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## Longitudinal study of hearing loss and subjective cognitive function decline in men

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### Abstract

**INTRODUCTION:** We examined the relation of self-reported hearing loss, hearing aid use, and risk of subjective cognitive function (SCF) decline.

**METHODS:** We conducted an 8-year (2008–2016) longitudinal study of 10,107 men aged 62 years who reported their hearing status in 2006 and had no subjective cognitive concerns in 2008. Change in SCF score was assessed by a 6-item questionnaire and subjective decline was defined as new report of at least one SCF concern during follow-up.

**RESULTS:** Hearing loss was associated with higher risk of SCF decline. Compared with no hearing loss, the multivariable-adjusted relative risk (MVRR, 95% CI) of incident SCF decline was 1.30(1.18, 1.42), 1.42(1.26, 1.61), and 1.54(1.22, 1.96) among men with mild, moderate and severe hearing loss (no hearing aids), respectively (p-trend < 0.001). Among men with severe hearing loss who used hearing aids, the MVRR was 1.37(1.18, 1.60).

**DISCUSSION:** Hearing loss was associated with substantially higher risk of subsequent subjective cognitive decline in men.

### Keywords

Cognition; Subjective cognitive function; Hearing loss; Hearing aids; Aging; Longitudinal study

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## 1. Introduction

Dementia poses a growing public health challenge as the population ages, and effective treatments to prevent progression or reverse its course are lacking.<sup>1</sup> In 2015, an estimated 47 million people worldwide were living with dementia,<sup>2</sup> and this number is projected to triple by 2050.<sup>3</sup> Examining measures of earlier stage memory decline and cognitive deterioration may be important for the development of preventive interventions that could be more effective than treatment of later stage dementia.<sup>4</sup> Self-perceived cognitive concerns can reflect subtle features of cognitive decline that are experienced by an individual even with normal performance on cognitive tests.<sup>5</sup> Subjective cognitive function (SCF) is a measure that is associated with objective brain changes that predict dementia in neuroimaging studies<sup>6-9</sup> and may be on a continuum with clinical manifestations of mild cognitive impairment and pre-dementia.<sup>4</sup>

Hearing loss, the most prevalent sensory deficit, has been associated with poorer cognitive performance in older adults and may be a risk factor for accelerated cognitive decline.<sup>10</sup> Both hearing loss and cognitive decline have multifactorial causes and are often progressive, likely reflecting cumulative auditory and neurodegenerative damage that accrue over the lifespan.<sup>11,12</sup> NHANES audiometric data show 61 million US adults have hearing loss in at least 1 ear.<sup>13</sup> The prevalence of hearing loss increases with age and is higher among men than women; one-third of men aged 40 years or older are estimated to have hearing loss.<sup>13</sup> Thus, understanding whether hearing loss may influence early cognitive decline could reveal a valuable opportunity for identifying determinants of early cognitive decline and provide crucial insights for earlier intervention and prevention. Further, hearing aid use could possibly curtail the trajectory of cognitive decline among those with hearing loss. However, findings from studies of hearing aid use and cognition are conflicting.<sup>14-18</sup> Therefore, we prospectively investigated the relation of self-reported hearing loss and risk of subjective cognitive function decline using longitudinal data collected from a well-characterized cohort of 10,107 men. In addition, among those with hearing loss, we examined whether the risk of subjective cognitive decline was moderated by hearing aid use.

## 2. Methods

### 2.1 Study Population

We evaluated the association between self-reported hearing loss and subjective cognitive function decline using data from the Health Professionals Follow-up Study (HPFS). The HPFS is a prospective cohort study that enrolled 51,529 male dentists, optometrists, osteopaths, pharmacists, podiatrists, and veterinarians who were 40–75 years of age at inception in 1986. Participants have completed questionnaires about diet, lifestyle factors, medical history, and medication use every two years. The 30-year follow-up exceeds 90% of eligible person-time, the time at risk that all participants contributed to the study. Most variables are updated every 2 years and diet information is updated every 4 years. In total, 28,367 men answered the question about hearing on the 2006 questionnaire and 25,848 of these also answered questions on subjective cognitive function on the 2008, 2012 and/or 2016 questionnaires. To evaluate the relation between hearing loss and incident SCF decline, we excluded men who reported one or more subjective cognitive concerns on the 2008

questionnaire or did not answer the SCF questions (n=11,022); men who answered the 2008 questions but not the 2012 or the 2016 SCF questions (n=1,301); and men who reported Parkinson's disease, cancer (other than non-melanoma skin cancer), or stroke (n=3,418) to minimize potential residual confounding due to varying severity of these conditions or treatment related effects. Thus, 10,107 men were included in the analysis.

