



Repositorio Institucional de la Universidad Autónoma de Madrid https://repositorio.uam.es

Esta es la **versión de autor** del artículo publicado en: This is an **author produced version** of a paper published in:

JAMA Otolaryngol: Head Neck Surg 147.11 (2021): 951-958

DOI: https://doi.org/10.1001/jamaoto.2021.2399

Copyright: © 2021 American Medical Association

El acceso a la versión del editor puede requerir la suscripción del recurso Access to the published version may require subscription

Association between hearing loss and impaired physical function, frailty and disability in older adults. A cross-sectional study

Subtitle: Hearing loss and physical function, frailty, and disability

Humberto Yévenes-Briones, MS¹; Francisco Félix Caballero, PhD^{1,*}; Ellen A Struijk, PhD¹; Jorge Rey-Martinez, MD, PhD²; Lourdes Montes-Jovellar, MD, PhD³; Auxiliadora Graciani, MD, PhD^{1,4}; Fernando Rodríguez-Artalejo, MD, PhD^{1,4}; Esther Lopez-Garcia, PhD^{1,4,*}

¹ Department of Preventive Medicine and Public Health. School of Medicine. Universidad Autónoma de Madrid-IdiPaz and CIBERESP (CIBER of Epidemiology and Public Health), Madrid, Spain.

² Neurotology Unit, ENT Department, Hospital Universitario Donostia, San Sebastián-Donostia, Spain.

³ Otolaryngology Department, Head and Neck Section, Hospital Universitario Ramón Y Cajal, Madrid, Spain.

⁴ IMDEA-Food Institute. CEI UAM+CSIC, Madrid, Spain.

* Corresponding author

Address for correspondence:

Francisco Félix Caballero, PhD Department of Preventive Medicine and Public Health School of Medicine Universidad Autónoma de Madrid C/ Arzobispo Morcillo, s/n 28029 Madrid, Spain E-mail: felix.caballero@uam.es

Esther Lopez-Garcia, PhD Department of Preventive Medicine and Public Health School of Medicine Universidad Autónoma de Madrid C/ Arzobispo Morcillo, s/n 28029 Madrid, Spain E-mail: esther.lopez@uam.es

Date of the revision: July, 23, 2021

Manuscript word count: 3426

1 Key points

2	Question: Is hearing loss associated with impaired physical function, frailty and
3	disability in older adults?

- 4 Findings: In this cross-sectional study of 1644 older adults, hearing loss at speech
- 5 frequency PTA (0.5, 1, 2, 4 kHz) was strongly associated with impaired physical
- 6 function, frailty and disability, independently of lifestyles, comorbidities, cognitive
- 7 status and social isolation. The results were similar for hearing loss at standard
- 8 frequency PTA (0.5, 1, 2 kHz).
- 9 Meaning: These results contribute to better characterize the nature of this association.

12 Abstract

13 **Importance:** Several studies have examined the association between hearing loss and physical function, with inconsistent results. Few of them used pure-tone thresholds and 14 15 considered the impact of important confounders in the association. 16 **Objective:** To examine the association between hearing loss and impaired lower extremity function, frailty syndrome and disability in older adults. 17 18 **Design:** Cross-sectional study with 1644 community-dwelling individuals aged 65 years and older (range 66 to 91 years). 19 20 Setting: The Seniors-ENRICA-2 is a cohort study that was established in 2015-2017 in 21 Spain. 22 Participants: Older adults of both genders with hearing threshold measurements and data on impaired lower extremity function, frailty syndrome and disability. 23 24 Exposures: Hearing loss defined as pure tone-average (PTA) >40 dB-HL in the better ear for standard frequency (0.5, 1, 2 kHz), speech frequency (0.5, 1, 2, 4 kHz) and high-25 frequency (3, 4, 8 kHz). 26 27 Main outcome and measure: Impaired lower extremity function was defined with the 28 Short Physical Performance Battery; the frailty syndrome was defined with five criteria 29 including weakness, slow walking speed, low physical activity, exhaustion, and weight 30 loss; and disability in instrumental activities of daily living (IADL) was evaluated with the Lawton and Brody scale. 31

32 **Results:** The prevalence of hearing loss was 13.6%. After adjustment for age, gender,

33 lifestyle, comorbidities, impaired cognition, and social isolation, hearing loss in

34 standard frequency was associated with impaired lower extremity function, with an

35	odds ratio (95% confidence interval) of 2.20 (1.25-3.88); the corresponding estimate for
36	the frailty syndrome was 1.85 (0.98-3.49); and for IADL disability was 2.25 (1.29-
37	3.94). When considering speech frequency PTA, hearing loss was also associated with
38	impaired function: 2.59 (1.57-4.28); for frailty syndrome: 1.85 (1.06-3.22); and for
39	IADL disability: 2.18 (1.32-3.60).
40	Conclusions and relevance: Hearing loss was associated with impaired lower
41	extremity function, frailty syndrome and IADL disability. This association should be
42	replicated and its mechanisms elucidated in further studies.

- **Keywords**: hearing loss, physical function, frailty syndrome, aging, instrumental
- 44 activities of daily living.

