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Literature Review

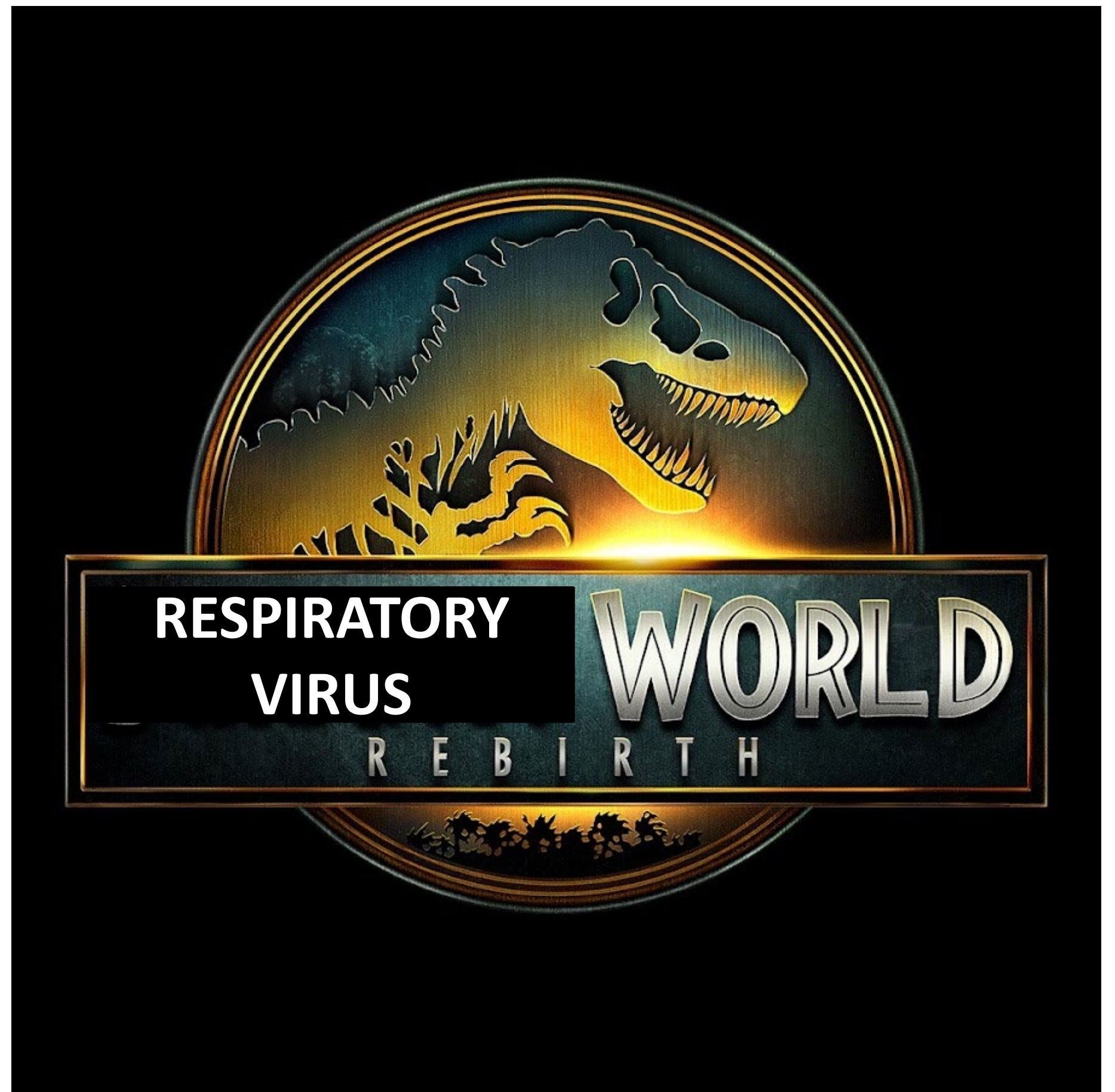
Respiratory Viruses

Emily Toth Martin, PhD MPH

Conflicts of Interest

My group receives research funding from the Centers for Disease Control and Prevention, NIH (including the CEIRR program), Flu Lab and has previously been funded by Pfizer and Merck.

