2026 Updates on Vaccine Safety for Viral Illnesses

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Wisconsin Virology Conference

May 2026

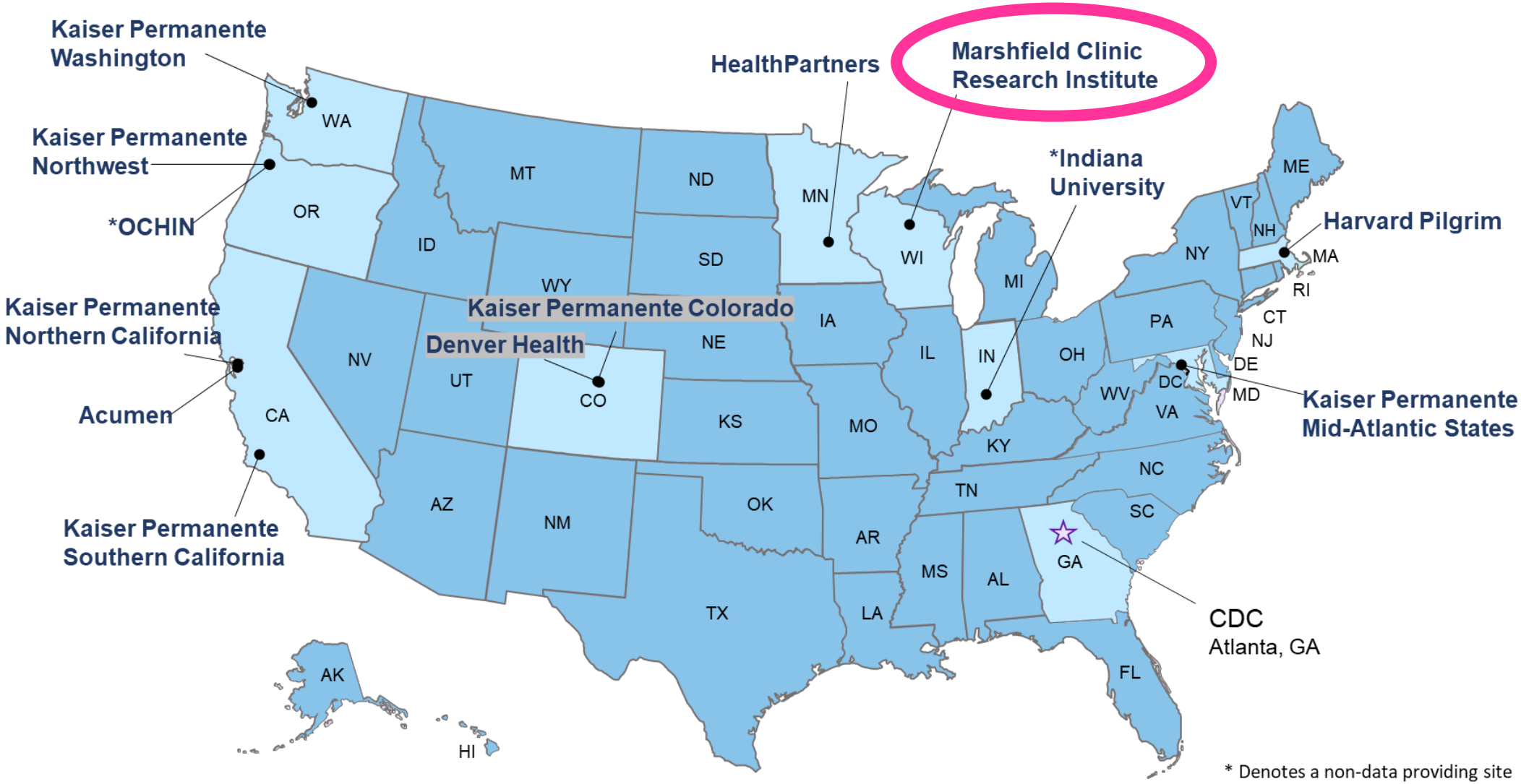
Vaccine Safety Systems in the US

- Vaccines are required to be monitored for safety and effectiveness after licensure
- We need very large datasets in order to find rare outcomes after vaccination
- In the US, these mechanisms include:
  - VAERS (Vaccine Adverse Event Reporting System)
  - VSD (Vaccine Safety Datalink)
  - V-safe (a real-time monitoring network for new vaccines by self-report)

VSD

- The Vaccine Safety Datalink is funded by CDC through their Immunization Safety Office, and involves 13 integrated healthcare organizations across the US
- Electronic health record data on >12 million persons annually
- Capability to conduct medical record review, unlike other large data systems (TriNetX)
- Capability to compare vaccinated to an appropriate control group

