PUBLIC HEALTH
UNIVERSITY OF MICHIGAN

UM Influenza Outbreak 2021

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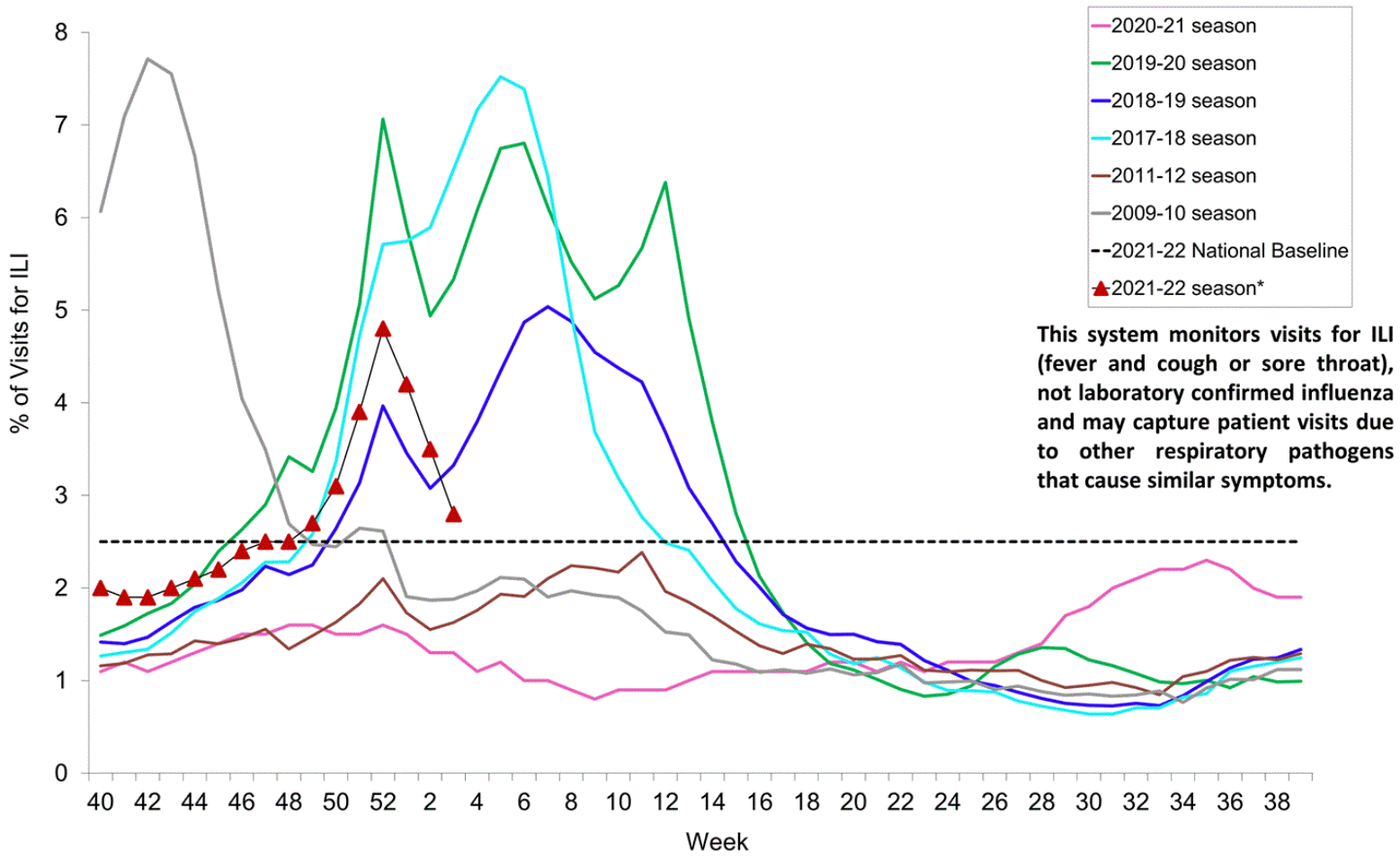
Disclosures

- Consultant to Sanofi on matters related to oseltamivir
- Roche, paid member of steering committee for baloxavir clinical trial
- This talk includes data from my laboratory, which is supported by

  grants and contracts from the NIH and CDC

2021-2022: The Year After The Year With No Flu



Out of the frying pan and into the fire

The New York Times

The Coronavirus Pandemic › | LIVE Covid-19 Updates | Coronavirus Map and Cases | Timeline of a BA.2 Infection

After a 'Covid Semester,' the University of Michigan Gets Tougher on the Virus

Like many big state universities, it tried to open with some semblance of normalcy. Outbreaks ensued.

