Original Research

Mediation Pathways from Lifestyle to Hearing Impairment: The Role of Inflammatory and Metabolic Biomarkers in a Prospective Cohort Study

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ABSTRACT

Background: The mechanisms linking lifestyle to hearing impairment remain unclear. This study seeks to examine the associations of lifestyle factors with hearing impairment and to quantify the mediating effects of inflammatory and metabolic biomarkers in these associations.

Methods: In 441,844 UK Biobank participants, lifestyle was scored across seven behaviors. Biomarkers included an inflammatory score, metabolic score for insulin resistance (METS-IR) and their individual components. Cox proportional hazards regression was used to examine the independent associations of lifestyle and biomarkers with hearing impairment. Mediation analysis was then performed to evaluate the mediating role of these biomarkers.

Results: Over a median follow-up of 14.22 years, 20,743 incident hearing impairment cases were documented. Adherence to an ideal lifestyle was associated with a 14% lower risk (HR = 0.86, 95% CI: 0.82–0.90) compared with a poor lifestyle, while elevated inflammatory score (HR = 1.03, 95% CI: 1.02–1.04) and metabolic score for insulin resistance (HR = 1.08, 95% CI: 1.06–1.10) significantly increased risk. Mediation analyses showed that inflammatory and metabolic biomarkers collectively explained 1%–20% of the lifestyle-hearing impairment association, with metabolic factors (body mass index, high-density lipoprotein cholesterol) contributing most substantially.

Conclusion: Adherence to a healthy lifestyle was associated with lower hearing impairment risk, with inflammation and metabolic dysregulation acting as partial mediators. This offers mechanistic insights and supports lifestyle-based interventions for hearing impairment prevention.

KEYWORDS

hearing impairment, inflammation, metabolism, lifestyle, UK biobank

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1 Introduction

Hearing impairment represents a prevalent public health challenge across the life course, affecting not only older adults but also increasingly mid-life and younger populations. Currently, age-related hearing impairment was the third largest contributor to the global disability burden, ranking first among all sensory disorders[1]. By 2050, 2.45 billion people are expected to have hearing impairment[2]. Moreover, hearing impairment has a number of adverse health effects, including but not limited to mental illness[3], cognitive impairment[4], reduced physical activity[5] and fall risk[6].

Despite its substantial global burden, hearing impairment remains largely preventable through modifiable lifestyle interventions. Several studies have shown a longitudinal association between healthy lifestyle and reduced hearing impairment[7,8], primarily focusing on traditional factors (smoking, alcohol, physical activity and sleep)[9-12]. However, alongside the transformation of modern lifestyles and the increasing prevalence of hearing impairment among younger populations, emerging behavioral factors—including sedentary behavior[13], social engagement[14] and supplements usage[15]—remain underexplored within multidimensional lifestyle profiles. Furthermore, the estimated population attributable fraction (PAF) has yet to be employed to quantify and compare the preventive potential of these diverse lifestyle factors[16]. Nevertheless, while behavioral factors provide critical intervention targets, the biological mechanisms through which they influence hearing impairment remain to be elucidated.

Hearing impairment arises from complex intrinsic pathophysiological mechanisms. Inflammatory and metabolic biomarkers not only act as biological mediators linking lifestyle behaviors to auditory aging, but also reflect key pathological processes—such as oxidative stress and mitochondrial dysfunction[17-19]—that damage diverse structures of the auditory system. These mechanisms drive cochlear hair cell apoptosis, microvascular deterioration in the stria vascularis, and otitis media, thereby facilitating sensorineural, conductive, or mixed hearing impairment. Therefore, elucidating not only whether but also to what extent these biomarkers mediate the relationship with lifestyle is of critical importance.

In this large-scale prospective cohort study, we systematically investigated the independent effects of lifestyle factors and inflammatory/metabolic biomarkers on hearing impairment, and the extent to which these biomarkers mediate the lifestyle-hearing association, providing a basis for developing hearing protection strategies.

2 Materials and Methods

2.1 Study design and population

This study was based on UK Biobank, a large-scale community-based cohort with long-term follow-up, details of which are described above[20]. The prospective study, conducted at 22 standardized assessment centers, recruited over 500,000 UK adults aged 40 to 69 between 2006 and 2010. Data collection included: (1) demographic characteristics and lifestyle factors through touchscreen questionnaires; (2) physical measurements (including hearing assessments); (3) biological samples.

The UK Biobank study was conducted with written informed consent from all participants and approval from the North West Multicenter Research Ethics Committee. The study was conducted using UKB resources under application number 92718[20]. Figure 1 depicts the participant selection flowchart. Participants were excluded for withdrawal of consent, baseline hearing impairment, or missing lifestyle data. Missing values (< 5%) were handled using multiple imputation by chained equations (MICE) with 10 imputations. The imputation model included all analysis variables, including the outcome, lifestyle factors, biomarkers, and covariates. Results from the imputed datasets were pooled using Rubin's rules. Final analytical samples included 441,844 participants for lifestyle analysis, 416,348 for biomarker analysis, and 378,177 for mediating effects analysis.

2.2 Lifestyle score assessment

We constructed a comprehensive lifestyle score (range 0–7) incorporating four traditional factors—smoking

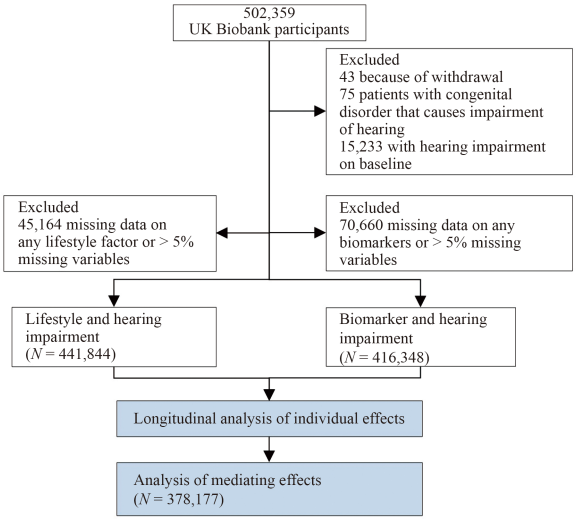

Fig. 1 Flowchart of the study design.

status, alcohol consumption, physical activity, and sleep duration[8] —and three emerging factors: sedentary time, social contact frequency, and supplement use[21]. Supplement use was included given its high prevalence in Western populations and emerging—though inconsistent—evidence suggesting potential links to hearing health, such as through antioxidant mechanisms[22]. All factors were assessed at baseline via touch-screen questionnaires. Participants were assigned 1 point for each factor meeting predefined health criteria (no smoking, no drinking alcohol, regular physical activity, optimal sleep, supplement use, low sedentary time, and moderate social engagement); otherwise, 0 points were assigned. Based on the total score distribution, participants were categorized into poor (0–2 points), intermediate (3–4 points), and ideal (5–7 points) lifestyle groups. Detailed operational definitions are provided in (Suppl. Table 1).