VSD



https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/index.html

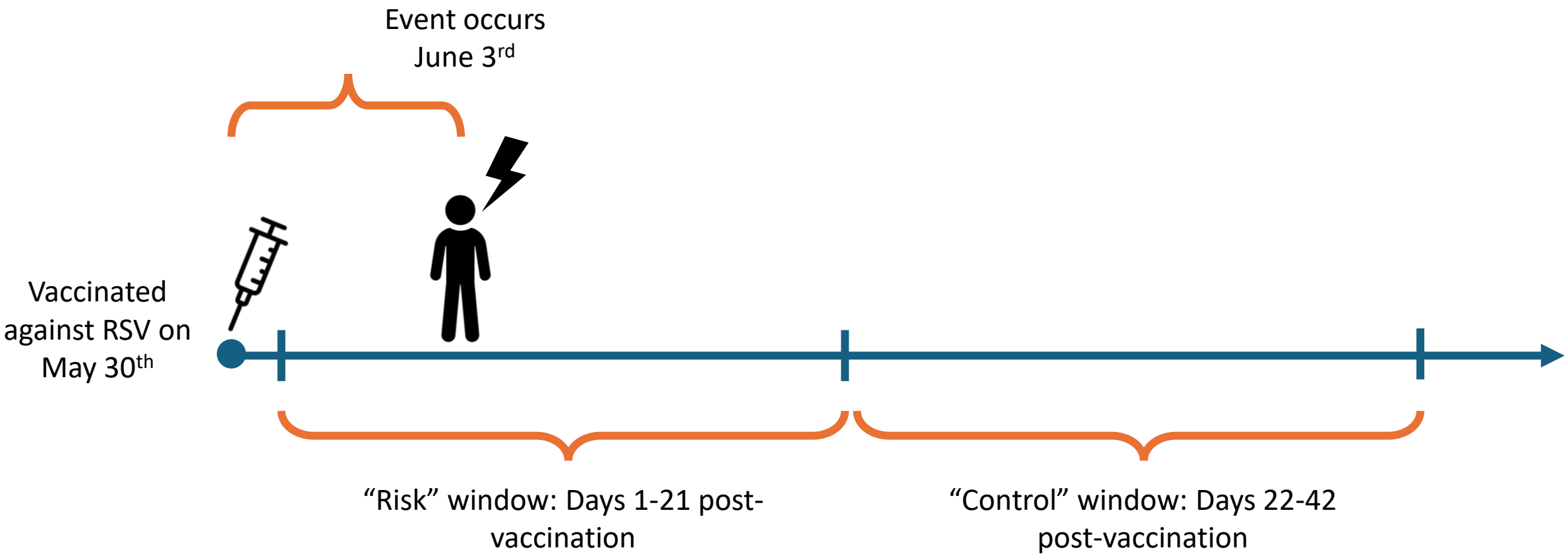
VSD

- VSD can conduct **retrospective analyses** of vaccine safety, after data has already been collected for several years
- VSD can also do **near real-time monitoring** of new vaccines, using a method called Rapid Cycle Analysis (RCA)
  - In this method, data are updated regularly (usually weekly or biweekly) and re-analyzed, looking for potential statistical signals of a safety concern
  - Outcomes of interest are pre-specified, using information from VAERS and clinical trials, as well as other safety monitoring systems

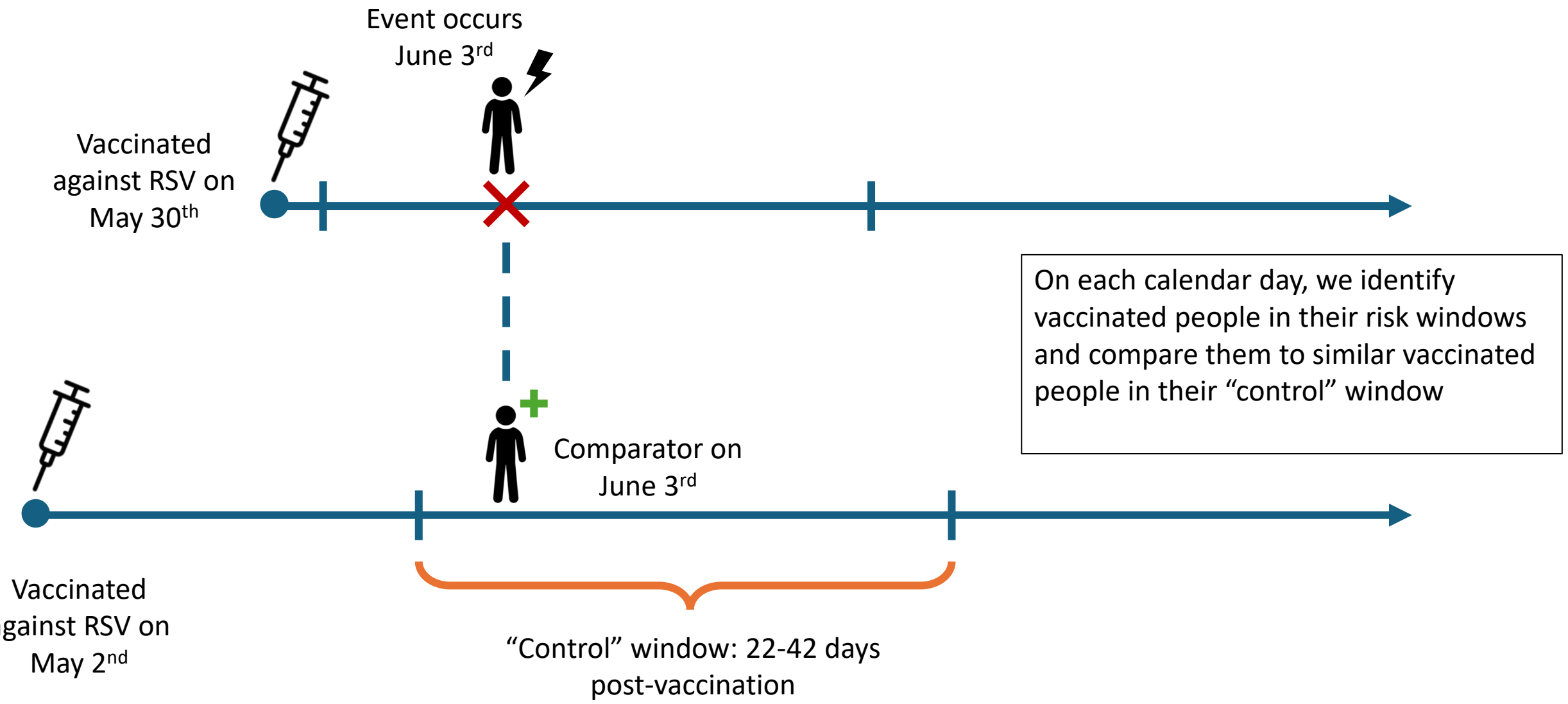
VSD Rapid Cycle Analysis (RCA)

- Permits rapid assessment of vaccine safety
- Outcome incidence in vaccinated persons is compared to outcome incidence in a comparator group
- Many current RCA analyses (including assessments of influenza, RSV, and COVID-19 vaccine safety) use a **vaccinated concurrent comparator**
- Using this type of comparator reduces the risk of bias inherent in comparing vaccinated to unvaccinated people

Vaccinated Concurrent Comparator Design



Vaccinated Concurrent Comparator Design



On each calendar day, we identify vaccinated people in their risk windows and compare them to similar vaccinated people in their "control" window

RCA of RSV Vaccine in Older Adults

- Near real-time surveillance among a cohort of persons ≥60 years old who received an RSV vaccine
- Surveillance period: 8/1/2023 through 6/1/2026
- Sequential analytic methods used to detect ‘statistical signals’ while maintaining a pre-defined type I error rate
- Statistical signals are interpreted as **potential** associations that warrant further investigation
  - Additional statistical analyses
  - Temporal scan analyses
  - Medical record review to confirm outcome and true date of onset

RCA of RSV Vaccine in Older Adults

Near real-time surveillance and tree-based data mining to assess the safety of respiratory syncytial virus vaccines in older adults in the vaccine safety datalink