## 2.2 Ascertainment of Hearing Loss

The 2006 questionnaire asked whether the participant had a hearing problem and, if so, the severity of the hearing problem (mild; moderate; severe, no hearing aid; severe, use a hearing aid). Findings using self-reported hearing loss in this and similar cohorts have been published previously.<sup>19–21</sup>

## 2.3 Ascertainment of Outcome

Subjective cognitive function (SCF) was assessed on questionnaires administered in 2008, 2012 and 2016. The SCF score is based on 6 questions (yes/no): (1) Do you have more trouble than usual remembering recent events? (2) Do you have more trouble than usual remembering a short list of items, such as a shopping list? (3) Do you have trouble remembering things from one second to the next? (4) Do you have any difficulty in understanding things or following spoken instructions? (5) Do you have more trouble than usual following a group conversation or a plot in a TV program due to your memory? (6) Do you have trouble finding your way around familiar streets? The SCF score ranges from 0 to 6, with one point assigned for each cognitive concern reported by the participant. SCF decline was defined as the new report of at least one SCF concern over follow-up. Thus, among those with SCF score = 0 (did not report any cognitive concerns) in 2008, incident subjective cognitive decline was defined as an SCF score of 1 or greater (reported one or more cognitive concerns) in 2012 or 2016. In the HPFS, higher SCF scores were strongly associated with age and with apolipoprotein-E (APOE) gene status,<sup>22</sup> and associations between other risk factors and SCF have been demonstrated using these methods.<sup>22,23</sup>

## 2.4 Ascertainment of Covariates

We considered covariates purported to be risk factors for hearing loss and/or for cognitive decline: age, race, occupation, body mass index, waist circumference, smoking (never, past, current), physical activity, hypertension, diabetes, hypercholesterolemia, Alternate Mediterranean dietary pattern (AMED adherence score, range 0–9), regular aspirin use (2+ /week), regular nonsteroidal anti-inflammatory drug (NSAID) use (2+ /week), regular acetaminophen use (2+ /week), and depression (defined as the use of anti-depressants in the past 2 years, or self-reported diagnosis, assessed in 2008). Information on covariates was obtained from biennial questionnaires and updated in each time period. AMED score was calculated from a validated semi-quantitative food frequency questionnaire administered every 4 years. Waist circumference was only assessed once during the study period (2008), thus only the baseline measure was used.

## 2.5 Statistical Analysis

The analyses were prospective, using information on hearing loss and hearing aid use collected before the ascertainment of SCF decline. Among men with SCF=0 in 2008, we examined the relation between hearing status and risk of incident decline in cognitive function during follow-up (SCF = 1). For each participant, person-time was allocated based on the response at the beginning of each follow-up period. We calculated the rate of incident SCF decline as the number of new cases during study follow-up divided by the person-time at risk throughout the observation period. Age- and multivariable-adjusted relative risks (MVRs) were calculated using Cox proportional hazards regression models with a binary outcome. To examine whether the relation was statistically significantly different among men with severe hearing loss who did and did not use hearing aids, we conducted analyses in which men with severe hearing loss who did not use hearing aids were the referent group and examined the comparison with men with severe hearing loss who used hearing aids. To evaluate the risk of more pronounced cognitive decline, we performed secondary analyses that examined incident SCF scores = 2. We calculated the p for linear trend for the age- and multivariable-adjusted analyses for incident SCF Score = 1 and for incident SCF Score = 2, according to increasing category of hearing loss severity among the men who did not use hearing aids.

To further evaluate the temporal relation of hearing loss to SCF, we performed a lag analysis examining hearing loss and risk of SCF decline after 8 years; individuals who reported SCF concerns in 2012 were excluded. We performed analyses stratified by age <70 versus 70+ years in 2006 and analyses stratified by current depression (defined as the use of anti-depressants in the past 2 years, or self-reported diagnosis, assessed in 2008). We conducted statistical tests of interaction by constructing interaction terms between age and hearing loss and between depression and hearing loss. To evaluate the possibility that responses to questions included in the SCF score might be influenced by hearing ability, we performed sensitivity analyses that removed questions from the SCF score that potentially could be influenced by hearing loss: “Do you have difficulty in understanding things or following spoken instructions?” and “Do you have more trouble than usual following a group conversation or a plot in a TV program due to your memory?”