2.3 Inflammatory and metabolic biomarkers assessment

Inflammatory and metabolic biomarkers were selected based on their established biological roles in aging-related pathologies and cochlear dysfunction[23-25]. We measured systemic inflammation using white blood cell count (WBC) and high-sensitivity C-reactive protein (hs-CRP), as these represent widely available, clinically standardized measures of innate immune activation and low-grade inflammation, respectively. An inflammatory score was calculated for each participant as the sum of the *z*-scores for hs-CRP and WBC, with z-scores derived using the formula: $Z = (X - M)/SD$, where X is the individual biomarker level, M is the mean, and SD is the standard deviation[26].

Metabolic dysfunction was assessed using glucose (GLU), triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), and body mass index (BMI). Meanwhile, we calculated metabolic score for insulin resistance (METS-IR)[27]:

$$\text{METS-IR} = \frac{\ln[(2 \times \text{GLU} + \text{TG}) \times \text{BMI}]}{\ln(\text{HDL} - \text{c})}$$

Where GLU, TG, and HDL-c are expressed in mg/dL, and BMI is expressed in kg/m^2. For biomarkers with repeated measurements, values were averaged if the intraclass correlation coefficient (ICC) was below 0.40. Cut-offs for all biomarkers are provided in (Suppl. Table 2).

2.4 Assessment of hearing impairment

The study started on the baseline assessment (2006–2010) and participants were followed until hearing impairment events, death, lost to follow-up or the end of last follow-up (18 June 2023), whichever occurred first. The diagnosis of hearing impairment was established based on the earliest incidence records of hospital inpatient, primary care and death register, with cross-validation between hospital admission records and general practitioner registries to confirm case ascertainment. Hearing impairment was defined using the International Classification of Diseases (ICD-10), codes H90 to H91 (includes sensorineural, conductive and other hearing impairment), according to the UKB recommended algorithm definition. Details of outcome definitions are provided in (Suppl. Table 3).

2.5 Covariate

Covariates were selected based on established associations with hearing impairment from previous studies and clinical relevance. These included baseline demographic characteristics (age, sex, qualifications, household income, and ethnicity), medical histories (hypertension, type 2 diabetes mellitus, and hypercholesterolemia), and hearing-related factors (use of ototoxic drugs, noisy workplace, and loud music exposure frequency)[8]. Detailed descriptions of covariates are provided in (Suppl. Table 4).

2.6 Statistical analysis

Participant characteristics were summarized by hearing impairment status and compared using Mann-Whitney U tests for continuous variables or χ^2 tests for categorical variables.

We conducted the analysis in two sequential phases to study the relationships between lifestyle, biomarkers, and hearing impairment.

First, to evaluate the independent effects, we fitted multivariate Cox proportional hazards models (with follow-up time as the time scale) to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Separate models were fitted for the lifestyle score, individual lifestyle factors, inflammatory score, METS-IR, and each biomarker. We constructed three hierarchical adjustment models: Model 1 was unadjusted; Model 2 was adjusted for age, sex, ethnicity, qualifications, and average total household income before tax; Model 3 was further adjusted for medical histories (hypertension, type 2 diabetes mellitus, hypercholesterolemia) and hearing-related exposures (use of ototoxic drugs, noisy workplace, and loud music exposure frequency), with the exception that diabetes and hypercholesterolemia were not adjusted for in the analyses of metabolic biomarkers to avoid overadjustment. The proportional hazards assumption was verified for all models using Schoenfeld residuals.

Second, to assess mediating effects, we performed causal mediation analysis for biomarkers that showed significant associations with both lifestyle and hearing

impairment in the previous steps. Biomarkers with skewed distributions were normalized using Z-score transformation prior to analysis. Using the R package mediation[28] with 1000 bootstrap samples, we estimated the direct and indirect effects, under the assumptions of no unmeasured confounding and correct temporal ordering.

Stratified analyses were conducted by age, sex, use of ototoxic drugs, noisy workplace, and loud music exposure frequency. Dose-response relationships were examined using restricted cubic splines. Sensitivity analyses included: (1) excluding cases within the first 5 years; (2) restricting to white participants; (3) adjusting for biomarkers in analysis of lifestyle; (4) adjusting for lifestyle and other biomarkers in analysis of biomarkers; (5) using a weighted lifestyle score by multiplying dichotomous lifestyle variables by the β coefficients, summing up, dividing by the sum of coefficients, and multiplying by 7. In addition, we performed two additional sensitivity analyses to strengthen the mediation analysis framework: (1) repeating the mediation analyses after excluding participants with baseline diabetes or hyperlipidemia to address reverse causation by pre-existing metabolic disease; (2) repeating the mediation analyses using biomarker measurements from the first follow-up assessment (2012–2013) to better satisfy the temporal ordering assumption.

All analyses were performed using R version 4.4.2. A two-sided P value < 0.05 was considered statistically significant， which were then adjusted for multiple testing by controlling the false discovery rate (FDR) using the method of Benjamini and Hochberg (1995) for independent effects and mediating effects.

3 Results

3.1 Population characteristics

During a median follow-up of 14.22 years (interquartile range [IQR], 13.36–14.96 years), 20,743 incident hearing impairment cases were identified in the primary analysis cohort, which had a mean age of 56.26 years and 46.2% were male. As shown in Table 1, participants who developed hearing impairment were older, more likely to be male, and had lower household income and educational attainment than those without incident hearing impairment. Notably, all biomarkers except HDL-c were higher at baseline in those who later developed hearing impairment (Suppl. Table 5). All biomarkers except hs-CRP showed moderate to good consistency (ICC, 0.41–0.72) between repeated measurements (Suppl. Table 6). The study population was categorized as follows: 18.7% had an ideal lifestyle, 61.6% had an intermediate lifestyle, and 19.8% had a poor lifestyle.

Table 1 Demographic characteristics at baseline of participants.