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CRediT authorship contribution statement

James G. Donahue: Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Noelle M. Cocoros:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Burney A. Kieke:** Writing – review & editing, Validation, Software, Methodology, Formal analysis, Conceptualization. **Kayla E. Hanson:** Writing – review & editing, Project administration, Investigation, Formal analysis, Conceptualization. **Eric S. Weintraub:**

https://pmc.ncbi.nlm.nih.gov/articles/PMC12704511/pdf/nihms-2124561.pdf

RCA of RSV Vaccine in Older Adults

- From 8/1/2023 – 9/28/2024: 55,479 doses of Abrysvo and 381,344 doses of Arexvy
- In 15 biweekly runs of sequential analysis, and 4788 analyses performed across outcomes over time, **no statistical signals in primary comparison interval** (1-21 day risk interval, 43-63 day comparison interval)

RCA of RSV Vaccine in Older Adults: signal investigation

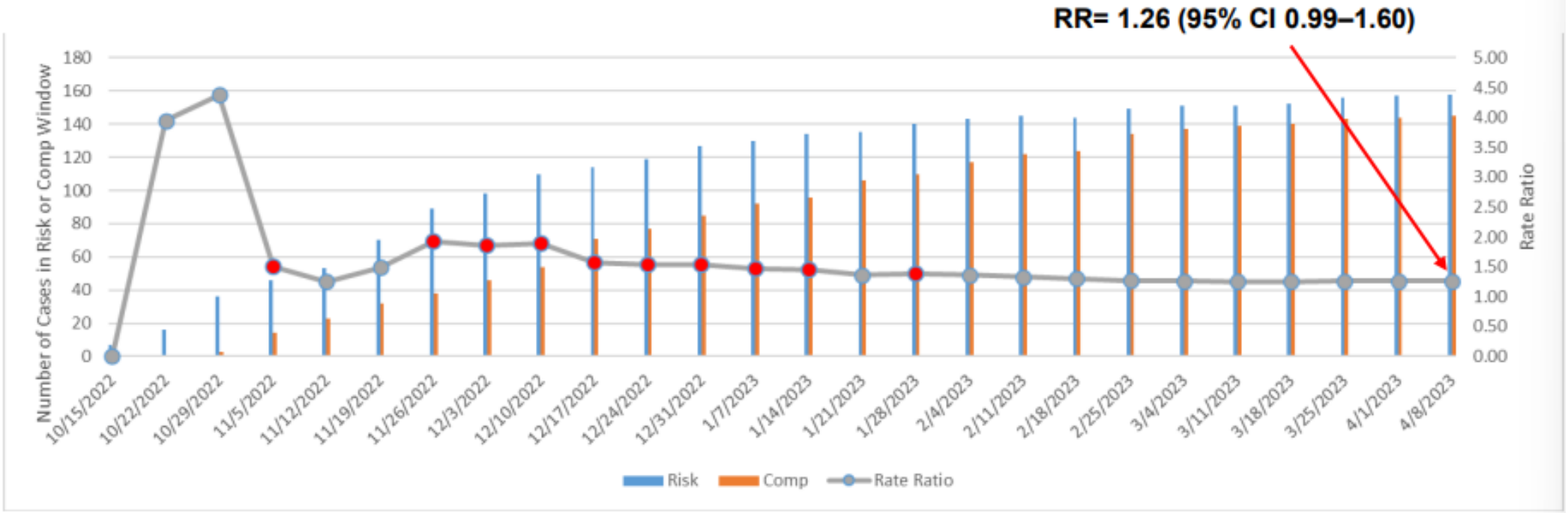
- A signal for immune thrombocytopenia (ITP) was observed in the first biweekly analysis
  - 1-21 day risk interval and 22-42 day comparison interval
  - Adults ≥60 years
  - Arexvy recipients without simultaneous vaccination

- Investigation of this statistical signal included manual chart review of 51 ITP cases; of these, 40 cases (78%) indicated chronic or unspecified thrombocytopenia, with onset before RSV vaccination
- Re-analysis of chart-confirmed data revealed no statistical relationship

RCA of COVID-19 vaccines

- A similar method, using the vaccinated concurrent comparator, is being used to assess the safety of COVID-19 vaccines and influenza vaccines
- In November 2022, a statistical signal for ischemic stroke was observed after receipt of Pfizer-BioNTech bivalent COVID-19 booster
- However, other safety monitoring systems did not observe similar findings

VSD RCA ischemic stroke after Pfizer-BioNTech bivalent booster, age ≥65 years, counts and adjusted rate ratios, Oct 16, 2022–April 8, 2023



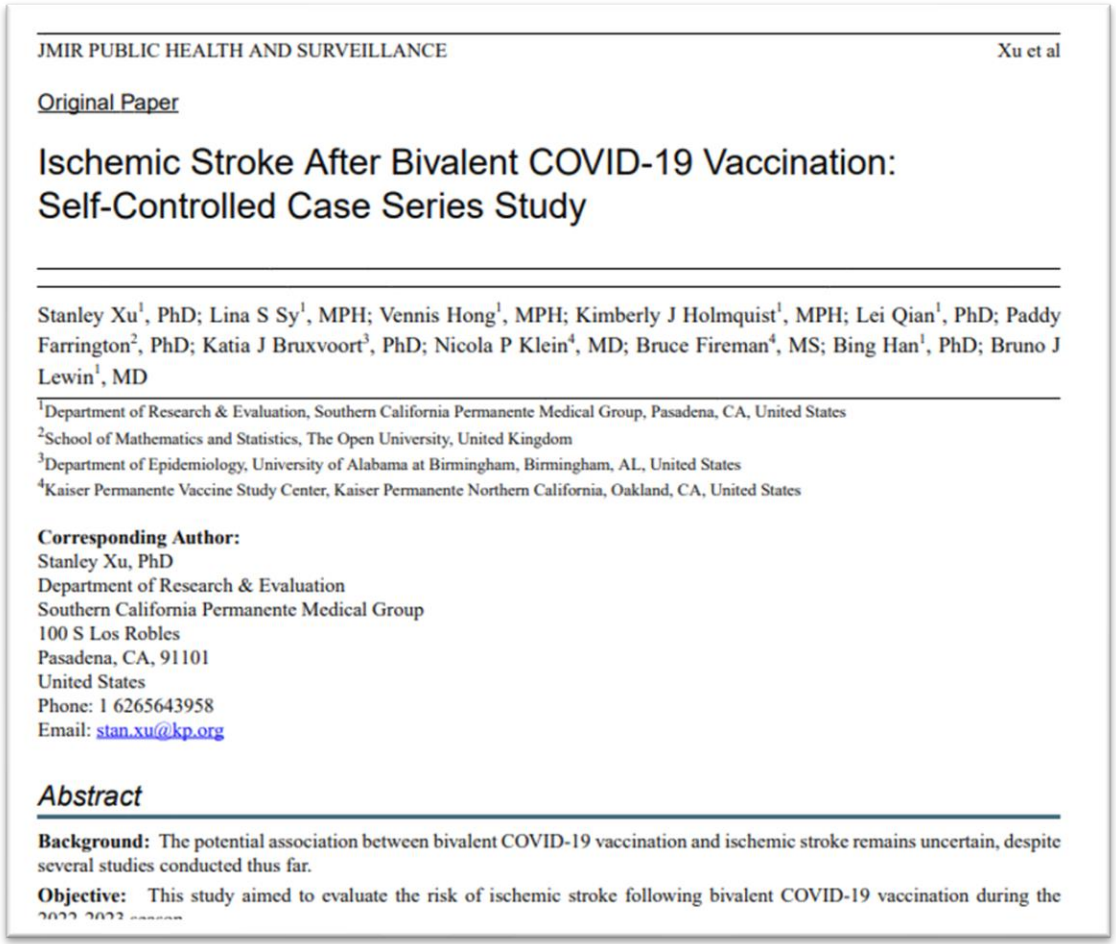
● Red dot represents sequential signal: p-value <0.01 (1-sided)

