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Depressive Symptoms and Risk of Hearing Loss Among Adults Aged 55 Years and Older: A Population-Based Study

Erjie Xie, Yuedi Tang

Department of Otolaryngology-Head and Neck Surgery, West China Hospital, Sichuan University, Sichuan, China

Background: Depression and hearing loss (HL) commonly occur in the aging population and may arise from shared mechanisms.

Aims: To investigate the observational associations between depression and HL.

Study Design: Observational study.

Methods: Adults aged ≥ 55 years from three nationally representative study cohorts were included: the National Health and Nutrition Examination Survey, the Health and Retirement Study, and the English Longitudinal Study of Ageing. Multiple linear regression was applied to examine the association between depressive severity and audiometric thresholds. Cox regression models were applied to evaluate the associations between depressive symptoms and HL.

Results: Cross-sectional analyses revealed that depression was significantly associated with higher pure-tone average thresholds. In pooled longitudinal analyses of 6,956 participants, individuals with baseline depression exhibited a higher incidence of HL when compared to their non-depressed counterparts. Longitudinal trajectory analyses identified three significant patterns: increasing [hazard ratio (HR) 1.48, 95% confidence interval (CI) 1.09-2.21] and fluctuating (HR 1.25, 95% CI 1.12-1.39) depressive symptom trajectories as independent predictors of HL, whereas decreasing trajectories indicated no significant association.

Conclusion: Depression and specific longitudinal trajectories are associated with elevated risk of HL. To further understand this association, integrated care models that synergistically address depression and HL in older adults are warranted.

INTRODUCTION

Hearing loss (HL), the most prevalent sensory deficit across the world, has emerged as a critical public health crisis, affecting over 466 million individuals.[1-3] Age-related HL (presbycusis) accounts for > 90% of all relevant cases, which imposes disproportionate burdens on older adults, as one-third of individuals aged ≥ 65 years are disabled due to HL.[3,4] With the rapid aging of the world population, HL prevalence is projected to escalate dramatically, necessitating urgent identification of modifiable risk factors to mitigate this "silent epidemic."

Depressive symptoms correlate with elevated risks of sleep disorders, cardiovascular diseases, systemic inflammation, and chronic pain.[5-7] When left untreated, subclinical depression often progresses to clinical depressive disorder, increasing the risks of self-harm and mortality.[8-10] Although HL has been recognized to exacerbate psychosocial distress, such as by increasing risks of depression, social isolation, and cognitive decline[11-14], the reverse causal pathway remains unclear.[11,15] This knowledge gap persists despite compelling biological plausibility: depressive disorders correlate with multisystem pathophysiology, including neuroendocrine dysregulation[16], chronic inflammation[17], and behavioral adaptations[18] that may directly impact auditory structures.

Here, we have proposed a structured conceptual model wherein chronic depression accelerates auditory decline through synergistic direct and indirect pathways. The direct neurobiological mechanisms comprise: (1) sustained systemic inflammation that activates TLR4/NF-κB signaling[19], resulting in cochlear hair cell apoptosis and spiral ganglion neuron degeneration[20,21]; (2) oxidative stress-induced mitochondrial dysfunction in the stria vascularis[22], disrupting endocochlear potential generation[23]; (3) HPA axis dysregulation causing glucocorticoid-mediated excitotoxicity in auditory cortex synapses.[24-26] Concurrently, depression triggers indirect behavioral cascades, including social withdrawal that reduces auditory-cognitive engagement and accelerates central auditory processing decline[27]; healthcare avoidance behavior delaying HL diagnosis and intervention; and maladaptive coping strategies[28] (e.g., prolonged use of headphones at high volume) promoting noise-induced cochlear synaptopathy.

Corresponding author: Yuedi Tang, Department of Otolaryngology-Head and Neck Surgery, West China Hospital, Sichuan University, Sichuan, China

e-mail: tangyd@hotmail.com

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ORCID iDs of the authors: E.X. 0009-0007-4721-9789; Y.T. 0000-0002-7193-5095.

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The bidirectional nature of the HL-depression relationship is increasingly being recognized. For instance, a recent longitudinal study by Tsimpida et al.[29] provided important evidence on this complex interplay, demonstrating that HL was associated with subsequent depressive symptoms, but also the potential for reverse causality. Nevertheless, extant research efforts and reviews continue to predominantly focus on HL as a predictor of depression[30,31], with limited longitudinal data examining depressive symptomatology as a precursor to HL.[32,33] Cross-sectional analysis, though suggestive of associations[34], suffers from three critical limitations: (1) an overreliance on cross-sectional designs that cannot establish temporality; (2) failure to disentangle domain-specific effects of depressive subtypes (cognitive-affective vs. somatic); (3) neglect of dynamic symptom trajectories that may differentially impact auditory pathology.

To overcome these limitations, we integrated data from multiple population-based cohorts, including the National Health and Nutrition Examination Survey (NHANES), Health and Retirement Study (HRS), and English Longitudinal Study of Ageing (ELSA). We aimed to examine the cross-sectional associations between depression severity and hearing thresholds across diverse frequency ranges and investigate the longitudinal relationships between depressive symptom trajectories and the risk of HL over a 10-year follow-up period, with the hope of advancing our current understanding of the interplay between mental health and sensory function.

