Comparative Analysis of TriNetX and Cosmos Databases: Assessing Sensorineural Hearing Loss in Chronic Kidney Disease

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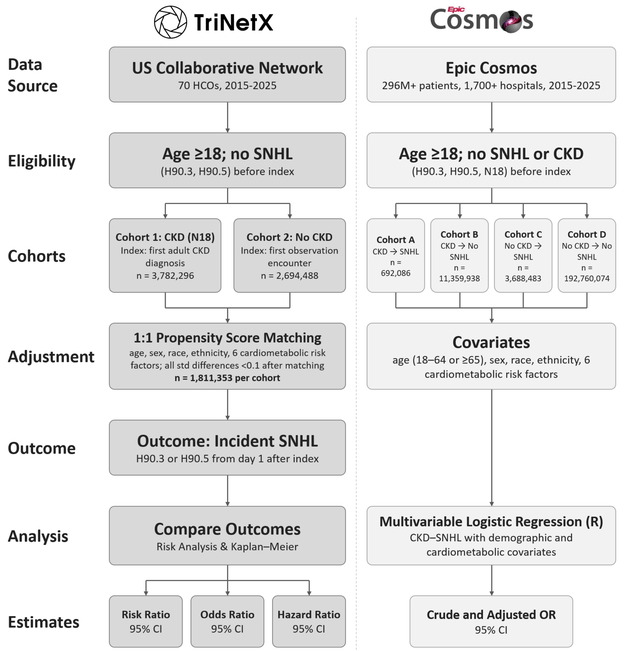
BACKGROUND:

- Large EHR-derived databases enable observational studies involving millions of patients, but estimates may differ across platforms because of network composition, cohort construction, covariate availability, and analytic workflow.
- Cross-platform reproducibility has rarely been evaluated in otolaryngology.
- Used the previously described association between CKD and SNHL as a clinical test case.

Objective

- To cross-validate TriNetX and Epic Cosmos by measuring the association between CKD and SNHL in each and comparing the results.

STUDY DESIGN:



RESULTS:

Despite identical diagnosis codes and similar demographic and cardiometabolic adjustment, TriNetX and Epic Cosmos produced discordant estimates of the association between CKD and SNHL.

TriNetX: Adults with CKD had 15.7% higher odds of developing SNHL (OR 1.16, 95% CI 1.14-1.17).

Epic Cosmos: Adults with CKD had 9.2% lower odds of developing SNHL after full adjustment (OR 0.91, 95% CI 0.91-0.91).

Populations

- **TriNetX:** 1,811,353 patients per cohort after 1:1 propensity score matching
- **Epic Cosmos:** 12,052,004 adults with CKD and 196,434,557 without CKD

Adjustment (both platforms)

- Age (matched in TriNetX; 18-64 vs ≥65 in Cosmos), sex, race (White vs non-White), and ethnicity (Hispanic vs non-Hispanic)
- Six cardiometabolic conditions defined by identical ICD-10 codes: diabetes, hypertension, hyperlipidemia, obesity, ischemic heart disease, and metabolic syndrome

CKD and SNHL: Effect Estimates Across Platforms

TriNetX propensity matched, n = 1,811,353 per cohort

Measure	Estimate	95% CI
Risk difference	0.004	0.003-0.004
Risk ratio	1.153	1.139-1.167
Odds ratio	**1.157**	**1.143-1.172**
Hazard ratio	1.128	1.114-1.142

SNHL-free at end of follow-up
CKD 89.84% vs no CKD 90.43%
Log-rank χ^2 = 353.1, P < .001

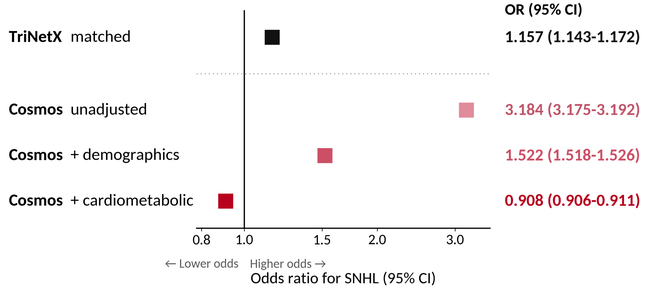
All TriNetX estimates P < .001.