An Update From:



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What's
New



What's
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What the
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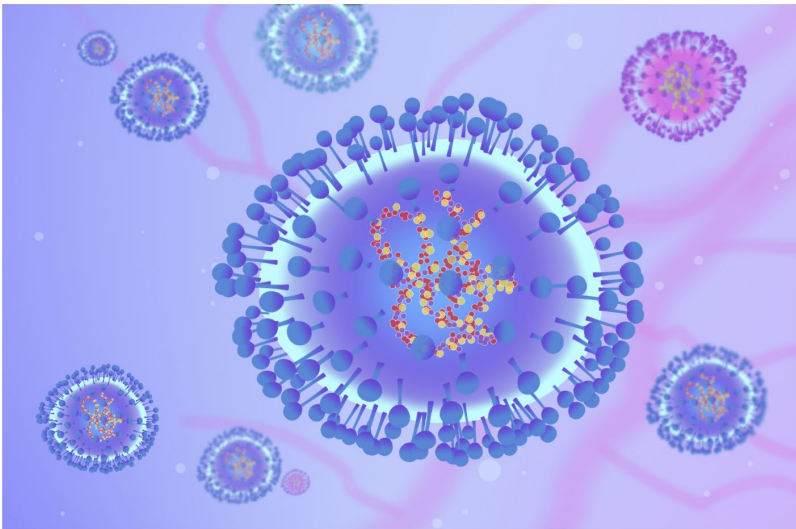
What’s “New”

CHINA / SOCIETY

HMPV not new emerging virus, residents advised to take precautions

By Global Times

Published: Jun 05, 2023 01:15 PM Updated: Jun 05, 2023 01:12 PM



THE HILL

Cases of HMPV are trending up in the US, especially in these states, CDC data shows

BY ADDY BINK AND MICHAEL BARTIROMO - 01/14/25 2:48 PM ET



HMPV

- First identified in 2001
- Molecular detection
- Single stranded, negative-sense RNA virus with a non-segmented genome
- Clinical syndrome and epidemiology is similar to RSV
- Season is often similar to RSV
- Estimates of prevalence vary (30-50% of RSV in a typical year)
- Emerging vaccine target



The global burden of human metapneumovirus-associated acute respiratory infections in older adults: a systematic review and meta-analysis

Durga Kulkarni*, Bingbing Cong*, Mamata Jyothish Kumar Ranjini, Geetika Balchandani, Shuting Chen, Jingyi Liang, Lina González Gordon, Ajoke Sobanjo-ter Meulen, Xin Wang, You Li, Richard Osei-Yeboah, Kate Templeton, Harish Nair

Summary

Background The human metapneumovirus (hMPV)-associated disease burden in older adults remains under-researched. We aimed to systematically estimate the global burden of hMPV-associated disease in older adults.

Methods We searched MEDLINE, Embase, Global Health, CINAHL, Web of Science, and Global Index Medicus in February, 2023, November, 2023, and October, 2024; and CNKI, Wanfang, and CQVip, in April, 2024, and October, 2024. We included studies conducted over at least 12 consecutive months, reporting on adults aged 60 years or older.



Lancet Healthy Longev 2025;
6: 100679
Published Online February 12, 2025
<https://doi.org/10.1016/j.lanhl.2024.100679>
*Joint first authors

Brothers in arms: RSV and hMPV

Human metapneumovirus (hMPV) is an enveloped virus with a single-stranded, negative-sense, non-segmented, 13-kb RNA genome. Although hMPV was formally identified in 2001, accompanying serological evidence indicated that hMPV had been circulating in the human population since at least 1958. hMPV belongs to the Pneumoviridae family (genus *Metapneumovirus*), which also includes avian metapneumoviruses.¹ hMPV poses a substantial clinical and public health burden among children and older adults, similar to respiratory syncytial virus (RSV). Currently, hMPV has no specific licensed

[HICs] and 288 000 in low-income and middle-income countries [LMICs]) in 2019 alone. Yet, the true numbers of hMPV cases will still be underestimated, particularly in cases in which hMPV-related clinical illness is mild and in regions where access to affordable health care is scarce, which will result in fewer hMPV-infected individuals getting tested. One small counterpoint to this assumption is that co-infections with hMPV and other respiratory viruses causing more severe disease might have led to more hospital admissions and testing than any milder disease caused by hMPV infection.

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Lancet Healthy Longev 2025;
6: 100684
Published Online January 23, 2025
<https://doi.org/10.1016/j.lanhl.2025.100684>
See **Articles** <https://doi.org/10.1016/j.lanhl.2024.100679>

- Searched English language and Chinese language databases. Collaboration included institutions from UK, China, Ireland, US, and South Africa
- 46 studies from 2005 to 2023 to determine percent positivity. Applied to 2019 hospitalization estimates.
- Global estimate for adults 65 and older: 473,000 (95% C.I. 396,000 – 777,000) hMPV-associated hospitalizations globally
 - 185,000 in High Income Countries
 - 288,000 in Low Income Countries
- US Incidence, 65 years and older: 231 per 100,000 people (95% C.I. 41-421)

