

Appendicitis No More Likely After COVID-19 and Influenza Infections and Vaccinations Than Prior to Vaccination or Infection

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Last updated 11 February 2025 • Check for updates at EpicResearch.org

Key Findings:

- There is no statistically significant change in likelihood of appendicitis or appendectomy among patients who have a COVID-19 or influenza vaccination or infection.

Some reports have suggested an increased likelihood of appendicitis following viral infections, including COVID-19 and influenza infections, as well as following a COVID-19 vaccination.^{1,2,3} We aimed to understand the relationship between COVID-19 and influenza infections and vaccinations.

We studied 2.7 million patients who had an influenza or COVID-19 vaccination or infection in 2022 or 2023. We adjusted for patient age, race, ethnicity, sex, smoking history, rural or urban status, history of infection or vaccination, and social vulnerability. We compared the likelihood of appendicitis or appendectomy in the 30 days following the vaccine or infection exposure to the same 30-day window one year prior.

We found no statistically significant change in the likelihood of being diagnosed with appendicitis or having an appendectomy for patients who had a COVID-19 infection, COVID-19 vaccination, influenza infection, or influenza vaccination compared to those without the exposure, as seen in Figure 1.

Likelihood of Appendicitis or Appendectomy After an Infection or Vaccination

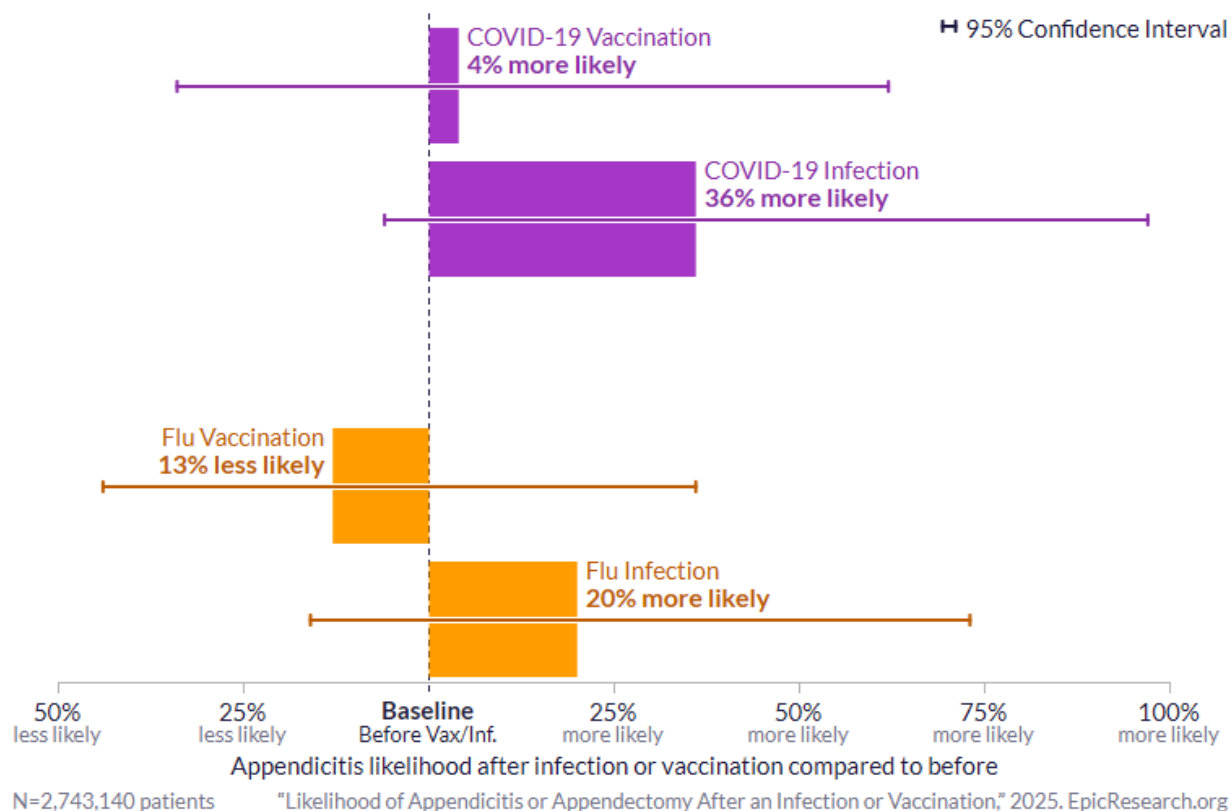


Figure 1. The likelihood of a patient experiencing appendicitis in the 30 days after a vaccination or infection compared to the likelihood a year prior.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 293 million patient records from 1,600 hospitals and more than 37,000 clinics from all 50 states, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Georgakopoulou VE, Gkoufa A, Damaskos C, et al. COVID-19-associated acute appendicitis in adults. A report of five cases and a review of the literature. *Exp Ther Med.* 2022;24(1):482. Published 2022 Jun 1. doi:10.3892/etm.2022.11409
2. Soltani S, Kesheh MM, Siri G, et al. The role of viruses in human acute appendicitis: a systematic literature review. *Int J Colorectal Dis.* 2023;38(1). doi:10.1007/s00384-023-04391-z
3. Oganesyanyan A, Schäfer M, Lesh C. Acute appendicitis following the COVID-19 vaccine. *J Surg Case Rep.* 2022;2022(6):rjac295. doi:10.1093/jscr/rjac295