Epic Cosmos sequential adjustment

Adjustment	OR	95% CI
Unadjusted	3.184	3.175-3.192
+ Age	1.515	1.511-1.519
+ Sex	1.515	1.511-1.519
+ Race/ethnicity	1.522	1.518-1.526
+ Diabetes	1.195	1.192-1.198
+ Hypertension	1.000	0.998-1.003
+ Hyperlipidemia	0.942	0.939-0.945
+ Obesity	0.925	0.922-0.927
+ Heart disease/metabolic syndrome	**0.908**	**0.906-0.911**

Adjusted odds ratios: TriNetX 1.157 (1.143-1.172) vs Cosmos 0.908 (0.906-0.911). The association persists after matching in TriNetX but reverses after cardiometabolic adjustment in Cosmos.

Effect estimates (OR) for the association between CKD and SNHL across platforms and adjustment models



DISCUSSION:

Several factors may explain the differences in effect estimates:

- **Different analytic approaches.** TriNetX used 1:1 propensity score matching on continuous age, while Cosmos used regression with a binary age adjustment (18-64 vs ≥65), so residual age confounding may contribute to the discordance. The Cosmos estimate was highly sensitive to adjustment, falling from 3.18 unadjusted to 1.52 after adjusting for age, sex, race, and ethnicity, with most of this drop occurring when the binary age covariate was added. It crossed 1.0 once hypertension was added, reaching 0.91 after full cardiometabolic adjustment. This finding shows how strongly results from aggregate EHR data depend on analytic choices.
- **Different populations and covariate timing.** The platforms draw on different health systems, patient populations, and coding practices. Covariates were measured before the index date in TriNetX, but their timing was not specified in Cosmos.
- **EHR coding and healthcare utilization.** Diagnosis dates reflect when a condition was coded, not necessarily when it began. Patients with CKD tend to have more clinical visits, giving hearing loss more opportunities to be diagnosed and coded.
- **TriNetX aligns with prior evidence.** The matched TriNetX estimate (OR 1.16) is consistent in direction with published adjusted estimates, including studies that adjusted for diabetes, hypertension, and dyslipidemia [1-3]. This finding suggests the Cosmos reversal likely reflects model specification rather than a true absence of association.

CONCLUSIONS:

TriNetX and Epic Cosmos produced materially different adjusted estimates for the same clinical association. These findings demonstrate that use of identical diagnosis codes and very large populations does not guarantee reproducible real-world evidence. Cross-platform studies require harmonized cohort entry, follow-up, covariate timing, and careful analysis of target parameters.

Key Take Away:
Large sample sizes do not protect against design-dependent results. Using the association between CKD and SNHL as a test case, we found substantial discordance between TriNetX and Epic Cosmos.

REFERENCES:

1. Shim YJ, Choi HG, Wee JH. Association between chronic kidney disease and sudden sensorineural hearing loss: a longitudinal follow-up study using ICD-10 codes in a national health screening cohort. *J Clin Med*. 2023;12(8):2861. doi:10.3390/jcm12082861
2. Wu KL, Shih CP, Chan JS, et al. Investigation of the relationship between sensorineural hearing loss and associated comorbidities in patients with chronic kidney disease: a nationwide, population-based cohort study. *PLoS One*. 2020;15(9):e0238913. doi:10.1371/journal.pone.0238913
3. Seo YJ, Ko SB, Ha TH, et al. Association of hearing impairment with chronic kidney disease: a cross-sectional study of the Korean general population. *BMC Nephrol*. 2015;16:154. doi:10.1186/s12882-015-0151-0