In a cross-sectional analysis (n=19,130) consistent with previous studies using this measure in this cohort,<sup>6,22,23</sup> SCF score was used to categorize all participants for whom we had information on hearing status and SCF. To reduce random error, the average SCF score was computed and the possible range was 0 to 6 points. Participants were categorized into one of three levels of SCF: “good” (SCF score = 0), “moderate” (SCF score = 0.5–2.5), or “poor” subjective cognitive function (SCF score = 3+). If a participant reported SCF data on only one questionnaire, then we used the single SCF score. Multivariable-adjusted logistic regression models with a binary outcome were used to estimate the odds ratio of SCF according to hearing status. Comparisons were made between (1) the moderate and good SCF groups and (2) the poor and good SCF groups. All P-values are two-tailed and considered statistically significant at P<0.05. Statistical tests were performed with SAS statistical software, version 9.4 (SAS Institute Inc., Cary, NC).

### 3. Results

The characteristics of study participants in 2006 according to severity of self-reported hearing loss are shown in Table 1. Men who reported greater hearing loss were more likely to be older, however there were no other large differences. After 52,752 person-years of follow-up, there were 2,771 cases of incident SCF decline (SCF 1). Hearing loss was associated with higher risk of SCF decline (Table 2). Compared with men with no hearing loss, the multivariable-adjusted relative risk (MVRR, 95%CI) of incident cognitive decline was 1.30 (1.18,1.42) among men with mild hearing loss, 1.42 (1.26,1.61) among men with moderate hearing loss, and 1.54 (1.22,1.96) among men with severe hearing loss but did not use hearing aids ( $p$ -trend<0.001). Among men with severe hearing loss who used hearing aids, the magnitude of the elevated risk was somewhat attenuated [1.37 (1.18,1.60)] but was not statistically significantly different from the risk among men with severe hearing loss who did not use hearing aids ( $p$ =0.4).

In a secondary analysis examining the relation of hearing loss and risk of more pronounced SCF decline (SCF 2), the magnitude of the association was slightly greater among those with mild or moderate hearing loss (Table 2), but there were only 23 cases among those with severe hearing loss who did not use hearing aids. Among men who did not use hearing aids, increasing severity of hearing loss tended to be associated with higher risk ( $p$ -trend<0.001). The risk among those with severe hearing loss who used hearing aids was similar to that found in the primary analysis. In a lag analysis that examined the relation of hearing loss and cognitive decline after 8 years, the trend was similar but the magnitudes of the point estimates were smaller (Supplemental Table S1). The relation between hearing loss and cognitive decline did not vary by age ( $p$ -interaction=0.9) or by depression ( $p$ -interaction=0.5). In sensitivity analyses that removed questions potentially related to hearing ability from the SCF score, hearing loss remained associated with higher risk of SCF decline, with greater risk among men with more severe hearing loss who did not wear hearing aids ( $p$ -trend<0.001); however, the magnitudes of the association were attenuated (Table 3). In sensitivity analyses in which individuals with Parkinson's, cancer or stroke were not excluded, but these conditions were adjusted for, the results did not appreciably differ (data not shown).

In cross-sectional analyses that compared the odds of moderate versus good SCF and poor versus good SCF according to hearing status, hearing loss was significantly and substantially associated with a higher likelihood of both moderate and poor SCF (Supplemental Table S2). Specifically, the multivariable-adjusted odds ratio (MVOR, 95%CI) for moderate SCF was 1.54 (1.43,1.65) for men with mild hearing loss, 1.62 (1.47,1.80) for men with moderate hearing loss, and 2.50 (2.06,3.03) for men with severe hearing loss who did not use hearing aids. Among men with severe hearing loss who wore hearing aids, the MVOR for moderate versus good SCF was 1.82 (1.62,2.05). In the analysis that compared poor versus good SCF, the magnitudes of the association were even greater. Compared with no hearing loss, the MVOR (95% CI) was 2.07 (1.76,2.43) for mild hearing loss, 2.49 (2.04,3.04) for moderate hearing loss, and 4.92 (3.61,6.71) for men with severe hearing loss who did not use hearing aids. Among men with severe hearing loss who used hearing aids, the MVOR for poor versus good SCF was 2.92 (2.37,3.60).