	HICs	LMICs	Global*
Number of data points	6	10	NA
Pooled hMPV-proportion positive, %	2.46 (1.33–4.51)	2.01 (1.69–2.40)	NA
Number of all-cause LRI hospital admissions (thousands)†	7507 (7151–7938)	14 377 (11 356–18 227)	21 897 (18 702–25 744)
Number of hMPV- associated hospital admissions (thousands)	185 (105–340)	288 (193–436)	473 (396–777)

Data in parentheses are 95% CIs. HICs=high-income countries. hMPV=human metapneumovirus. LMICs=low-income and middle-income countries. LRI=lower respiratory infection. NA=not applicable. *Global estimates are sum of estimates from HICs and LMICs. †Estimated using Global Burden of Disease Study 2017 data (applied to 2019 population estimates); both are from the Institute For Health Metrics and Evaluation.

Table 1: Number of hMPV-associated LRI hospitalisation episodes in individuals aged ≥65 years in 2019 based on data from proportion-positive studies

	Proportion positive analysis	Hospitalisation rate analysis	Annual incidence of outpatient visits for hMPV-associated ARIs	hMPV-associated ARIs in community incidence rate
Number of data points	2	5	1	1
Pooled estimate	5.50% (3.17–9.36)	231 (41–421) per 100 000 people	40 (0–180) per 100 000 people	500 (431–569) per 100 000 person-years
Number of all-cause LRI hospital admissions in 2019 (thousands)	2494 (2157–2880)	..	..	..
Number of hMPV- associated hospital admissions in 2019 (thousands)	135 (78–256)	122 (41–398)	..	..

Data in parentheses are 95% CIs. ARI=acute respiratory infection. hMPV=human metapneumovirus. LRI=lower respiratory infection.

Table 2: hMPV-associated ARI burden in the USA in individuals aged ≥65 years in 2019 based on data from studies using multiple study designs

Vaccine and Therapeutic Development

- 13 trials on ClinicalTrials.gov
- Many HMPV vaccines under development are combined with RSV and/or PIV

 **National Library of Medicine**
National Center for Biotechnology Information

ClinicalTrials.gov

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Active, not recruiting ⓘ

Study of a Respiratory Syncytial Virus/Human Metapneumovirus Vaccine Candidate

ClinicalTrials.gov ID ⓘ **NCT06134648**

Sponsor ⓘ Sanofi Pasteur, a Sanofi Company

Information provided by ⓘ Sanofi (Sanofi Pasteur, a Sanofi Company) (Responsible Party)

Last Update Posted ⓘ 2024-08-14

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New Findings on Influenza Drift Impacting Epidemic Size and Strain

- Many factors might drive yearly influenza epidemics & dominant subtypes
 - H3N2 vs H1N1 circulation history
 - HA antigenic drift
 - NA antigenic drift
 - Age of susceptible individuals
- Solving this may improve forecasting and strain selection



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[Epidemiology and Global Health, Microbiology and Infectious Disease](#)

Antigenic drift and subtype interference shape A(H3N2) epidemic dynamics in the United States

