

Self-Reported Hearing Loss, Hearing Aids, and Cognitive Decline in Elderly Adults: A 25-Year Study

Hélène Amieva, PhD, Camille Ouvrard, MSc, Caroline Giulioli, MSc, Céline Meillon, MSc, Laetitia Rullier, PhD, and Jean-François Dartigues, MD, PhD

OBJECTIVES: To investigate the association between hearing loss, hearing aid use, and cognitive decline.

DESIGN: Prospective population-based study.

SETTING: Data gathered from the Personnes Agées QUID study, a cohort study begun in 1989–90.

PARTICIPANTS: Individuals aged 65 and older (N = 3,670).

MEASUREMENTS: At baseline, hearing loss was determined using a questionnaire assessing self-perceived hearing loss; 137 subjects reported major hearing loss, 1,139 reported moderate problems (difficulty following the conversation when several persons talk at the same time or in a noisy background), and 2,394 reported no hearing trouble. Cognitive decline was measured using the Mini-Mental State Examination (MMSE), administered at follow-up visits over 25 years.

RESULTS: Self-reported hearing loss was significantly associated with lower baseline MMSE score ($\beta = -0.69$, $P < .001$) and greater decline during the 25-year follow-up period ($\beta = -0.04$, $P = .01$) independent of age, sex, and education. A difference in the rate of change in MMSE score over the 25-year follow-up was observed between participants with hearing loss not using hearing aids and controls ($\beta = -0.06$, $P < .001$). In contrast, subjects with hearing loss using a hearing aid had no difference in cognitive decline ($\beta = 0.07$, $P = .08$) from controls.

CONCLUSION: Self-reported hearing loss is associated with accelerated cognitive decline in older adults; hearing aid use attenuates such decline. *J Am Geriatr Soc* 63:2099–2104, 2015.

Key words: hearing loss; hearing aids; cognitive decline; elderly

From Epidemiology and Biostatistics, Institut National de la Santé et de la Recherche Médicale U897, University of Bordeaux, Bordeaux, France.

Address correspondence to Prof. Hélène Amieva, INSERM U897, Epidemiology and Biostatistics, Université de Bordeaux, 146 Rue Léo Saignat, 33076 Bordeaux Cedex, France. E-mail: Helene.Amieva@isped.u-bordeaux2.fr

DOI: 10.1111/jgs.13649

Hearing loss is the third most common chronic health condition affecting older adults. Approximately 30% of individuals aged 65 and older have some degree of hearing loss, with estimates ranging from 70% to 90% of those aged 85 and older.^{1,2} Individuals with hearing loss often experience depressive symptoms and social isolation.^{3–7} There is also evidence that older adults with hearing loss have poorer cognitive performance.^{8–13} Two longitudinal studies showed an association between hearing loss and cognitive decline over 6 years of follow-up.^{14,15} In particular, the Health, Aging and Body Composition (Health ABC) Study, conducted in a sample of 1,984 community-dwelling individuals aged 70 to 79 showed that hearing loss measured using audiometric testing was independently associated with accelerated cognitive decline and incident cognitive impairment during the 6 years of follow-up.¹⁵

Despite its high prevalence and consequences for health outcomes, hearing loss is largely underdiagnosed and thus undertreated.¹⁶ Almost two-thirds of older adults with hearing impairment do not use hearing aids.¹⁷ Little is known about the effect of hearing aids on health outcomes in older adults, in particular cognitive decline. In one study,¹⁵ hearing aid use was associated with slightly lower rates of cognitive decline and risk of incident cognitive impairment in individuals with hearing loss, but the results were not statistically significant, possibly because of the short follow-up and lack of statistical power. In the other longitudinal study,¹⁴ because of small sample size, the association between hearing aid use and cognitive decline could not be properly examined.

With the ongoing follow-up of the Personnes Agées QUID (PAQUID) cohort specifically designed to study brain aging, the 25-year follow-up of the cohort was used to assess the relationship between hearing loss and long-term age-related cognitive decline. Using self-reported measure of hearing loss, the association between hearing loss and cognitive trajectories over 25 years was investigated in a community-based cohort of older adults, and the trajec-

jectories of those using hearing aids were compared with trajectories of those who were not.