This information was previously presented to the Advisory Committee on Immunization Practices (ACIP) meeting on April 19, 2023

https://www.cdc.gov/acip/downloads/slides-2025-09-18-19/05-su-covid-508.pdf

RCA of COVID-19 vaccines

- A subsequent self-controlled case series analysis did not identify statistically significant increased risk for ischemic stroke, either for separate or same-day administration of Pfizer vaccine



JMIR PUBLIC HEALTH AND SURVEILLANCE Xu et al

Original Paper

Ischemic Stroke After Bivalent COVID-19 Vaccination: Self-Controlled Case Series Study

Stanley Xu[1], PhD; Lina S Sy[1], MPH; Vennis Hong[1], MPH; Kimberly J Holmquist[1], MPH; Lei Qian[1], PhD; Paddy Farrington[2], PhD; Katia J Bruxvoort[3], PhD; Nicola P Klein[4], MD; Bruce Fireman[4], MS; Bing Han[1], PhD; Bruno J Lewin[1], MD

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Abstract

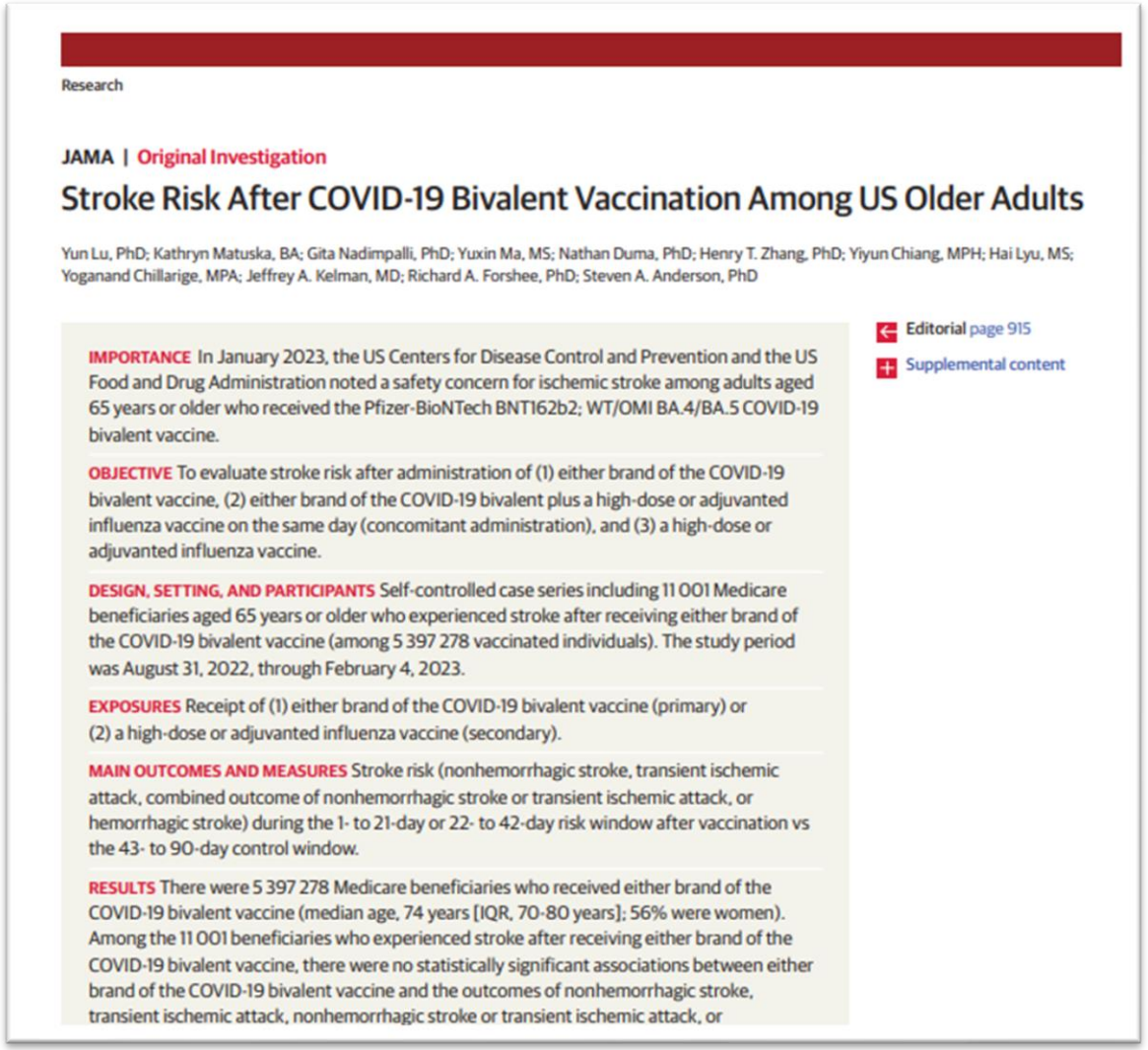
Background: The potential association between bivalent COVID-19 vaccination and ischemic stroke remains uncertain, despite several studies conducted thus far.