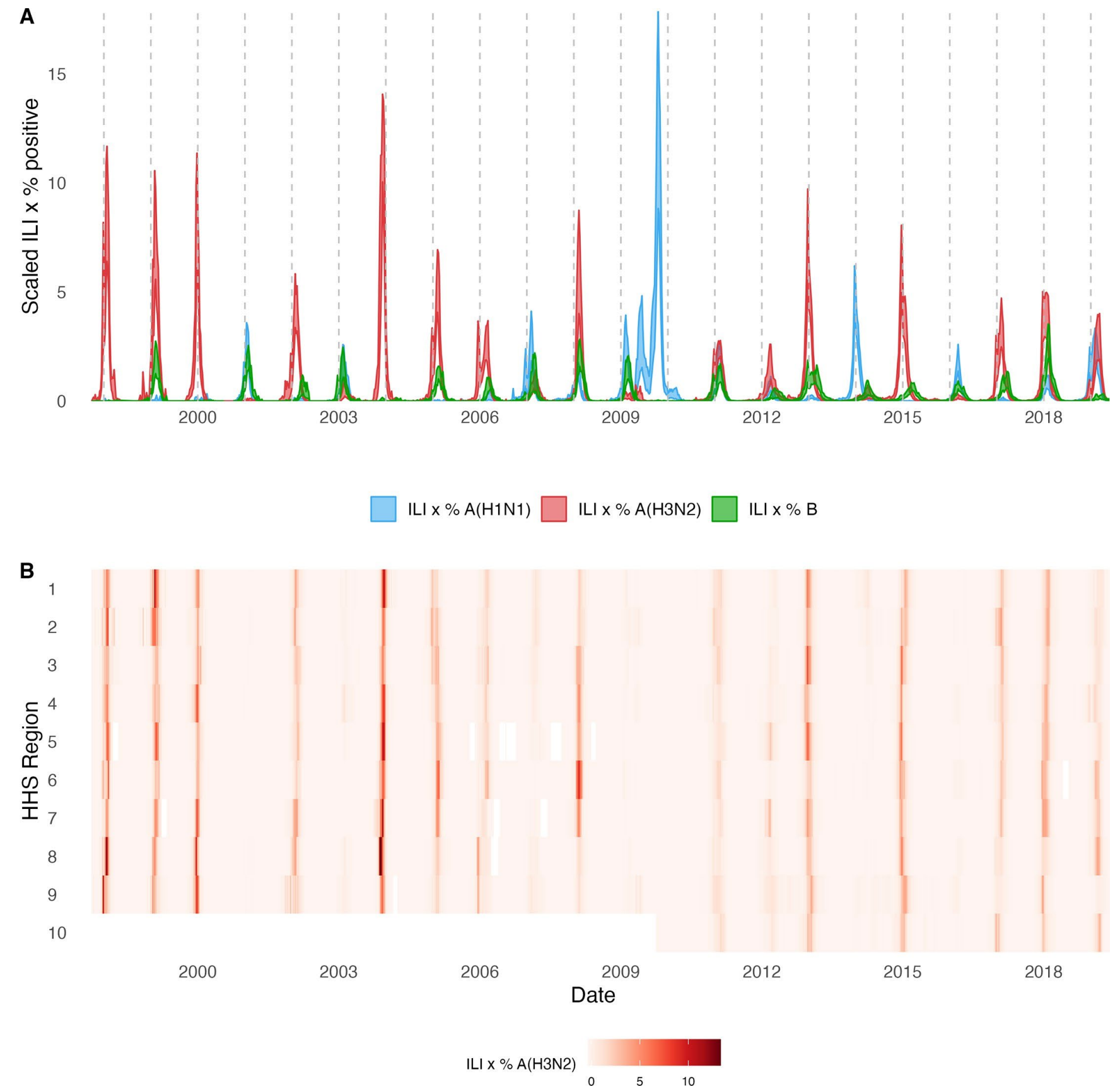
Amanda C Perofsky , John Huddleston, Chelsea L Hansen, John R Barnes, Thomas Rowe, Xiyan Xu, Rebecca Kondor, David E Wentworth, Nicola Lewis, Lynne Whittaker, Burcu Ermetal, Ruth Harvey, Monica Galiano, Rodney Stuart Daniels, John W McCauley, Seiichiro Fujisaki, Kazuya Nakamura, Noriko Kishida, Shinji Watanabe, Hideki Hasegawa, Sheena G Sullivan, Ian G Barr, Kanta Subbarao, Florian Krammer, Trevor Bedford, Cécile Viboud [« see less](#)