METHODS

Study Population and Protocol

PAQUID is a French epidemiological study of a sample of elderly participants randomly selected from the general population using electoral rolls. Three thousand seven hundred seventy-seven community-dwelling individuals aged 65 and older were included at baseline.¹⁸ Ethics committee of Bordeaux University Hospital approved the study, and all participants provided written informed consent to participate. Subjects were evaluated at home at the initial visit and at 1, 3, 5, 8, 10, 13, 15, 17, 20, 22, and 25 years. Each visit included a neuropsychological evaluation and a criteria checklist for dementia diagnosis completed by a psychologist. Individuals who met these criteria saw a neurologist, who confirmed or rejected the diagnosis according to current standards. Finally, an independent panel of specialized neurologists reviewed the diagnosis.

At each follow-up visit, tests and scales of cognitive performance, cognitive complaints, functional ability, and depressive symptomatology were administered to participants. The Mini-Mental State Examination (MMSE)¹⁹ was used as an index of global cognitive performance. Instrumental activities of daily living (IADLs)²⁰ were assessed using the French version of the Lawton scale. Four of the eight IADLs shown to be associated with cognitive performance and not influenced by sex were used for this study (telephone use, transportation, medication, domestic finances). Participants were considered dependent in each of these activities if they could not perform the activity at the highest level of performance. The IADL score was the number of IADLs in which the subject was considered to be dependent (range 0–4).²¹ Depressive symptomatology was assessed using the Center for Epidemiologic Studies Depression Scale.²² Information on psychotropic drug use, information regarding social network (number of visits, living situation, satisfaction with relationships) was also collected during the interview.

Measures of Hearing Impairment and Hearing Aid Use

A short questionnaire assessing self-perceived hearing loss was administered at baseline. Participants were asked, “Do you have hearing trouble?” Possible responses were “I do not have hearing trouble”; “I have trouble following the conversation with two or more people talking at the same time or in a noisy background”; and “I have major hearing loss.” Participants were also asked whether they had a hearing aid.

Study Sample

All 3,777 members of the PAQUID cohort were eligible for this analysis, with the exception of those with a diagnosis of dementia at the time of inclusion ($n = 102$) and those who did not complete the questionnaire on hearing loss ($n = 5$). The 3,670 eligible subjects were divided into three groups: major degree of hearing loss, difficulties fol-

lowing conversations in a noisy background or multiple conversations, and no hearing trouble.

Statistical Analysis

Baseline characteristics of participants were compared using chi-square tests, analyses of variance, and mean comparisons as appropriate. $P < .05$ was considered statistically significant. The association between hearing loss and hearing aid use and decline in MMSE score over the 25-year follow-up period was assessed using a linear mixed-effect model,²³ which is designed to analyze longitudinal data. Intrasubject correlation is modeled using a subject-specific random intercept and a subject-specific random slope with an unstructured covariance matrix. This model offers the advantage of taking into account multiple observations within a subject and intrasubject correlation. It also allows for adjustment of numerous potential confounding variables.

In the first step, only one interaction term, between hearing impairment and time (age used as time-variable), was included in the model, to assess the effect of hearing loss at baseline on cognitive decline (Model 1). In a second model, a variable was constructed taking into account the presence of hearing aids, providing three categories of participants: no hearing loss, hearing loss and no hearing aid, hearing loss with a hearing aid. This model (Model 2) assessed the effect of hearing aids on further cognitive decline using an interaction term between the previously defined variable and the time variable. These two models were controlled for age, sex, and educational level (defined as no formal education vs primary school certificate or higher). Finally, the third statistical model (Model 3) was adjusted for depressive symptomatology measured using the Center for Epidemiologic Studies Depression Scale (cut-off score of 23 for women and 17 for men), social network variables (number of visits, living situation, satisfaction with relationships), comorbidities, IADL dependency, psychotropic drug consumption (antidepressants, benzodiazepines, antipsychotics), and dementia.

RESULTS

Participants

There were 3,670 participants, of whom, at baseline, 137 (4%) reported major hearing loss, 1,139 (31%) reported moderate hearing loss (trouble following a conversation with two or more people talking at the same time or in a noisy background), and 2,394 (65%) reported no hearing trouble. For the study of cognitive decline, the analysis was restricted to subjects for whom MMSE scores and information on all relevant confounding variables were available. In the successive analyses, there were 3,670 subjects for the first statistical model, 3,577 for the second model (93 missing values regarding hearing aids), and 3,414 for the final model (163 missing values for confounding factors).