Characteristic	Overall	Incident hearing impairment	No. hearing impairment	*P* value*
No. of participants	441,844	20,743	421,101	
Follow-up time, [IQR], year	14.22 [13.36,14.96]	6.34 [3.28,10.23]	14.28 [13.53,15.00]	< 0.001
Age, mean (SD), year	56.26 (8.10)	60.35 (7.00)	56.06 (8.09)	< 0.001
Sex, No. (%)				< 0.001
Female	237,729 (53.80)	9593 (46.20)	228,136 (54.20)	< 0.001
Male	204,115 (46.20)	11,150 (53.80)	192,965 (45.80)	
Educational level, No. (%)				< 0.001
College or University degree	152,803 (34.60)	5930 (28.60)	146,873 (34.90)	
A levels/AS levels or equivalent	51,694 (11.70)	2024 (9.80)	49,670 (11.80)	
O levels/GCSEs or equivalent	95,743 (21.70)	4339 (20.90)	91,404 (21.70)	
CSEs or equivalent	23,673 (5.40)	846 (4.10)	22,827 (5.40)	
NVQ or HND or HNC or equivalent	28,888 (6.50)	1710 (8.20)	27,178 (6.50)	
Other professional qualifications	89,043 (20.20)	5894 (28.40)	83,149 (19.70)	
Average total household income before tax, No. (%)				< 0.001
Less than £18,000	96,816 (21.90)	6234 (30.10)	90,582 (21.50)	
£18,000 to £30,999	112,072 (25.40)	6024 (29.00)	106,048 (25.20)	
£31,000 to £51,999	116,683 (26.40)	4822 (23.20)	111,861 (26.60)	
£52,000 to £100,000	91,787 (20.80)	2984 (14.40)	88,803 (21.10)	
Greater than £100,000	24,486 (5.50)	679 (3.30)	23,807 (5.70)	

(*Continued*)

Characteristic	Overall	Incident hearing impairment	No. hearing impairment	*P* value*
Ethnicity, No. (%)				< 0.001
White	402,749 (91.20)	19,324 (93.20)	383,425 (91.10)	
Mixed	16,065 (3.60)	616 (3.00)	15,449 (3.70)	
Asian or Asian British	15,748 (3.60)	589 (2.80)	15,159 (3.60)	
Black or Black British	2280 (0.50)	66 (0.30)	2214 (0.50)	
Chinese	1358 (0.30)	37 (0.20)	1321 (0.30)	
Other ethnic group	3644 (0.80)	111 (0.50)	3533 (0.80)	
Hypertension, No. (%)	118,784 (26.90)	7132 (34.40)	111,652 (26.50)	< 0.001
Type 2 diabetes mellitus, No. (%)	24,342 (5.50)	1717 (8.30)	22,625 (5.40)	< 0.001
Hypercholesterolemia, No. (%)	196,831 (44.50)	10,641 (51.30)	186,190 (44.20)	< 0.001
Use of ototoxic drugs, No. (%)	117,595 (26.60)	6318 (30.50)	111,277 (26.40)	< 0.001
Noisy workplace, No. (%)				< 0.001
No	346,788 (78.50)	15,491 (74.70)	331,297 (78.70)	
Yes, for less than a year	23,541 (5.30)	1125 (5.40)	22,416 (5.30)	
Yes, for around 1–5 years	23,739 (5.40)	1243 (6.00)	22,496 (5.30)	
Yes, for more than 5 years	47,776 (10.80)	2884 (13.90)	44,892 (10.70)	
Loud music exposure frequency, No. (%)				0.624
No	388,418 (87.90)	18,265 (88.10)	370,153 (87.90)	
Yes, for less than a year	14,024 (3.20)	635 (3.10)	13,389 (3.20)	
Yes, for around 1–5 years	20,505 (4.60)	978 (4.70)	19,527 (4.60)	
Yes, for more than 5 years	18,897 (4.30)	865 (4.20)	18,032 (4.30)	
Healthy lifestyle factors, No. (%)				
No smoking	243,446 (55.10)	10,185 (49.10)	233,261 (55.40)	< 0.001
No drinking alcohol	17,378 (3.90)	859 (4.10)	16,519 (3.90)	0.119
Regular physical activity	275,054 (62.30)	12,876 (62.10)	262,178 (62.30)	0.594
Optimal sleep	53,064 (12.00)	1910 (9.20)	51,154 (12.10)	< 0.001
Supplement use	224,989 (50.90)	11,341 (54.70)	213,648 (50.70)	< 0.001
Low sedentary time	314,215 (71.10)	14,068 (67.80)	300,147 (71.30)	< 0.001
Moderate social engagement	405,326 (91.70)	19,092 (92.00)	386,234 (91.70)	0.104
Lifestyle categories, No. (%)				< 0.001
Poor	87,277 (19.80)	4560 (22.00)	82,717 (19.60)	
Intermediate	272,097 (61.60)	12,701 (61.20)	259,396 (61.60)	
Ideal	82,470 (18.70)	3482 (16.80)	78,988 (18.80)	
Lifestyle score, mean (SD)	3.47 (1.15)	3.39 (1.16)	3.47 (1.15)	< 0.001

IQR, interquartile range; SD, standard deviation.

**P* value: *T*-test/*Chi*-squared test was used to compare the differences in basic characteristics between participants without incident hearing impairment and participants with incident hearing impairment for continuous/categorical variables.

3.2 Association of lifestyle factors with hearing impairment

Analysis of lifestyle factors revealed a consistent association with hearing impairment, with all factors except frequency of visits from friends/family showing significant effects after full adjustment (Table 2). Notably, not using dietary supplements was associated with a reduced risk of hearing impairment (HR = 0.96, 95% CI: 0.93–0.98), whereas most other lifestyle factors

Table 2 Association of lifestyle factors with hearing impairment.

Lifestyle factors	PAF% (95% CI)	Model 1		Model 2		Model 3	
		HR (95% CI)	*P* value*	HR (95% CI)	*P* value*	HR (95% CI)	*P* value*
Smoking status	**10.89 (9.69,12.1)**						
Never		1 (reference)		1 (reference)		1 (reference)	
Previous		**1.37 (1.33,1.41)**	< 0.001	**1.14 (1.11,1.18)**	< 0.001	**1.13 (1.10,1.17)**	< 0.001
Current		**1.09 (1.04,1.14)**	< 0.001	**1.08 (1.03,1.13)**	0.003	**1.07 (1.02,1.12)**	0.010
Alcohol drinker status	−5.29 (−11.76,1.12)						
Never		1 (reference)		1 (reference)		1 (reference)	
Previous		**1.24 (1.13,1.36)**	< 0.001	**1.17 (1.07,1.29)**	0.001	**1.16 (1.06,1.28)**	0.002
Current		**0.93 (0.87,0.99)**	0.039	0.94 (0.88,1.01)	0.102	0.94 (0.88,1.01)	0.082
Sleep duration	**3.51 (2.50,4.42)**						
7–8 hours/d		1 (reference)		1 (reference)		1 (reference)	
< 7 hours/d		**1.05 (1.01,1.08)**	0.006	**1.04 (1.00,1.07)**	0.029	**1.03 (1.00,1.07)**	0.049
> 8 hours/d		**1.41 (1.35,1.48)**	< 0.001	**1.18 (1.12,1.23)**	< 0.001	**1.17 (1.12,1.23)**	< 0.001
Physical activity	**1.06 (0.55,1.52)**						
Regular		1 (reference)		1 (reference)		1 (reference)	
Irregular		0.98 (0.94,1.01)	0.127	**1.03 (1.00,1.06)**	0.048	**1.03 (1.00,1.07)**	0.049
None		**1.11 (1.06,1.15)**	< 0.001	**1.14 (1.10,1.19)**	< 0.001	**1.14 (1.09,1.19)**	< 0.001
Supplement use	/						
Yes		1 (reference)		1 (reference)		1 (reference)	
No		**0.86 (0.83,0.88)**	< 0.001	**0.95 (0.93,0.98)**	< 0.001	**0.96 (0.93,0.98)**	0.002
Sedentary time	**4.63 (3.64,5.40)**						
< 6 hours/d		1 (reference)		1 (reference)		1 (reference)	
6–12 hours/d		**1.20 (1.16,1.23)**	< 0.001	**1.06 (1.03,1.10)**	< 0.001	**1.06 (1.02,1.09)**	< 0.001
> 12 hours/d		1.09 (0.98,1.21)	0.112	**1.15 (1.03,1.27)**	0.010	**1.13 (1.02,1.25)**	0.020
Frequency of friend/family visits	/						
Once a month or more		1 (reference)		1 (reference)		1 (reference)	
Less than once a month		0.97 (0.92,1.02)	0.218	1.01 (0.96,1.06)	0.784	1.01 (0.96,1.06)	0.771