## 4. Discussion

In this longitudinal study among 10,107 US men, hearing loss was associated with higher risk of subjective cognitive decline, and the magnitude of the risk was greater with increasing severity of hearing loss. Compared with men with no hearing loss, the risk of subjective cognitive decline was 30% higher among men with mild hearing loss, and 42–54% higher among men with moderate or worse hearing loss.

SCF appraises subjective cognitive concerns that reflect changes in memory or thinking experienced by individuals who may or may not demonstrate abnormal performance on cognitive tests.<sup>24</sup> A decline in SCF may capture an individual's self-perceived experience of cognitive decline before evidence of impairment is apparent on standardized neuropsychological tests,<sup>25,26</sup> and thus may be an early manifestation of preclinical Alzheimer's disease (AD) and other dementias.<sup>27</sup> In our female cohort of nurses, strong linear trends of increasingly worse scores on cognitive tests were associated with increasing numbers of memory concerns; the odds of objective cognitive impairment increased ~20% with each additional cognitive concern that was reported.<sup>7</sup> In other cohorts, SCF predicted accelerated memory decline,<sup>28</sup> and cognitively normal older adults with subjective cognitive concerns had higher risk of progression to minimal cognitive impairment (MCI).<sup>29</sup> Further, SCF was associated with increased risk of dementia<sup>30,31</sup> and predicted dementia 6–9 years before physician diagnosis.<sup>32</sup>

Several plausible mechanisms could explain an association between hearing loss and cognitive decline, but the underlying pathophysiology remains unclear. Hearing loss related degradation or deprivation of sound stimuli may lead to more effortful listening, increased cognitive load, and alterations in neural networks.<sup>33,34</sup> Poorer scores on cognitive tests may be due to compensatory deployment of cognitive resources that otherwise would be available for task performance.<sup>35</sup> As the integrity of the auditory input signal diminishes, there may be an increasing reliance on additional cognitive processes to infer meaning from heard speech. As a result, performance on cognitive tests that rely on auditory input may be adversely influenced by inadequate auditory signal processing requiring the recruitment of additional cognitive processes for listening and speech processing. As additional cognitive resources are allocated to processing the degraded auditory signal, cognitive spare capacity may be reduced. Chronic compensation for hearing loss may induce neural reorganization, alter cognitive resource allocation and deplete cognitive resources.<sup>34,36</sup> Further, common mechanisms may underlie both auditory and cognitive changes that occur with advancing age,<sup>37</sup> and evidence shows declines in other sensory modalities are also associated with declines in cognition.<sup>38,39</sup> Common neurodegenerative etiologies may involve vascular, oxidative, and inflammatory processes,<sup>40</sup> and genetics.<sup>41</sup> Likely, a combination of shared causative processes and sensory-related factors cumulatively contribute to cognitive decline.<sup>42,43</sup> Hearing loss may also encumber social engagement, leading to social isolation and depression that may increase the risk of cognitive decline.<sup>44,45</sup>

Previous studies suggested lower scores on objective tests of cognition are more prevalent and cognitive function may decline more rapidly among individuals with hearing loss, but findings have not been consistent and longitudinal data are limited. A meta-analysis of

cross-sectional studies suggested individuals without hearing loss had better general cognition than those with hearing loss, but the studies were predominantly small, had limited adjustment for potential confounding factors, and there was substantial heterogeneity.<sup>46</sup> Our cross-sectional multivariable-adjusted results revealed hearing loss was associated with substantially higher odds of worse SCF.