45 **INTRODUCTION**

46

morbidity. Aging is associated with a greater prevalence of impaired sensory, motor and 47 cognitive function, which lowers quality of life and increases dependency at this stage 48 49 of life.¹ One of the most prevalent sensory impairments in the older population is hearing loss,² which is the fifth leading cause of disability worldwide,³ and entails high 50 economic costs for the society.⁴ Hearing difficulties in older adults are undertreated, a 51 situation that results in several adverse consequences, such as increased risk of 52 depression⁵ and lower quality of life.⁶ 53 The association between hearing loss on physical function limitation, frailty and 54 disability is unclear. Some chronic diseases, including hypertension, type 2 diabetes and 55 cardiovascular disease have been associated with hearing loss⁷⁻⁹ and are also related to 56 disability.^{10,11} In addition, sensorineural hearing loss is closely related to impaired 57 cognition, and probably shares several age-related degenerative alterations,¹² so that 58 cognitive impairment may lead to physical function limitation.¹³ Hearing loss in the 59 older adults may also restrict social participation, which is a determinant of disability.¹⁴ 60 In fact, hearing impairment might be an early physiological marker of physical function 61 limitation.¹⁵ 62

Increased life expectancy has been accompanied by a heavy burden of late-life

Previous studies have examined the association between hearing loss and physical function, frailty syndrome and disability with inconsistent results.¹⁶⁻²⁴ Research to better characterize hearing capacity in relation to functional capacity is needed, as well as to better understand the role of comorbidities, cognitive impairment, and social isolation in this relation. Therefore, our objective was to examine the association between hearing loss, using pure-tone average of air conduction hearing thresholds in a wide frequency

- range, in association with impaired lower-extremity function, frailty and disability, in a
- 70 well-characterized population of older adults.

72 METHODS

73 *Study design and participants*

We analyzed data from the Seniors-ENRICA-2 study, a cohort study of 3273
community-dwelling individuals aged 65 years and older. Study participants were
residents of the city of Madrid and four large surrounding cities holding a national
health card. Participants were recruited in 2015-2017, using a random sampling
stratified by gender and district. In 2019, a new data collection was conducted, updating
baseline information and adding new measures, including the assessment of hearing
function.

At the baseline and follow-up, data were collected in three stages, (a) telephone 81 82 interview for lifestyles, morbidity, health status, use of health care information; (b) a 83 first home visit to perform a physical examination, including an audiogram, and collect blood and urine samples; and (c) a second home visit to collect information on habitual 84 diet and place an accelerometer in the wrist of the participants. The procedures, 85 instruments and questionnaires were like those used in the Seniors-ENRICA I cohort.²⁵ 86 87 In particular, for the performance of the audiograms, interviewers were provided with a 88 specific protocol for an optimal realization, and training sessions were programmed. All 89 study participants provided written informed consent, and the Clinical Research Ethics 90 Committee of 'La Paz' University Hospital in Madrid approved the study. 91 A total of 1894 participants provided data in 2019. We selected those who had a hearing 92 assessment that followed the specified protocol and information for the covariates of 93 interest, so that analyses were performed with 1644 persons. Participants who rejected 94 to perform the audiology were older, with more comorbidity, and with more prevalence

95 of social isolation than participants who accepted to be examined.

96

97 Hearing assessment

Hearing was assessed by measuring air conduction thresholds using a hearing test at 98 99 frequencies 0.5, 1, 2, 3, 4 and 8 kilohertz (kHz) in both ears. The hearing test was performed with AudCal, an application for iPhone and iPad. The evaluation was carried 100 101 out in a quiet environment, face to face with the evaluator, with the mobile screen made 102 only visible for the evaluator. The headphones used were wired in-ear headphones, 103 distributed in iPhone packages (Earpods[®]). The earbuds were fitted under the standard headphones. We began evaluating the frequency 1 kHz at 0 dB-HL, increasing the 104 105 sound in 5 dB-HL intervals until the participant started hearing the stimulus. After the hearing threshold was identified at that frequency, the other frequencies were completed 106 107 for that ear. The same procedure was carried out for the other ear. This application has been shown high sensitivity and specificity in both ears with respect to the gold 108 109 standard test, tonal audiometry in a soundproof booth, and has shown a high intra-class 110 correlation (r = 0.93) with the standard evaluation, using an ISO-standard audiometer and standard headphones in the Spanish population.²⁶ 111

112 To determine hearing capacity in our study population, we calculated three pure-tone 113 averages (PTAs) according to different frequency ranges: the first one by using the 114 standard PTA definition (0.5, 1 and 2 kHz); the second one considering the speech 115 frequency (0.5, 1, 2 and 4 kHz); and the third one considering the high-frequency (3, 4 116 and 8 kHz). We defined hearing loss in relation to three cut-off points, according to the 117 American Speech-Language-Hearing Association: >15 dB-HL, indicating slight to 118 profound hearing loss; >25 dB-HL reflecting mild to profound hearing loss; and >40 dB-HL, which indicates moderate to profound hearing loss.²⁷ We considered the hearing 119

threshold of the better ear, following the World Health Organization (WHO) 120

recommendations.²⁸ 121

131

122 *Physical function, frailty syndrome and disability*

Physical function was measured using the Short Physical Performance Battery (SPPB), which 123 assesses gait speed, the degree of ability to get up from a chair, and balance assessment. Gait 124 speed was calculated as the shortest time, in seconds (s), to complete two times a walking 125 126 distance of 2.44 meters at a normal pace. The ability to rise from a chair was evaluated by asking the participants to stand up and sit down five consecutive times without using their 127 hands. For the standing balance test, participants were asked to stand in three progressively 128 challenging positions. Each component was scored on a four-point scale, and the total SPPB 129 score was calculated by the sum of the components, ranging from 0 (worst) to 12 (best 130 performance). Impaired lower extremity function was defined as a total score ≤ 6 points.²⁹

