1. **Full Title**: The impact of noise exposure on subclinical speech in noise deficits: epidemiologic insights into hidden hearing loss

   **b. Abbreviated Title (Length 26 characters)**: hidden hearing loss

2. **Writing Group**:
   Writing group members: Osama Tarabichi (first author), Jennifer A. Deal, Joshua Betz, Frank R Lin, Adele Goman, Nicholas Reed (senior author)

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. ___ OT ___ [please confirm with your initials electronically or in writing]

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3. **Timeline**:  
   Data Analysis - 6 months, manuscript preparation - 3 months

4. **Rationale**:  
   Traditional clinical evaluations of hearing loss include measuring behavioral pure tone audiometric thresholds to determine the mechanism and severity of hearing loss. While audiometry is undoubtedly an effective and useful tool, clinical observations that
individuals with normal audiometric thresholds can have significantly different hearing experiences, particularly in noisy environments, has motivated research into pathologic mechanisms of hearing loss that are not detectable by audiometry\(^2\). There is a growing body of evidence from both animal and human studies that in the noise-exposed and/or aging ear, degradation of synaptic connections between the cochlear inner hair cells and auditory nerve neurons could potentially explain perceived difficulties listening in noisy environments despite normal audiometric testing\(^3\)\(^4\). The absence of evidence on standard clinical testing has led to investigators coining the term “hidden hearing loss (HHL)” to describe this phenomenon\(^6\).

The ability to detect pure tones relies on intact cochlear hair cell mechanics and spiral ganglion neurons (SGN)\(^7\). SGNs are the primary messengers that carry sound information transduced by the inner ear from the cochlea to the brain for processing. SGN’s are classified based on physiologic properties as high and low threshold SGNs and both types are equally distributed across the frequency map of the cochlea\(^8,9\). It is thought that low threshold neurons are typically reserved for hearing in quiet environments and are the main type of neuron activated in pure tone audiometric testing. In noisy environments, the background level of noise rises above the threshold level of activation for low-threshold SGN’s and we rely on our high threshold neurons to discriminate signals of interest\(^10,11\).

Evidence from human, rodent and primate temporal bone histology has revealed that synaptic degradation between hair cells and SGN’s occurs in the aging/ noise exposed cochlea\(^12\)\(^-\)\(^14\) and disproportionately affects synaptic terminals of high threshold SGNs\(^7\). This differential degradation of high threshold SGN synapses could theoretically impact an individual’s ability to understand speech in noise without affecting their ability to perform audiometric tasks and provide a plausible biologic explanation for the HHL paradigm.

The discovery of these findings in animal studies has led to some investigators evaluating physiologic tests that could potentially detect these deficits in humans. In a seminal report, Maison et al found that music students with a documented history of noise exposure, speech in noise deficits and normal audiograms had reductions in their auditory brainstem implant wave 1 amplitudes and increased ultra-high frequency audiometric thresholds (10-20KHz)\(^15\). Despite extensive research aiming to better understand HHL and develop diagnostic tools that could detect it in clinical settings, epidemiologic research attempting to estimate the burden of this problem is limited\(^15\). Spankovic et al investigated the prevalence of subjective hearing difficulty in individuals with normal audiograms age 20-69 participating in NHANES and reported that it was about 15%\(^16\). Spankovic et al did not find a significant association between self-reported hearing problems and history of noise exposure in individuals with normal audiograms. Tremblay et al performed a similar analysis in the beaver dam offspring study and found that 12% of individuals with normal audiograms reported subjective hearing difficulty and that it was associated with recreational and fire-arm related noise exposure.\(^17\).
In the ARIC study, participants underwent an evaluation of their ability to understand speech in noise (QuickSIN). This data will allow us to evaluate the proposed mechanism of HHL by examining the association between noise exposure and speech in noise performance in individuals with normal audiograms. We hypothesize that individuals with normal audiograms and a history of noise exposure will demonstrate poorer speech in noise performance than those without a history of noise exposure. To our knowledge, this study will be the first to explore this hypothesis using an objective measure of speech in noise deficits in a large cohort study. This analysis could provide important insights into the proposed association between noise exposure and subclinical speech in noise deficits and identify other factors associated with this clinical paradigm.

5. **Main Hypothesis/Study Questions:**

Aim: Investigate the impact of noise exposure on the ability to comprehend speech in noise in a cohort of older adults with normal audiometric results.

Hypothesis: Older adults with normal audiograms and a history of noise exposure have poorer speech in noise performance than those without a history of noise exposure.