Give this article | 127

After welcoming students to campus for a hybrid fall semester, the University of Michigan in Ann Arbor is adding more virtual classes and asking most students to remain home. Erin Kirkland for The New York Times

The New York Times

C.D.C. Investigates Flu Outbreak at University of Michigan

There have been 528 cases of the flu on the university's campus in Ann Arbor, a vast majority in students who have not had flu shots, school officials said.

The University of Michigan campus in Ann Arbor on Tuesday. Ryan Garza/Detroit Free

What’s going on at UHS?

Email 11/10

Hi all -

I'm worried there is an early flu season starting (320 cases at UHS with a percent positivity of 27.2% last week and 35.1% this week). We have one case in MFIVE so far.

We have a number of loose ends in each of the studies that we should think about tying up in case of an early season. Can we have a last minute meeting together? I could do 2:30-3:30 today if anyone else can?

Emily

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Emily Toth Martin, Ph.D.
Associate Professor, Epidemiology
University of Michigan School of Public Health

Infrastructure matters!

STUDENT LIFE
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Test results / samples available daily for COVID response

MICHIGAN CENTER FOR
RESPIRATORY VIRUS RESEARCH AND RESPONSE
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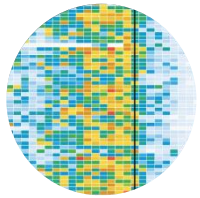
Existing Collaboration with CDC

Protocol for Vaccine Data Retrieval / COVID-19 Surveillance data collaboration

HEALTH DEPARTMENT
WASHTENAW
COUNTY Michigan

Reviewed for related cases outside campus



Lauring laboratory

CDC

MDHHS
Michigan Department of Health & Human Services

Timeline of the investigation

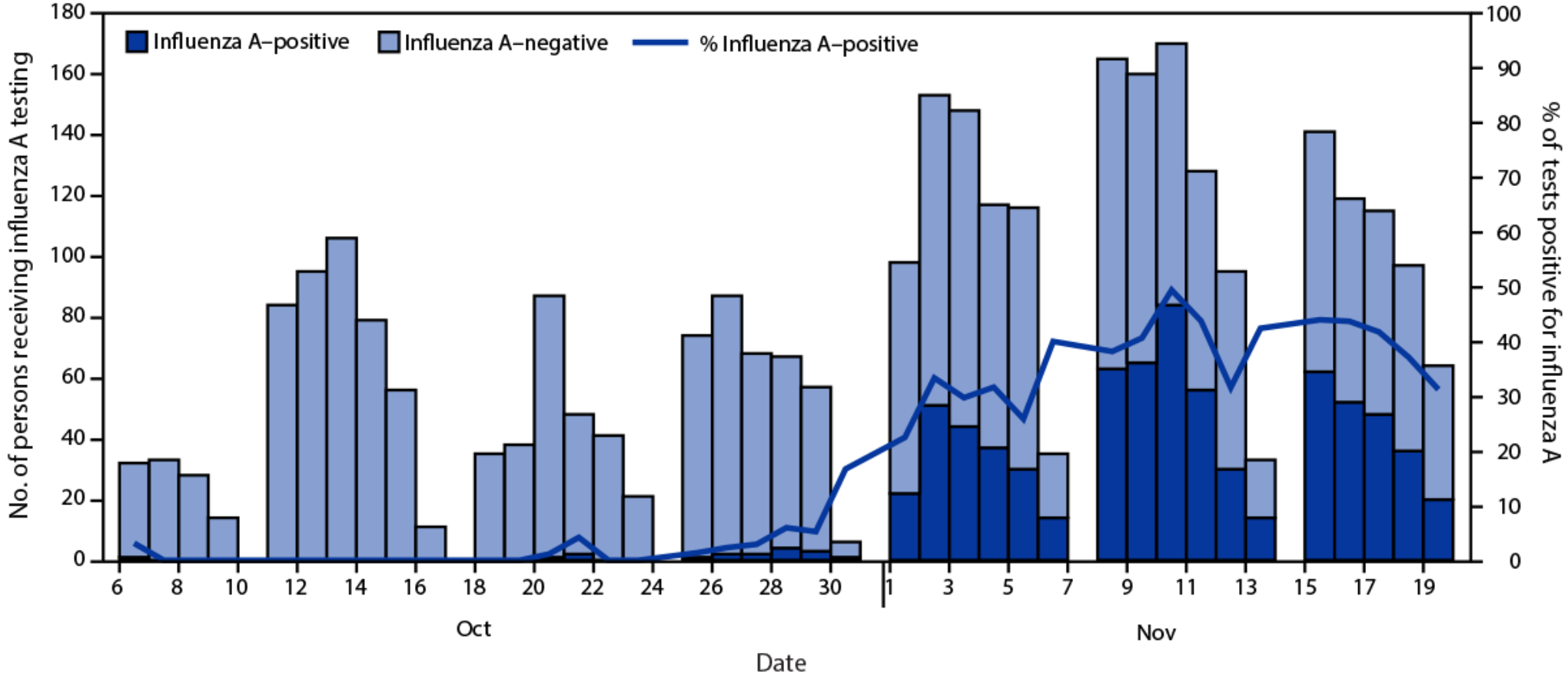
- Nov 2 – University health service notes increase in flu activity
  (from 13 cases the week before to 47 on Nov 1-2)
- Nov 10 – MDHHS notified of outbreak
- Nov 11 – MDHHS invites CDC to initiate an EPI-AID for a joint investigation
- Nov 14 – CDC EIS arrives on campus
- Nov 16 – Regulatory approvals in place across university, MDHHS, and CDC
- Nov 18 – Blood draws and serial sample collection begins
- Nov 18 – State vaccination registry data transferred to CDC
- Nov 18 (later that evening) – First VE estimate!
- Nov 24 – CDC Health Advisory – *2 weeks from notification of outbreak*
- Dec 10 – MMWR released

