (20/20)	B: 78.9 (7.6) M: 77.2 (7)	B: 11.6 (4.5) M: 13.6 (3.5)	Assess brain atrophy differences between monolinguals and bilinguals AD patients	Bilingual had greater amounts of brain atrophy in areas traditionally used to distinguish AD patients. No significant differences between groups in age at diagnosis (p 0.5)
Woumans et al [20]	5 stars	Hospital/Belgium	AD	134 (65/69)[b]	B: 77.9 (7.8) M: 76.4 (8.5)	B: 14.7 (3.1) M: 13.5 (2.8)	Evaluate the bilingual advantage in a non-immigrant sample of European patients	Delay of 4.6 years in the onset of AD symptoms (p 0.014) and 4.8 years in AD diagnosis in bilinguals compared to monolinguals (p 0.009)
Zheng et al. [21]	5 stars	Memory Clinic/ China	AD	129 (61/68)	B: 74.4 (9.4) M: 67.7 (9.9)	B: 10.8 (4.3) M: 7.9 (3.8)	Determine if Cantonese/Mandarin bilingualism can delay the onset of AD	Cantonese/Mandarin bilingual AD patients were significantly older at AD symptoms onset ($p < 0.001$)

B bilinguals, *M* monolinguals, *SD* Standard Deviation, *AD* Alzheimer's disease, *MMSE* mini-mental state examination, *FTD* frontotemporal dementia, *VaD* vascular dementia, *DLB* dementia with lewy bodies, *BANC* bilingualism as a protective factor in age-related neurodegenerative conditions, *CR* cognitive reserve

[a]Data from AD patients specifically, in studies including other dementias

[b]Studies that defined bilingualism as the ability of speaking two (or more) languages

Discussion

This is the first systematic review with meta-analysis to demonstrate that the bilingualism may delay AD onset. In this review, the pooled results of 7 studies indicate that bilingualism is related to a delay of nearly 4.05 years in the onset of AD symptoms and 2 years in the age at AD diagnosis compared to monolinguals.

A recent review [23] assessed the effects of bilingualism on the risk of cognitive decline and dementia. This review found that bilingualism do not reduce the incidence of dementia. This is probably because Mukadam et al. [23] considered patients with any type of dementia. Currently, there are at least ten different types of dementia. Each type of dementia has distinguished characteristics, causes, symptoms and prognosis. Therefore, it is likely that different factors may influence AD onset and other types of dementia.

The available evidence suggests that bilinguals might be able to withstand more disease pathology than monolinguals, probably accruing symptoms later in life. This hypothesis is supported by previous data from studies that have evaluated brain atrophy differences between monolinguals and bilinguals AD patients. The bilingual population has shown substantially greater amounts of brain atrophy in areas commonly impaired in AD patients [24]. Perani et al. assessed the cerebral resting-state metabolic activity in bilingual and monolingual AD participants. Bilinguals showed a more severe cerebral hypometabolism but increased connectivity in the executive control system [15, 25]. Recent studies have also reported that bilinguals present increased gray and white matter densities in cerebral regions related to executive control [10, 11]. Together, these results suggest that bilingualism may lead to the creation of a broader neural network and may increase CR, probably through its effects on executive control. These executive abilities and neural network may result in compensation mechanisms for early cognitive symptoms, which could help delay the clinical onset but not the neuropathology of AD.

We found moderate to high heterogeneity in both our meta-analysis. This may be mainly justified by clinical heterogeneity in included studies. We could not address the influence of age of acquisition of the second language on bilingual advantages, years of schooling, and language used during the assessments (dominant or non-dominant), since these characteristics were not reported in the included studies. Kowoll et al. [26] showed that while the dominant language is more vulnerable to brain damage, the non-dominant is affected later in the course of AD. It is therefore plausible that differences in the choice of dominant or non-dominant language to be applied in the study assessments might affect the results. Therefore, the clinical heterogeneity should be addressed in future studies, considering baseline differences between groups.