The frailty syndrome was assessed according to the Fried criteria,³⁰ which defines frailty 132 133 as the presence of at least three of the following criteria: 1) unintentional weight loss of 134 \geq 4.5 kg in the preceding year; 2) exhaustion, based on an affirmative response to any of the following questions from the Centre for Epidemiologic Studies Depression Scale: 'I 135 felt that anything I did was a big effort' or 'I felt that I could not get going' at least 3 or 136 4 days a week; 3) low physical activity, defined as walking ≤ 2.5 h/week for males and 137 \leq 2.0 h/week for females; 4) slow walking speed, defined as the lowest cohort-specific 138 quintile of gait speed over 2.44 m, adjusted for gender and height; 5) and muscle 139 140 weakness, set as the cohort-specific lowest quintile of grip strength, measured with a Jamar dynamometer in the dominant hand, adjusted for gender and body mass index. 141 Participants were classified as frail if they met at least 3 of the criteria. 142

To evaluate disability in instrumental activities of daily living (IADL) we used the Lawton and 143 144 Brody scale, which evaluates complex everyday functional competences, such as shopping, doing housework, using the phone, doing laundry, preparing meals, using public transportation, 145 managing money, and taking medications.³¹ Each domain was rated dichotomously (0=capable 146 in some degree, 1=incapable). Due to the idiosyncrasy of this population, the score for men was 147 148 calculated without considering the tasks housework, laundry and preparing meals, so it ranged 0-5, whereas for women, the score included all the tasks and ranged 0-8. The score was directly 149 150 proportional to the degree of dependence; disability was defined when there was a need of assistance for performing two or more IADL.³² 151

152 *Other variables*

153 We collected self-reported information on age, educational level, tobacco and alcohol

154 consumption. For the measurement of physical activity (metabolic equivalent tasks-

155 h/week), an ActiGraph GT9X accelerometer was used and participants were asked to

use the accelerometer for seven consecutive days.³³ We calculated the body mass index

157 (BMI) as the weight (kg) divided by the squared height (m^2) measured under

158 standardized conditions. Diet quality was evaluated according to the adherence to the

159 Mediterranean Diet using the Mediterranean Diet Adherence Screener (MEDAS),

160 whose score ranges from 0 to 14, and a higher score reflects a greater adherence to this

diet.³⁴ The hours of sleep were evaluated with the question: *Can you tell me*,

162 *approximately, how long do you usually sleep?* To assess sedentary behaviors, we

163 considered information about television viewing (h/week). Besides, we collected the

164 number of habitual drug treatments currently used. Since the consumption of ototoxic

165 medication was very low (<1.1% reported consumption of aspirin, acetaminophen or

166 ibuprofen), we added these drugs to the total number. We defined hypertension as

systolic blood pressure \geq 140 mm Hg or diastolic blood pressure \geq 90 mm Hg or being

under antihypertensive medication. In addition, diabetes was defined as fasting glucose
levels ≥126 mg/dL or use of antidiabetic medication.

170 Participants reported if they had received a physician-based diagnosis of cancer, 171 cardiovascular diseases (heart attack, stroke, heart failure or atrial fibrillation) and musculoskeletal diseases (arthritis, osteoarthritis or hip fracture). We also evaluated the 172 cognitive status of the participants with the Mini Mental State Examination (MMSE), in 173 174 which orientation, memory, fixation, calculation and language construction were 175 measured; impaired cognition was defined as a score <23. Lastly, we evaluated the 176 social participation through 5 questions: 1) How often do you see or talk on the phone with family members (other than those who live with you)?; 2) How often do you see or 177 178 talk on the phone with friends or neighbors?; 3) How much time do you usually spend alone at home?; 4) How often do you attend church or religious services?; and 5) How 179 180 often do you attend senior club meetings, centers or associations to which you belong? Each response was scored between 1 and 5, then we added the score of each question 181 182 and created a scale with a range from 5 to 25, with a higher score indicating greater social participation.³⁵ Social isolation was defined a score below the median (<17). 183

184 Statistical analysis

185 We assessed differences in sociodemographic characteristics, lifestyles, comorbidities, 186 cognitive function, and social participation between the categories of hearing status. The 187 unpaired *t*-test or Chi-square test were used to compare continuous or categorical 188 variables, as appropriate across the categories of hearing loss. Then, we used logistic 189 regression to examine the association of moderate to profound hearing loss, at standard 190 PTA, speech frequency and high-frequency PTA, with impaired lower extremity 191 function, frailty syndrome and IADL disability. The estimates of the associations were expressed as odds ratios and 95% confidence interval. We built three logistic regression 192

models: 1) adjusted for age and gender; 2) additionally adjusted for educational level 193 194 (primary or less, secondary and university), smoking status (current smoker, former 195 smoker, never smoker), current alcohol drinker, physical activity (tertiles of METsh/wk), BMI (tertiles of kg/m²), MEDAS (tertiles of the score), hours of daily sleep 196 197 (tertiles), time viewing television (tertiles of h/week), and number of habitual drug 198 treatments; 3) a third model additionally adjusted for hypertension, cancer, diabetes, 199 cardiovascular diseases, musculoskeletal diseases, impaired cognitive function, and 200 social isolation. We also modeled the association of the continuous PTA (per 5 dB-HL 201 increment) in association with the studied outcomes. An analysis between hearing loss 202 and individual subscales of the SPPB was performed; the cutoff point to define 203 difficulty to raise from a chair, slow gait, and balance impairment was a score of ≤ 3 in 204 each scale. 205 As a sensitivity analysis, we replicated the analyses defining hearing loss as PTA >25

205 The a sensitivity analysis, we repredice the analyses defining nouring 1000 as 1 111 > 20

dB-HL in the better ear, in the three frequency ranges, to understand if the association

- varied for milder degrees of severity of hearing loss. The analyses were performed with
- the STATA Software (version 15.0; Stata Corp., College Station).