The baseline characteristics of the three groups are presented in Table 1. Significant differences were observed for nearly all variables. Subjects reporting hearing loss were more likely to be male; were less educated; and had

Table 1. Baseline Characteristics of the Three Hearing Loss Groups

Characteristic	No Hearing Loss, n = 2,394	Self-Reported Moderate Hearing Loss, n = 1,139	Self-Reported Major Hearing Loss, n = 137	Global P-Value	P-Value ^a
Age, mean ± SD	73.8 ± 6.2	76.7 ± 7.0	81.7 ± 7.7	<.001 ^b	<.001 ^c
Mini-Mental State Examination score, mean ± SD	26.1 ± 3.2	25.3 ± 3.4	24.1 ± 5.1	<.001 ^b	.01 ^c
Female, n (%)	1,499 (62.6)	564 (49.5)	67 (48.9)	<.001 ^d	.89 ^d
≥Primary school certificate, n (%)	1,617 (67.5)	703 (61.7)	73 (53.3)	<.001 ^d	.06 ^d
Depressive symptomatology, n (%)	244 (10.4)	212 (19.1)	27 (21.4)	<.001 ^d	.54 ^d
Psychotropic medication use, n (%)	875 (36.6)	482 (42.3)	63 (42.3)	<.001 ^d	.41 ^d
≥1 Comorbidities, n (%)	906 (38.1)	563 (49.7)	74 (54.0)	<.001 ^d	.34 ^d
Instrumental activity of daily living score, mean ± SD	0.4 ± 0.8	0.7 ± 1.1	1.4 ± 1.4	<.001 ^c	<.001 ^c
Living alone, n (%)	988 (41.3)	512 (44.9)	68 (49.6)	.03 ^d	.30 ^d
Satisfied with relationships, n (%)	1,943 (82.9)	882 (80.7)	101 (81.5)	.30 ^d	.84 ^d

SD = standard deviation.

^a Comparison between subjects with major hearing loss and subjects with moderate hearing loss.

^b Analysis of variance: global comparison of the three groups.

^c Estimated using the *t*-test.

^d Estimated using the chi-square test.

higher depressive symptomatology, more comorbidities, and a higher level of dependency than those without hearing impairment.

Compared to subjects reporting moderate degree of hearing loss (i.e., those reporting difficulties tracking a conversation when there is background noise or multiple conversations), subjects reporting major hearing loss were older ($P < .001$) and more dependent ($P < .001$) and had lower MSSE scores ($P = .01$). No significant difference was observed for the other variables. Therefore, for subsequent analyses, only two groups were considered: a group without hearing impairment and another group pooling subjects reporting moderate and severe degrees of hearing loss.

Effect of Hearing Loss and Hearing Aids on Cognitive Decline

Table 2 shows results of the first model assessing the association between hearing loss and cognitive decline. Hearing loss was significantly associated with a lower score on MMSE ($P < .001$) and greater cognitive decline during the

Table 2. Relationship Between Self-Reported Hearing Loss and Change in Cognitive Score over the 25 Years of the PAQUID Study Follow-Up

Variable	β (Standard Error) P-Value > t
Time	-0.16 (0.01) < .001
Initial MMSE: self-reported hearing loss (reference no self-reported hearing loss)	-0.69 (0.11) < .001
MMSE decline self-reported hearing loss × time (reference no hearing loss × time)	-0.04 (0.02) .01

Estimated from mixed-effect models adjusted for age, sex, and educational level.

25-year follow-up period ($P = .01$) independently of age, gender and educational level.

Table 3 shows the results of the models including information regarding hearing aids. Of the 1,276 participants reporting hearing loss, 150 used hearing aids (89 of those reporting moderate hearing loss, 61 of those with severe loss). Model 2 examined the association between hearing loss, hearing aid use, and cognitive decline, adjusted for age, sex, and educational level. At baseline, both groups reporting hearing loss (using and not using hearing aids) had a lower MMSE score than the control group (subjects without hearing trouble). A significant difference in the rate of change of MMSE score over the 25-year follow-up period was observed between the group of participants reporting hearing impairment and not using hearing aids and the control group ($\beta = -0.06, P < .001$). Figure 1 illustrates the evolution of MMSE scores in the three groups. Subjects reporting hearing loss not using hearing aids declined more rapidly on the MMSE than the control group, with a mean difference of 0.06 points per year (~1.5 points over the entire follow-up period). In contrast, subjects reporting hearing loss using a hearing aid had no significant difference in cognitive decline from the control group; the opposite trend ($\beta = 0.07, P = .08$) was observed, which suggests that the absence of a significant difference in the rate of cognitive decline for this group is not simply due to lack of statistical power. Finally, Model 3 assessed the same relationship as Model 2, with additional adjustment on several psychoenvironmental factors (depressive symptomatology, social network variables, comorbidities, IADL dependency, psychotropic drug use, dementia). After controlling for these factors, the difference in cognitive decline was no longer significant for any of the groups reporting hearing loss (Table 3).