Establishing depression as a modifiable risk factor for HL carries significant clinical implications. Critically, no FDA-approved disease-modifying drugs currently exist for HL, leaving management limited to devices (e.g., hearing aids) with inherent shortcomings. Within this therapeutic vacuum, treating depression offers a unique preventive opportunity. Evidence-based interventions may interrupt the bidirectional cycle, providing dual benefits: alleviating affective symptoms and mitigating auditory decline. This mechanistic hypothesis merits incorporation into public health strategies for aging populations.

MATERIALS AND METHODS

Study population

We first conducted a cross-sectional analysis using data from the NHANES, a CDC-led program designed to evaluate the health and nutritional status of the United States (US) population. Participants from the NHANES 2015-2016 and 2017-2018 cycles were included. After applying exclusion criteria, 1,736 participants were included in the final analysis; the detailed exclusion process is outlined in Figure 1. The HRS and ELSA are harmonized prospective cohort studies that employ multistage probability sampling of nationally representative aging populations. Data were analyzed from HRS Waves 4-12 (1998-2014) and ELSA Waves 1-9 (2002-2019). The baseline assessments were anchored at HRS Wave 4 (1998) and ELSA Wave 1 (2002). Depressive symptom trajectories were constructed using four biennial survey waves: HRS Waves 4-7 (1998-2004) and ELSA Waves 1-4 (2002-2009), which captured dynamic symptom evolution. Extended surveillance for incident HL spanned 16 years post-baseline through HRS Wave 12 (2014) and ELSA Wave 9 (2018-2019), thus enabling comprehensive time-to-event analyses.

Figure 1 details the participant selection process. From 41,186 initially eligible participants in the HRS and ELSA cohorts, we excluded 13,230 individuals aged < 55 years. Subsequent exclusions differed by the analysis type: baseline depression analyses excluded 2,211 with missing depression assessments, 17,509 with incomplete hearing assessments follow-up, and 1,280 with pre-existing HL, leaving 6,956 participants. For depressive trajectory analyses, we further excluded 12,598 participants with incomplete depression data during follow-up, 7,418 with insufficient hearing assessments, and 2,456 individuals with pre-existing or incident HL before/during the exposure period to minimize any potential confounding factors by preclinical HL and mitigate reverse causality concerns. This approach yielded a final analytical cohort of 5,484 participants.

Definitions and measurements

Depressive symptom assessment

In NHANES, depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9), a validated self-report scale aligned with the diagnostic criteria for major depressive disorder in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition. The total scores were categorized into four levels: 0-4 (non-depressed), 5-9 (mild depression), 10-14 (moderate depression), and ≥ 15 (severe depression).[35] The PHQ-9 demonstrated strong reliability and validity in both clinical and population-based settings.[36,37]

In HRS and ELSA, depressive symptoms were assessed using an 8-item version of the center for epidemiologic studies depression scale; this tool was validated for use in older adult populations.[38,39] Participants reported the presence of each symptom over the past week, with responses summed to create a total score (range: 0-8). A score of ≥3 indicated clinically relevant depressive symptoms.[40,41] The symptoms were further categorized into two domains: the cognitive-affective domain, which reflected fundamental emotional disturbances; and the somatic domain, which represented physical manifestations of depression.[42] The scores of both cognitive-affective and somatic domains were categorized using upper tertile thresholds, with CES-D scores ≥ 2 representing clinically significant symptoms in each respective domain.[43]

The depressive symptom trajectories were constructed based on the CES-D score changes across HRS waves 4-7 and ELSA waves 1-4. Five distinct trajectories were identified: consistently low, as characterized by no elevated symptoms at any time point; decreasing, as defined by elevated symptoms at the initial time point(s) followed by a consistent decline; increasing, marked by no elevated symptoms initially, but consistent elevation thereafter; consistently high, indicating elevated symptoms at all-time points; and fluctuating, encompassing trajectories that did not fit the abovementioned categories. Participants exhibiting consistently low symptoms were designated as the reference group.[44] Similar categorizations were applied to somatic and cognitive-affective