Relatively few longitudinal studies of hearing and cognitive function have been conducted. These included mostly older adults, and study size, duration, and rates of follow-up were limited. In the Health ABC study (n=1984, mean age 77.4y), baseline hearing loss was associated with a 41% greater annual rate of decline in scores on the Modified Mini-Mental State Examination and a 32% greater annual rate of decline in scores on the Digit Symbol Substitution Test, compared with those without hearing loss.<sup>10</sup> A smaller study in the Atherosclerosis Risk in Communities Neurocognitive Study (ARIC)(n=253, mean age 76.9y), observed faster declines in memory and global function, assessed using the Delayed Word Recall Test, the Word Fluency Test, and the Digit Symbol Substitution Test, among participants with moderate/severe hearing loss compared with no hearing loss; however, hearing was not measured until the end of the study.<sup>16</sup> A study among 2,002 individuals (mean age 63y) examined self-reported hearing difficulty (queried as “even with the use of a hearing aid”) and subjective cognitive function, assessed using 4 questions, and found self-reported hearing difficulty was associated with a 22% (14–29%) higher odds of poor subjective cognitive function 5 years later.<sup>47</sup> In contrast, several studies did not observe longitudinal associations between hearing loss and various measures of global or domain-specific cognition.<sup>48–51</sup> One longitudinal study in Australia among 1,352 older adults found no differences in 5- or 10-year risk of cognitive decline, assessed using the Mini-Mental State Examination, between those with or without hearing loss.<sup>49</sup> Another Australian study among 2,087 older adults observed no association between hearing loss and cognitive measures of verbal reasoning, speed and memory, including the Digit Substitution Subscale and other sections of the WAIS-R, the Boston Naming Test, and the National Adult Reading Test.<sup>50</sup> A study among older US adults found moderate/severe hearing loss was associated with higher risk of dementia but found no association with domain specific cognitive change.<sup>52</sup> To our knowledge, this is the first longitudinal study to examine the relation of hearing loss and change in subjective cognitive function that distinguished between those who did and did not use hearing aids and that used a previously validated measure to assess SCF.

Hearing aid use may reduce listening effort and cognitive fatigue among individuals with hearing loss,<sup>53</sup> but findings from studies of hearing aid use and cognitive decline have been inconsistent.<sup>10,16,54,55</sup> Increased listening effort and fatigue related to hearing loss have been demonstrated,<sup>56</sup> but may persist among those who wear hearing aids.<sup>57</sup> A small cross-sectional study found better cognitive performance in older adults with moderate/severe hearing loss who reported hearing aid use, compared with those who did not (n=85, mean age=77y),<sup>16</sup> and a large cross-sectional study in the UK Biobank (n=164,770; age 40–69y) found hearing aid use was associated with better cognition, independent of social isolation and depression.<sup>15</sup> However, a study among older adults with hearing loss in the Epidemiology of Hearing Loss Study (n=666) found no significant differences between hearing aid users and non-users for any of several cognitive measures that were assessed, but

there were only 69 hearing aid users, thus power was limited.<sup>58</sup> A French longitudinal study among 3,777 older adults, which found self-reported hearing trouble was associated with an overall 21% (4–40%) higher risk of dementia, observed no association between hearing loss and dementia among those who used hearing aids, but the confidence intervals were wide.<sup>59</sup> Our findings show a higher risk of subjective cognitive decline, even among those who used hearing aids. In our cross-sectional analysis, the magnitudes of the association were attenuated by hearing aid use. In our longitudinal analysis, although the point estimates among men with severe hearing loss who used hearing aids were slightly lower than among men with hearing loss who did not use hearing aids, the difference was not statistically significant. This may have been due to limited power or could suggest that if a difference truly exists, the magnitude of the effect may be modest. More information, particularly on whether hearing aid use provides cognitive benefits for individuals with mild or moderate hearing loss, is needed. A randomized trial to determine whether hearing aid use reduces the risk of cognitive decline and dementia among older adults is currently underway.<sup>60</sup>

In our study, SCF was assessed with methods used previously in this and similar cohorts.<sup>9,22</sup> At present, there is no gold standard questionnaire or single “best” approach for assessment of SCF.<sup>61</sup> Notably, assessments have evolved over time and more recent measures capture additional aspects regarding memory concerns and self-perception in relation to peers.<sup>24,61,62</sup> In our sensitivity analysis that did not include questions potentially influenced by hearing status in the SCF score, the magnitudes of the relations were somewhat attenuated. This is consistent with a study that demonstrated age-related differences in cognitive function varied as a function of hearing loss and the influence of age on cognitive decline may be overestimated if hearing loss is not taken into account,<sup>63</sup> and suggests that some measures typically used in cognitive research may be sensitive to hearing ability.<sup>64</sup> Therefore, hearing status could be an important methodologic consideration in studies of cognitive decline and dementia.