PAF, estimated population attributable fraction; CI, confidence interval; HR, hazards ratio.
Model 1: crude model.
Model 2: adjusted for age, sex, ethnicity, qualifications, and average total household income before tax.
Model 3: model 2 + hypertension, type 2 diabetes mellitus, hypercholesterolemia, use of ototoxic drugs, noisy workplace, and loud music exposure frequency.
**P* value: *P* values were adjusted for multiple testing by controlling the false discovery rate.
Bold: *P* value < 0.05.

showed adverse associations. Specifically, both former (HR = 1.13, 95% CI: 1.10–1.17) and current smokers (HR = 1.07, 95% CI: 1.02–1.12) showed elevated risks, as did former alcohol consumers (HR = 1.16, 95% CI: 1.06–1.28). Both long sleep duration (HR = 1.17, 95% CI: 1.12–1.23) and short sleep duration (HR = 1.03, 95% CI: 1.00–1.07) were associated with higher risk relative to 7–8 h/d, while no physical activity (HR = 1.14, 95% CI: 1.09–1.19) increased risk compared to regular activity. Sedentary behavior exhibited a clear dose-response relationship, with progressively higher risks for 6–12 h/d (HR = 1.06, 95% CI: 1.02–1.09) and > 12 h/d (HR = 1.13, 95% CI: 1.02–1.25) compared to the reference (< 6 h/d).

3.3 Association of lifestyle categories and lifestyle score with hearing impairment

A strong dose-response relationship was observed between lifestyle score and hearing impairment risk (*P* for trend < 0.001) (Suppl. Table 7). Compared to the poor lifestyle group, risks were significantly lower in the intermediate (HR = 0.93, 95% CI: 0.90–0.96) and ideal (HR = 0.86, 95% CI: 0.82–0.90) groups. RCS analysis

confirmed that the risk of hearing impairment decreased linearly with increasing lifestyle score (Suppl. Figure 1).

3.4 Association of inflammatory and metabolic biomarkers with hearing impairment

As detailed in Table 3, elevated levels of both inflammatory and metabolic biomarkers were independently associated with an increased risk of hearing impairment.

We first analyzed inflammatory score and its components (WBC, hs-CRP) in association with outcome. After full adjustment, a higher inflammatory score was significantly associated with increased hearing impairment risk, both per 1-point increment (HR = 1.03, 95% CI: 1.02–1.04) and when comparing the highest (Q3) (HR = 1.17, 95% CI: 1.13–1.21) to the lowest tertile (Q1). Consistent results were observed across WBC and hs-CRP.

Similarly, dysregulation across multiple metabolic pathways was associated with elevated risk. Each 1-standard-deviation increase in the standardized METS-IR

Table 3 Association of biomarkers with hearing impairment.

Biomarker	Level	Model 1		Model 2		Model 3	
		HR (95% CI)	*P* value [b]	HR (95% CI)	*P* value [b]	HR (95% CI)	*P* value [b]
Inflammatory score	Low	1 (reference)		1 (reference)		1 (reference)	
	Moderate	**1.15 (1.11,1.19)**	< 0.001	**1.05 (1.01,1.09)**	0.005	**1.05 (1.01,1.09)**	0.009
	High	**1.34 (1.29,1.38)**	< 0.001	**1.18 (1.14,1.22)**	< 0.001	**1.17 (1.13,1.21)**	< 0.001
	Per 1-point	**1.03 (1.02,1.04)**	< 0.001	**1.03 (1.02,1.04)**	< 0.001	**1.03 (1.02,1.04)**	< 0.001
Inflammatory biomarkers							
WBC, 10^9/L	Low	1 (reference)		1 (reference)		1 (reference)	
	Moderate	**1.10 (1.06,1.14)**	< 0.001	1.03 (0.99,1.06)	0.149	1.02 (0.99,1.06)	0.194
	High	**1.22 (1.18,1.26)**	< 0.001	**1.12 (1.08,1.15)**	< 0.001	**1.11 (1.07,1.15)**	< 0.001
hs-CRP, mg/L	Low	1 (reference)		1 (reference)		1 (reference)	
	Moderate	**1.25 (1.21,1.29)**	< 0.001	**1.09 (1.06,1.13)**	< 0.001	**1.09 (1.05,1.13)**	< 0.001
	High	**1.36 (1.32,1.41)**	< 0.001	**1.18 (1.14,1.22)**	< 0.001	**1.18 (1.13,1.22)**	< 0.001
METS-IR	Low	1 (reference)		1 (reference)		1 (reference)	
	Moderate	**1.24 (1.20,1.28)**	< 0.001	**1.09 (1.06,1.13)**	< 0.001	**1.08 (1.05,1.12)**	< 0.001
	High	**1.41 (1.36,1.46)**	< 0.001	**1.19 (1.14,1.24)**	< 0.001	**1.17 (1.13,1.22)**	< 0.001
	Per 1-point [a]	**1.16 (1.14,1.18)**	< 0.001	**1.08 (1.07,1.10)**	< 0.001	**1.08 (1.06,1.10)**	< 0.001
Metabolic biomarkers							
HDL-c, mg/dL	Low	1 (reference)		1 (reference)		1 (reference)	
	High	**0.90 (0.87,0.93)**	< 0.001	**0.90 (0.87,0.93)**	< 0.001	**0.91 (0.88,0.94)**	< 0.001
TG, mg/dL	Low	1 (reference)		1 (reference)		1 (reference)	
	High	**1.21 (1.17,1.24)**	< 0.001	**1.06 (1.03,1.09)**	< 0.001	**1.05 (1.02,1.08)**	< 0.001
GLU, mg/dL	Low	1 (reference)		1 (reference)		1 (reference)	
	High	**1.37 (1.31,1.44)**	< 0.001	**1.15 (1.10,1.20)**	< 0.001	**1.13 (1.08,1.19)**	< 0.001
BMI, kg/m^2	Normal	1 (reference)		1 (reference)		1 (reference)	
	Low	1.04 (0.84,1.28)	0.727	1.08 (0.87,1.33)	0.488	1.08 (0.88,1.34)	0.453
	Overweight	**1.27 (1.23,1.31)**	< 0.001	**1.10 (1.06,1.14)**	< 0.001	**1.09 (1.06,1.13)**	< 0.001
	Obesity	**1.36 (1.31,1.41)**	< 0.001	**1.18 (1.13,1.22)**	< 0.001	**1.16 (1.12,1.20)**	< 0.001