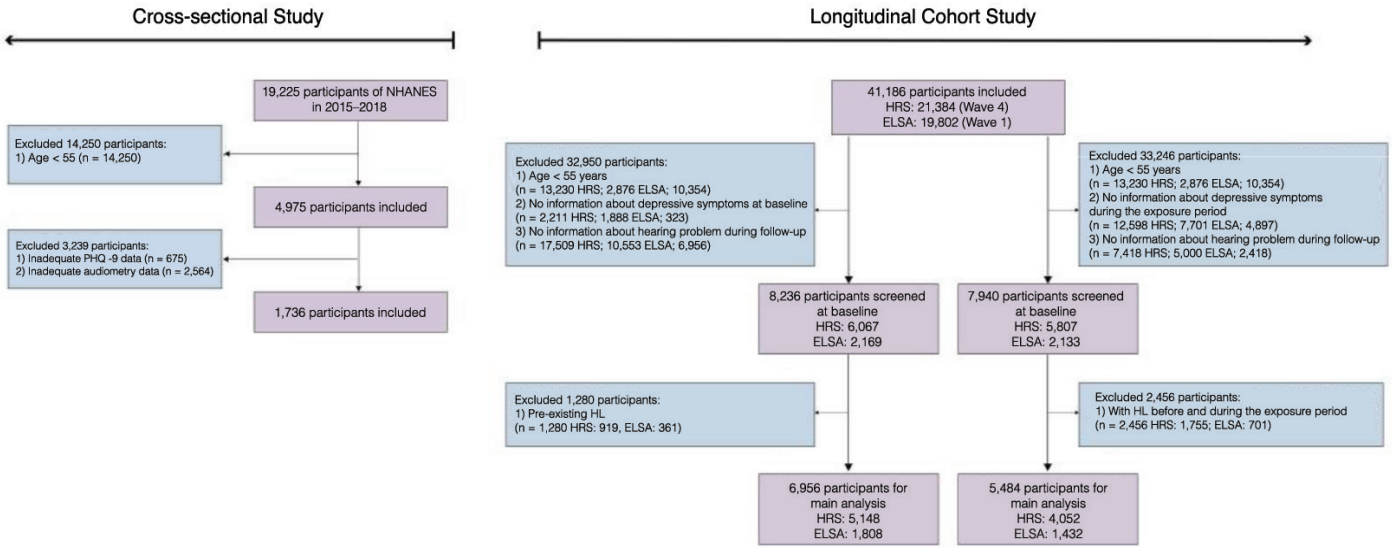

FIG. 1. Flowchart of the study selection process.

HRS, the Health and Retirement Study; ELSA, the English Longitudinal Study of Ageing; PHQ, Patient Health Questionnaire-9; NHANES, National Health and Nutrition Examination Survey.

symptom trajectories. Definitions of depressive symptom domains (i.e., cognitive-affective and somatic) and trajectory classifications are detailed in Supplementary Tables 1 and 2.

Hearing assessment

Hearing thresholds were measured using pure-tone audiometry (PTA). The thresholds for each frequency were calculated as the mean of binaural PTA values, excluding data with interaural threshold differences exceeding 10 dB at the same frequency. Low-frequency PTA was defined as the mean of thresholds at 0.5, 1, and 2 kHz; speech-frequency PTA as the mean of thresholds at 0.5, 1, 2, and 4 kHz; and high-frequency PTA as the mean of thresholds at 4, 6, and 8 kHz.[45,46]

Hearing problems were assessed across HRS waves 8-12 and ELSA waves 5-9 by using a standardized self-report measure. The participants rated their hearing ability on a 5-point Likert scale (1 = excellent to 5 = poor), and the responses were categorized into two groups: normal hearing (excellent/very good/good) and HL (fair/poor).[47] The onset of HL was defined as the first survey wave in which participants reported a score of 4 (fair) or 5 (poor).[48] The self-reported question demonstrated sensitivity of 43.0%-81.5% and specificity of 76.4%-93% in prior studies.[49,50]

Statistical analysis

Continuous variables were summarized by mean and standard deviation (SD); categorical variables were presented as counts and percentages.

In NHANES, we applied the recommended 4-year sampling weights derived from the original 2-year mobile examination center weights (WTMEC2YR) to ensure nationally representative estimates. This weighting approach accounted for NHANES' complex survey design and non-response, allowing all analyses to produce unbiased estimates generalizable to the non-institutionalized US civilian population during the study period. Kaplan-Meier (K-M) curves were used for univariate survival analysis. Multiple linear regression models were employed to explore the associations between depressive symptoms and hearing thresholds, after adjusting for potential confounders. To explore the potential threshold effects, we systematically evaluated each integer value of PHQ-9 as a candidate cut-off. At each threshold, the participants were dichotomized into subclinical (PHQ < cut-off) and clinically significant (PHQ ≥ cut-off) depression groups. Differences in the hearing thresholds between the groups were assessed by using complex survey linear regression. The optimal clinical threshold was defined as the PHQ-9 value, yielding the largest statistically significant ($p < 0.05$) hearing threshold differences. In HRS and ELSA, multivariate Cox proportional hazards models were employed to estimate associations between depressive symptoms and the risk of HL. The proportional hazards assumptions for these models were assessed and validated using Schoenfeld residuals.

For our core exposure (depression) and primary outcome (hearing assessment), we maintained complete-case analysis by excluding individuals with missing data. To address the missing covariate data, we applied chained-equation multiple imputation using the "mice" package in R. A total of five imputed datasets were generated, each undergoing a maximum of 50 iterations per imputation round. All five imputed datasets were analyzed separately, and results were combined using Rubin's rules to obtain the pooled-effect estimates. False discovery rate (FDR) correction was applied independently per frequency band (low/speech/high), depressive symptom subscale, and trajectory group using the Benjamini-Hochberg procedure. Associations were considered suggestive at $p < 0.05$ with $q \geq 0.05$, and statistically significant at FDR $q < 0.05$.

To assess the effect modification, we incorporated interaction terms between the depression levels and covariates in survey-weighted

TABLE 1. Baseline Characteristics of Participants Stratified by Depression Status at Baseline in the HRS and ELSA Cohorts.