DISCUSSION

This study showed that self-reported hearing loss is independently associated with accelerated cognitive decline in

Table 3. Relationship Between Self-Reported Hearing Loss, Hearing Aids, and Change in Cognitive Score over the 25 Years of the PAQUID Study Follow-Up

Variable	Model 2 ^a	Model 3 ^b
	β (Standard Error) P-Value > t	
Time	–0.15 (0.01) < .001	–0.65 (0.03) < .001
Initial MMSE (reference no hearing loss)		
Self-reported hearing loss without hearing aids	–0.68 (0.11) < .001	–0.14 (0.22) .15
Self-reported hearing loss with hearing aids	–0.70 (0.25) .006	–0.04 (0.22) .86
MMSE decline (reference no hearing loss \times time)		
Self-reported hearing loss without hearing aids \times time	–0.06 (0.02) < .001	–0.01 (0.01) .46
Self-reported hearing loss with hearing aids \times time	0.07 (0.04) .08	0.05 (0.03) .08

MMSE = Mini-Mental State Examination.

^a Estimated from mixed-effect models adjusted for age, sex, and educational level.

^b Estimated from mixed-effects models adjusted for age, sex, educational level, depressive symptomatology, social network (number of visits, living situation, satisfaction with relationships), comorbidities, dependency, psychotropic consumption, dementia.

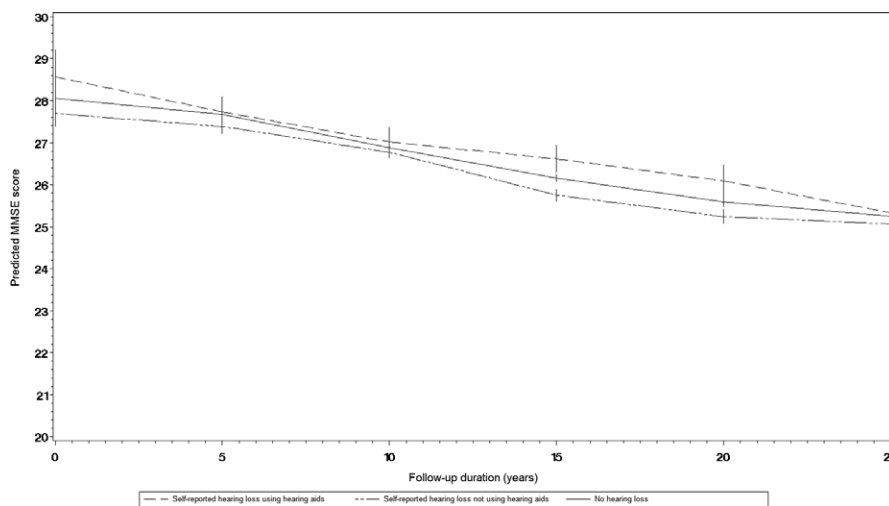


Figure 1. Estimated change in Mini-Mental State Examination (MMSE) score over 25 years of follow-up.

community-dwelling older adults. Prior research has found an association between self-reported hearing loss and cognitive decline.^{14,15} With a larger sample and a longer follow-up period than prior studies, the current study strongly reinforces the plausibility of such association.

The opposite statistical trend was observed in participants reporting hearing loss who used hearing aids. Contrary to participants who did not report using hearing aids, cognitive decline of those wearing hearing aids was not significantly different from that of controls. In other words, elderly adults with hearing loss using hearing aids had similar rates of cognitive decline as those with no hearing impairment. Such a result had never been reported. In the previous study,¹⁵ of 1,984 elderly adults followed for 6 years, hearing aid use was associated with slightly lower rates of cognitive decline in individuals reporting hearing loss, although, probably because of low statistical power, the results were not statistically significant.

Hearing loss has often been associated with depressive symptoms and social isolation,^{3–7} which supports the hypothesis that social isolation and depressive symptomatology may mediate the association between hearing loss

and cognitive decline. This hypothesis would be consistent with the results of the third statistical model of the present study. After controlling for numerous psychosocial variables such as depression, social network, and psychotropic consumption, cognitive decline in individuals with hearing impairment was no longer significantly different. This suggests that there is no direct effect of hearing loss on cognitive decline but rather that depressive symptoms and social isolation mediate the association. Therefore, by at least partially restoring communication abilities, hearing aids may help improve mood, increase social interactions, and enable participation in cognitively stimulating activities and consequently could slow cognitive decline.