CI, confidence interval; HR, hazards ratio; WBC, white blood cell count; hs-CRP, high-sensitivity C-reactive protein; METS-IR, metabolic score for insulin resistance; HDL-c, high-density lipoprotein cholesterol; TG, triglycerides; GLU, glucose; BMI, body mass index.

Model 1: crude model. Model 2: adjusted for age, sex, ethnicity, qualifications, and average total household income before tax. Model 3: Inflammatory biomarkers: model 2 + hypertension, type 2 diabetes mellitus, hypercholesterolemia, use of ototoxic drugs, noisy workplace, and loud music exposure frequency; Metabolic biomarkers: model 2 + hypertension, use of ototoxic drugs, noisy workplace, and loud music exposure frequency.

[a] HR (95% CI) of incidence risk per point increment in METS-IR after standardization.

[b] *P* value: *P* values were adjusted for multiple testing by controlling the false discovery rate.

Bold: *P* value < 0.05.

was associated with an 8% higher risk (HR = 1.08, 95% CI: 1.06–1.10). Participants with a METS-IR above 2.48 had a 17% higher risk (HR = 1.17, 95% CI: 1.13–1.22) compared to those with a METS-IR below 2.25. Analyses of its components revealed that higher levels of TG (HR = 1.05, 95% CI: 1.02–1.08), GLU (HR = 1.13, 95% CI: 1.08–1.19), and BMI (HR = 1.16, 95% CI: 1.12–1.20) were associated with increased risk, whereas higher HDL-c was associated with a 9% risk reduction (HR = 0.91, 95% CI: 0.88–0.94).

Kaplan-Meier curves confirmed significant divergence in cumulative incidence by levels of both inflammatory score and METS-IR (Suppl. Figure 2).

3.5 Mediation analysis

Mediation analysis revealed that the association between lifestyle score and hearing impairment was partially mediated by several inflammatory and metabolic biomarkers, including WBC, hs-CRP, HDL-c, TG, BMI, and GLU (Figure 2a). Metabolic biomarkers, particularly BMI and HDL-c, exhibited the strongest mediating effects, accounting for 16.52% and 14.00% of the total association, respectively. In contrast, inflammatory biomarkers such as WBC contributed less than 6%. Further analysis of seven lifestyle factors confirmed that their associations with hearing impairment were also mediated by these biomarkers, with the exception of moderate social engagement (*P* for indirect effect > 0.05) (Figure 2b).

In summary, although both inflammatory and metabolic biomarkers partially mediated the association between lifestyle and hearing impairment, metabolic factors (notably BMI and HDL-c) explained a substantially larger proportion (14.00%–16.52%) of the association compared with inflammatory factors (< 6.00%).

3.6 Subgroup analysis and sensitivity analysis

Stratified analysis showed that the association between lifestyle and biomarkers and hearing impairment remained consistent in different age, sex, history of ototoxic drug use, and noise exposure populations (Suppl. Tables 8–15). Sensitivity analysis (including exclusion of early onset patients, race limitation, additional model adjustments, and use of weighted lifestyle scores) further confirmed the robustness of the results (Suppl. Tables 16–22). In additional sensitivity analyses, after excluding participants with baseline metabolic diseases, most biomarkers (except WBC and GLU) remained significant mediators of the lifestyle score–hearing impairment association (Suppl. Figure 3 and Suppl. Table 23). When using repeated biomarker measurements from follow-up, only HDL-c, TG, and BMI showed significant mediating effects in the associations of no smoking, no drinking alcohol, and regular physical activity with hearing impairment (Suppl. Figure 4).

4 Discussion

This study demonstrated that adherence to a healthy lifestyle was associated with reduced hearing risk, while elevated inflammatory and metabolic biomarkers independently increased risk. Crucially, we further revealed that distinct lifestyle factors operated through different pathways. To our knowledge, this is the first study to quantitatively integrate these mediation pathways for hearing impairment, offering novel mechanistic and public health insights into hearing problems prevention[29].

Previous studies on lifestyle and hearing impairment have been predominantly cross-sectional[30-32] and focused on traditional factors such as smoking, physical activity, and occupational noise[8,33]. While Yévenes-Briones et al. combined five health behaviors, only physical activity showed a significant association[7], and Jung et al. emphasized noise-related exposures without considering emerging lifestyle factors[8]. Our study extends this work by incorporating sedentary behavior, social engagement, and supplement use into a comprehensive lifestyle score, and by being the first to compare estimated PAF across multiple behaviors. In addition to traditional factors, we find that sedentary behavior may increase long-term hearing impairment risk. Exogenous nutrient intake from supplements may adversely affect cochlear health. Several explanations exist: first, early subclinical symptoms may drive supplement use, creating an apparent positive association; second, residual confounding by health consciousness or healthcare access cannot be ruled out, as supplement users may seek more care, increasing hearing loss detection; third, our analysis only covered vitamin/mineral products—other supplements (omega-3 or amino acids)[34] could have different or protective effects. Future studies should include detailed supplement type. Meanwhile, we found that adherence to an ideal lifestyle could prevent approximately 10.06% of hearing impairment cases, underscoring the significant preventive potential of composite behavioral modification. Notably, among seven lifestyle factors, smoking cessation offered the greatest preventive potential (estimated PAF = 10.89%), followed by reduced sedentary time (estimated PAF = 4.63%).