Characteristic	Overall (n = 6956)	Non-depressive (n = 5767)	Depressive (n = 1189)	*p*
Age, mean (SD)	63.3 (6.2)	63.3 (6.2)	63.2 (6.5)	0.569
Sex, n (%)				< 0.001
Female	4494 (64.6)	3578 (62.0)	916 (77.0)	
Male	2462 (35.4)	2189 (38.0)	273 (23.0)	
Education, n (%)				< 0.001
Below high school	1510 (21.7)	1106 (19.2)	404 (34.0)	
High school	2310 (33.2)	1912 (33.2)	398 (33.5)	
College or above	2955 (42.5)	2606 (45.2)	349 (29.4)	
Other	181 (2.6)	143 (2.5)	38 (3.2)	
Marital status, n (%)				< 0.001
Married or partnered	5162 (74.2)	4434 (76.9)	728 (61.2)	
Unmarried and others	1794 (25.8)	1333 (23.1)	461 (38.8)	
Household income, n (%)				< 0.001
High tertile	2943 (42.3)	2615 (45.3)	328 (27.6)	
Medium tertile	2308 (33.2)	1929 (33.4)	379 (31.9)	
Low tertile	1705 (24.5)	1223 (21.2)	482 (40.5)	
Smoking status, n (%)				0.114
Ever smokers	3758 (54.1)	3089 (53.6)	669 (56.3)	
Never smokers	3192 (45.9)	2672 (46.4)	520 (43.7)	
Drinking status, n (%)				< 0.001
Ever drinkers	4473 (64.3)	3810 (66.1)	663 (55.8)	
Never drinkers	2483 (35.7)	1957 (33.9)	526 (44.2)	
Hypertension, n (%)				< 0.001
No	4531 (65.1)	3830 (66.4)	701 (59.0)	
Yes	2425 (34.9)	1937 (33.6)	488 (41.0)	
Diabetes, n (%)				0.002
No	6481 (93.2)	5398 (93.6)	1083 (91.1)	
Yes	475 (6.8)	369 (6.4)	106 (8.9)	
Cognition, mean (SD)	0.3 (0.1)	0.3 (0.1)	0.4 (0.1)	< 0.001
Depressive symptoms (CES-D)				
Total score, mean (SD)	1.2 (1.7)	0.6 (0.7)	4.5 (1.5)	< 0.001
Cognitive-affective score, mean (SD)	0.4 (0.8)	0.1 (0.4)	1.8 (1.0)	< 0.001
Somatic score, mean (SD)	0.7 (0.9)	0.4 (0.6)	2.0 (0.9)	< 0.001

HRS, Health and Retirement Study; ELSA, English Longitudinal Study of Ageing; SD, standard deviation; CES-D, central depression scale.

linear regression models. Estimates from multiply imputed datasets were pooled via Rubin's rules, with interaction significance tested by Wald tests ($\alpha = 0.05$). Significant interactions underwent marginal effects visualization to demonstrate the depression effect heterogeneity across subgroups.

Model adequacy was confirmed through normality (Shapiro-Wilk), homoscedasticity (Breusch-Pagan), and global and covariate-specific Schoenfeld tests, with $\alpha = 0.05$. The functional form of each continuous predictor was assessed with restricted cubic splines (3-5 knots) via the "rms" package. Where assumptions were violated, we applied quantile regression ($\tau = 0.5$) or rank transformations after re-fitting each model across 15 imputed datasets under Rubin's rules.

Statistical analyses were performed using R software (version 4.3.2, R Foundation for Statistical Computing, Vienna, Austria).

TABLE 2. Baseline Characteristics of Participants Stratified by Depressive Symptom Trajectories.

Characteristic	Overall (n = 5484)	Consistently low (n = 3612)	Consistently high (n = 156)	Decreasing (n = 117)	Fluctuating (n = 1486)	Increasing (n = 113)	*p* value
Age, y, mean (SD)	63.0 (6.1)	63.1 (6.0)	63.6 (6.6)	62.7 (6.5)	62.9 (6.2)	63.4 (6.0)	0.510
Sex, n (%)							< 0.001
Male	1786 (32.6)	1368 (37.9)	24 (15.4)	18 (15.4)	350 (23.6)	26 (23.0)	
Female	3698 (67.4)	2244 (62.1)	132 (84.6)	99 (84.6)	1136 (76.4)	87 (77.0)	
Educational attainment, n (%)							< 0.001
Below high school	1092 (19.9)	595 (16.5)	63 (40.4)	34 (29.1)	375 (25.2)	25 (22.1)	
High school	1850 (33.7)	1187 (32.9)	51 (32.7)	41 (35.0)	529 (35.6)	42 (37.2)	
College or above	2396 (43.7)	1746 (48.3)	34 (21.8)	38 (32.5)	534 (35.9)	44 (38.9)	
Other	146 (2.7)	84 (2.3)	8 (5.1)	4 (3.4)	48 (3.2)	2 (1.8)	
Marital status, n (%)							< 0.001
Married and partnered	4056 (74.0)	2817 (78.0)	74 (47.4)	74 (63.2)	1005 (67.6)	86 (76.1)	
Unmarried and others	1428 (26.0)	795 (22.0)	82 (52.6)	43 (36.7)	481 (32.4)	27 (23.9)	
Household income, n (%)							< 0.001
High tertile	2378 (43.4)	1752 (48.5)	27 (17.3)	30 (25.6)	525 (35.3)	44 (38.9)	
Medium tertile	1816 (33.1)	1190 (32.9)	51 (32.7)	42 (35.9)	491 (33.0)	42 (37.2)	
Low tertile	1290 (23.5)	670 (18.5)	78 (50.0)	45 (38.5)	470 (31.6)	27 (23.9)	
Smoking status, n (%)							0.223
Never	2574 (46.9)	1729 (47.9)	65 (41.7)	57 (48.7)	669 (45.0)	54 (47.8)	
Ever	2910 (53.1)	1883 (52.1)	91 (58.3)	60 (51.3)	817 (55.0)	59 (52.2)	
Alcohol consumption, n (%)							< 0.001
Never	1925 (35.1)	1147 (31.8)	86 (55.1)	49 (41.9)	591 (39.8)	52 (46.0)	
Ever	3559 (64.9)	2465 (68.2)	70 (44.9)	68 (58.1)	895 (60.2)	61 (54.0)	
Hypertension, n (%)							< 0.001
No	3629 (66.2)	2451 (67.9)	87 (55.8)	71 (60.7)	957 (64.4)	63 (55.8)	
Yes	1855 (33.8)	1161 (32.1)	69 (44.2)	46 (39.3)	529 (35.6)	50 (44.2)	
Diabetes, n (%)							< 0.001
No	5126 (93.5)	3415 (94.5)	142 (91.0)	103 (88.0)	1362 (91.7)	104 (92.0)	
Yes	358 (6.5)	197 (5.5)	14 (9.0)	14 (12.0)	124 (8.3)	9 (8.0)	
Cognition function, mean (SD)	0.3 (0.1)	0.3 (0.1)	0.4 (0.1)	0.3 (0.1)	0.3 (0.1)	0.3 (0.1)	0.004