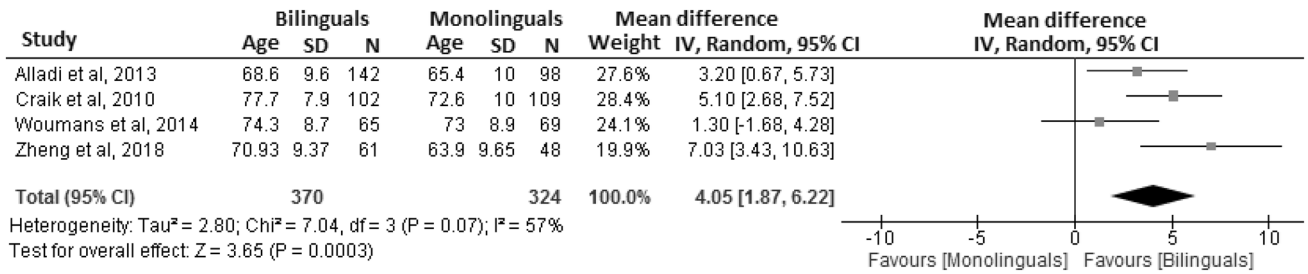

Fig. 2 Age at onset of Alzheimer's disease symptoms. Age is expressed in years (mean); *N* number of participants, *SD* Standard Deviation, *IV* inverse-variance, Confidence interval

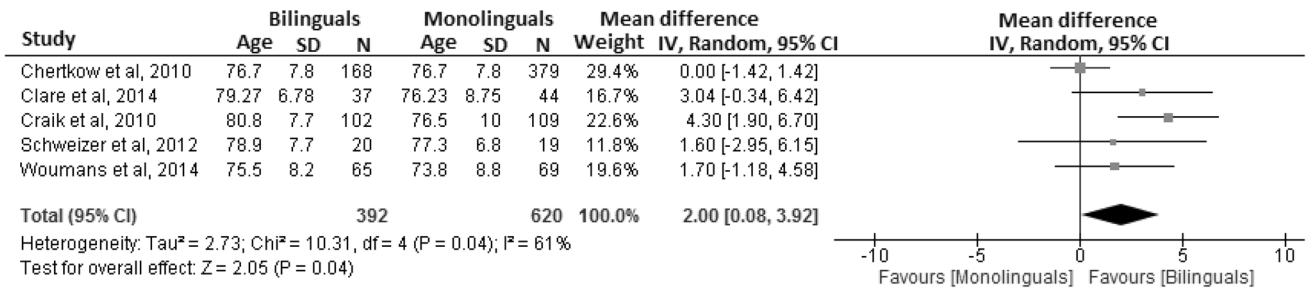

Fig. 3 Age at Alzheimer's disease diagnosis. Age is expressed in years (mean); *N* number of participants, *SD* Standard Deviation, *IV* inverse-variance, Confidence interval

This review is not without limitations. Our data should be interpreted with caution, since some shortcomings in the methodology of the included studies, such as the presence of confounding factors, can interfere in the precision of the results. A possible confounding previously reported is the "healthy migrant effect", in which healthier people are more likely to migrate [27]. However, the results of the studies that included non-immigrant participants in this review [12, 14, 20, 21] (Figs. 2 and 3) have the same direction of the effect as the studies that included immigrants. Some of the included studies have also controlled for other confounding factors. Alladi et al. [12] reported a delay of 4.5 years for bilinguals, independent of sex, occupation, immigration status, education, and setting (urban or rural). Craik et al. [19] demonstrated that bilinguals showed symptoms of dementia 5.1 years later than monolinguals, even after controlling for education, gender, cognitive, and occupational levels. Furthermore, most of the studies included in this review do not have a reliable instrument that indicates to which extent each individual can be considered bilingual. It is a limitation for most studies to rely on the patients and caregivers' information for the bilingualism factor. It is noteworthy that it may be very difficult to quantify a life experience such as bilingualism, and reliable instruments for use in each language are scarce. However, it is important to assess bilingual usage as fully as possible, considering both measures of daily usage and age of acquisition of the second language [like in the Language and Social Background Questionnaire (LSBQ)] [28]. Additionally, although bilingualism commonly refers to the ability of speaking two languages, we have included 4 studies [12, 13, 19, 20] that defined bilingualism as the ability to speak two or more languages. Further studies can clarify if the multilingualism may have a more important effect on neural plasticity than bilingualism in patients with AD. Finally, in our study, the relation between bilingualism and the incidence of AD could not be evaluated, since none of the included studies were prospective.