Data Definitions

Term	Definition
Study period	2022 and 2023
Study population	Patient's first exposure during the study period . The patients were required to have at least one outpatient face-to-face visit more than a year prior to

	<p>the exposure date and their most recent vaccine registry query must have occurred at least 30 days after their index event.</p> <p>Exclusions:</p> <ul style="list-style-type: none"> • IBD at any time: ICD-10-CM code K50*-K52* • Appendicitis or appendectomy prior to or on the exposure date.
<p>Exposures</p>	<p>Receipt of COVID or Influenza vaccine</p> <p>COVID Vaccine: CVX codes 230, 301, 302, 300, 229, 218, 207, 311, 219, 208, 217, 312, 221, 228, 227, 310, 308, 309, 211, 313, 212</p> <p>Influenza Vaccine: CVX codes 160, 205, 168, 197, 135, 161, 166, 149, 111, 186, 171, 320, 153, 185, 155, 231, 201, 202, 200, 194, 158, 150, 141, 140</p> <p>COVID-19 or influenza infection</p> <p>COVID-19 infection: A diagnosis with ICD-10-CM code O07.1, U00, U49, U50, or J12.82 or a positive lab with LOINC code 96119-3, 94558-4, 97097-0, 95209-3, 102048-6, 101928-0, 101289-7, 96986-5, 94565-9, 95608-6, 94763-0, 101721-9, 103202-8, 94759-8, 94845-5, 96763-8, 96764-6, 95409-9, 94760-6, 94533-7, 95425-5, 94766-3, 94316-7, 94510-5, 97098-8, 98132-4, 98494-8, 94559-2, 95824-9, 94639-2, 96899-0, 94644-2, 94511-3, 98131-6, 98493-0, 94534-5, 96120-1, 96123-5, 96091-4, 94314-2, 94646-7, 94645-9, 94819-0, 95406-5, 96797-6, 94500-6, 94660-8, 94309-2, 96829-7, 94745-7, 94746-5, 96897-4, 94531-1, 95826-4, 94306-8, 94640-0, 96765-3, 94642-6, 94643-4, 100156-9, 96094-8, 98080-5, 96957-6, 95522-9, 95521-1, 96898-2, 97104-4, 94767-1, 94641-8, 96900-6, 96448-6, 94756-4, 94307-6, 94311-8, 96958-4, 94757-2, 94308-4, 94312-6, 94822-4, 95424-8, 96741-4, 95609-4, 95970-0, 104451-0, 60275-5, 60534-5, 41458-1, 94647-5, 94758-0, 96121-9, 96122-7, 95823-1, 94765-5, 94315-9, 94509-7, 94310-0, 94313-4, 94502-2, 96896-6, 96895-8, 96894-1, 99314-7, 96752-1, 96751-3, 96756-2, 96757-0, 103557-5, 94764-8, 100157-7, 77106-3, or 77107-1</p> <p>Influenza Infection: a diagnosis with ICD-10-CM code J09*-J11* or a positive lab mapped to LOINC code 40981-3, 48310-7, 44559-3, 43874-7, 46082-4, 44558-5, 80382-5, 44563-5, 44564-3, 44560-1, 31858-4, 5861-0, 31859-2, 5862-8, 5863-6, 72365-0, 72366-8, 61102-0, 72356-9, 48509-4, 38381-0, 80588-7, 49531-7, 92977-8, 82166-0, 76078-5, 34487-9, 85477-8, 22827-0, 55463-4, 33535-6, 44567-6, 72367-6, 24015-0, 6437-8, 6438-6, 62462-7, 38382-8, 44572-6, 49534-1, 43895-2, 46083-2, 80383-3, 44577-5, 44575-9, 44573-4, 5864-4, 5865-1, 31864-2, 5866-9, 5867-7, 80591-1, 49535-8, 92976-0, 82170-2, 76080-1, 40982-1, 85478-6, or 6604-3</p> <p>Positive labs were identified based on a mapped result value of “Positive,” “Detected,” “Influenza A virus positive,” “Influenza B virus positive,” “Influenza A (H3),” or “Influenza A (H1)”</p>
<p>Outcome</p>	<p>Diagnosis with appendicitis or an appendectomy procedure</p>

Appendicitis	A diagnosis with ICD-10-CM K35*
Appendectomy	A procedure with CPT code 44950, 44955, 44960, 44970, or 44979
Confounders	<p>Patient age:</p> <ul style="list-style-type: none"> • 0-9 • 10-19 • 20-29 • 30-39 • 40-49 • 50-59 • 60-69 • 70+ <p>Legal sex Race and ethnicity Social Vulnerability Index score Past/current smoker RUCA</p>
Race and ethnicity	<p>Single category checking in this order:</p> <ul style="list-style-type: none"> • Hispanic ethnicity • Non-Hispanic of the following races <ul style="list-style-type: none"> ○ Only race being Black ○ Only race being White ○ Other races
Model specifications	<p>We matched our populations 1:1:1:1 on the patient age and calendar quarter of exposure to align the populations across the event types.</p> <p>For each population, we analyzed with Binomial regression:</p> <ul style="list-style-type: none"> • Outcome within 30 days after exposure compared to the same 30 days a year prior

Table 1: Likelihood of Appendicitis or Appendectomy After an Infection or Vaccination

Condition	Odds Ratio	Lower CI	Upper CI
COVID-19 Vaccination	1.04	0.66	1.62
COVID-19 Infection	1.36	0.94	1.97
Flu Vaccination	0.87	0.56	1.36
Flu Infection	1.20	0.84	1.73