SD, standard deviation.

Covariates

Covariates were selected based on the established epidemiological evidence, encompassing key demographic, socioeconomic, behavioral, and clinical factors. For the NHANES cohort, these included age, gender, educational attainment, poverty-income ratio, body mass index, triglyceride-glucose index, systemic inflammation response index (SIRI), smoking status, alcohol consumption, physical activity, noise exposures, comorbidity status, memory problems, and antidepressant use. In the HRS and ELSA cohorts, covariates comprised age, gender, educational attainment, marital status, household income, smoking status, alcohol consumption, hypertension, diabetes, and cognitive function. Comprehensive operational definitions for all variables are documented in the Supplementary Methods.

Ethical considerations

The NHANES was approved by the CDC's Institutional Review Board, and HRS and ELSA received ethical approval from their respective review committees. Written informed consent was obtained from all participants or their guardians before their inclusion.

RESULTS

Baseline characteristics of the study population

The baseline characteristics of 1,736 participants from NHANES, stratified by depression severity (no, mild, moderate, and severe depression), are summarized in Supplementary Table 3. The mean age was 66.3 years (SD = 7.5), with near-equal sex distribution (47.6% male).

In longitudinal analysis, two analytic frameworks were implemented: (1) baseline depression status (present/absent; n = 6,956) (Table 1) and (2) eight-year depressive trajectories (n = 5,484) (Table 2). At baseline, depressive individuals exhibited pronounced socioeconomic disparities: female predominance, lower education, and income inequality. Marital instability and cardiometabolic burdens were elevated. Adverse trajectories demonstrated socioeconomic vulnerability and female predominance.

Cross-sectional associations between depression severity and HL

In unadjusted analyses, severe depression was significantly associated with elevated hearing thresholds across all frequency ranges: low-frequency PTA [β = %95 ,6.86 confidence interval (CI): 2.35-11.36, $p = 0.003$, FDR q = 0.009] and speech-frequency PTA (β = 7.69, 95% CI: 2.24-13.14, $p = 0.006$, FDR q = 0.018). In contrast, mild and moderate depression showed no significant associations with hearing thresholds at any frequency.

After full adjustment, severe depression remained significantly associated with elevated low-frequency PTA (β = 7.46, 95% CI: 3.71-11.21, $p < 0.001$, FDR q = 0.003) and speech-frequency PTA (β = 7.76, 95% CI: 2.96-12.56, $p = 0.002$, FDR q = 0.006). For high-frequency PTA, the association with severe depression approached, but did not reach any nominal significance (β = 7.66, 95% CI: -0.61 to 15.93, $p = 0.070$) and did not survive multiple testing correction (FDR q = 0.210). No significant associations were detected for mild or moderate depression at any frequency after the adjustment (Table 3). Full diagnostic analyses and validation results have been presented in Supplementary Tables 4 and 5. Testing for non-linear characteristics of covariates has been summarized in Supplementary Table 6. Significant interactions identified both synergistic and protective modifiers of depression-hearing associations. Age intensified the effects of mild depression, while racial identity amplified the impacts of severe depression. Firearm noise exposure exerted protective effects across all levels of depression severity. Physical activity intensity differentially modified severe depression outcomes, with vigorous exertion providing the strongest protection. In contrast, memory impairment and systemic inflammation SIRI acted as synergistic risk amplifiers (Supplementary Table 7).

Longitudinal association of baseline depression status with incident HL

Figure 2 presents the K-M curves for the cumulative HL incidence across depressive status groups. Participants with total, cognitive-affective, or somatic depressive symptoms exhibited a higher

TABLE 3. Association Between Depression Severity (PHQ-9) and Hearing Thresholds in the NHANES.