209 **RESULTS**

Among study participants, 49.5% were women and the mean age was 73.8 ± 4.3 years 210 211 (range: 66 to 91 years). The frequency of hearing loss according to the different 212 definitions and cut-off points is presented in Table 1. We observed a high frequency of slight and mild hearing loss, in the three types of frequencies. For moderate hearing 213 loss, the prevalence at standard PTA was 9.3% for the total population, 9.9% for men 214 215 and 8.6% for women; at speech frequency PTA, the percentage was 13.6% (15.2% for men and 12.1% for women); and at high-frequency PTA, 45.1% (50.4% for men and 216 217 39.7% for women). The participants' characteristics according to hearing status are presented in Table 2. In 218 comparison with participants with normal hearing, those with moderate to profound 219 220 hearing loss were older, reported lower levels of physical activity, had lower adherence 221 to the Mediterranean diet, and spent more time watching television. In addition, they 222 were treated with more drugs, and showed a higher prevalence of diabetes, 223 cardiovascular diseases, and impaired cognitive function. The association of hearing loss with impaired lower extremity function, the frailty 224 225 syndrome and IADL disability is shown in Table 3. For standard PTA, hearing loss was 226 associated with all the three outcomes considered, in the models adjusted for age and 227 gender. The associations were slightly modified after further adjustment for socio-228 demographic and lifestyle characteristics, comorbidities, impaired cognitive function 229 and social isolation: for impaired lower extremity function, the odds ratio (95% 230 confidence interval) was 2.20 (1.25-3.88); for the frailty syndrome: 1.85 (0.98-3.49); 231 and for IADL disability: 2.25 (1.29-3.94). When using speech frequency PTA, hearing loss was associated with the outcomes, and the multivariable adjustment barely 232 modified the estimates: for impaired lower extremity function: 2.59 (1.57-4.28); for the 233

- frailty syndrome: 1.85 (1.06-3.22); and for IADL disability: 2.18 (1.32-3.60). Lastly,
- when we used high-frequency PTA, associations were found between hearing loss and

frailty and IADL disability in the less adjusted models; however, when we adjusted for

- additional confounders, no association was observed.
- 238 Continuous PTA in association with the outcomes showed a direct association (etable
- 1). More specific analyses examining the association for the subscales in the SPPB
- showed that difficulty to raise from a chair and balance impairment were associated
- with hearing loss after adjustment for all confounders (**etable 2**). Finally, when we
- focused on mild hearing loss, the associations were similar than those found for
- 243 moderate hearing loss (**etable 3**).

244 **DISCUSSION**

In this study of community-dwelling older adults, moderate to profound hearing loss at
standard and speech frequency PTA was associated with impaired lower extremity
function and IADL disability, independently of socio-demographic and lifestyle
characteristics, comorbidities, cognitive impairment, and social isolation. Moderate to
profound hearing loss at speech frequency PTA was also associated with the frailty
syndrome after adjustment for these confounders. Similar results were also found for
milder hearing loss.

252 In this population, 79.6 to 91.1% (depending on the PTA used) of the participants had 253 some degree of hearing loss. These figures are higher than the most recent data from the Spanish National Health Survey 2017,³⁶ where 34% of people 65-74 y, 49% of people 254 255 75-84 y, and 70% of people \geq 85 y reported some hearing impairment. This discrepancy reflects the fact that self-reported hearing impairment may underestimate the degree of 256 257 hearing loss, particularly for milder loss. On the other hand, the prevalence of moderate 258 to profound hearing loss in our study (9.3% for standard PTA, 13.6% for speech frequency and 45.1% for high-frequency PTA) was lower than in the United States of 259 America (USA) among people aged \geq 70 years (16.5, 26.5 and 74.1%, respectively).³⁷ 260 261 Reasons for the lower prevalence in the Spanish population are unknown. 262 Regarding the association between hearing loss and impaired lower extremity function, our results were consistent with those found by Bang et al.;¹⁶ in a cross-sectional study, 263 264 defining PTA at 0.5, 1, 2 and 3 kHz, they found that hearing loss (with a hearing threshold >40 dB-HL) was linked to postural instability, which is a key component of 265 266 the SPPB score. Furthermore, our results are consistent with the Health, Aging and Body Composition study, a prospective cohort of 2190 participants, where moderate 267 hearing loss was associated with lower SPPB.³⁷ In addition, Lin et al.¹⁷ using data from 268

the US National Health and Nutrition Examination Survey observed a strong association 269 270 between hearing loss and higher risk of falls. In two recent papers by Martinez-271 Amezcua et al., with data from the Baltimore Longitudinal Study of Aging and the Atherosclerosis Risk in Communities study, both in the USA, longitudinal analyses 272 273 showed that participants with hearing loss presented faster declines in physical function over time, compared with those with normal hearing.^{19,20} The same authors found that 274 gait speed and balance were independently associated with hearing impairment.²⁰ This 275 276 result is different to our findings, where the chair stand test showed a significant association but not gait speed. 277

