

Interim Estimates of 2022–23 Influenza Vaccine Effectiveness from Two Studies in Wisconsin: A Test-Negative Case-Control Study and a Community Cohort Study

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Huong McLean presenting on behalf of the study team

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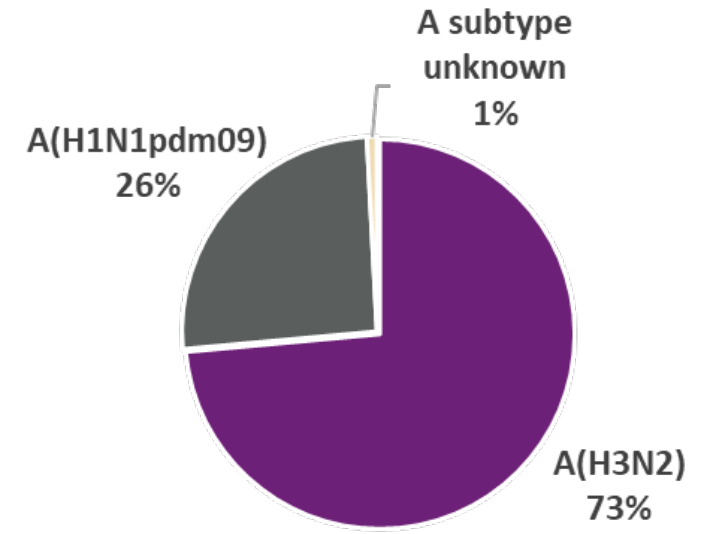
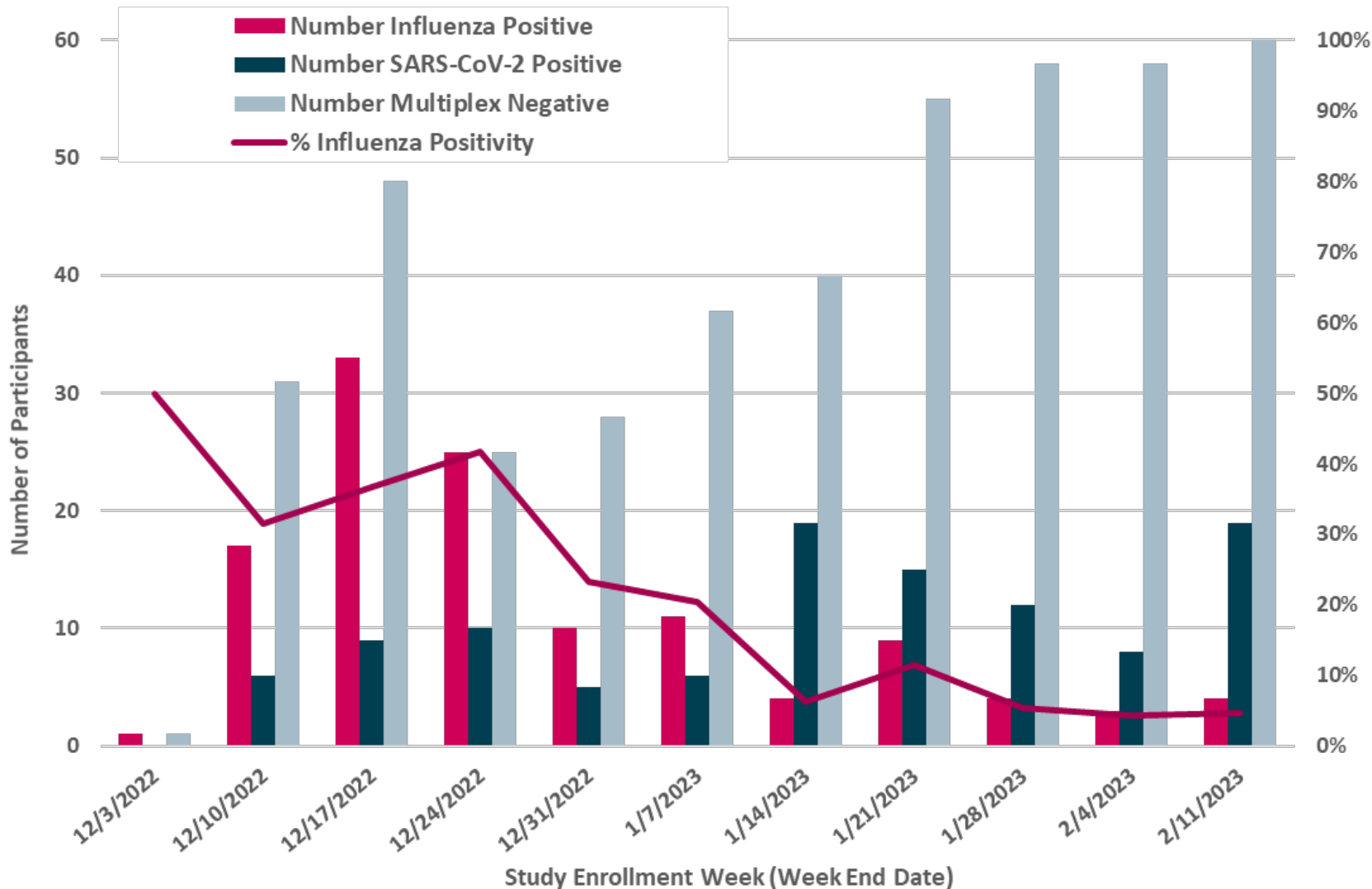