	Crude			Adjusted[a]		
Depression severity	**β (95% CI)**	***p***	**FDR q**	**β (95% CI)**	***p***	**FDR q**
Low-frequency PTA						
Non-depressed	Ref			Ref		
Mild depression	1.25 (-0.88, 3.39)	0.250	0.500	0.82 (-1.28, 2.92)	0.445	0.445
Moderate depression	2.61 (-1.50, 6.72)	0.213	0.500	1.70 (-2.52, 5.92)	0.430	0.445
Severe depression	6.86 (2.35, 11.36)	0.003	0.009	7.46 (3.71, 11.21)	< 0.001	0.003
Speech-frequency PTA						
Non-depressed	Ref			Ref		
Mild depression	0.75 (-1.26, 2.75)	0.466	0.699	0.46 (-1.66, 2.58)	0.670	0.670
Moderate depression	2.25 (-1.84, 6.34)	0.281	0.562	1.67 (-2.40, 5.74)	0.421	0.632
Severe depression	7.69 (2.24, 13.14)	0.006	0.018	7.76 (2.96, 12.56)	0.002	0.006
High-frequency PTA						
Non-depressed	Ref			Ref		
Mild depression	-1.76 (-4.25, 0.73)	0.165	0.330	-1.37 (-4.26, 1.52)	0.353	0.530
Moderate depression	0.63 (-4.21, 5.46)	0.800	0.800	1.15 (-2.99, 5.29)	0.587	0.587
Severe depression	8.58 (0.17, 16.99)	0.046	0.092	7.66 (-0.61, 15.93)	0.070	0.210

[a]Adjusted for age, sex, race, education attainment, marital status, PIR (poverty-income ratio), BMI (body mass index), tobacco and alcohol use, physical activity, comorbidities, firearm noise exposure, occupational noise exposure, recreational noise exposure, TyG (triglyceride-glucose index), SIRI (systemic inflammation response index), memory problems, and antidepressant use.
PHQ-9, Patient Health Questionnaire-9; NHANES, National Health and Nutrition Examination Survey; PTA, pure-tone audiometry; CI, confidence interval; FDR, false discovery rate

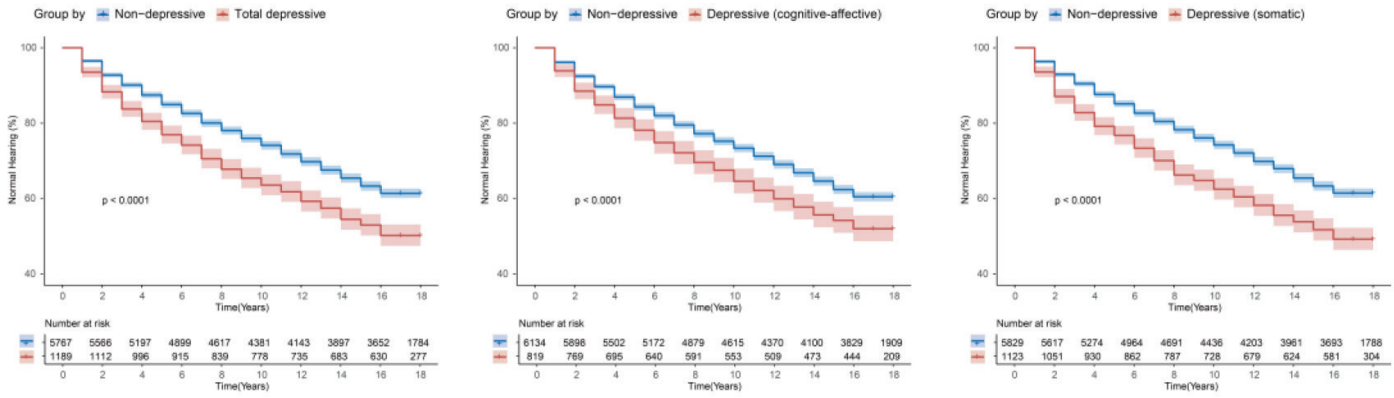

FIG. 2. Kaplan-Meier curves of cumulative hearing loss incidence in groups with different baseline depressive status.

incidence of HL compared to the non-depressive group. In unadjusted analyses, each SD increase in depressive symptoms was significantly associated with incident HL: total symptoms [hazard ratio (HR) = 1.07, 95% CI: 1.05-1.10, $p < 0.001$, FDR q = 0.002, E = 1.34], cognitive-affective symptoms (HR = 1.07, 95% CI: 1.01-1.14, $p = 0.027$, FDR q = 0.027, E = 1.34), and somatic symptoms (HR = 1.17, 95% CI: 1.11-1.23, $p < 0.001$, FDR q = 0.002, E = 1.62). After multivariable adjustment, these associations strengthened: total symptoms (aHR = 1.10, 95% CI: 1.07-1.13, $p < 0.001$, FDR q = 0.002, E = 1.43), cognitive-affective symptoms (aHR = 1.09, 95% CI: 1.03-1.17, $p = 0.007$, FDR q = 0.007, E = 1.40), and somatic symptoms (aHR = 1.22, 95% CI: 1.16-1.29, $p < 0.001$, FDR q = 0.002, E = 1.74). All associations remained statistically significant after FDR correction (q < 0.05) (Supplementary Table 8). Considering that somatic symptoms demonstrated stronger effects than cognitive-affective symptoms, we conducted component-level analyses of somatic symptoms, which revealed that "everything was an effort," suggesting the

TABLE 4. Associations Between Depressive Symptom Trajectories and Risk of Hearing Loss.