Our mediation analysis quantified the pathways underlying these relationships. The lifestyle–hearing impairment association was partially mediated by inflammatory (WBC, hs-CRP) and metabolic (BMI, HDL-c, TG, GLU) biomarkers (Figure 2a). Metabolic pathways, particularly involving BMI and HDL-c, accounted for a substantially larger proportion of the mediated effect (14%–17%) compared to inflammatory pathways (< 6%). This suggests that while both systems

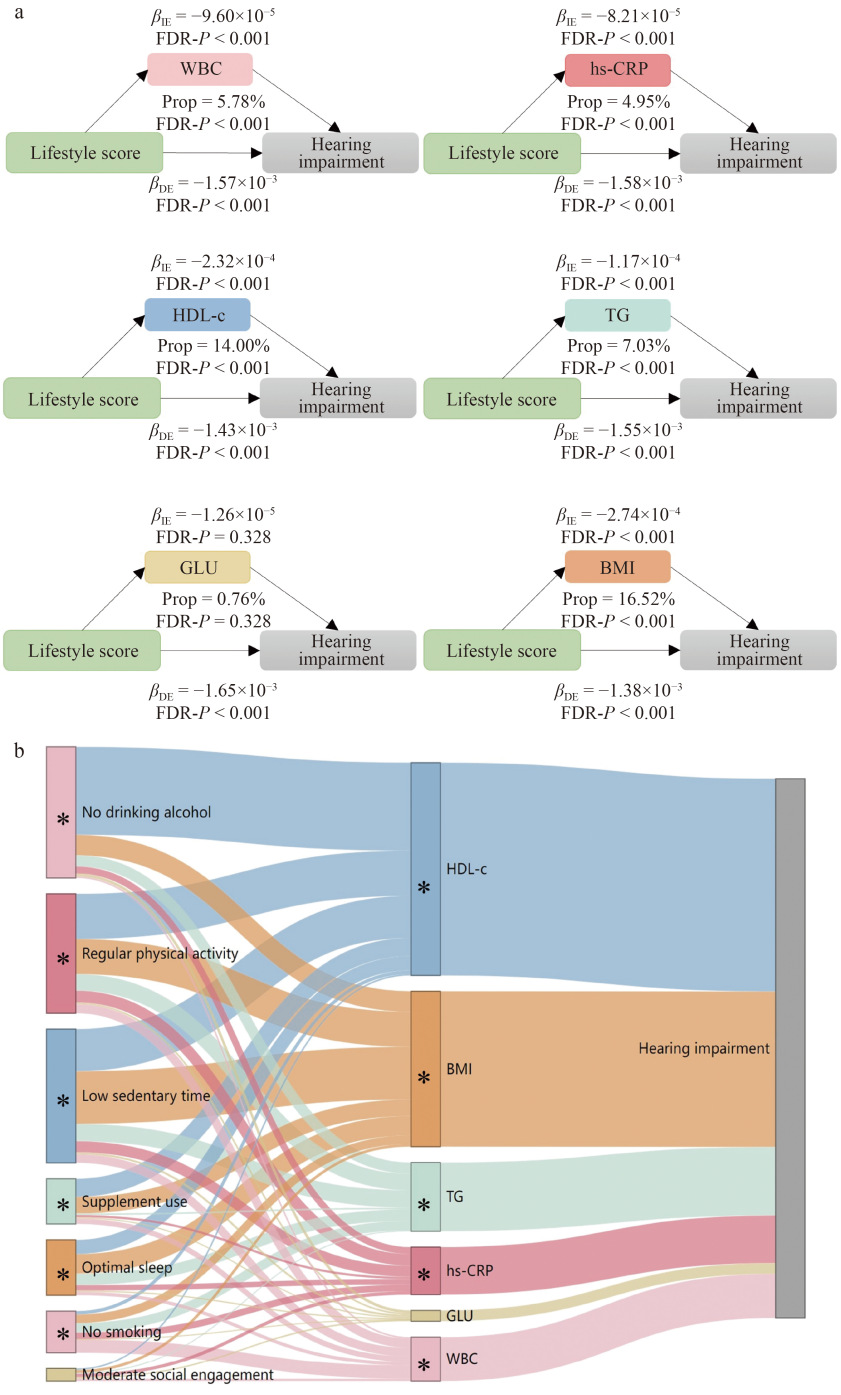

Fig. 2 Mediating role of biomarkers in the associations of lifestyle with hearing impairment. (a) Partial mediation of the lifestyle – hearing impairment association by inflammatory (WBC, hs‑CRP) and metabolic (BMI, HDL‑c, TG, GLU) biomarkers. (b) Mediating role of inflammatory and metabolic biomarkers examined separately for each lifestyle factor.

Note: β, original regression coefficient; Prop, the proportion of mediation effect; IE, indirect effects; DE, direct effect; WBC, white blood cell count; hs-CRP, high-sensitivity C-reactive protein; HDL-c, high-density lipoprotein cholesterol; TG, triglycerides; GLU, glucose; BMI, body mass index.

The branch width in the Sankey diagram represents the absolute value of the indirect effect ($|\beta_{IE}|$). The pathway between a lifestyle factor and a biomarker is considered to show a significant mediation effect (FDR-adjusted $P < 0.05$) only if both the lifestyle factor and the biomarker are marked with "*".

Inflammatory markers: Mediation models were adjusted for age, sex, ethnicity, qualifications, average total household income before tax, hypertension, type 2 diabetes mellitus, hypercholesterolemia, use of ototoxic drugs, noisy workplace, and loud music exposure frequency.

Metabolic markers: Mediation models were adjusted for age, sex, ethnicity, qualifications, average total household income before tax, hypertension, use of ototoxic drugs, noisy workplace, and loud music exposure frequency.

are involved, metabolic factors may be a more dominant pathway through which lifestyle influences hearing. The mediating role of biomarkers was further examined for each lifestyle factor (Figure 2b). Our findings reveal a distinct pattern: smoking cessation exerted its protective effect on hearing through a relatively balanced involvement of both inflammatory and metabolic pathways, whereas the benefits of other healthy lifestyle factors were primarily attributable to metabolic factors. For never smoking, most biomarkers significantly mediated the association, with WBC and TG showing the strongest effects. Never drinking alcohol exhibited a unique pattern in which HDL-c mediated a large proportion of the association. Regular physical activity, low sedentary time, and optimal sleep showed similar mediation profiles, with effects predominantly driven by HDL-c and BMI. These findings underscore that the auditory benefits of an active and well-rested lifestyle are largely mediated through metabolic pathways[35-40]. Two sensitivity analyses (excluding pre-existing metabolic diseases and using repeated biomarker measurements) confirmed the robustness of the mediation findings, with key metabolic markers remaining significant. Such behaviors may enhance insulin sensitivity, promote favorable lipid profiles, and reduce adiposity—all of which may protect against metabolic stress and microvascular damage in the cochlea, thereby preserving hearing function[11,41-43]. Supplement use displayed negative mediation proportions, which is consistent with its independent association with hearing impairment. This counterintuitive finding may reflect residual confounding or be related to the simultaneous measurement of exposure and mediating factors, warranting further investigation. Moderate social engagement was the only factor without significant mediation, implying that its effects may involve non-inflammatory or non-metabolic pathways—such as cognitive stimulation, stress reduction, or psychosocial support[44].