Objective: This study aimed to evaluate the risk of ischemic stroke following bivalent COVID-19 vaccination during the

https://pmc.ncbi.nlm.nih.gov/articles/PMC11234065/pdf/publichealth_v10i1e53807.pdf

RCA of COVID-19 vaccines

- Investigations in Medicare Fee-for-Service claims database, also using a self-controlled case series design, found no evidence for elevation in risk of non-hemorrhagic stroke



Research

JAMA | Original Investigation

Stroke Risk After COVID-19 Bivalent Vaccination Among US Older Adults

Yun Lu, PhD; Kathryn Matuska, BA; Gita Nadimpalli, PhD; Yuxin Ma, MS; Nathan Duma, PhD; Henry T. Zhang, PhD; Yiyun Chiang, MPH; Hai Lyu, MS; Yoganand Chillarige, MPA; Jeffrey A. Kelman, MD; Richard A. Forshee, PhD; Steven A. Anderson, PhD

Editorial page 915
Supplemental content

IMPORTANCE In January 2023, the US Centers for Disease Control and Prevention and the US Food and Drug Administration noted a safety concern for ischemic stroke among adults aged 65 years or older who received the Pfizer-BioNTech BNT162b2; WT/OMI BA.4/BA.5 COVID-19 bivalent vaccine.

OBJECTIVE To evaluate stroke risk after administration of (1) either brand of the COVID-19 bivalent vaccine, (2) either brand of the COVID-19 bivalent plus a high-dose or adjuvanted influenza vaccine on the same day (concomitant administration), and (3) a high-dose or adjuvanted influenza vaccine.

DESIGN, SETTING, AND PARTICIPANTS Self-controlled case series including 11 001 Medicare beneficiaries aged 65 years or older who experienced stroke after receiving either brand of the COVID-19 bivalent vaccine (among 5 397 278 vaccinated individuals). The study period was August 31, 2022, through February 4, 2023.

EXPOSURES Receipt of (1) either brand of the COVID-19 bivalent vaccine (primary) or (2) a high-dose or adjuvanted influenza vaccine (secondary).

MAIN OUTCOMES AND MEASURES Stroke risk (nonhemorrhagic stroke, transient ischemic attack, combined outcome of nonhemorrhagic stroke or transient ischemic attack, or hemorrhagic stroke) during the 1- to 21-day or 22- to 42-day risk window after vaccination vs the 43- to 90-day control window.

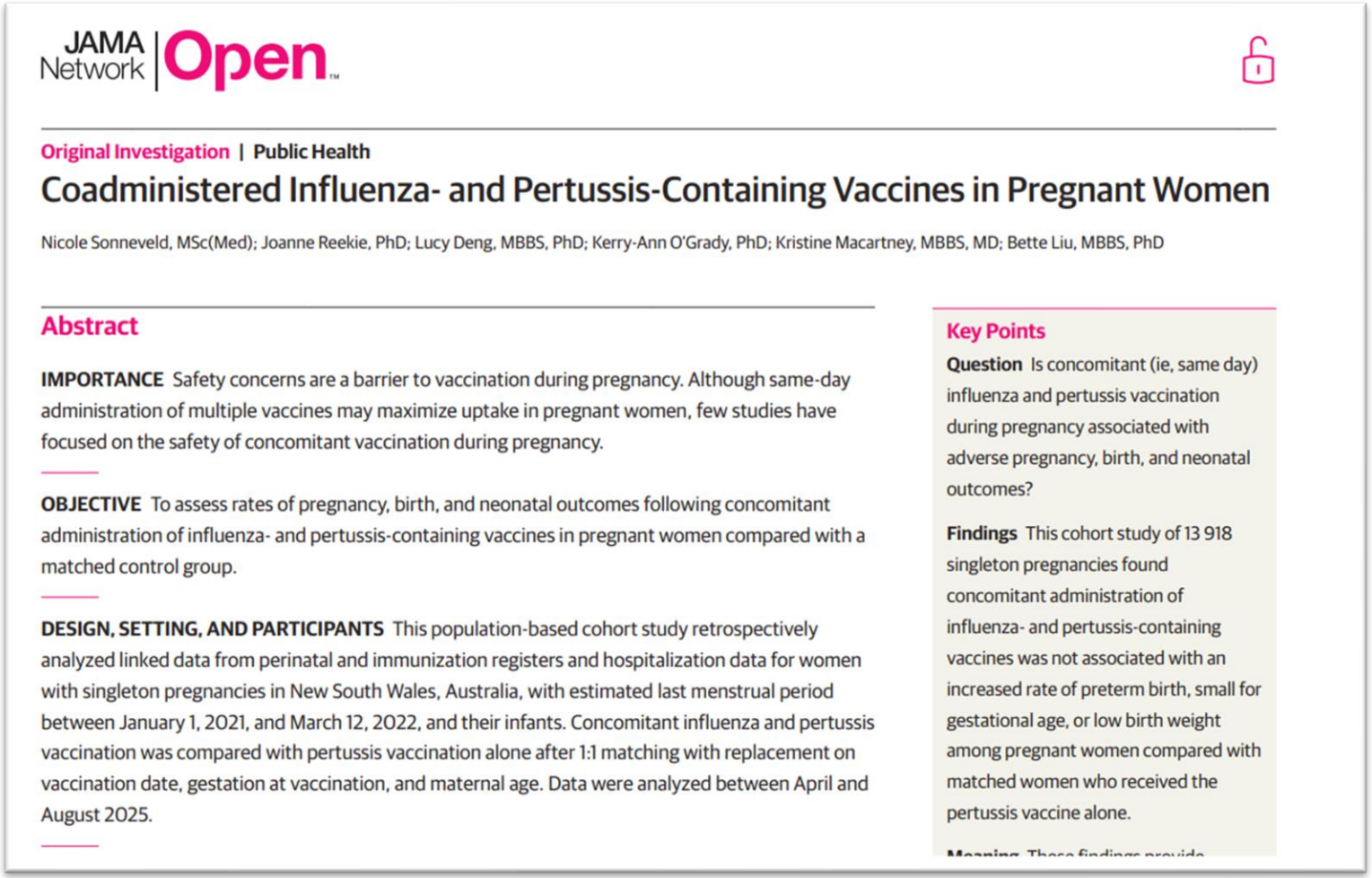
RESULTS There were 5 397 278 Medicare beneficiaries who received either brand of the COVID-19 bivalent vaccine (median age, 74 years [IQR, 70-80 years]; 56% were women). Among the 11 001 beneficiaries who experienced stroke after receiving either brand of the COVID-19 bivalent vaccine, there were no statistically significant associations between either brand of the COVID-19 bivalent vaccine and the outcomes of nonhemorrhagic stroke, transient ischemic attack, nonhemorrhagic stroke or transient ischemic attack, or