	Crude			Adjusted[a]			
Depressive symptom trajectory	**HR (95% CI)**	***p***	**FDR q**	**HR (95% CI)**	***p***	**FDR q**	**E value**
Total depressive symptom trajectory							
Consistently low	Ref			Ref			
Consistently high	1.24 (0.96-1.61)	0.103	0.137	1.21 (0.92-1.61)	0.179	0.239	
Decreasing	1.13 (0.83-1.54)	0.452	0.452	1.20 (0.86-1.68)	0.278	0.371	
Fluctuating	1.19 (1.08-1.32)	< 0.001	< 0.001	1.23 (1.10-1.37)	< 0.001	< 0.001	1.76
Increasing	1.47 (1.11-1.96)	0.007	0.014	1.50 (1.11-2.04)	0.009	0.018	2.37
Cognitive-affective depressive symptom trajectory							
Consistently low	Ref			Ref			
Consistently high	1.42 (1.02-1.97)	0.039	0.078	1.29 (0.92-1.82)	0.143	0.190	
Decreasing	0.96 (0.61-1.50)	0.844	0.844	0.91 (0.55-1.52)	0.723	0.723	
Fluctuating	1.10 (0.99-1.22)	0.084	0.112	1.12 (1.00-1.26)	0.059	0.118	
Increasing	1.60 (1.13-2.27)	0.009	0.018	1.75 (1.21-2.53)	0.003	0.012	2.90
Somatic depressive symptom trajectory							
Consistently low	Ref			Ref			
Consistently high	1.41 (1.08-1.85)	0.013	0.026	1.42 (1.07-1.90)	0.016	0.032	2.19
Decreasing	1.28 (0.88-1.87)	0.193	0.257	1.34 (0.89-2.03)	0.166	0.221	
Fluctuating	1.18 (1.07-1.31)	< 0.001	< 0.001	1.23 (1.10-1.37)	< 0.001	< 0.001	1.76
Increasing	1.24 (0.85-1.81)	0.273	0.364	1.20 (0.81-1.79)	0.364	0.364	

[a]The adjusted model accounted for potential confounders, including age, gender, education level, marital status, household income, cognition function, smoking status, alcohol consumption, hypertension and diabetes.
HR, hazard ratio; CI, confidence interval; FDR, false discovery rate

most robust association (aHR = 1.32, 95% CI: 1.21-1.45, $p < 0.001$, FDR q < 0.001), followed by "could not get going" (aHR = 1.31, 95% CI: 1.20-1.44, $p < 0.001$, FDR q < 0.001), and finally "restless sleep" (aHR = 1.22, 95% CI: 1.14-1.32, $p < 0.001$, FDR q < 0.001) (Supplementary Table 9).

Longitudinal association of depression symptom trajectories with incident HL

As shown in Supplementary Figure 1, distinct depressive symptom trajectories were identified. Longitudinal analyses demonstrated significant associations between these trajectories and HL risk (Table 4). The K-M curves indicated a progressive decline in normal hearing over the follow-up period, with consistently high and increasing depressive symptom groups experiencing the most rapid declines (Supplementary Figure 2). Details on incident HL events, median follow-up duration, censoring criteria, and log-rank statistics are provided in Supplementary Table 10.

In unadjusted analyses, fluctuating depressive symptoms revealed significantly elevated HL risk for total (HR = 1.19, 95% CI: 1.08-1.32, $p < 0.001$, FDR q < 0.001) and somatic symptoms (HR = 1.18, 95% CI: 1.07-1.31, $p < 0.001$, FDR q < 0.001), but not for cognitive-affective symptoms (HR = 1.10, 95% CI: 0.99-1.22, $p = 0.084$, FDR q = 0.112). Increasing trajectories demonstrated a significant risk for total (HR = 1.47, 95% CI: 1.11-1.96, $p = 0.007$, FDR q = 0.014) and cognitive-affective symptoms (HR = 1.60, 95% CI: 1.13-2.27, $p = 0.009$, FDR q = 0.018). Consistently high somatic symptoms indicated elevated risk (HR = 1.41, 95% CI: 1.08-1.85, $p = 0.013$, FDR q = 0.026). Adjusted models revealed consistent patterns: fluctuating symptoms remained significant for total (aHR = 1.23, 95% CI: 1.10-1.37, $p < 0.001$, FDR q < 0.001) and somatic symptoms (aHR = 1.23, 95% CI: 1.10-1.37, $p < 0.001$, FDR q < 0.001); increasing trajectories for total (aHR = 1.50, 95% CI: 1.11-2.04, $p = 0.009$, FDR q = 0.018) and cognitive-affective symptoms (aHR = 1.75, 95% CI: 1.21-2.53, $p = 0.003$, FDR q = 0.012); and consistently high somatic symptoms (aHR = 1.42, 95% CI: 1.07-1.90, $p = 0.016$, FDR q = 0.032). No other trajectories revealed significant associations after FDR correction (Table 4). Power analysis addresses concerns regarding smaller trajectory groups (Supplementary Table 11). Supplementary Table 12 presents covariate-specific proportional hazards assumption testing for the Cox regression models.