The strength of this study is the exceptionally long follow-up of participants. Age-related cognitive decline is a slowly evolving process, so unless the effect of a rehabilitative strategy is expected to be massive and immediate—which is rarely the case—a short study follow-up is insufficient to assess strategies that may have a significant but modest effect on cognitive decline. Such effect may be appreciable only over a long period of time, which is probably the case with the effect of hearing aids on cognitive decline. Another strength is that the study was performed

in a large sample of community-dwelling older adults randomly selected from the general population, allowing reasonably good generalizability of the results.

Several limitations should be also underlined. The first and probably most important is the observational design of the study, which means that the results should be interpreted with caution. Even though it was possible to control numerous demographic and psychosocial variables measured in the PAQUID study, participants using hearing aids could have differed from those not using hearing aids in unmeasured factors. The question of whether hearing rehabilitative strategies affect cognitive decline could be addressed only in a randomized controlled trial. The second limitation is that the study relied on a self-reported measure of hearing impairment; no objective auditory measure was available. The measure used was self-perceived hearing difficulty, which is far less precise than an audiometric measure. Nonetheless, from a practical point of view, such an inexpensive and easy-to-collect measure provides useful information on the possible consequences of hearing loss in elderly adults. In addition, numerous studies have shown that self-reported hearing loss is highly correlated with audiometric measures in older adults.^{24–29} Nonetheless, such correlation is still under debate, in particular for minimal degrees of hearing loss. Another limitation is that hearing loss was measured only at baseline, so information on the trajectory of hearing loss was unavailable. The last main limitation was that the study relied on information regarding possession of hearing aids, whereas reporting having a hearing aid does not necessarily mean that one uses it regularly.³⁰

This study also has several strengths, including its population-based design, long-term follow-up, and the full assessment of a wide range of cognitive, clinical, and dementia-related measures.

In conclusion, hearing loss is associated with accelerated cognitive decline in older adults. It was also found that hearing aid use attenuates such cognitive decline, which had never been reported. Taken together, these results underline the importance of addressing the problem of underdiagnosis and undertreatment of hearing loss in elderly adults. With the prevention of cognitive aging being one of the international priorities of research, along with cognitive training³¹ and physical exercise interventions,³² which have been shown to have a modest but positive effect on cognitive aging, auditory rehabilitation programs should be considered as additional potential candidates to promote successful aging. Hearing rehabilitative treatment is complex and does not simply consist of using a hearing aid, so a well-designed interventional trial is necessary to demonstrate the effect of a comprehensive auditory rehabilitation program on cognitive aging.

ACKNOWLEDGEMENTS

The PAQUID study was supported by ARMA (Bordeaux), Caisse Nationale d'Assurance Maladie des Travailleurs Salariés, Conseil Général de la Dordogne, Conseil Général de la Gironde, Conseil Régional d'Aquitaine, Fondation de France, France Alzheimer (Paris), GIS Longévité, Institut

National de la Santé et de la Recherche Médicale, Mutuelle Générale de l'Éducation Nationale, Mutualité Sociale Agricole, Novartis Pharma (France), and SCORInsurance (France).

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

Author Contributions: Amieva, Dartigues: study design. Amieva: writing the manuscript. Meillon: statistical analysis. Ouvrard, Giulioli, Dartigues, Meillon, Rullier: critical revisions of the manuscript.

Sponsor's Role: The funders had no role in study design, data collection or analysis, the decision to publish, or preparation of the manuscript.