The strengths of our study include its prospective, large-scale design within the UK Biobank, which provides stronger causal inference than cross-sectional studies. Second, we compared the estimated PAF of multiple lifestyle factors, identifying smoking cessation as the primary intervention target for hearing preservation. Third, our mediation analysis elucidated the underlying biological pathways, offering a mechanistic understanding of how modifiable behaviors influence cochlear health. Our study also has several limitations. First, despite adjusting for a wide range of confounders, residual confounding cannot be entirely ruled out in this observational study. Consequently, the estimated PAF should be interpreted as potential prevention fractions rather than definitive causal estimates. Second, the cross-sectional assessment of mediators is a limitation of the primary analysis, even though sensitivity analyses using repeated biomarker data produced essentially unchanged mediation results. Third, we did not consider the effect of biomarker changes on hearing. Fourth, hearing impairment was defined solely using ICD-10 codes (H90–H91), without objective audiometric measures. This may introduce some misclassification, making our findings conservative.

5 Conclusion

In conclusion, we found that adherence to healthy lifestyle was associated with a reduced risk of hearing impairment. Inflammation and metabolic dysregulation were found to partially mediate this association, providing mechanistic insights into the pathway linking lifestyle to auditory health. These findings offer actionable evidence for public health strategies and clinical guidance regarding modifiable behavioral interventions. Future studies should further validate these causal mechanisms and explore their relevance to specific hearing phenotypes, such as audiogram and different frequencies of hearing.

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Ethical statement

The North West Multi‐Centre Research Ethics Committee approved the collection and use of UK Biobank (UKB) data. The present research using the UKB Resource was approved under application number 92718. All participants consented to the use of their de-identified data and access to their national health-related hospital and death records.

Conflicts of interest

Author Wenyan Li serves as an Executive Editor-in-Chief of this journal. She was not involved in the editorial review or decision-making process for this manuscript. All editorial decisions were made independently by other members of the Editorial Board who have no conflicts of interest. The other authors confirm that they have no conflicts of interest to declare.

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Data availability statement

The data is accessible through the UKB project, contingent upon registration and an application process. The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

AI statement

The authors used (DeepSeek R1, online version) as a language-editing tool to improve grammar, clarity, and readability. The AI tool was not used for data analysis, data generation, image processing, or scientific content creation. All outputs were carefully reviewed and verified by the authors, who take full responsibility for the final content.

Author contributions

Wenyan Li, Yanfeng Jiang, Runhua Li, and Jialin Li conceptualized the study. Runhua Li, Shuaizhou Chen, and Yasi Zhang conducted the formal analysis. Gaogan Jia and Cenfei Li conducted the investigation. Runhua Li drafted the initial manuscript. Wenyan Li, Yanfeng Jiang, Jialin Li, Chen Suo, and Xingdong Chen critically revised the manuscript. Wenyan Li, Yanfeng Jiang, and Chen Suo acquired funding. All authors approved the final version for publication.

Supplementary files

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References

1. GBD 2019 AGEING COLLABORATORS. Global, regional, and national burden of diseases and injuries for adults 70 years and older: systematic analysis for the Global Burden of Disease 2019 Study. *Bmj*. 2022, 376: e068208.
2. GBD 2019 HEARING LOSS COLLABORATORS. Hearing loss prevalence and years lived with disability, 1990–2019: findings from the Global Burden of Disease Study 2019. *Lancet*. 2021, 397(10278): 996–1009.
3. Wang N, Gao B, Stewart SL, Hoch JS, Guo J. Associations of cumulative hearing and vision loss with depression among U. S. adults aged 50 and older: results from the health and retirement study. *BMC Psychiatry*. 2025, 25(1): 690.
4. Uhlmann RF, Larson EB, Rees TS, Koepsell TD, Duckert LG. Relationship of hearing impairment to dementia and cognitive dysfunction in older adults. *Jama*. 1989, 261(13): 1916–1919.
5. Assi S, Twardzik E, Deal JA, et al. Hearing Loss and Physical Activity Among Older Adults in the United States. *J Gerontol A Biol Sci Med Sci*. 2024, 79(1): glad186.
6. Heitz ER, Gianattasio KZ, Prather C, Talegawkar SA, Power MC. Self-Reported Hearing Loss and Nonfatal Fall-Related Injury in a Nationally Representative Sample. *J Am Geriatr Soc*. 2019, 67(7): 1410–1416.
7. Yévenes-Briones H, Caballero FF, Banegas JR, Rodríguez-Artalejo F, Lopez-Garcia E. Association of Lifestyle Behaviors With Hearing Loss: The UK Biobank Cohort Study. *Mayo Clin Proc*. 2022, 97(11): 2040–2049.
8. Jung SH, Lee YC, Shivakumar M, et al. Association between genetic risk and adherence to healthy lifestyle for developing age-related hearing loss. *BMC Med*. 2024, 22(1): 141.
9. Garcia Morales EE, Ting J, Gross AL, et al. Association of Cigarette Smoking Patterns Over 30 Years With Audiometric Hearing Impairment and Speech-in-Noise Perception: The Atherosclerosis Risk in Communities Study. *JAMA Otolaryngol Head Neck Surg*. 2022, 148(3): 243–251.
10. Piano MR, Marcus GM, Aycock DM, et al. Alcohol Use and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2025, 152(1): e7–e21.
11. Kuo PL, Di J, Ferrucci L, Lin FR. Analysis of Hearing Loss and Physical Activity Among US Adults Aged 60-69 Years. *JAMA Netw Open*. 2021, 4(4): e215484.
12. Liu M, Zhang H, Wang Z, et al. Independent and Combined Associations of Sleep Duration, Bedtime, and Polygenic Risk Score with the Risk of Hearing Loss among Middle-Aged and Old Chinese: The Dongfeng-Tongji Cohort Study. *Research (Wash D C)*. 2023, 6: 0178.
13. Sánchez-Sánchez JL, Ortolá R, Banegas JR, et al. Association between physical activity and sedentary behaviour and changes in intrinsic capacity in Spanish older adults (Seniors-ENRICA-2): a prospective population-based study. *Lancet Healthy Longev*. 2025, 6(5): 100681.
14. Huang AR, Cudjoe TKM, Rebok GW, Swenor BK, Deal JA. Hearing and vision impairment and social isolation over 8 years in community-dwelling older adults. *BMC Public Health*. 2024, 24(1): 779.
15. Lu W, Tang R, Jiahui X, et al. Protective effects of dietary nutrients on hearing loss: a systematic review and meta-analysis. *Front Nutr*. 2025, 12: 1528771.
16. Zapata-Diomedi B, Barendregt JJ, Veerman JL. Population attributable fraction: names, types and issues with incorrect interpretation of relative risks. *Br J Sports Med*. 2018, 52(4): 212–213.
17. Kitama T, Nishiyama T, Hosoya M, et al. Noise-Induced Hearing Loss: Overview and Future Prospects for Research on Oxidative Stress. *Int J Mol Sci*. 2025, 26(10): 4927.
18. Kros CJ, Steyger PS. Aminoglycoside- and Cisplatin-Induced Ototoxicity: Mechanisms and Otoprotective Strategies. *Cold Spring Harb Perspect Med*. 2019, 9(11): a033548.
19. He H, Han Z, Cheng S, Zhou Y. Hearing the call of mitochondria: Insight into its role in sensorineural hearing loss. *Neurobiol Dis*.