https://jamanetwork.com/journals/jama/fullarticle/2816237

Influenza vaccine safety

- Unfortunately, there have been limited opportunities to present safety data regarding influenza to the public via ACIP in the last 12 months
- However, seasonal influenza vaccines continue to have a strong track record of safety
- Additional recent analyses emphasize safety:
  - When co-administered with other vaccines
  - When given to immunocompromised populations and children

Influenza vaccine safety



JAMA Network | Open

Original Investigation | Public Health

Coadministered Influenza- and Pertussis-Containing Vaccines in Pregnant Women

Nicole Sonneveld, MSc(Med); Joanne Reekie, PhD; Lucy Deng, MBBS, PhD; Kerry-Ann O'Grady, PhD; Kristine Macartney, MBBS, MD; Bette Liu, MBBS, PhD

Abstract

IMPORTANCE Safety concerns are a barrier to vaccination during pregnancy. Although same-day administration of multiple vaccines may maximize uptake in pregnant women, few studies have focused on the safety of concomitant vaccination during pregnancy.

OBJECTIVE To assess rates of pregnancy, birth, and neonatal outcomes following concomitant administration of influenza- and pertussis-containing vaccines in pregnant women compared with a matched control group.

DESIGN, SETTING, AND PARTICIPANTS This population-based cohort study retrospectively analyzed linked data from perinatal and immunization registers and hospitalization data for women with singleton pregnancies in New South Wales, Australia, with estimated last menstrual period between January 1, 2021, and March 12, 2022, and their infants. Concomitant influenza and pertussis vaccination was compared with pertussis vaccination alone after 1:1 matching with replacement on vaccination date, gestation at vaccination, and maternal age. Data were analyzed between April and August 2025.

Key Points

Question Is concomitant (ie, same day) influenza and pertussis vaccination during pregnancy associated with adverse pregnancy, birth, and neonatal outcomes?

Findings This cohort study of 13 918 singleton pregnancies found concomitant administration of influenza- and pertussis-containing vaccines was not associated with an increased rate of preterm birth, small for gestational age, or low birth weight among pregnant women compared with matched women who received the pertussis vaccine alone.

Meaning These findings provide

https://pubmed.ncbi.nlm.nih.gov/41996114/

Influenza vaccine safety

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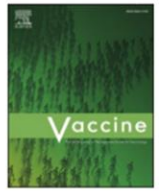
Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Check for updates

Safety of seasonal inactivated influenza vaccines in children 6 months–17 years of age in the Vaccine Adverse Events Reporting System (VAERS) 2018–2023: before, during, and after the COVID-19 pandemic public health emergency

E. Gloria Anyalechi [a,*], Paige L. Marquez [a], Mary N. Rubin [b], Sally-Ann P. Johannsen [a], Krystal Kohlman [a], Jyothi Gunta [a], Kimberly N. Works [a], Jared Woo [a], Brittney Romanson [a], Matthew B. Crist [a], John R. Su [a], Pedro Moro [a]

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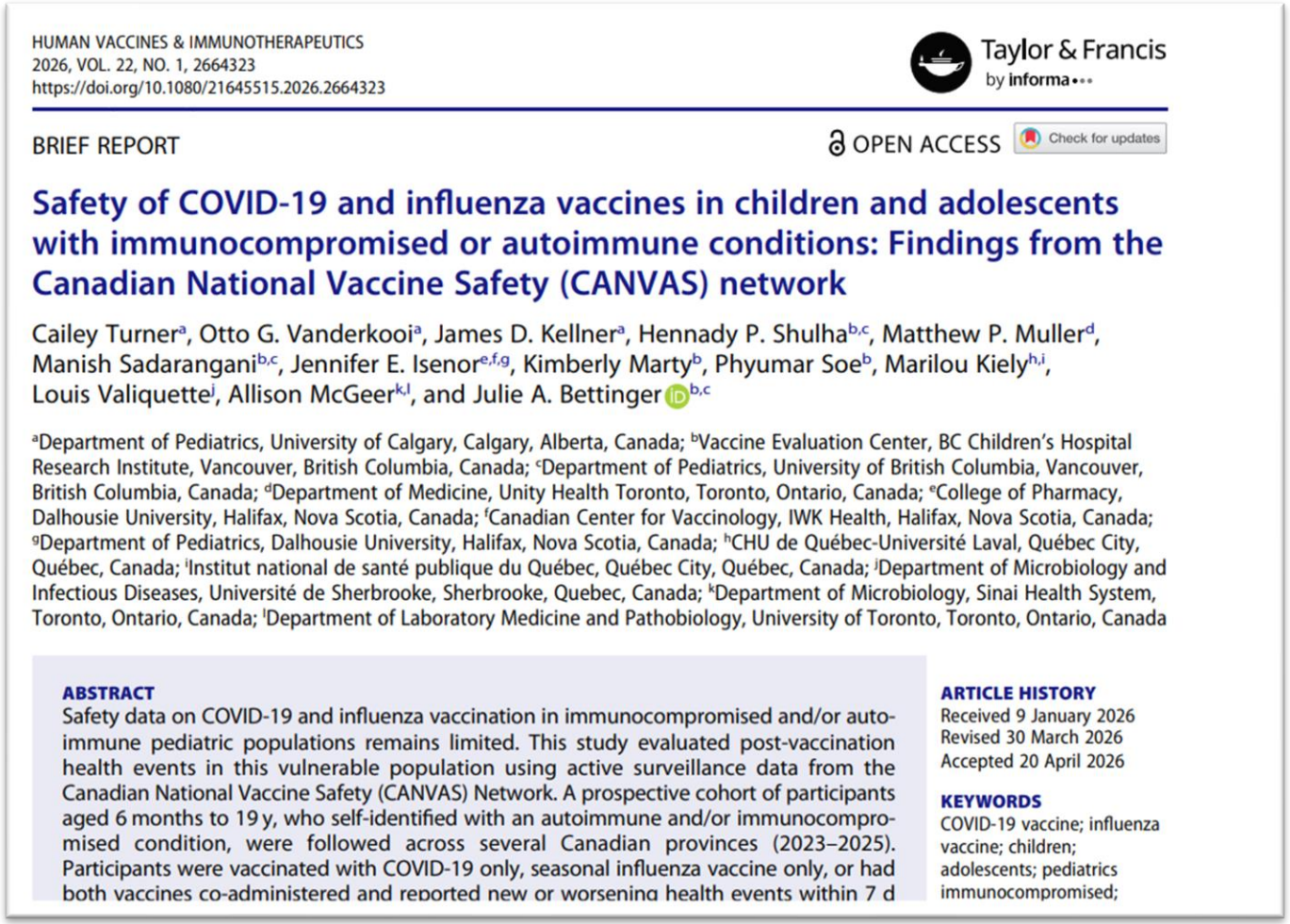
Vaccine pharmacovigilance
Adverse event following immunization