REFERENCES

- Chien W, Lin FR. Prevalence of hearing aid use among older adults in the United States. *Arch Intern Med* 2012;172:292–293.
- Weinstein BE. *Geriatric Audiology*. New York: Thieme Publishers Inc., 2000.
- Kiely KM, Anstey KJ, Luszcz A. Dual sensory loss and depressive symptoms: The importance of hearing, daily functioning, and activity engagement. *Front Hum Neurosci* 2013;7:837.
- Li CM, Zhang X, Hoffman HJ et al. Hearing impairment associated with depression in US adults, National Health and Nutrition Examination Survey 2005–2010. *JAMA Otolaryngol Neck Surg* 2014;140:293–302.
- Thomas PD, Hunt WC, Garry PJ et al. Hearing acuity in a healthy elderly population: Effects on emotional, cognitive, and social status. *J Gerontol* 1983;38:321–325.
- Strawbridge WJ, Wallhagen MI, Shema SJ et al. Negative consequences of hearing impairment in old age: A longitudinal analysis. *Gerontologist* 2000;40:320–326.
- Weinstein BE, Ventry IM. Hearing impairment and social isolation in the elderly. *J Speech Hear Res* 1982;25:593–599.
- Lin FR, Ferrucci L, Metter EJ et al. Hearing loss and cognition in the Baltimore Longitudinal Study of Aging. *Neuropsychology* 2011;25:763–770.
- Uhlmann RF, Larson EB, Rees TS et al. Relationship of hearing impairment to dementia and cognitive dysfunction in older adults. *JAMA* 1989;261:1916–1919.
- Gussekloo J, de Crean AJ, Oduber C et al. Sensory impairment and cognitive functioning in oldest-old subjects: The Leiden 85+ Study. *Am J Geriatr Psychiatry* 2005;13:781–786.
- Ohta RJ, Carlin MF, Harmon BM. Auditory acuity and performance on the mental status questionnaire in the elderly. *J Am Geriatr Soc* 1981;29:476–478.
- Granick S, Kleban MH, Weiss AD. Relationships between hearing loss and cognition in normally hearing aged persons. *J Gerontol* 1976;31:434–440.
- Lindenberger U, Baltes PB. Sensory functioning and intelligence in old age: A strong connection. *Psychol Aging* 1994;9:339–355.
- Valentijn SA, van Boxtel MP, van Hooren SA et al. Change in sensory functioning predicts change in cognitive functioning: Results from a 6-year follow-up in the Maastricht Aging Study. *J Am Geriatr Soc* 2005;53:374–380.
- Lin FR, Yaffe K, Xia J et al. Hearing loss and cognitive decline in older adults. *JAMA Intern Med* 2013;173:293–299.
- Lin FR. Hearing loss in older adults: Who's listening? *JAMA* 2012;307:1147–1148.
- Fischer ME, Cruickshanks KJ, Wiley TL et al. Determinants of hearing aid acquisition in older adults. *Am J Public Health* 2011;101:1449–1455.
- Dartigues JF, Gagnon M, Barberger-Gateau P et al. The Paquid epidemiological program on brain ageing. *Neuroepidemiology* 1992;11:14–18.
- Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
- Lawton MP, Brody EM. Assessment of older people: Self-maintaining and instrumental activities of daily living. *Gerontologist* 1969;9:179–186.
- Barberger-Gateau P, Commenges D, Gagnon M et al. Instrumental activities of daily living as a screening tool for cognitive impairment and dementia in elderly community dwellers. *J Am Geriatr Soc* 1992;40:1129–1134.

22. Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1:385–401.
23. Laird NM, Ware JH. Random-effects models for longitudinal data. *Biometrics* 1982;38:963–974.
24. Mingfang D, Jianjun S, Tao J et al. Comparison between self-reported hearing and measured hearing thresholds of the elderly in China. *Ear Hear* 2014;35:e228–e232.
25. Deepthi R, Kasthuri A. Validation of the use of self-reported hearing loss and the Hearing Handicap Inventory for elderly among rural Indian elderly population. *Arch Gerontol Geriatr* 2012;55:767–767.
26. Ferrite S, Santana VS, Marshall SW. Validity of self-reported hearing loss in adults: Performance of three single questions. *Rev Saude Publica* 2011;45:824–830.
27. Rosdina AK, Leelavathi M, Zaitun A et al. Self-reported hearing loss among elderly Malaysians. *Malays Fam Physician* 2010;5:91–94.
28. Valette-Rosalino C, Rozenfeld S. Auditory screening in the elderly: Comparison between self-reported and audiometry. *Rev Bras Otorrinolaringol* 2005;71:193–200.
29. Sindhusake D, Mitchell P, Smith W et al. Validation of self-reported hearing loss. The Blue Mountains Hearing Study. *Int J Epidemiol* 2001;30:1371–1378.
30. McCormack A, Fortnum H. Why do people fitted with hearing aids not wear them? *Int J Audiol* 2013;52:360–368.
31. Ball K, Berch DB, Helmers KF et al. Effects of cognitive training interventions with older adults: A randomized controlled trial. *JAMA* 2002;288:2271–2281.
32. Lautenschlager NT, Cox KL, Flicker L et al. Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: A randomized trial. *JAMA* 2008;300:1027–1037.