DISCUSSION

This study provides robust evidence linking depression severity and symptom trajectories with HL. Participants with baseline depressive symptoms faced an elevated risk of developing HL, with somatic symptoms emerging as the strongest predictor. Over eight years, trajectory analyses revealed higher HL risks among individuals with consistently high, increasing, or fluctuating symptoms. These findings underscore the importance of depressive symptom subtypes and their dynamic progression in HL pathogenesis.

The escalating global burden of depression in aging populations underscores the need to investigate its multisystemic health consequences. Our systematic review of longitudinal studies (Supplementary Table 13) highlighted critical methodological limitations in previous studies. Using prospective dual-cohort analysis, we showed a persistently elevated incidence of HL among depressed individuals compared with non-depressed controls, supporting previous meta-analytic findings.[11] Mechanistically, this association may reflect depression-related neuropathological changes in central auditory pathways and cochlear aging processes mediated by chronic inflammatory cascades.[24,25,51-56]

Beyond baseline assessments, our study is among the first to examine dynamic depression trajectories in HL pathogenesis. Distinct longitudinal depression patterns were confirmed in the HRS and ELSA cohorts, revealing trajectory-dependent HL risk. Participants with fluctuating depressive symptoms exhibited consistently elevated HL risk across total and somatic domains, while those with increasing trajectories showed pronounced risk for total and cognitive-affective symptoms. Consistently high somatic symptoms remained significantly associated with HL risk, whereas consistently high total or cognitive-affective symptoms showed no significant associations after full adjustment. Notably, the absence of a significant association for decreasing depressive symptoms suggests that effective depression management may mitigate HL risk, emphasizing the value of early intervention and sustained mental health care.

Collectively, these findings establish depression as a dynamic risk modulator for auditory decline, with trajectory patterns and symptom domains differentially affecting cochlear vulnerability. The pronounced impact of chronic somatic symptoms highlights the need for targeted monitoring in depressed patients exhibiting a high somatic symptom burden.

Our findings carry several key implications. First, we propose an integrated stepped-care model incorporating: (1) bidirectional screening (PHQ ≥ 15 triggering mandatory audiometry; HL patients completing PHQ-9), and (2) targeted prevention programs addressing somatic symptoms through sleep and nutrition interventions. Second, the stronger association with somatic depressive symptoms suggests that mitigating physiological dysregulation, via anti-inflammatory therapies or lifestyle changes, may reduce HL risk in depressed individuals. Finally, although the study demonstrates a temporally structured relationship between depression and HL, these results should be interpreted with caution.

Several limitations should be acknowledged. First, residual confounding from unmeasured variables (e.g., ototoxic antidepressants) may persist despite covariate adjustment. Second, reliance on self-reported or clinically assessed depressive symptoms could introduce measurement bias. Third, generalizability may be limited by cohort characteristics (e.g., predominantly Caucasian populations in ELSA). Future studies incorporating objective depression biomarkers (e.g., inflammatory or neuroimaging profiles), medication adherence data, and longitudinal audiometric assessments are needed to elucidate the underlying mechanisms.

Several limitations warrant consideration. First, residual confounding from unmeasured variables may persist despite covariate adjustment. Second, heterogeneity in depression assessment methods (PHQ-9, CES-D) across cohorts may bias estimates. Third, despite our longitudinal design, reverse

causality cannot be entirely excluded. Given the 8-year trajectory period, some depressive symptoms may partly reflect reactions to underlying or subclinical hearing decline not fully captured at baseline, rather than causally contributing to HL, an inherent limitation of observational studies. Fourth, the use of self-reported HL in HRS and ELSA, alongside objective audiometry in NHANES, is a major limitation. Self-report, while capturing broader functional and perceptual aspects of hearing, is not equivalent to audiometric thresholds and introduces potential measurement bias and misclassification. Fifth, our multiple imputation approach assumes data are missing-at-random, which may not fully hold. Although a wide range of variables was included to make this assumption more plausible, the potential for bias due to data missing not at random cannot be entirely ruled out. Sixth, generalizability may be limited by cohort characteristics, such as the predominantly White populations in ELSA. Seventh, significant potential for survival bias exists because our analysis required participants to survive and remain engaged throughout the extended follow-up. This may have selectively excluded individuals with more severe depression, greater HL, or other serious health conditions, potentially leading to underestimation of the true associations between depressive symptom trajectories and HL. Eighth, the use of a rule-based classification system for depressive symptom trajectories, rather than a data-driven statistical approach (e.g., latent class growth analysis), represents an additional limitation. While designed to maintain clinical relevance, this method relies on predefined rules and thresholds, introducing subjectivity and potentially limiting comparability with studies using model-based trajectories.

This study provides robust evidence linking depressive status, symptom trajectories, and HL. The findings underscore the importance of integrating mental health care into strategies for preserving auditory function, particularly in aging populations. Although the precise mechanisms remain unclear, the results suggest that effective management of depression, especially somatic symptoms, may help reduce HL risk. Future research should investigate the underlying pathways and develop targeted interventions to mitigate depression's impact on auditory health.

Ethics Committee Approval: Not applicable.

Informed Consent: Written informed consent was obtained from all participants or their guardians before their inclusion.

Data Sharing Statement: The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

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Supplementary 1: https://www.balkanmedicaljournal.org/img/files/balkan-2025.2025-6-78-9-supplement%281%29.pdf

Supplementary 2: https://www.balkanmedicaljournal.org/img/files/balkan-2025.2025-6-78-9-supplement-2%281%29.pdf

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