Strengths of our study include large sample size and prospective study design with longitudinal follow-up of SCF. Potential limitations include self-report of hearing loss and of cognitive function. Although self-reported hearing loss has been associated with objective measures of hearing, the onset of hearing loss is often insidious, and individuals may not be aware of their hearing loss. This may also apply to self-assessment of cognitive function. Information on hearing was collected prospectively, before the assessment of SCF, thus misclassification of hearing status would likely be at random with respect to the outcome and would attenuate associations towards the null. A study in NHANES examined the accuracy of subjective assessment of hearing (using a single question) compared with objective assessment of hearing loss, defined as better ear pure tone mean sensitivity (0.5, 1, 2, 4 kHz)  $\geq 25$  dB HL, and found self-reported and objective measures were in agreement among 72% of men in their 50's and 60's, and 71% in their 70's; some individuals with abnormalities on the audiogram did not report a hearing problem.<sup>65</sup> Moreover, accumulating evidence shows auditory deterioration and hearing difficulty may not be fully captured by the conventional audiogram.<sup>11,66,67</sup> Self-reported functional hearing ability may provide an ecologically valid assessment of hearing in real-world settings and identify a larger group of adults with meaningful hearing loss. The SCF questions used in this study have been validated against objective features of dementia and clinically established cognitive testing



questionnaires.<sup>6–9,29</sup> Early cognitive concerns and SCF score are strong predictors of future dementia and poor SCF may indicate imminent AD.<sup>9,68</sup> SCF scores were associated with mid- and later-stage biomarkers of AD, including amyloid plaques, neurofibrillary tangles, and grey matter atrophy.<sup>69–72</sup> In HPFS, higher SCF scores were strongly associated with age and with apolipoprotein-E (APOE) gene status.<sup>22</sup> Our study was limited to predominantly white male healthcare professionals with generally high socioeconomic status and education. This is useful to reduce variability in the study measures and enhance internal validity of health-related information. Notably, SCF may be a stronger predictor of longitudinal cognitive decline in those with higher educational attainment.<sup>73</sup> However, findings may not be generalizable, thus replication in women and other populations would be informative. This study was observational and residual confounding by unmeasured factors is possible, but the findings were robust to adjustments for numerous potential confounders which were measured repeatedly using well-validated instruments. This study examined SCF, which has been validated and correlates with objective measures,<sup>6</sup> however, our study did not examine objective outcome metrics.

#### 4.1 Conclusion

Hearing loss was associated with higher risk of subjective cognitive decline in men, and the magnitude of the risk was greater with increasing severity of hearing loss.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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#### Abbreviations:

<b>HPFS</b>	Health Professionals Follow-Up Study
<b>SCF</b>	Subjective cognitive function
<b>MVRR</b>	multivariable-adjusted relative risk
<b>METs</b>	Metabolic equivalents
<b>AMED</b>	Alternate Mediterranean diet

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### Research in Context

- 1.** Systematic review: We reviewed the literature on hearing loss as a potential risk factor for accelerated cognitive decline. We noted the scarcity of longitudinal data and the lack of studies investigating the relation of hearing loss and subjective cognitive decline, an early at-risk state of AD dementia.
- 2.** Interpretation: Our findings revealed that hearing loss is associated with substantially higher risk of subjective cognitive decline, and the magnitude of the risk is greater with increasing severity of hearing loss. There is higher risk of subjective cognitive decline even among those who used hearing aids. We also note that hearing status could be an important consideration in studies of cognitive decline and dementia.
- 3.** Future directions: Future studies need to address the following issues: (1) to replicate these findings among women and other populations and (2) to investigate whether hearing aid use provides cognitive benefits for individuals with hearing loss.

**Table 1:**

Age-adjusted characteristics of men in the Health Professionals Follow-up Study (HPFS), according to hearing status (2006)

	No hearing difficulty	Mild hearing loss	Moderate hearing loss	Severe hearing loss, no hearing aid	Severe hearing loss, use hearing aid
N	5403	2836	1049	196	623
Age, years *	66.4 (6.2)	67.7 (6.6)	69.8 (7.4)	69.2 (7.1)	72.7 (7.6)
White race, %	95.9	97.4	97.6	96.3	99.0
BMI, kg/m <sup>2</sup>	26.0 (3.8)	26.5 (3.9)	26.6 (3.9)	27.4 (4.9)	26.4 (3.8)
Waist circumference (2008), cm	99.4 (10.7)	100.8 (11.1)	100.5 (10.4)	102.4 (10.4)	100.7 (11.4)
Smoking, %					
Never	53.4	49.3	44.6	45.6	50.0
Past	43.2	47.5	53.3	51.5	49.2
Current	3.4	3.2	2.1	2.8	0.8
Physical activity, METs/week †	48.9	50.0	54.5	49.2	49.5
Hypertension, %	47.7	48.7	54.0	48.3	49.5
Diabetes, %	7.8	8.0	8.4	8.7	9.9
Elevated cholesterol, %	59.8	61.6	64.3	62.0	68.7
AMED diet score ‡	4.5	4.4	4.5	4.2	4.3
Aspirin use (2+/wk), %	60.3	63.5	65.2	54.9	63.4
Ibuprofen use, (2+/wk), %	19.2	22.5	24.3	21.8	23.4
Acetaminophen use, (2+/wk), %	11.3	11.8	12.7	14.2	13.7

Values are means (SD) or percentages and are standardized to the age distribution of the study population.

