Chronic Opioid Therapy and Risk of Sensorineural Hearing Loss and Vestibular Dysfunction: A Propensity-Matched Cohort Study

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Introduction

Several case reports describe sensorineural hearing loss following opioid overdose, but the association with long-term prescribed opioid use remains unclear. Using a large, real-world cohort, we evaluated whether chronic opioid therapy is associated with adverse hearing and vestibular outcomes compared to the non-ototoxic analgesic duloxetine, a guideline-recommended alternative for musculoskeletal pain.

Methods

Study Design and Cohort Selection

1. Data Source
TriNetX Research Network, 2006–2024

2. Eligible Population
- Adults >18 with a diagnosis of dorsalgia, osteoarthritis or chronic pain
- ≥ 1 year of opioid or duloxetine therapy — initial Rx within 1 yr of diagnosis; prescription continued between 6–12mo since the initial treatment, and continued further at least once >12mo of initial treatment

3. Exclusions
- Ototoxic medication exposure (aminoglycosides, platinum compounds, loop diuretics, vancomycin)
- Depression, anxiety, or substance use disorder diagnoses

4. Treatment Cohorts
- Chronic opioid therapy with no exposure to duloxetine
- Chronic duloxetine therapy with no exposure to opioids

5. Propensity Score Matching
1:1 matching for age, sex, race and Charlson comorbidity markers

6. Outcomes Assessed
Sudden idiopathic hearing loss, Bilateral SNHL, Unilateral SNHL, tinnitus, and vestibular dysfunction at 3, 5, and 10 years

7. Control Outcomes
- Positive control: constipation
- Negative controls: conductive hearing loss, atopic dermatitis

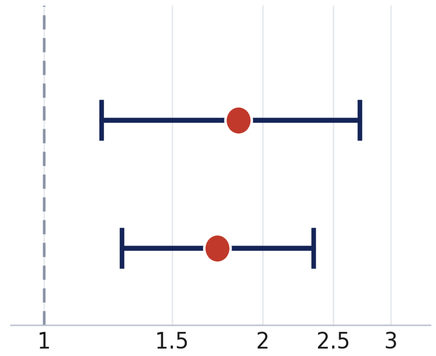
8. Secondary Analyses
Matched comparisons of opioid vs. no opioid, and duloxetine vs. no duloxetine

Results

4,001	4,001	8,002
Opioid-Treated Patients	Duloxetine-Treated Comparators	Total Patients

Opioid vs. Duloxetine (1:1 Propensity-Matched): Hearing & Vestibular Outcomes

Outcome	Opioid vs. Duloxetine
Vestibular Dysfunction *5-Year Outcome*	**RR 1.85 (95% CI 1.20–2.72)** **p = 0.004**
Bilateral SNHL *10-Year Outcome*	**RR 1.73 (95% CI 1.28–2.35)** **p < 0.001**



Sudden idiopathic hearing loss, unilateral sensorineural hearing loss, and tinnitus were not significant at any timepoint

Validity Checks

✓ **Positive Control: Constipation**
Significantly more common in the opioid cohort at all time points ($p < 0.001$), confirming expected detection of known opioid-related effects

✓ **Negative Controls: Conductive Hearing Loss and Atopic Dermatitis**
Too few outcomes to detect conductive hearing loss, but no significant difference in atopic dermatitis at 10 years ($p = 0.235$), supporting the specificity of the observed hearing and vestibular associations.

Duloxetine vs. No Duloxetine (n = 4,001 per group)
No association observed between duloxetine treatment and hearing or vestibular outcomes.

Opioid vs. No Opioid (n = 102,164 per group)
All outcomes were higher among opioid-exposed patients; however, this comparison did not pass negative control testing

Conclusion

Chronic prescribed opioid use may be associated with higher rates of sensorineural hearing loss and vestibular dysfunction compared with the non-ototoxic analgesic duloxetine, supporting investigation into mechanisms of opioid ototoxicity to inform prescribing practices for pain management.

Limitations

- Retrospective design using structured EHR data with diagnosis and prescription data depend on coding accuracy and completeness across contributing health systems
- Sample size limits the number of covariates possible for propensity score matching; unmeasured cofounders may skew the data without disrupting the chosen positive and negative control outcomes

Clinical Implications & Future Directions

- Supports further mechanistic investigation into opioid-related ototoxicity and its dose or duration dependence.
- May inform more hearing-conscious prescribing strategies for long-term management of musculoskeletal pain.
- Warrants prospective, audiometrically confirmed follow-up in patients on chronic opioid therapy.