Tinnitus Risk After COVID-19 XBB.1.5 Vaccination: A Self-Controlled Case Series Study

EPH33

Kaiser Permanente Research

Stanley Xu, PhD [a,b], Lina S. Sy, MPH [a], Vennis Hong, MPH [a], Lei Qian, PhD [a], Kimberly J. Holmquist, MPH [a], Katia J. Bruxvoort, PhD [a,c], Bing Han, PhD [a], Bruno Lewin, MD [a,d].

[a] Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena, CA, United States; [b] Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA, United States; [c] School of Public Health, University of Alabama at Birmingham, Birmingham, AL, United States; [d] Department of Clinical Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA, United States

BACKGROUND

- COVID-19 vaccines have undergone thorough safety evaluations in the U.S. and globally, with numerous studies confirming their favorable safety profile.
- Serious adverse events such as myocarditis, pericarditis, Guillain-Barré syndrome (GBS), thrombotic events, and mortality are exceedingly rare following COVID-19 vaccination.
- During December 14, 2020–May 4, 2023, VAERS received 17,859 reports of tinnitus after COVID-19 vaccination, representing a small fraction of vaccinated individuals.
- Most observational studies found no clear association between COVID-19 vaccination and tinnitus, though some suggested a potential link.

OBJECTIVE

- To assess the risk of tinnitus following administration of updated COVID-19 vaccine targeting the XBB.1.5 variant (COVID-19 XBB.1.5 vaccine) using a self-controlled case series (SCCS) design.

METHODS

- **Study Population and Period**: The SCCS study analyzed electronic health records of individuals aged ≥12 years enrolled at Kaiser Permanente Southern California (KPSC), covering tinnitus events between September 1, 2023, and March 31, 2024. Participants needed at least one year of continuous enrollment prior to September 1, 2023.
- **Vaccine Exposures and Observation Period**: The study included individuals who received Pfizer or Moderna COVID-19 XBB.1.5 vaccines between September 1, 2023, and March 31, 2024, with or without coadministration of the influenza vaccine. The observation period ended on March 31, 2024, or upon death, receipt of a second vaccine dose, or disenrollment, whichever occurred first.
- **Outcome Definition**: Tinnitus events were identified using ICD-10 code H93.1* in inpatient, emergency department, or outpatient settings. The primary outcome was first-ever tinnitus in individuals with no documented history of tinnitus since October 1, 2015, while the secondary outcome was first-in-1-year tinnitus in individuals with no documented history of tinnitus in the year prior to the first diagnosis during the observation period.
- **Statistical analyses**: A modified SCCS approach was used to estimate relative incidence (RI) and 95% confidence intervals (CI) for tinnitus, comparing risk intervals (1–14 days and 1–28 days post-vaccination) to control intervals (person-time outside of the risk intervals). The analysis included adjustments for seasonality and subgroup analyses by age and coadministration with the influenza vaccine. We excluded Day 0 from the observation period due to potential ambiguity in the temporal relationship between vaccination and tinnitus onset.

Our findings suggest no increased tinnitus risk following COVID-19 XBB.1.5 vaccination, either administered alone or coadministered with influenza vaccine, and by age group. These results provide reassuring evidence of the safety of COVID-19 vaccines with respect to tinnitus risk.

RESULTS

Demographic characteristics of recipients of COVID-19 XBB.1.5 vaccines who experienced tinnitus

- Among the 13,940 recipients of COVID-19 XBB.1.5 vaccines who experienced first-ever tinnitus, nearly half were aged 60 years or older, and there was a slightly higher proportion of females (Table 1).
- Most cases occurred among Non-Hispanic White and Hispanic individuals, with the majority identified in the outpatient setting. Of the COVID XBB.1.5 vaccinees who had a first-ever tinnitus, 922 had co-administration of influenza vaccine.

Table 1. Demographic characteristics of recipients of COVID-19 XBB.1.5 vaccines who experienced a first-ever tinnitus event in inpatient, emergency department, and outpatient settings at Kaiser Permanente Southern California during the period from September 1, 2023, to March 31, 2024.

	All (N=13,940)	Coadministered with influenza vaccine (N=922)	Not coadministered with influenza vaccine (N=13,018)
	n (%)	n (%)	n (%)
Age (years)			
12-39	2,526 (18.1)	164 (17.8)	2,362 (18.1)
40-59	4,481 (32.1)	274 (29.7)	4,207 (32.3)
60+	6,933 (49.7)	484 (52.5)	6,449 (49.5)
Sex			
Female	7,382 (53.0)	422 (45.8)	6,960 (53.5)
Male	6,556 (47.0)	500 (54.2)	6,056 (46.5)
Missing	2 (0.0)	0 (0.0)	2 (0.0)
Race/ethnicity			
Hispanic	5,884 (42.2)	325 (35.2)	5,559 (42.7)
Non-Hispanic White	4,971 (35.7)	372 (40.3)	4,599 (35.3)
Non-Hispanic Asian/Pacific Islander	1,503 (10.8)	109 (11.8)	1,394 (10.7)
Non-Hispanic Black	930 (6.7)	58 (6.3)	872 (6.7)
Other/Unknown	652 (4.7)	58 (6.3)	594 (4.6)
Setting			
Outpatient	13,521 (97.0)	909 (98.6)	12,612 (96.9)
Inpatient	75 (0.5)	2 (0.2)	73 (0.6)
Emergency department	344 (2.5)	11 (1.2)	333 (2.6)

Table 2. Relative incidences (95% confidence intervals) of first-ever tinnitus in inpatient, emergency department, and outpatient settings after COVID-19 XBB.1.5 vaccination during the period from September 1, 2023, to March 31, 2024.