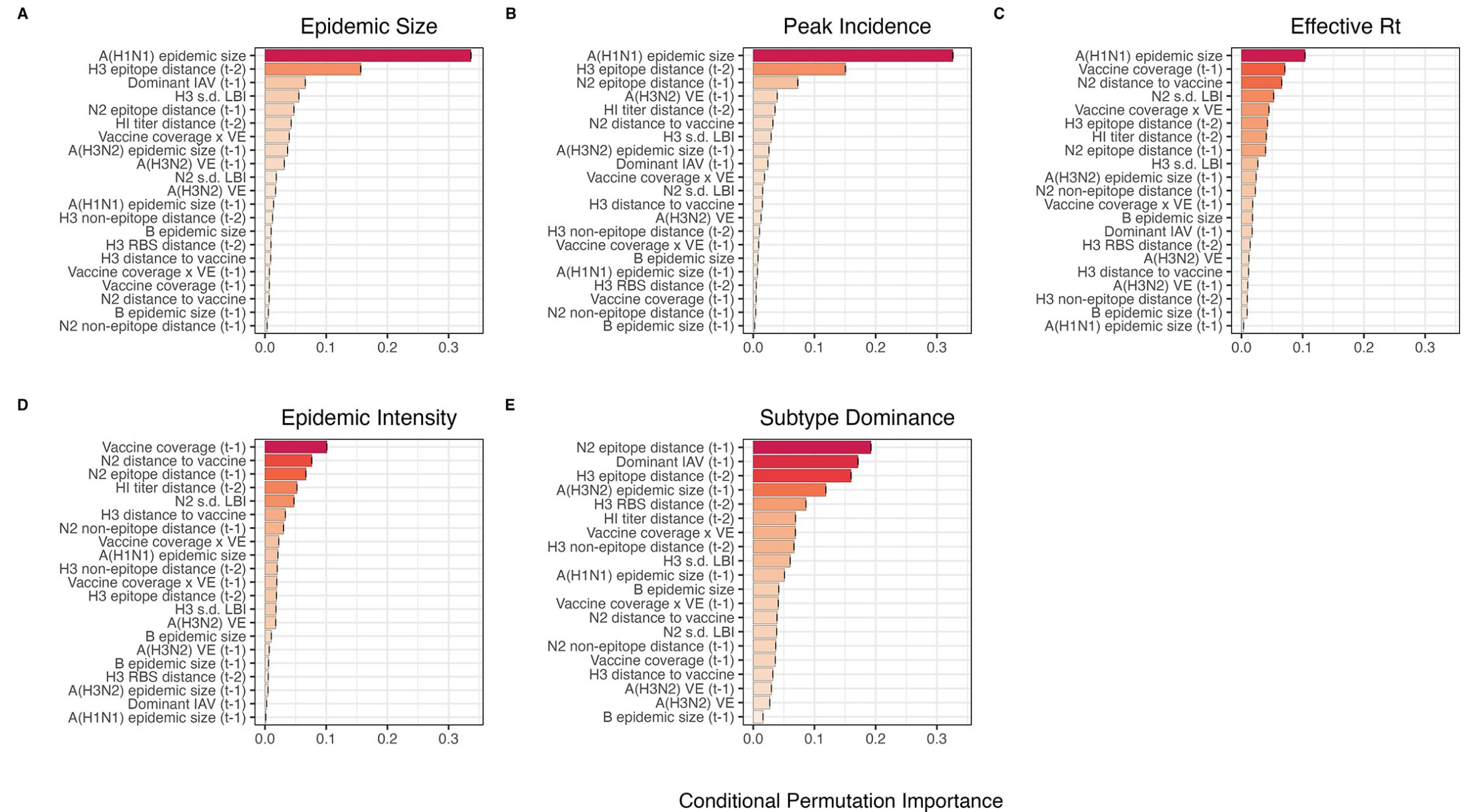
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Study Methods

- Seasons 1997-1998 to 2018-2019 in the U.S.
- Data Sources
 - ILINet
 - Type and subtype distribution from NREVSS & U.S. WHO Collaborating Labs
 - HA and NA sequence data
 - Hemagglutination inhibition (HI) serology data



Results



- Change in N2 is associated with faster epidemics and relatively more infections in adults vs children.
- Intensity of A(H3N2) outbreaks is more heavily influenced by the co-occurrence of A/H1N1 then by the degree of viral evolution.

The problem of influenza evolution...



Researchers sailing around the Antarctic Peninsula on the *Australis* found animals infected with H5N1 at 24 out of the 27 locations where they disembarked to take samples. ANTONIO ALCAMÍ

Antibody testing to assess scope of exposure to H5N1

Morbidity and Mortality Weekly Report

Serologic Evidence of Recent Infection with Highly Pathogenic Avian Influenza A(H5) Virus Among Dairy Workers — Michigan and Colorado, June–August 2024

Alexandra M. Mellis¹; Joseph Coyle²; Kristen E. Marshall^{3,4}; Aaron M. Frutos^{1,5}; Jordan Singleton^{5,6}; Cara Drehoff^{3,5}; Angiezel Merced-Morales¹; H. Pamela Pagano¹; Rachel O. Alade^{5,7}; Elizabeth B. White¹; Emma K. Noble¹; Crystal Holiday¹; Feng Liu¹; Stacie Jefferson¹; Zhu-Nan Li¹; F. Liani Gross¹; Sonja J. Olsen¹; Vivien G. Dugan¹; Carrie Reed¹; Sascha Ellington¹; Sophia Montoya³; Allison Kohnen³; Ginger Stringer³; Nisha Alden³; Peter Blank²; Derick Chia²; Natasha Bagdasarian²; Rachel Herlihy³; Sarah Lyon-Callo²; Min Z. Levine¹

7% of dairy workers had serologic evidence of recent infection with A(H5).