Extent of investigation

- 866 Total Influenza Cases out of of 4,164 Visits (Oct 6 through Dec 14)
  - First sample processed for sequencing Nov 11
  - Clade identified Nov 13
  - 442 samples sequenced between 11/11-11/29
  - Overall 535 with clades assigned, 361 with whole genome sequence
- 111 Acute Serum Specimens Collected
- 66 Kits distributed for Shedding Study
- 831 Responses to Risk Factor Survey

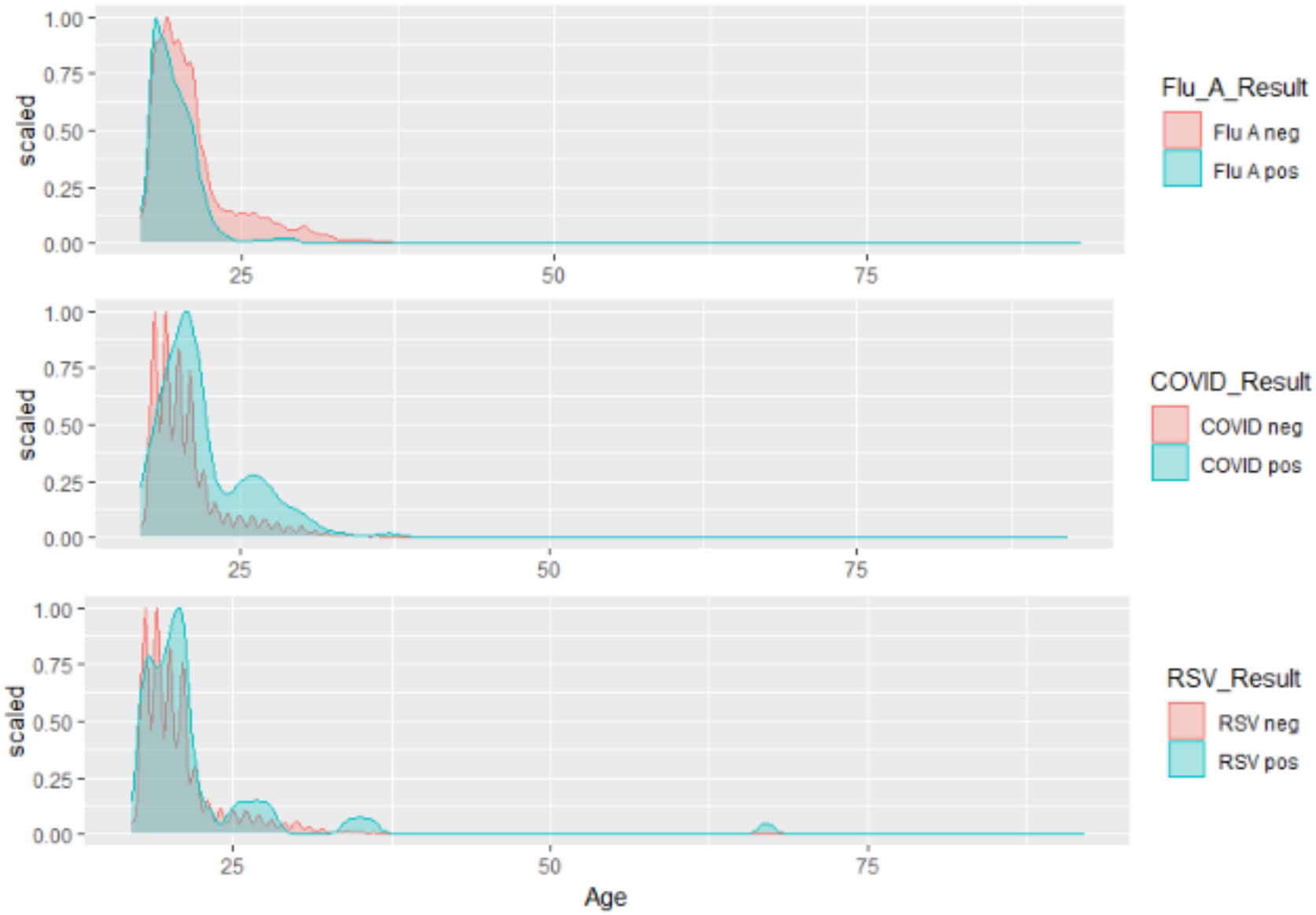
Symptomatic testing and cases at UHS

FIGURE. Number of symptomatic persons who received testing for influenza A at University Health Service (N = 3,121)* and percentage of tests positive for influenza A, by date of influenza test† — University of Michigan, October 6–November 19, 2021