ABSTRACT

Introduction: Annual influenza vaccination is recommended for persons aged ≥6 months to prevent influenza illness and its potential complications. Young children are at a higher risk of developing severe influenza. We describe characteristics and reporting of Vaccine Adverse Event Reporting System (VAERS) reports following seasonal inactivated influenza vaccines (IIV) in children aged 6 months–17 years over five influenza seasons spanning the COVID-19 pandemic

https://pubmed.ncbi.nlm.nih.gov/41990612/

Influenza vaccine safety



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Taylor & Francis
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BRIEF REPORT

OPEN ACCESS Check for updates

Safety of COVID-19 and influenza vaccines in children and adolescents with immunocompromised or autoimmune conditions: Findings from the Canadian National Vaccine Safety (CANVAS) network

Cailey Turner[a], Otto G. Vanderkooi[a], James D. Kellner[a], Hennady P. Shulha[b,c], Matthew P. Muller[d], Manish Sadarangani[b,c], Jennifer E. Isenor[e,f,g], Kimberly Marty[b], Phyumar Soe[b], Marilou Kiely[h,i], Louis Valiquette[j], Allison McGeer[k,l], and Julie A. Bettinger[b,c]

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ABSTRACT

Safety data on COVID-19 and influenza vaccination in immunocompromised and/or autoimmune pediatric populations remains limited. This study evaluated post-vaccination health events in this vulnerable population using active surveillance data from the Canadian National Vaccine Safety (CANVAS) Network. A prospective cohort of participants aged 6 months to 19 y, who self-identified with an autoimmune and/or immunocompromised condition, were followed across several Canadian provinces (2023–2025). Participants were vaccinated with COVID-19 only, seasonal influenza vaccine only, or had both vaccines co-administered and reported new or worsening health events within 7 d

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KEYWORDS
COVID-19 vaccine; influenza vaccine; children; adolescents; pediatrics immunocompromised;

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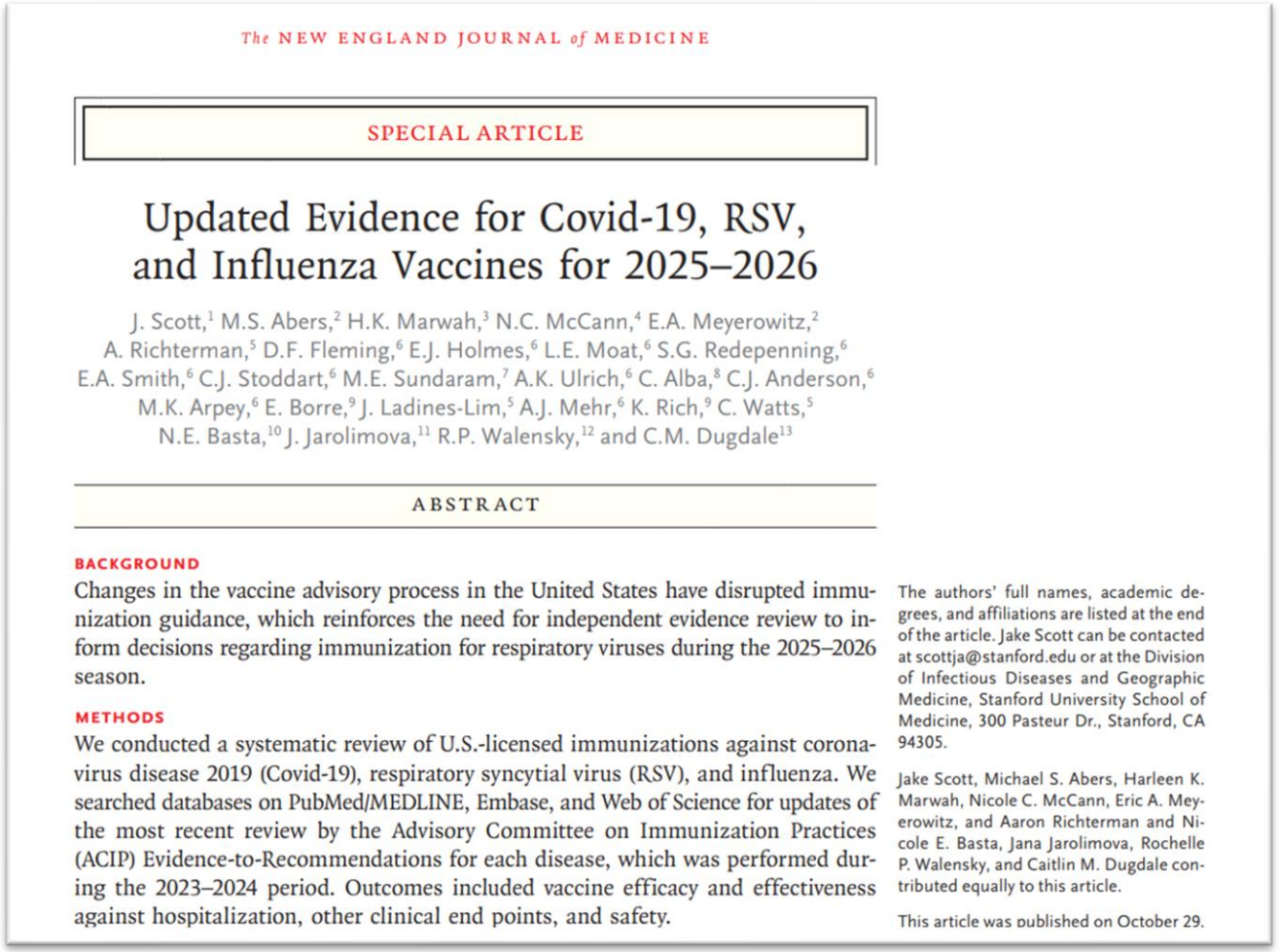
Influenza vaccine safety