In this systematic review, we conducted extensive searches on large databases with a sensitive search strategy. To minimize the likelihood of bias, we followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions [17]. We found promising results suggesting that bilingual patients may exhibit symptoms and diagnosis of AD later than a comparable group of monolingual patients. Of note, the late diagnosis does not necessarily prove that bilingualism delays AD. Instead, it may be the result of a delay in the diagnosis and consequently in the disease management. Nevertheless, the fact that bilinguals have also exhibited symptoms later than monolinguals and that no other obvious reasons explain why monolinguals could have been systematically diagnosed earlier than bilinguals are additional arguments that strengthen the hypothesis that bilingualism actually delays the disease onset.

While current drugs may help to slow the progression of AD, none of them have showed to delay the onset of AD [29]. On the other hand, and more importantly, this study exposes a critical issue: the need of future strong prospective studies with more rigorous methodology, including comprehensive clinical, imaging, and neuropathological data, to improve the precision of these results and address the possible underlying mechanism of this advantage. Large prospective studies using reliable instruments for evaluating bilingualism, with good follow-up rates, and controlling for confounders such as the years of schooling, age of acquisition of the second language, number of spoken languages, native language, and immigrant status, are necessary to improve the precision of the results.

Conclusion

Bilingualism may delay the manifestation of symptoms and diagnosis of AD. Further studies with more rigorous methodology are needed to improve the precision of the results.

Funding This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior-Brasil (CAPES)-Finance Code 001.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval The protocol for this systematic review was first published on May 5th 2017 on CEP/ UNIFESP (Federal University of Sao Paulo) platform under the number 5207180317.

Informed consent Informed consent not applicable.

References

1. Alzheimer's Disease International (2019) World Alzheimer Report 2019: Attitudes to dementia. Alzheimer's Disease International, London
2. Alzheimer's Association (2020) 2020 Alzheimer's disease facts and figures. Alzheimer's Dement 16(3):391–460. https://doi.org/10.1002/alz.12068
3. Alzheimer's Association (2019) 2019 Alzheimer's disease facts and figures. Alzheimers Dement 15(3):321–387
4. Bruggenjurgen B, Andersohn F, Burkowitz J, Ezzat N, Gaudig M, Willich SN (2016) Cohort study on predictors of need for nursing care in Alzheimer's disease: an analysis of