Delahoy et al. MMWR 70:1712, 2021

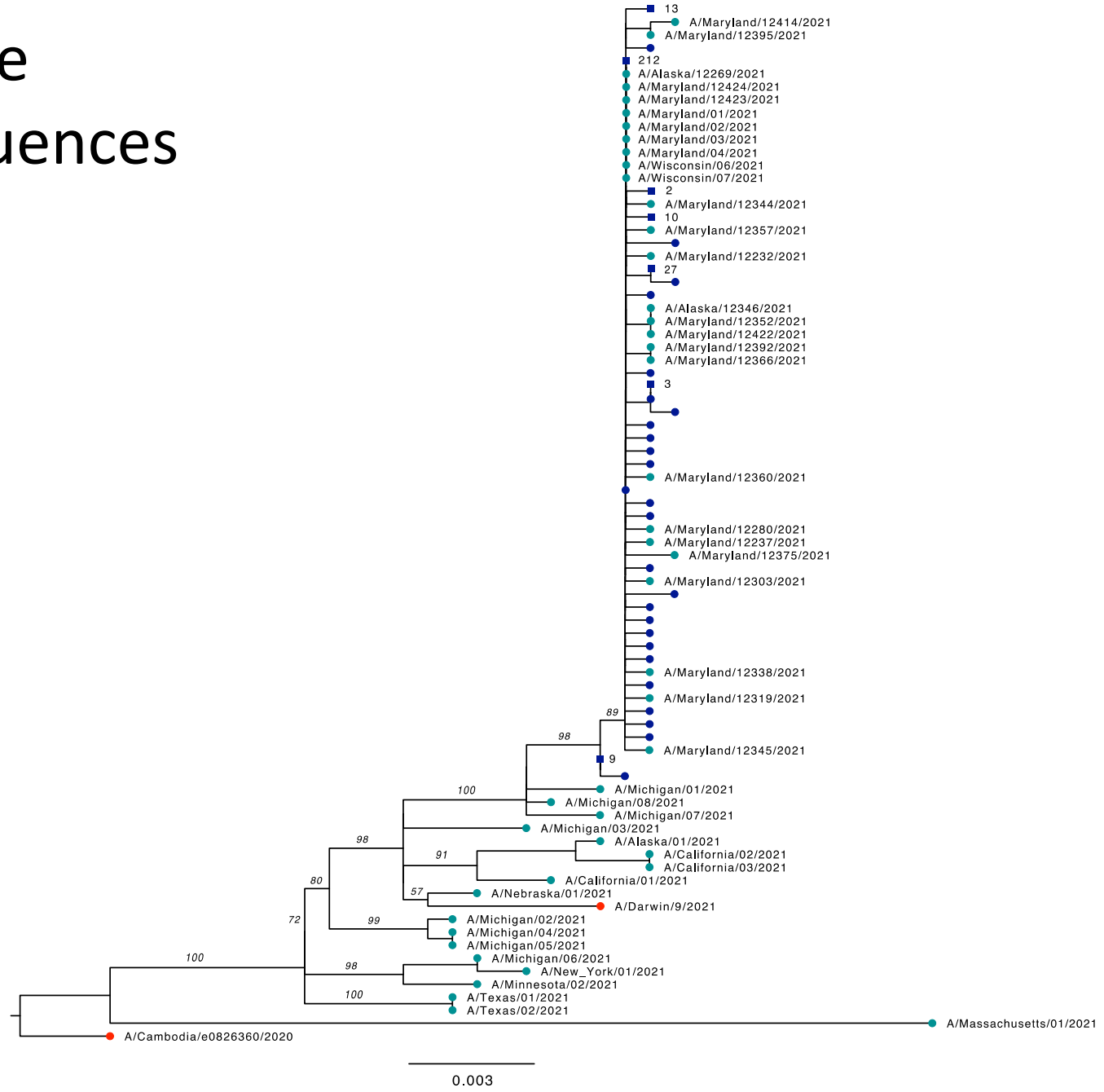
Age distribution by virus (through Nov 12)