Morbidity and Mortality Weekly Report

Highly Pathogenic Avian Influenza A(H5N1) Virus Infection of Indoor Domestic Cats Within Dairy Industry Worker Households — Michigan, May 2024

Ramya Naraharisetti, PhD^{1,2}; Meghan Weinberg, PhD²; Becky Stoddard³; Mary Grace Stobierski, DVM²; Kimberly A. Dodd, DVM⁴; Nora Wineland, DVM⁵; Mathew Beal, DVM⁴; Jennifer Morse, MD³; Samantha Hatter, DVM⁴; Dodd Sledge, DVM⁴; Katelynn Youatt, DVM⁴; Joseph Coyle, MPH²; Jevon McFadden, MD^{2,6}; Timothy M. Uyeki, MD⁷; Lizette O. Durand, VMD, PhD⁷

A(H5N1) recovered from 2 domestic cats living in dairy industry worker households.

Notes from the Field

Seroprevalence of Highly Pathogenic Avian Influenza A(H5) Virus Infections Among Bovine Veterinary Practitioners — United States, September 2024

Jerome Leonard^{1,2}; Elizabeth J. Harker¹; Christine M. Szablewski¹; Sara F. Margrey³; K. Fred Gingrich II⁴; Keyana Crossley⁵; Emily Fletcher³; Claire J. McCreavy¹; Sabrina Weis-Torres⁶; Dennis Wang^{2,7}; Emma K. Noble¹; Min Z. Levine¹; H. Pamela Pagano¹; Crystal Holiday¹; Feng Liu¹; Stacie Jefferson¹; Zhu-Nan Li¹; F. Liaini Gross¹; Carrie Reed¹; Sascha Ellington¹; Alexandra M. Mellis¹; Samantha M. Olson¹

Survey of 150 bovine veterinary practitioners with cattle exposure within three months found 2% (n=3) with serologic evidence of recent A(H5).

New Results

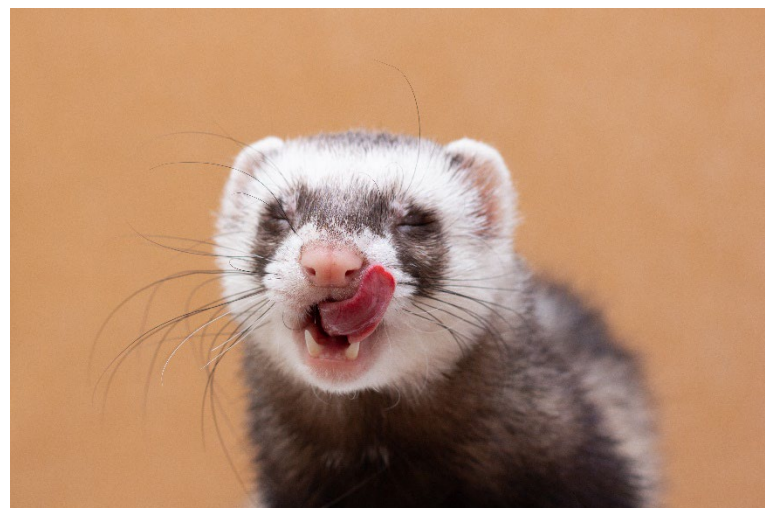
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Pre-existing H1N1 immunity reduces severe disease with bovine H5N1 influenza virus

Valerie Le Sage, Bailee D. Werner, Grace A. Merrbach, Sarah E. Petnuch, Aoife K. O'Connell, Holly C. Simmons,
 Kevin R. McCarthy,  Douglas S. Reed, Louise H. Moncla, Disha Bhavsar, Florian Krammer,
 Nicholas A. Crossland, Anita K. McElroy,  W. Paul Duprex,  Seema S. Lakdawala

doi: <https://doi.org/10.1101/2024.10.23.619881>

This article is a preprint and has not been certified by peer review [what does this mean?].