278 We also observed an association between hearing loss and the frailty syndrome, as did the meta-analysis by Tan et al.²¹ However, although the meta-analysis included studies 279 at low and moderate risk of bias, more than half of the studies used self-reported 280 281 measures of hearing loss, which could be susceptible to recall bias. Also, only two studies used audiometric measures to determine hearing loss and none considered 282 283 lifestyles, comorbidities and social isolation simultaneously in their analyses. Regarding 284 the association between hearing loss and IADL disability, our results are consistent with the systematic review carried out by Lin et al.²³ We have extended the above results by 285 286 considering the impact of comorbidities, cognitive function, and social isolation to this association. 287

Hearing loss in older adults can be due to multiple causes that affect the peripheral
auditory system. Among the most common causes are degenerative processes associated
with age.³⁸ For example, adults with chronic vestibular loss have shown gait deficits.³⁹
Vestibular function is responsible for balance, a key component of physical function.
Thus, the age-related deterioration of the hair cells that participate in both, the vestibular
system and auditory system may imply that hearing loss is a surrogate of vestibular

dysfunction,⁴⁰ and then, the association observed in this study may not be causal. Other 294 295 mechanisms include the close relation between movement and coordination with the 296 acoustic inputs from the environment; hearing difficulty would impede an appropriate physical response.¹⁵ The presence of comorbidities may also indicate that several 297 298 underlying common mechanisms are damaged, such as the modulation of response to stress, impaired immune response, and impaired cardiometabolic function.⁴¹ Lastly, 299 other non-causal explanations include the social isolation related to hearing loss, which 300 301 can lead to a reduction in physical activity, and a subsequent deterioration of the physical function.¹⁵ We adjusted our analyses for the presence of comorbidity as well as 302 303 for social isolation in an effort to exclude these non-causal mechanisms.

304 The main limitation of our study was the cross-sectional design, so we could not attribute directionality to the observed associations. In addition, although we used pure-305 306 tone audiometry to assess hearing function, which has been proposed as the optimal metric in both, clinical settings and epidemiological studies,⁴² this was performed with a 307 308 portable device in at-home environment. Therefore, bias related to environmental noise 309 and interviewer performance, as well as bias related to the instrument, cannot be 310 discarded. Moreover, the number of cases of hearing loss for standard PTA was small. 311 Lastly, we did not measure vestibular function, and it would have been relevant to 312 determine its impact on the study associations. On the other hand, well established 313 measurement tools such as the SPPB and the IADL scale were used, as well as the Fried 314 criteria to define the frailty syndrome. Also, the analyses were adjusted for main 315 potential confounders, including comorbidity, cognitive impairment and social isolation, which suggests that hearing impairment may be a predictor of deterioration of physical 316 317 function. Finally, given that participants who accepted to perform audiometry were

- different than those who rejected the test, the results obtained cannot be extrapolated to
- 319 a general population of community-dwelling older adults.
- 320 In conclusion, hearing loss was associated with impaired lower extremity function, the
- 321 frailty syndrome and IADL disability, all common conditions in older adults.
- 322 Longitudinal studies are necessary to establish causal relationships between hearing loss
- and these outcomes.

325 Acknowledgments

- 326 Conflict of Interest and Funding Disclosure: the authors declare that they have no327 conflicts of interest.
- **Sources of Support:** This work was supported by FIS grants 20/1040 and 19/319
- 329 (Instituto de Salud Carlos III, State Secretary of R+D+I, and FEDER/FSE).

330 Authors' contributions

- 331 The authors' contributions were as follows: HYB, FFC and ELG: designed the research;
- HYB and FFC: performed the statistical analyses; all authors: contributed to
- interpretation of the results; HYB, FFC and ELG: drafted the manuscript; ELG:
- supervised the conduct of research and had primary responsibility for final content; and
- all authors: reviewed the manuscript for important intellectual content, and read and

approved the final manuscript.

REFERENCES

1. Partridge L, Deelen J, Slagboom PE. Facing up to the global challenges of ageing. Nature. 2018;561(7721):45-56.

2. Agrawal Y, Platz EA, Niparko JK. Prevalence of hearing loss and differences by demographic characteristics among US adults: data from the National Health and Nutrition Examination Survey, 1999-2004. Arch Intern Med. 2008 Jul 28;168(14):1522-

3. Vos T, Allen C, Arora M, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388(10053):1545-602.

4. Binti Ida Umaya. Global costs of unaddressed hearing loss and cost-effectiveness of interventions: a WHO report. Universitas Nusantara PGRI Kediri. 2017.

Lawrence BJ, Jayakody DMP, Bennett RJ, Eikelboom RH, Gasson N, Friedland PL.
 Hearing loss and depression in older adults: a systematic review and meta-analysis.
 Gerontologist. 2020; 60(3):e137-e154.

6. Tseng Y-C, Liu SH-Y, Lou M-F, Huang G-S. Quality of life in older adults with sensory impairments: a systematic review. Qual Life Res. 2018; 27(8):1957-71.