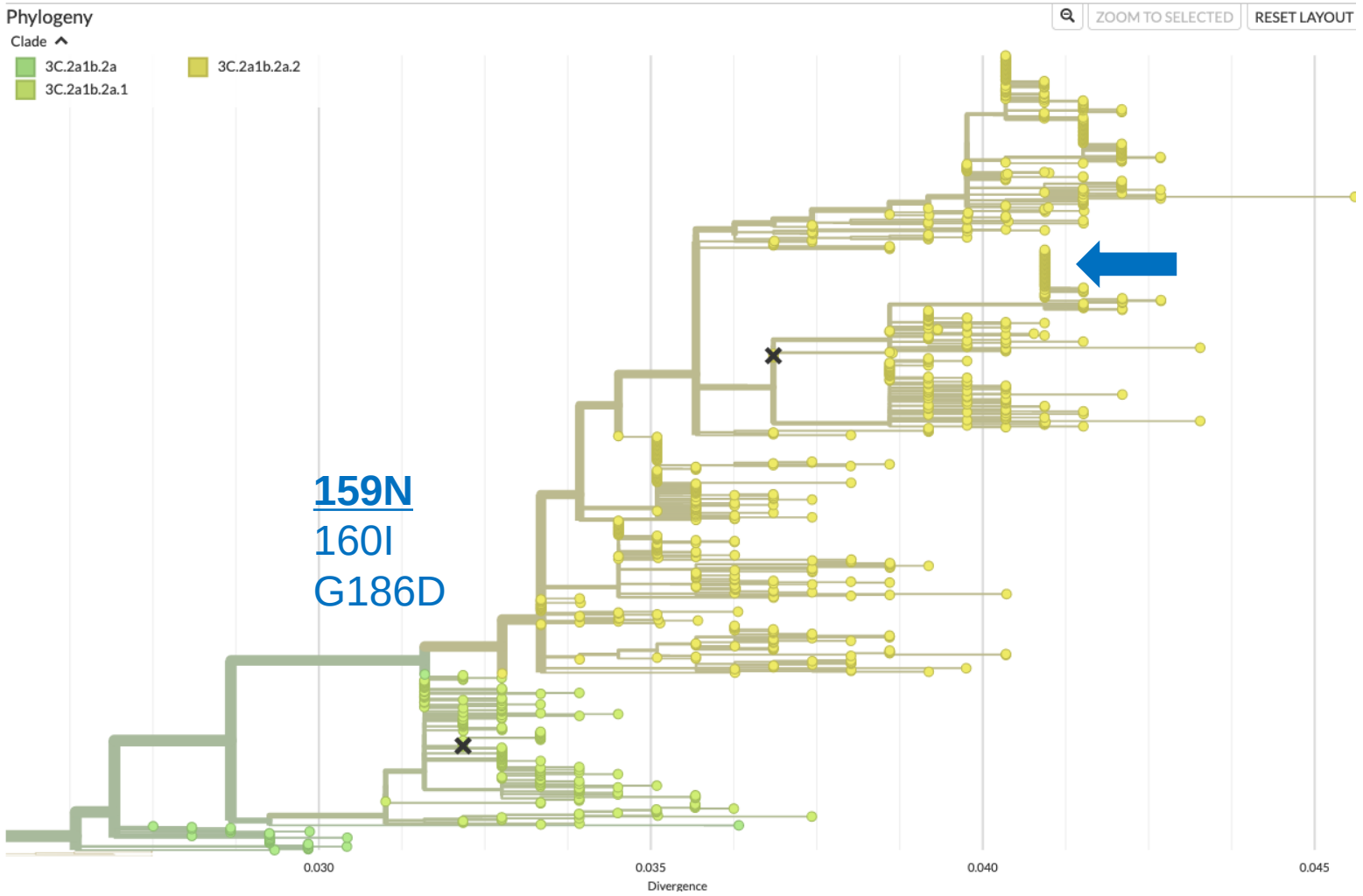
Demographic breakdown

Category	Influenza A Positive n / N (%)
Female	272 / 1589 (17%)
Male	241 / 992 (24%)
White	310 / 1628 (19%)
Black	13 / 77 (17%)
Asian	129 / 560 (23%)
Hispanic	32 / 153 (21%)
Non-Hispanic	451 / 2292 (20%)