Values of polytomous variables may not sum to 100% due to rounding.

\* Value is not age-adjusted

† Metabolic equivalents from recreational and leisure-time activities

‡ AMED Score: measure of adherence to the Alternate Mediterranean diet (range 0–9)

Hearing loss and risk of incident subjective cognitive decline\* in the Health Professionals Follow-up Study

Table 2:

Hearing Status	SCF Score > 1			SCF Score > 2		
	Cases	Age-adjusted RR(95% CI)	Multivariable-adjusted RR <sup>†</sup> (95% CI)	Cases	Age-adjusted RR(95% CI)	Multivariable-adjusted RR <sup>†</sup> (95% CI)
No difficulty	1250	1.00 (ref)	1.00 (ref)	438	1.00 (ref)	1.00 (ref)
Mild hearing loss	845	1.32 (1.21, 1.45)	1.30 (1.18, 1.42)	335	1.49 (1.29, 1.72)	1.45 (1.25, 1.68)
Moderate hearing loss	378	1.48 (1.32, 1.67)	1.42 (1.26, 1.61)	140	1.56 (1.29, 1.90)	1.51 (1.24, 1.84)
Severe, nohearing aid	77	1.63 (1.29, 2.06)	1.54 (1.22, 1.96)	23	1.44 (0.94, 2.20)	1.33 (0.86, 2.04)
<b>p-trend</b>		<b>&lt;0.001</b>	<b>&lt;0.001</b>		<b>&lt;0.001</b>	<b>&lt;0.001</b>
Severe, usea hearing aid	221	1.44(1.24, 1.68)	1.37(1.18, 1.60)	86	1.48(1.15, 1.90)	1.40(1.09, 1.80)

\* Incident subjective cognitive decline defined as Subjective Cognitive Function Score (SCF) 1 or 2 at follow-up

<sup>†</sup> Adjusted for: Age, race, occupation, BMI, waist circumference, smoking (past/current), physical activity, hypertension, diabetes, hypercholesterolemia, depression, aspirin use, ibuprofen use, acetaminophen use, and AMED adherence score.

Abbreviations:

RR: relative risk

BMI: body mass index

AMED: Alternate Mediterranean diet



**Table 3:**

Hearing loss and risk of incident subjective cognitive decline\* in the Health Professionals Follow-up Study, after excluding two questions that potentially could be influenced by hearing status

Hearing Status	Person-years	Cases	Age-adjusted RR (95% CI)	Multivariable-adjusted RR <sup>†</sup> (95% CI)
No difficulty	28623	1208	1.00 (ref)	1.00 (ref)
Mild hearing loss	14638	790	1.28 (1.17, 1.41)	1.26 (1.15, 1.38)
Moderate hearing loss	5438	326	1.34 (1.18, 1.52)	1.29 (1.13, 1.46)
Severe, no hearing aid	986	65	1.44 (1.12, 1.86)	1.37 (1.06, 1.77)
<b>p-trend</b>			<b>&lt;0.001</b>	<b>&lt;0.001</b>
Severe, use a hearing aid	3068	179	1.24 (1.05, 1.46)	1.18 (1.00, 1.39)

\* Incident subjective cognitive decline defined as Subjective Cognitive Function Score (SCF) - 1. Score does not include questions on “difficulty in understanding or following spoken instructions” or “trouble following a group conversation or plot in a TV program.”

<sup>†</sup> Adjusted for: Age, race, occupation, BMI, waist circumference, smoking (past/current), physical activity, hypertension, diabetes, hypercholesterolemia, depression, aspirin use, ibuprofen use, acetaminophen use, and AMED, adherence score.

Abbreviations:

MVRR: multivariable-adjusted relative risk

BMI: body mass index

AMED: Alternate Mediterranean diet