nature medicine

Brief Communication

<https://doi.org/10.1038/s41591-025-03599-6>

Immune history shapes human antibody responses to H5N1 influenza viruses

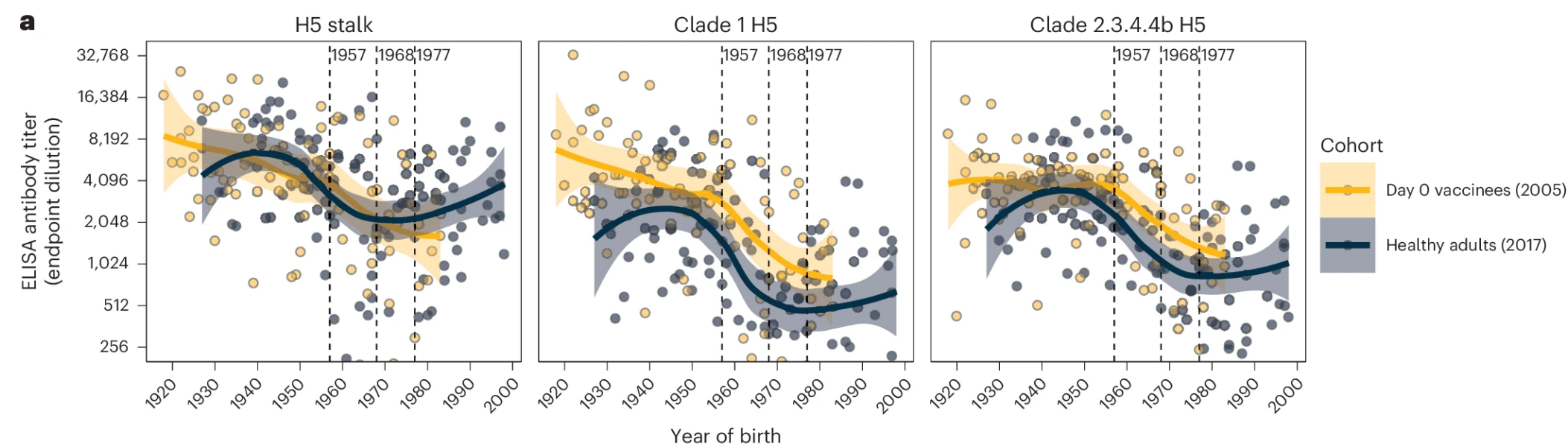
Received: 31 October 2024

Accepted: 20 February 2025

Published online: 13 March 2025

 Check for updates

Tyler A. Garretson^{1,5}, Jiaojiao Liu^{1,5}, Shuk Hang Li^{1,5},  Gabrielle Scher^{1,5},
 Jefferson J. S. Santos^{1,5},  Glenn Hogan², Marcos Costa Vieira³, Colleen Furey¹,
 Reilly K. Atkinson¹, Naiqing Ye¹,  Jordan T. Ort¹, Kangchon Kim³,
 Kevin A. Hernandez¹, Theresa Eilola¹, David C. Schultz¹,  Sara Cherry²,
 Sarah Cobey³ & Scott E. Hensley¹ 



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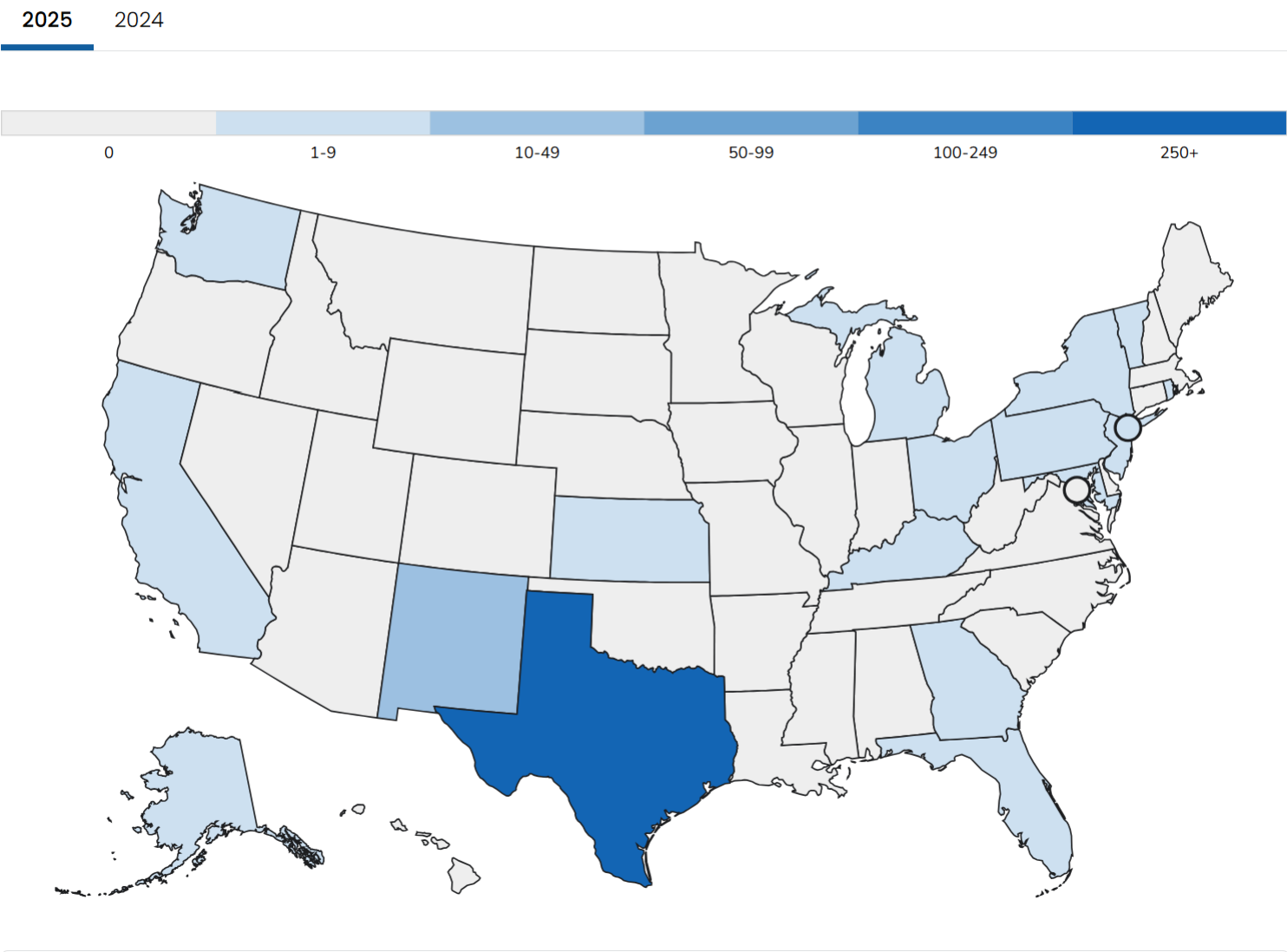
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Map of measles cases in 2024 & 2025