healthcare data. J Alzheimers Dis 54(4):1365–1372. https://doi.org/10.3233/jad-160137
5. Norton S, Matthews FE, Barnes DE, Yaffe K, Brayne C (2014) Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. Lancet Neurol 13(8):788–794. https://doi.org/10.1016/s1474-4422(14)70136-x
6. Mendez MF (2019) Bilingualism and dementia: cognitive reserve to linguistic competency. J Alzheimers Dis 71(2):377–388. https://doi.org/10.3233/jad-190397
7. Heim S, Stumme J, Bittner N, Jockwitz C, Amunts K, Caspers S (2019) Bilingualism and "brain reserve": a matter of age. Neurobiol Aging 81:157–165. https://doi.org/10.1016/j.neurobiolaging.2019.05.021
8. Bialystok E (2017) The bilingual adaptation: how minds accommodate experience. Psychol Bull 143(3):233–262. https://doi.org/10.1037/bul0000099
9. Gold BT, Kim C, Johnson NF, Kryscio RJ, Smith CD (2013) Lifelong bilingualism maintains neural efficiency for cognitive control in aging. J Neurosci 33(2):387–396. https://doi.org/10.1523/jneurosci.3837-12.2013
10. Luk G, Bialystok E, Craik FI, Grady CL (2011) Lifelong bilingualism maintains white matter integrity in older adults. J Neurosci 31(46):16808–16813. https://doi.org/10.1523/jneurosci.4563-11.2011
11. Abutalebi J, Canini M, Della Rosa PA, Sheung LP, Green DW, Weekes BS (2014) Bilingualism protects anterior temporal lobe integrity in aging. Neurobiol Aging 35(9):2126–2133. https://doi.org/10.1016/j.neurobiolaging.2014.03.010
12. Alladi S, Bak TH, Duggirala V, Surampudi B, Shailaja M, Shukla AK et al (2013) Bilingualism delays age at onset of dementia, independent of education and immigration status. Neurology 81(22):1938–1944. https://doi.org/10.1212/01.wnl.0000436620.33155.a4
13. Bialystok E, Craik FI, Freedman M (2007) Bilingualism as a protection against the onset of symptoms of dementia. Neuropsychologia 45(2):459–464. https://doi.org/10.1016/j.neuropsychologia.2006.10.009
14. Clare L, Whitaker CJ, Craik FI, Bialystok E, Martyr A, Martin-Forbes PA et al (2016) Bilingualism, executive control, and age at diagnosis among people with early-stage Alzheimer's disease in Wales. J Neuropsychol 10(2):163–185. https://doi.org/10.1111/jnp.12061
15. Schweizer TA, Ware J, Fischer CE, Craik FI, Bialystok E (2012) Bilingualism as a contributor to cognitive reserve: evidence from brain atrophy in Alzheimer's disease. Cortex 48(8):991–996. https://doi.org/10.1016/j.cortex.2011.04.009
16. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 339:b2535. https://doi.org/10.1136/bmj.b2535
17. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (eds) Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available from https://www.training.cochrane.org/handbook
18. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M et al. (2014) The Newcastle–Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analysis. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
19. Craik FI, Bialystok E, Freedman M (2010) Delaying the onset of Alzheimer disease: bilingualism as a form of cognitive reserve. Neurology 75(19):1726–1729. https://doi.org/10.1212/WNL.0b013e3181fc2a1c
20. Woumans E, Santens P, Sieben A, Versijpt J, Stevens M, Duyck W (2014) Bilingualism delays clinical manifestation of Alzheimer's disease. Biling Lang Cognit 18:568–574. https://doi.org/10.1017/S136672891400087X
21. Zheng Y, Wu Q, Su F, Fang Y, Zeng J, Pei Z (2018) The protective effect of cantonese/mandarin bilingualism on the onset of Alzheimer disease. Dement Geriatr Cogn Disord 45(3–4):210–219. https://doi.org/10.1159/000488485
22. Chertkow H, Whitehead V, Phillips N, Wolfson C, Atherton J, Bergman H (2010) Multilingualism (but not always bilingualism) delays the onset of Alzheimer disease: evidence from a bilingual community. Alzheimer Dis Assoc Disord 24(2):118–125. https://doi.org/10.1097/WAD.0b013e3181ca1221
23. Mukadam N, Sommerlad A, Livingston G (2017) The relationship of bilingualism compared to monolingualism to the risk of cognitive decline or dementia: a systematic review and meta-analysis. J Alzheimer's Dis JAD. https://doi.org/10.3233/JAD-170131
24. Duncan HD, Nikelski J, Pilon R, Steffener J, Chertkow H, Phillips NA (2018) Structural brain differences between monolingual and multilingual patients with mild cognitive impairment and Alzheimer disease: evidence for cognitive reserve. Neuropsychologia 109:270–282. https://doi.org/10.1016/j.neuropsychologia.2017.12.036
25. Perani D, Farsad M, Ballarini T, Lubian F, Malpetti M, Fracchetti A et al (2017) The impact of bilingualism on brain reserve and metabolic connectivity in Alzheimer's dementia. Proc Natl Acad Sci USA 114(7):1690–1695. https://doi.org/10.1073/pnas.1610909114
26. Kowoll M, Degen C, Gladis S, Schröder J (2015) Neuropsychological profiles and verbal abilities in lifelong bilinguals with mild cognitive impairment and Alzheimer's disease. J Alzheimer's Dis JAD. https://doi.org/10.3233/JAD-142880
27. Fuller-Thomson E, Kuh D (2014) The healthy migrant effect may confound the link between bilingualism and delayed onset of Alzheimer's disease. Cortex 52:128–130. https://doi.org/10.1016/j.cortex.2013.08.009
28. Anderson JAE, Mak L, Keyvani Chahi A, Bialystok E (2018) The language and social background questionnaire: Assessing degree of bilingualism in a diverse population. Behav Res Methods 50(1):250–263. https://doi.org/10.3758/s13428-017-0867-9
29. Selkoe DJ (2011) Resolving controversies on the path to Alzheimer's therapeutics. Nat Med 17(9):1060–1065. https://doi.org/10.1038/nm.2460