7. Lin BM, Curhan SG, Wang M, Eavey R, Stankovic KM, Curhan GC. Hypertension, Diuretic Use, and Risk of Hearing Loss. Am J Med. 2016 Apr;129(4):416-22.

8. Kim MB, Zhang Y, Chang Y, et al. Diabetes mellitus and the incidence of hearing loss: a cohort study. Int J Epidemiol. 2017 Apr 1;46(2):717-726.

9. Wattamwar K, Qian ZJ, Otter J, et al. Association of Cardiovascular Comorbidities with Hearing Loss in the Older Old. JAMA Otolaryngol Head Neck Surg. 2018 Jul 1;144(7):623-629.

10. Buford TW. Hypertension and aging. Ageing Res Rev. 2016/02/01. 2016Mar;26:96-111.

11. Koye DN, Shaw JE, Magliano DJ. Diabetes and disability in older Australians: The Australian Diabetes, Obesity and Lifestyle (AusDiab) study. Diabetes Res Clin Pract. 2017;126:60-7.

12. Singer L, Green M, Rowe F, Ben-Shlomo Y, Kulu H, Morrissey K. Trends in multimorbidity, complex multimorbidity and multiple functional limitations in the ageing population of England, 2002-2015. J Comorbidity. 2019 Sep 4;9:2235042X19872030-2235042X19872030.

13. Robertson DA, Savva GM, Kenny RA. Frailty and cognitive impairment--a review of the evidence and causal mechanisms. Ageing Res Rev. 2013 Sep;12(4):840-51

14. Gopinath B, Hickson L, Schneider J, et al. Hearing-impaired adults are at increased risk of experiencing emotional distress and social engagement restrictions five years later. Age Ageing. 2012 Sep 1;41(5):618–23.

15. Brenowitz WD, Wallhagen MI. Does Hearing Impairment Affect PhysicalFunction?: Current Evidence, Potential Mechanisms, and Future Research Directionsfor Healthy Aging. JAMA Netw Open. 2021 Jun 1; 4(6):e2114782.

16. Bang S-H, Jeon J-M, Lee J-G, Choi J, Song J-J, Chae S-W. Association Between Hearing Loss and Postural Instability in Older Korean Adults. JAMA Otolaryngol Neck Surg. 2020 Jun 1;146(6):530-4.

17. Lin FR, Ferrucci L. Hearing loss and falls among older adults in the United States. Arch Intern Med. 2012 Feb 27;172(4):369-71.

 Cosiano MF, Jannat-Khah D, Lin FR, Goyal P, McKee M, Sterling MR. Hearing Loss and Physical Functioning Among Adults with Heart Failure: Data from NHANES. Clin Interv Aging. 2020; May 6;15:635-43.

19. Martinez-Amezcua P, Kuo PL, Reed NS, Simonsick EM, Agrawal Y, Lin FR, Deal JA, Ferrucci L, Schrack JA. Association of hearing impairment with higher level physical functioning and walking endurance: Results from the Baltimore Longitudinal Study of Aging (BLSA). J Gerontol A Biol Sci Med Sci. 2021 May 18:glab144. doi: 10.1093/gerona/glab144. Online ahead of print.

20. Martinez-Amezcua P, Powell D, Kuo PL, Reed NS, Sullivan KJ, Palta P, Szklo M, Sharrett R, Schrack JA, Lin FR, Deal JA. Association of Age-Related Hearing Impairment With Physical Functioning Among Community-Dwelling Older Adults in the US. JAMA Netw Open. 2021 Jun 1;4(6):e2113742.

21. Tan BKJ, Man REK, Gan ATL, et al. Is Sensory Loss an Understudied Risk Factor for Frailty? A Systematic Review and Meta-analysis. J Gerontol A Biol Sci Med Sci.2020 Nov 13;75(12):2461-2470.

22. Sardone R, Castellana F, Bortone I, et al. Association Between Central and Peripheral Age-Related Hearing Loss and Different Frailty Phenotypes in an Older Population in Southern Italy. JAMA Otolaryngol Neck Surg. 2021 Feb 11; Available from: https://doi.org/10.1001/jamaoto.2020.5334 23. Lin T-C, Yen M, Liao Y-C. Hearing loss is a risk factor of disability in older adults: A systematic review. Arch Gerontol Geriatr. 2019;85:103907.

24. Mueller-Schotte S, Zuithoff NPA, van der Schouw YT, Schuurmans MJ,
Bleijenberg N. Trajectories of Limitations in Instrumental Activities of Daily Living in
Frail Older Adults With Vision, Hearing, or Dual Sensory Loss. J Gerontol A Biol Sci
Med Sci. 2019 May;74(6):936-42.

25. Rodríguez-Artalejo F, Graciani A, Guallar-Castillón P, et al. Rationale and methods of the study on nutrition and cardiovascular risk in Spain (ENRICA). Rev Esp Cardiol.
2011; 64(10):876-882.

26. Larrosa F, Rama-Lopez J, Benitez J, et al. Development and evaluation of an audiology app for iPhone/iPad mobile devices. Acta Otolaryngol. 2015; 135(11):1119-27.

27. Degree of Hearing Loss [Internet]. [cited 2021 Mar 2]. Available from: https://www.asha.org/public/hearing/degree-of-hearing-loss/

28. WHO Report of the Informal Working Group On Prevention Of Deafness And Hearing Impairment Programme Planning. Geneva, 1991.

29. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive Models, and value of gait speed alone compared with the short physical performance battery. Journals Gerontol Ser A. 2000; 55(4):M221-31.

30. Fried LP, Tangen CM, Walston J, et al. Frailty in Older Adults: Evidence for a Phenotype. Journals Gerontol Ser A. 2001;56(3):M146-57.

31. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969; 9(3):179-186.

32. Machado-Fragua MD, Struijk EA, Graciani A, Guallar-Castillon P, Rodríguez-Artalejo F, Lopez-Garcia E. Coffee consumption and risk of physical function impairment, frailty and disability in older adults. Eur J Nutr. 2019; 58(4):1415-27.

33. Cabanas-Sánchez V, Esteban-Cornejo I, Migueles JH, et al. Twenty four-hour activity cycle in older adults using wrist-worn accelerometers: The seniors-ENRICA-2 study. Scand J Med Sci Sport. 2020 Apr;30(4):700-708.

34. Schröder H, Fitó M, Estruch R, et al. A short screener is valid for assessingMediterranean Diet adherence among older Spanish men and women. J Nutr. 2011;141(6):1140-5.

35. Levasseur M, Richard L, Gauvin L, Raymond É. Inventory and analysis of definitions of social participation found in the aging literature: Proposed taxonomy of social activities. Soc Sci Med. 2010;71(12):2141-9.

36. Spanish Statistical Office [Internet]. [cited 2021 Mar 11]. Available from: https://www.ine.es/en/index.htm

37. Lin FR, Thorpe R, Gordon-Salant S, Ferrucci L. Hearing Loss Prevalence and Risk Factors Among Older Adults in the United States. Journals Gerontol Ser A. 2011 May 1;66A(5):582-90.

38. Jayakody DMP, Friedland PL, Martins RN, Sohrabi HR. Impact of Aging on the Auditory System and Related Cognitive Functions: A Narrative Review. Front Neurosci. 2018 Mar 5; 12:125.

39. Grove CR, Whitney SL, Pyle GM, Heiderscheit BC. Instrumented Gait Analysis to Identify Persistent Deficits in Gait Stability in Adults With Chronic Vestibular Loss. *JAMA Otolaryngol Head Neck Surg*. Published online July 01, 2021. doi:10.1001/jamaoto.2021.1276

40. Cunningham LL, Tucci DL. Hearing loss in adults. N Engl J Med. 2017. Dec 21;377(25):2465-2473.

41. Spankovich C., Le Prell C. G. Healthy diets, healthy hearing: National Health and Nutrition Examination Survey, 1999-2002. Int J Audiol. 2013. 52:369-76.

42. Lin FR, Reed NS. The Pure-Tone Average as a Universal Metric—Knowing Your Hearing. JAMA Otolaryngol Head Neck Surg. 2020 Dec 23. doi:
10.1001/jamaoto.2020.4862. Online ahead of print.

Table 1. Prevalence of hearing loss in the participants according to the definitions of hearing loss, by gender.^{1,2} N=1644

	All Participants			Men			Women		
	>15 dB-HL ³	$>25 \text{ dB-HL}^4$	$>40 \text{ dB-HL}^5$	>15 dB-HL ³	$>25 \text{ dB-HL}^4$	$>40 \text{ dB-HL}^5$	>15 dB-HL ³	>25 dB-HL ⁴	>40 dB-HL ⁵
Standard PTA 0.5, 1, 2 kHz, n (%)	1308 (79.6)	659 (40.1)	152 (9.3)	658 (79.2)	333 (40.1)	82 (9.9)	650 (80.0)	326 (40.1)	70 (8.6)
Speech frequency PTA 0.5, 1, 2, 4 kHz, n (%)	1388 (84.4)	866 (52.7)	224 (13.6)	715 (86.0)	465 (56.0)	126 (15.2)	673 (82.8)	401 (49.3)	98 (12.1)
High-frequency PTA _{3, 4, 8 kHz} , n (%)	1498 (91.1)	1259 (76.6)	742 (45.1)	768 (92.4)	668 (80.4)	419 (50.4)	730 (90.0)	591 (72.7)	323 (39.7)

PTA: pure total average.

¹Hearing loss in the better ear of the participants.

²The prevalence values are represented as number of cases and percentage in each definition of hearing loss.

³ Definition from slight to profound hearing loss.

⁴ Definition from mild to profound hearing loss.

⁵ Definition from moderate to profound hearing loss.

Table 2. Participants' characteristics, at different frequency ranges (N=1644)^{1,2,3}