2025, 213: 107030.
20. Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med*. 2015, 12(3): e1001779.
21. Han H, Cao Y, Feng C, et al. Association of a Healthy Lifestyle With All-Cause and Cause-Specific Mortality Among Individuals With Type 2 Diabetes: A Prospective Study in UK Biobank. *Diabetes Care*. 2022, 45(2): 319–329.
22. Curhan SG, Stankovic KM, Eavey RD, Wang M, Stampfer MJ, Curhan GC. Carotenoids, vitamin A, vitamin C, vitamin E, and folate and risk of self-reported hearing loss in women. *Am J Clin Nutr*. 2015, 102(5): 1167–1175.
23. Lassale C, Vullo P, Cadar D, Batty GD, Steptoe A, Zaninotto P. Association of inflammatory markers with hearing impairment: The English Longitudinal Study of Ageing. *Brain Behav Immun*. 2020, 83: 112–119.
24. Verschuur CA, Dowell A, Syddall HE, et al. Markers of inflammatory status are associated with hearing threshold in older people: findings from the Hertfordshire Ageing Study. *Age Ageing*. 2012, 41(1): 92–97.
25. Han X, Wang Z, Wang J, et al. Metabolic syndrome is associated with hearing loss among a middle-aged and older Chinese population: a cross-sectional study. *Ann Med*. 2018, 50(7): 587–595.
26. Chen Y, Ju H, Xie K, Zhao X. Association of inflammatory score with all-cause and cardiovascular mortality in patients with metabolic syndrome: NHANES longitudinal cohort study. *Front Immunol*. 2024, 15: 1410871.
27. Bello-Chavolla OY, Almeda-Valdes P, Gomez-Velasco D, et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. *Eur J Endocrinol*. 2018, 178(5): 533–544.
28. Zhang Z, Zheng C, Kim C, Van Poucke S, Lin S, Lan P. Causal mediation analysis in the context of clinical research. *Ann Transl Med*. 2016, 4(21): 425.
29. Sun S, Zhao Q, He H, Liu Y, Nie Y, Zhou Y. Pathophysiological insights and therapeutic developments in age-related hearing loss: a narrative review. *Front Aging Neurosci*. 2025, 17: 1657603.
30. Jiang K, Spira AP, Reed NS, Lin FR, Deal JA. Sleep Characteristics and Hearing Loss in Older Adults: The National Health and Nutrition Examination Survey 2005-2006. *J Gerontol A Biol Sci Med Sci*. 2022, 77(3): 632–639.
31. Cai Y, Martinez-Amezcua P, Betz JF, et al. Hearing Impairment and Physical Activity and Physical Functioning in Older Adults: Baseline Results From the ACHIEVE Trial. *J Gerontol A Biol Sci Med Sci*. 2024, 79(7): glae117.
32. Dawes P, Cruickshanks KJ, Moore DR, et al. Cigarette smoking, passive smoking, alcohol consumption, and hearing loss. *J Assoc Res Otolaryngol*. 2014, 15(4): 663–674.
33. Akamatsu Y, Ojima T, Nakanishi H, Misawa K, Nakayama T. Association of high-frequency hearing loss with examination data and lifestyle in 36 000 middle-aged and older adults. *Geriatr Gerontol Int*. 2025, 25(3): 366–373.
34. Mao H, Ni W, Ma L, et al. Targeting Phospholipid Metabolism as an Effective Hearing Protection Strategy. *Neurosci Bull*. 2026, 42(1): 1–18.
35. Nwanaji-Enwerem JC, Khodasevich D, Gladish N, et al. Sensory impairments and epigenetic aging: insights from self-rated hearing and vision in United States adults. *Geroscience*. 2026, 48(1): 1037–1050.
36. Rim HS, Kim MG, Park DC, et al. Association of Metabolic Syndrome with Sensorineural Hearing Loss. *J Clin Med*. 2021, 10(21): 4866.
37. Terreros HG, Munoz F, D'Espessailles Tapia A. Obesity and Hearing Loss: Mechanisms and Future Challenges. *Obesity (Silver Spring)*. 2025, 33(12): 2264–2276.
38. Cha YJ, Yeo JH, Kim SS, et al. Effects of Nitric Oxide Expression on Hearing Loss. *Int J Mol Sci*. 2025, 26(17): 8416.
39. Murillo-Cuesta S, Seoane E, Cervantes B, Zubeldia JM, Varela-Nieto I. NLRP3 inflammasome and hearing loss: from mechanisms to therapies. *J Neuroinflammation*. 2025, 22(1): 225.
40. Guo Q, Li Z, Luo C, et al. Metabolic shifts in murine inner ears mimicking erythrocytes and plasma reveal diagnostics and early predictors for age-related hearing loss. *iScience*. 2025, 28(9): 113285.
41. Gispen FE, Chen DS, Genther DJ, Lin FR. Association between hearing impairment and lower levels of physical activity in older adults. *J Am Geriatr Soc*. 2014, 62(8): 1427–1433.
42. Wu L, Yang H, Ding Z, He Q. Association between hearing loss and insulin resistance as measured by metabolic score for insulin resistance in NHANES 1999 to 2018. *Sci Rep*. 2025, 15(1): 29328.
43. Yévenes-Briones H, Caballero FF, Estrada-deLeón DB, et al. Duration and Quality of Sleep and Risk of Self-reported Hearing Loss: The UK Biobank Study. *Ear Hear*. 2023, 44(5): 1182–1189.
44. Beadle J, Yuwono E, Levasseur M, Wister A. Effectiveness of interventions for social isolation, loneliness, and social participation in older adults with hearing loss: results from a systematic review. *Syst Rev*. 2026, 15(1): 155.