Analyses	All	Coadministered with influenza vaccine	Not coadministered with influenza vaccine
14-day risk interval			
Overall	0.72 (0.61-0.85)	1.10 (0.79-1.53)	0.67 (0.55-0.81)
By age (years)			
12-39	0.84 (0.51-1.37)	1.22 (0.51-2.95)	0.86 (0.47-1.60)
40-59	0.79 (0.57-1.10)	1.49 (0.85-2.63)	0.67 (0.44-1.02)
60+	0.68 (0.56-0.83)	0.98 (0.62-1.56)	0.64 (0.51-0.81)
28-day risk interval			
Overall	0.86 (0.77-0.96)	1.21 (0.94-1.56)	0.83 (0.73-0.94)
By age (years)			
12-39	0.93 (0.65-1.33)	0.97 (0.49-1.94)	1.13 (0.73-1.74)
40-59	0.86 (0.68-1.08)	1.24 (0.78-1.98)	0.83 (0.63-1.10)
60+	0.86 (0.75-0.98)	1.36 (0.98-1.90)	0.80 (0.69-0.93)

RESULTS

Table 3. Relative incidences (95% confidence intervals) of first-in-1-year tinnitus in inpatient, emergency department, and outpatient settings after COVID-19 XBB.1.5 vaccination during the period from September 1, 2023, to March 31, 2024.

Analyses	All	Coadministered with influenza vaccine	Not coadministered with influenza vaccine
14-day risk interval			
Overall	0.72 (0.62-0.83)	1.11 (0.83-1.49)	0.66 (0.56-0.78)
By age (years)			
12-39	0.79 (0.48-1.29)	1.18 (0.49-2.83)	0.81 (0.44-1.49)
40-59	0.82 (0.61-1.09)	1.48 (0.90-2.42)	0.68 (0.47-0.99)
60+	0.68 (0.57-0.81)	0.98 (0.66-1.47)	0.65 (0.53-0.78)
28-day risk interval			
Overall	0.87 (0.79-0.96)	1.17 (0.94-1.47)	0.84 (0.76-0.94)
By age (years)			
12-39	0.90 (0.64-1.27)	0.92 (0.47-1.83)	1.09 (0.72-1.65)
40-59	0.85 (0.69-1.05)	1.22 (0.81-1.83)	0.80 (0.62-1.03)
60+	0.88 (0.79-0.99)	1.27 (0.94-1.70)	0.84 (0.74-0.96)

First-ever tinnitus

- The relative incidence (RI) of first-ever tinnitus after COVID-19 XBB.1.5 vaccination was 0.72 (95% CI: 0.61-0.85) for the 1–14 day risk interval and 0.86 (95% CI: 0.77-0.96) for the 1–28 day risk interval, indicating no increased risk (Table 2).
- For the 1–14 day risk interval, the RI was 1.10 (95% CI: 0.79-1.53) with influenza vaccine coadministration and 0.67 (95% CI: 0.55-0.81) without coadministration.
- For the 1–28 day risk interval, the RI was 1.21 (95% CI: 0.94-1.56) with influenza vaccine coadministration and 0.83 (95% CI: 0.73-0.94) without coadministration.
- No increased risk of first-ever tinnitus was observed across age subgroups or by influenza vaccine coadministration for both 1–14 and 1–28 day risk intervals.

First-in-1-year tinnitus

- The relative incidence (RI) of first-in-1-year tinnitus following COVID-19 XBB.1.5 vaccination was 0.72 (95% CI: 0.62-0.83) for the 1–14 day risk interval and 0.87 (95% CI: 0.79-0.96) for the 1–28 day risk interval (Table 3).
- For the 1–14 day risk interval, the RI was 1.11 (95% CI: 0.83-1.49) with influenza vaccine coadministration and 0.66 (95% CI: 0.56-0.78) without coadministration.
- For the 1–28 day risk interval, the RI was 1.17 (95% CI: 0.94-1.47) with influenza vaccine coadministration and 0.84 (95% CI: 0.76-0.94) without coadministration.
- No increased risk of first-in-1-year tinnitus was observed across age groups, with similar patterns noted for individuals with and without influenza vaccine coadministration for both 1–14 and 1–28 day risk intervals.

KAISER PERMANENTE®