as of March 20, 2025



RESEARCH BRIEF

Appropriateness of Immunoglobulin M Testing for Measles, Mumps, and Rubella



Thomas D. Filardo, MD,^{1, #} Nina B. Masters, PhD,^{1, #} Jessica Leung, MPH,¹ Sarah Baca, BS,^{2, 3}
Heartley Egwuogu, PhD,^{2, 3} Oscar Rincon Guevara, PhD,² Julia Raykin, PhD,²
David E. Sugerman, MD¹

Introduction: Testing for immunity to measles, mumps, and rubella should include only immunoglobulin G (IgG); immunoglobulin M (IgM) testing is appropriate only if acute illness is suspected. The appropriateness of measles, mumps, and rubella IgM testing was evaluated in a national administrative dataset.

Methods: Laboratory testing for measles, mumps, and rubella during 2019–2022 was analyzed in 2024 using HealthVerity administrative claims and laboratory data. IgG, IgM, and reverse-transcriptase polymerase chain reaction (RT-PCR) testing are described by year, demographics, and region. IgM testing was examined for appropriateness, defined as an IgM test combined with diagnostic codes indicative of acute illness.

Results: During 2019–2022, IgM testing represented a small proportion of serologic testing (measles: 3.3%, mumps: 2.4%, rubella: 2.1%) but appeared to be appropriately performed in only 15.4% of cases for measles, 32.8% of cases for mumps, and 10.2% of cases for rubella. IgM testing was more commonly performed for female patients, with the largest discrepancy seen for rubella (90.5% female vs 9.5% male). IgM for measles and mumps was more often performed appropriately for persons aged 0–19 years (37.6% and 60.1%) compared with persons aged 20–49 years (11.8% and 22.0%) and 50+ years (16.5% and 33.8%).

Conclusions: The majority of IgM testing for measles, mumps, and rubella during this period appeared inappropriate. Clinicians and health systems could ensure that IgG testing alone is performed when evaluating for immunity through modifications to electronic medical records and commercial laboratories could ensure that providers are able to test for IgG alone when evaluating immunity.

Am J Prev Med 2024;67(6):973–977. Published by Elsevier Inc.

Real-Time Use of a Dynamic Model To Measure the Impact of Public Health Interventions on Measles Outbreak Size and Duration — Chicago, Illinois, 2024

Nina B. Masters, PhD¹; Inga Holmdahl, PhD²; Paige B. Miller, PhD²; Chirag K. Kumar^{2, 3}; Catherine M. Herzog, PhD²;
Peter M. DeJonge, PhD^{4, 5}; Stephanie Gretsche, MPH⁴; Sara E. Oliver, MD¹; Manisha Patel, MD¹; David E. Sugerman, MD¹;
Beau B. Bruce, MD, PhD²; Brian F. Borah, MD⁴; Scott W. Olesen, PhD²

“Counterfactual analysis of different intervention scenarios demonstrated the importance of early deployment of public health interventions in Chicago, with a **69% chance of an outbreak of 100 or more cases** had there been no mass vaccination or active case-finding compared with only a **1% chance when those interventions were deployed.**”





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Thank You

Contact me for slides at etmartin@umich.edu

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