6. **Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).**

Primary outcome:

- Signal to noise ratio (SNR) loss: ARIC participants received a speech in noise perception test (QuickSIN). This test involves playing tracks of six sentences with five key words in each at varying SNR ratios to determine SNR loss. One point is awarded for each key word that is correctly identified. SNR loss is calculated by subtracting the total number of correct words from 25.5. SNR loss will be analyzed as a continuous outcome in our model. We will also model SNR loss as an ordinal outcome by dividing our observed dataset into quartiles and studying distribution of exposures between quartiles.

**Exposure:**

- Hearing ability: Hearing ability was assessed at ARIC Visit 6 (N=3,625) using pure-tone audiometry in a sound treated booth. Pure-tone audiometry is the gold standard method for assessing objective hearing ability. Only individuals with normal thresholds (<25dB) at 0.5, 1, 2, 4 and 8 KHz will be included in this analysis.

- Noise Exposure: The following questions are asked as part of the HNE form to determine history of noise exposure. Noise exposure will be modelled as a dichotomous outcome (ever vs. never noise exposed) with questions 1, 3 and 5 below. We will report occupational and firearm
related noise exposure as two separate ordinal scales and assess their relationship to the outcome as well (Q2/4).

1) Have you ever used firearms for target shooting, hunting, or any other purposes? (Y/N)
   Purpose of firearm use?
   • Target Shooting (Y/N)
   • Hunting (Y/N)
   • Military (Y/N)
   • Job/other (Y/N)

2) How many TOTAL rounds have you fired (include target shooting, hunting, military, and/or job/other experience)?
   • 1 to less than 100 rounds ......................... 1
   • 100 to less than 1000 rounds ..................... 2
   • 1000 to less than 10,000 rounds ................ 3
   • 10,000 to less than 50,000 rounds ............. 4
   • 50,000 or more rounds .......................... 5

3) Have you ever had a job or combination of jobs where you were exposed to very loud sounds or noise for 10 or more hours per week? By loud noise I mean noise so loud that you had to shout to be heard. (Y/N)

4) For how many months or years have you been or were you exposed at work to loud sounds or noise for 10 or more hours per week?
   • Less than 3 months ............................... 1
   • 3 to 11 months ..................................... 2
   • 1 to 2 years ....................................... 3
   • 3 to 4 years ....................................... 4
   • 5 to 9 years ....................................... 5
   • 10 to 14 years .................................... 6
   • 15 or more years ................................. 7

5) Outside of a job, have you ever been exposed to very loud noise or music for 10 or more hours a week? This is noise so loud that you have to shout to be understood 3 feet away. Examples are noise from power tools, lawn mowers, farm machinery, cars, trucks, motorcycles, or loud music. (Y/N)

Covariates:

-Age: The association between age and QuickSIN scores will be modeled using splines to account for potential non-linear relationships. We may also consider stratifying our analyses by age group as we expect our outcome may vary significantly by age.
- Sex
- Education level
  - Categorical outcome with three categories: Less than high school, high school, more than high school
- Race
- Health related factors: hypertension, stroke, smoking, diabetes.

**Statistical approach**

A multivariable linear regression model will be constructed to assess the relationship between SNR loss as measured by QuickSIN and history of noise exposure. We are going to stratify our analysis based on the cognitive status of participants as that will likely to play in to their ability to perform QuickSIN test tasks. Stratification of participants will be based on Mini-Mental State Examination scores. Age and race specific cut-offs derived from normative data reported by Schneider et al will be used\(^{18}\). Covariates listed above will be adjusted for in our analysis.

7.a. Will the data be used for non-CVD analysis in this manuscript? _____ Yes  _X___ No

   b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? _____ Yes  _____ No
   (This file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? _____ Yes  _X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = “No use/storage DNA”? _____ Yes  _____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: [http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html](http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html)

   _____X__ Yes  ________ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

   ARIC proposal #3112: Factors Predicting Speech-in-Noise Change: Results from the Aging, Cognition, and Hearing Evaluation in Elders Pilot (ACHIEVE-P) Study
ARIC proposal #3253: Using Self-Reported Hearing Quality to Infer About Epidemiological Associations between Functional Outcomes and Objective Hearing Loss in ARIC

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _____ Yes ___X__ No

11.b. If yes, is the proposal
   ____   A. primarily the result of an ancillary study (list number* __________)
   ____   B. primarily based on ARIC data with ancillary data playing a minor role
          (usually control variables; list number(s)* __________ __________ __________)

*ancillary studies are listed by number at https://www2.cscc.unc.edu/aric/approved-ancillary-studies

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PubMed Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.
References