Phylogenetic tree of outbreak sequences



Where does this fit in big picture?



What's really different about these clades?

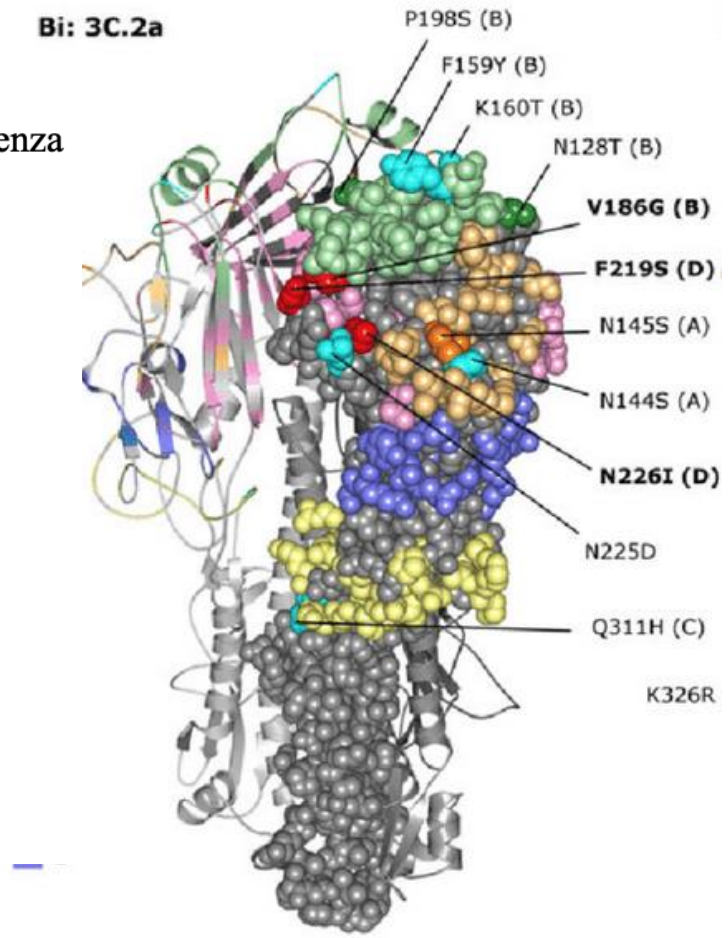
The WHO recommends that quadrivalent vaccines for use in the 2022 southern hemisphere influenza season contain the following:

Egg-based vaccines

- **an A/Victoria/2570/2019 (H1N1)pdm09-like virus;**
- **an A/Darwin/9/2021 (H3N2)-like virus;**
- **a B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and**
- **a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.**

Cell- or recombinant-based vaccines

- **an A/Wisconsin/588/2019 (H1N1)pdm09-like virus;**
- **an A/Darwin/6/2021 (H3N2)-like virus;**
- **a B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and**
- **a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.**



Preliminary VE Analysis through Nov 12

	Influenza-positive			Influenza-negative			Vaccine effectiveness			
							Unadjusted		Adjusted*	
	No. vaccinated	Total	(%)	No. vaccinated	Total	(%)	(%)	(95% CI)	(%)	(95% CI)
Flu A >13 days	128	481	27	512	1924	27	0	(-25 to 20)	**-3**	**(-30 to 18)**
Flu A >20 days	110	463	24	427	1839	23	-3	(-31 to 19)	**-5**	**(-34 to 18)**

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 71 / No. 10
March 11, 2022

Interim Estimates of 2021–22 Seasonal Influenza Vaccine Effectiveness — United States, February 2022

Jessie R. Chung, MPH[1]; Sara S. Kim, MPH[1]; Rebecca J. Kondor, PhD[1]; Catherine Smith, MS[1]; Alicia P. Budd, MPH[1]; Sara Y. Tartof, PhD[2]; Ana Florea, PhD[2]; H. Keipp Talbot, MD[3]; Carlos G. Grijalva, MD[3]; Karen J. Wernli, PhD[4]; C. Hallie Phillips, MEd[4]; Arnold S. Monto, MD[5]; Emily T. Martin, PhD[5]; Edward A. Belongia, MD[6]; Huong Q. McLean, PhD[6]; Manjusha Gaglani, MBBS[7,8]; Michael Reis, MD[7,8]; Krissy Moehling Geffel, PhD[9]; Mary Patricia Nowalk, PhD[9]; Juliana DaSilva, MA[1]; Lisa M. Keong[1,10]; Thomas J. Stark, PhD[1]; John R. Barnes, PhD[1]; David E. Wentworth, PhD[1]; Lynnette Brammer, MPH[1]; Erin Burns, MA[1]; Alicia M. Fry, MD[1]; Manish M. Patel, MD[1]; Brendan Flannery, PhD[1]

TABLE 2. Number and percentage of persons receiving 2021–22 seasonal influenza vaccine among 3,636 outpatients with acute respiratory infection, by influenza test result status and vaccine effectiveness* against all influenza A and against virus type A(H3N2) — U.S. Influenza Vaccine Effectiveness Network, United States, October 4, 2021–February 12, 2022