The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Updated Evidence for Covid-19, RSV, and Influenza Vaccines for 2025–2026

J. Scott,[1] M.S. Abers,[2] H.K. Marwah,[3] N.C. McCann,[4] E.A. Meyerowitz,[2] A. Richterman,[5] D.F. Fleming,[6] E.J. Holmes,[6] L.E. Moat,[6] S.G. Redepenning,[6] E.A. Smith,[6] C.J. Stoddart,[6] M.E. Sundaram,[7] A.K. Ulrich,[6] C. Alba,[8] C.J. Anderson,[6] M.K. Arpey,[6] E. Borre,[9] J. Ladines-Lim,[5] A.J. Mehr,[6] K. Rich,[9] C. Watts,[5] N.E. Basta,[10] J. Jarolimova,[11] R.P. Walensky,[12] and C.M. Dugdale[13]

ABSTRACT

BACKGROUND

Changes in the vaccine advisory process in the United States have disrupted immunization guidance, which reinforces the need for independent evidence review to inform decisions regarding immunization for respiratory viruses during the 2025–2026 season.

METHODS

We conducted a systematic review of U.S.-licensed immunizations against coronavirus disease 2019 (Covid-19), respiratory syncytial virus (RSV), and influenza. We searched databases on PubMed/MEDLINE, Embase, and Web of Science for updates of the most recent review by the Advisory Committee on Immunization Practices (ACIP) Evidence-to-Recommendations for each disease, which was performed during the 2023–2024 period. Outcomes included vaccine efficacy and effectiveness against hospitalization, other clinical end points, and safety.

The authors' full names, academic degrees, and affiliations are listed at the end of the article. Jake Scott can be contacted at scottja@stanford.edu or at the Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, 300 Pasteur Dr., Stanford, CA 94305.

Jake Scott, Michael S. Abers, Harleen K. Marwah, Nicole C. McCann, Eric A. Meyerowitz, and Aaron Richterman and Nicole E. Basta, Jana Jarolimova, Rochelle P. Walensky, and Caitlin M. Dugdale contributed equally to this article.

This article was published on October 29.

https://pubmed.ncbi.nlm.nih.gov/41160817/

Additional slides

Pros/cons of the vaccinated concurrent comparator design

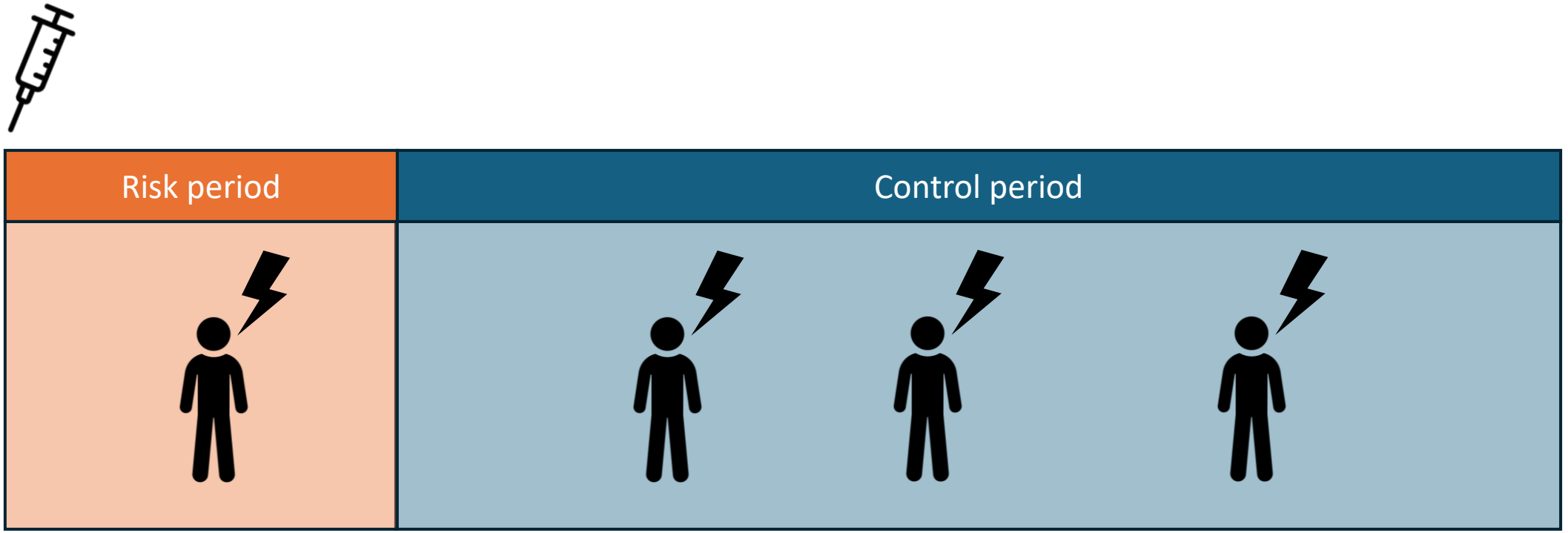
- Pros:
  - Not confounded by time-stable comorbidities, healthcare seeking behavior, or demographics
  - Follow-up time in “control” window is on the same **calendar dates** as follow-up time in “risk” window
  - Avoids bias that can arise from day-to-day variation in health services
  - Reduces potential bias from data lags

- Cons:
  - Early in the season, it can be challenging to find appropriate comparators (22-42 days after vaccination) for people with events in the “risk” window

Self-controlled case series design

- In this design, we still compare incidence of events during a risk window and a control window
- However, instead of matching on date, each individual **serves as their own control** (as the name suggests)
- And all individuals **are cases**/have the outcome (as the name suggests)
- This allows for the elimination of any confounding that does not vary over time

Self-controlled case series design



An incidence rate ratio is then calculated as follows:

$$\frac{Events\ per\ person - time\ in\ risk\ period}{Events\ per\ person - time\ in\ control\ period}$$

Self-controlled case series design: variations