			Hearin	ng status		
	Standard PTA 0.5,1,2 kHz		Speech frequen	ncy PTA 0.5,1,2,4 kHz	High-frequency PTA 3,4,8 kHz	
-	Normal	Hearing loss	Normal	Hearing loss	Normal	Hearing loss
N	1,492	152	1,420	224	902	742
Age, y	73.5±4.2	$76.8 \pm 4.8^{\circ}$	73.4±4.1	$76.4 \pm 4.8^{\circ}$	72.7±3.9	75.1±4.5°
Educational level; primary or less, %	58.9	65.1	59.1	61.6	57.8	61.5
Current smoker, %	8.9	5.3	9.1	4.5	9.0	7.8
Current alcohol drinker, %	33.4	29.6	33.0	33.0	32.9	33.2
Physical activity, MET-h/week	23.7±8.9	21.1±9.7°	23.9±8.8	20.2±9.4°	24.6±8.7	22.0±9.1°
Body mass index, kg/m ²	27.6±4.4	28.1±4.9	27.6±4.4	28.1±4.8	27.5±4.5	27.8±4.4
Adherence to the MEDAS score	7.3±1.7	6.9 ± 1.7^{a}	7.3±1.7	$6.9 \pm 1.6^{\circ}$	7.3±1.7	7.2±1.6
Hours of daily sleep	6.7±1.3	6.6±1.5	6.7±1.3	6.7±1.5	6.7±1.2	6.7±1.4
Television viewing, h/week	24.6±12.8	28.4±14.7°	24.5±12.7	27.7±14.8°	24.3±12.6	25.7±13.6 ^a
Number of habitual drugs	4.1±3.0	5.1±3.3°	4.0±3.0	5.1±3.2°	3.7±2.9	4.7 ± 3.1^{a}
Chronic diseases,						
Hypertension, %	68.2	71.7	68.2	70.5	66.1	71.6 ^a
Diabetes, %	22.7	32.2 ^b	22.1	32.6 ^b	20.5	27.2 ^b
Cancer, %	10.7	12.5	10.8	11.6	10.8	11.1
Cardiovascular diseases*, %	7.3	7.9	6.8	10.7ª	6.2	8.8 ^a
Musculoskeletal diseases ^{**} , %	48.1	50.0	48.2	49.1	48.5	48.1
Impaired cognitive function, %	2.2	5.3ª	2.1	4.9^{a}	2.1	3.0
Social isolation, %	43.4	42.1	43.7	40.6	44.0	42.5
Impaired lower extremity function	6.0	17.8°	5.4	17.9 ^c	4.4	10.2 ^c
(SPPB score ≤ 6), %						
Frailty syndrome ⁴ , %	4.2	11.8 ^c	3.9	11.2 ^c	3.1	7.1 ^c
IADL disability ⁵ , %	5.8	19.1°	5.4	17.4°	4.6	10.1°

¹ Defined as normal (PTA \leq 40 dB-HL) and as moderate to profound hearing loss (PTA >40 dB-HL) in the better ear.

² Abbreviations. PTA: pure-tone average; METs: metabolic equivalent tasks; MEDAS: Mediterranean Diet Adherence Screener; SPPB: Short Physical Performance Battery; IADL: Instrumental Activities of Daily Living.

 3 Values are means \pm SD unless otherwise indicated. P values based on Student's *T* test, for continuous variables or chi-square test for qualitative variables.

⁴The diagnosis of the frailty syndrome was based on the Fried criteria (weakness, low speed, low physical activity, exhaustion, and weight loss).

⁵ IADL disability was defined as need of assistance for performing two or more IADL.

^{*} Includes heart attack, stroke, heart failure and atrial fibrillation.

**Includes arthritis, osteoarthritis and hip fracture.

^ap<0.05 ^bp<0.01 ^cp<0.001

	Hearing loss, standard PTA _{0.5,1,2 kHz}	Hearing loss, speech frequency PTA _{0.5,1,2,4 kHz}	Hearing loss, high- frequency PTA 3,4,8 kHz
	Odds ratio (95% confidence interval)	Odds ratio (95% confidence interval)	Odds ratio (95% confidence interval)
Impaired lower extremity function			
Number of cases	27	40	76
Model 1	2.14 (1.28-3.58)*	2.59 (1.64-4.09)*	1.75 (1.14-2.68)*
Model 2	2.06 (1.18-3.60)*	2.48 (1.52-4.05)*	1.47 (0.93-2.33)
Model 3	2.20 (1.25-3.88)*	2.59 (1.57-4.28)*	1.50 (0.95-2.39)
Frailty syndrome			
Number of cases	18	25	53
Model 1	2.22 (1.23-4.00)*	2.34 (1.37-3.98)*	2.00 (1.22-3.29)*
Model 2	1.90 (1.02-3.54)*	1.88 (1.09-3.26)*	1.59 (0.95-2.65)
Model 3	1.85 (0.98-3.49)*	1.85 (1.06-3.22)*	1.59 (0.95-2.67)
IADL disability			
Number of cases	29	39	75
Model 1	2.39 (1.45-3.94)*	2.41 (1.53-3.78)*	1.63 (1.07-2.49)*
Model 2	2.21 (1.30-3.78)*	2.18 (1.35-3.51)*	1.29 (0.83-2.03)
Model 3	2.25 (1.29-3.94)*	2.18 (1.32-3.60)*	1.33 (0.83-2.12)

Table 3. Association between moderate to profound hearing loss and impaired lower extremity function, frailty syndrome and IADL disability. N=1644.

Abbreviations: PTA: pure total average; IADL: Instrumental Activities of Daily Living.

Hearing loss defined as PTA >40 dB-HL in the better ear.

* Statistically significant at alpha = 0.05

Model 1: adjusted for age and gender.

Model 2: Additionally adjusted for educational level (primary or less, secondary and university), smoking status (current smoker, former smoker, never smoker), current alcohol drinker, physical activity (tertiles of METs-h/wk, BMI (tertiles of kg/m²), MEDAS (tertiles of score), hours of daily sleep (tertiles), time viewing television (tertiles, h/week) and number of drugs currently used.

Model 3: Additionally adjusted for hypertension, diabetes, cancer, cardiovascular diseases, musculoskeletal diseases, impaired cognitive function and social isolation.