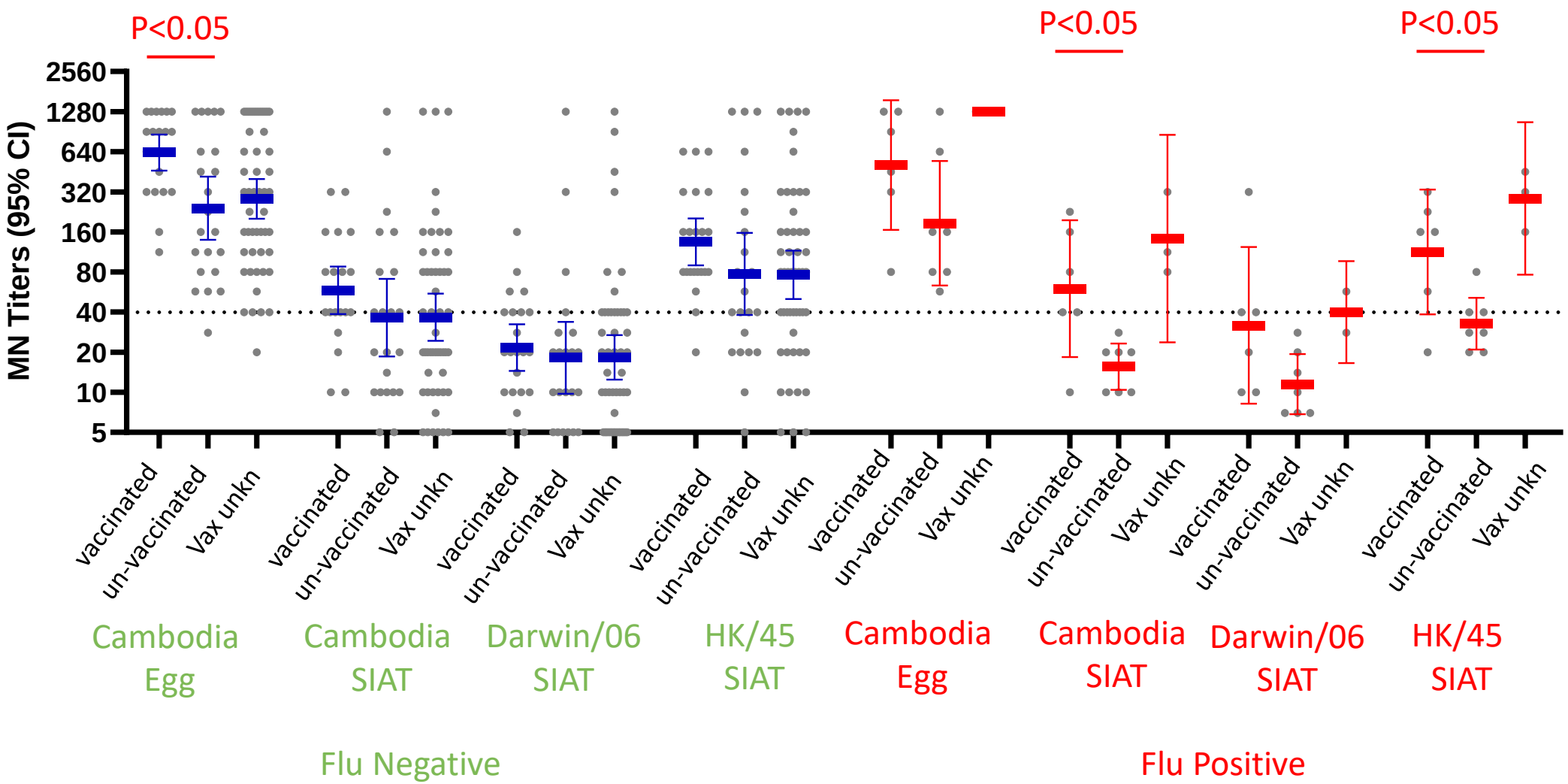
	Influenza-positive		Influenza-negative		VE*	
Influenza type, all ages	Total	Vaccinated no. (%)	Total	Vaccinated no. (%)	Unadjusted % (95% CI)	Adjusted % (95% CI)†
Influenza A	**194**	79 (41)	**3,442**	1,738 (50)	32 (10 to 50)	14 (–17 to 37)
Influenza A/H3N2	**177**	69 (39)	**3,174**	1,564 (49)	34 (11 to 52)	16 (–16 to 39)

Abbreviations: OR = odds ratio; VE = vaccine effectiveness.

* VE was estimated using the test-negative design as 100% x (1 – OR [ratio of odds of being vaccinated among outpatients who received influenza-positive test results to odds of being vaccinated among outpatients who received influenza-negative test results]); ORs were estimated using logistic regression. https://www.cdc.gov/flu/vaccines-work/us-flu-ve-network.htm

† Adjusted for study site, age group, number of days from illness onset to enrollment, and month of illness using logistic regression.

Microneutralization antibodies in acute sera by vaccination and infection status



What did we learn from this outbreak?

- Preparedness matters
  - Outbreak happened “at the right place, at the right time”
- Rapid and efficient investigation
  - Clade assignment and VE estimate within 2 weeks!
  - Wealth of serological and interview data
- Antigenic drift from vaccine
  - Serological responses were low against circulating strain
- In this population vaccine effectiveness against mild disease was low
  - Only estimated for H3N2
  - VE against more severe disease? Other groups?

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