Test-negative case-control study

Methods: Test-negative case-control study

- **Enrollees:** Outpatients aged 6 months – 64 years with acute respiratory illness with cough ≤ 7 days duration
- **Dates of enrollment:** December 2, 2022 – February 10, 2023
- Nasal and oropharyngeal swabs tested for influenza and SARS-CoV-2
- **Vaccination status:** documented (in health record) receipt ≥ 14 days before illness onset per ACIP recommendations
- **Analysis:** $VE = (1 - \text{adjusted OR}) \times 100\%$
 - Logistic regression model adjusted for age, month of onset, higher-risk condition (self report)

RT-PCR results by week of enrollment



- 34/34 sequenced A(H3N2) viruses belonged to **subclade 2a2**
- 9/9 A(H1N1pdm09) belonged to **subclade 5a.2**



Participant* characteristics

		Total no. of patients	No. (%) vaccinated†	No. (%) influenza positive	No. (%) influenza- and SARS-CoV-2 negative
Total		545	186 (34)	116 (21)	249 (79)
Age	6 mos – 17 years	223	69 (31)	42 (19)	181 (81)
	18 – 64 years	322	117 (36)	74 (23)	248 (77)
Sex	Female	318	127 (40)	65 (20)	253 (80)
	Male	227	59 (26)	51 (22)	176 (78)
Race/ethnicity	Non-Hispanic White	482	161 (33)	105 (22)	377 (78)
	Hispanic	35	12 (34)	6 (17)	29 (83)
	Non-Hispanic non-White	28	13 (46)	5 (18)	23 (82)
Self report of higher-risk condition§	Yes	154	69 (45)	30 (19)	124 (81)
	No	391	117 (30)	86 (22)	305 (78)
Self report of ≥2 COVID-19 vaccine doses	Yes	258	133 (52)	51 (20)	207 (80)
	No	287	53 (18)	65 (23)	222 (77)

*109 patients had a positive test result for SARS-CoV-2 virus infection and were excluded.

†84% received cell-culture based vaccine (ccIV4).

§Based on self-report of asthma or another chronic lung disease, cancer, diabetes, heart disease including high blood pressure, immunocompromising condition, kidney disease, liver disease, obesity, and pregnancy in the 12 months preceding enrollment.

Vaccine effectiveness (VE) against outpatient influenza, children and adults aged 6 months – 64 years

	Influenza positive		Influenza- and SARS-CoV-2 negative		Adjusted VE*
	No. vaccinated / Total	%	No. vaccinated / Total	%	% (95% CI)
Influenza A	26 / 116	22	160 / 429	37	54 (23-73)
A(H3N2)	16 / 86	19	160 / 429	37	60 (25-79)

Study period: December 2, 2022 – February 10, 2023.

*VE was estimated using the test-negative design as $100\% \times (1 - aOR)$ where aOR represents ratio of odds of being vaccinated among influenza positive cases to odds of being vaccinated among influenza-negative and SARS-CoV-2-negative controls; ORs were estimated using logistic regression with adjustment for age, month of illness onset, and presence of one or more higher-risk condition.

Prospective community cohort study

Methods: Community cohort study

- Ongoing community cohort in central Wisconsin
- 241 children aged 1 – 17 years followed weekly since September 5, 2022
- Weekly reporting for absence or presence of symptoms
 - Fever, cough, loss of smell or taste, sore throat, muscle/body aches, shortness of breath, diarrhea, nasal congestion/runny nose, or nausea/vomiting
- New symptom onset prompts self- or guardian-collection of anterior nasal swab for influenza and SARS-CoV-2 testing
- Information collected from surveys and extracted from electronic health records (e.g., vaccination history, clinical influenza test results)

Analysis: Community cohort study

Cox proportional hazards model with time-varying vaccination status

At risk	October 23, 2022 – February 10, 2023 or positive influenza infection date
Vaccinated	≥14 days after influenza vaccine receipt*
Unvaccinated	Time before influenza vaccination
Censored	Person-time for the 13 days after vaccine receipt

- **Influenza case:** positive RT-PCR influenza result (research or clinical sample)
- $VE = \left(1 - \text{adjusted } HR_{\frac{\text{rate of influenza infection among vaccinated person-time}}{\text{rate of influenza among unvaccinated person-time}}} \right) * 100\%$
- Adjusted for age, higher-risk condition (self-report), COVID-19 vaccination

*Based on documentation in health record according to ACIP recommendations

Characteristics of community cohort

		Total no. of participants*	No. (%) vaccinated†	No. (%) influenza positive¶
Total		241	94 (39)	34 (14)
Age	1 – 8 years	71	31 (44)	9 (13)
	9 – 17 years	170	63 (37)	25 (15)
Sex	Female	116	49 (42)	17 (15)
	Male	125	45 (36)	17 (14)
Race/ethnicity	Non-Hispanic White	233	92 (39)	33 (14)
	Hispanic	2	2 (100)	1 (50)
	Non-Hispanic non-White	6	0 (0)	0 (0)
Self report of higher-risk condition§	Yes	31	13 (42)	6 (19)
	No	210	84 (39)	28 (13)
≥2 COVID-19 vaccine doses	Yes	115	61 (53)	20 (17)
	No	126	33 (26)	14 (11)

*242 participants enrolled; 1 was excluded because they were partially vaccinated per ACIP recommendations prior to the start of the analysis period.

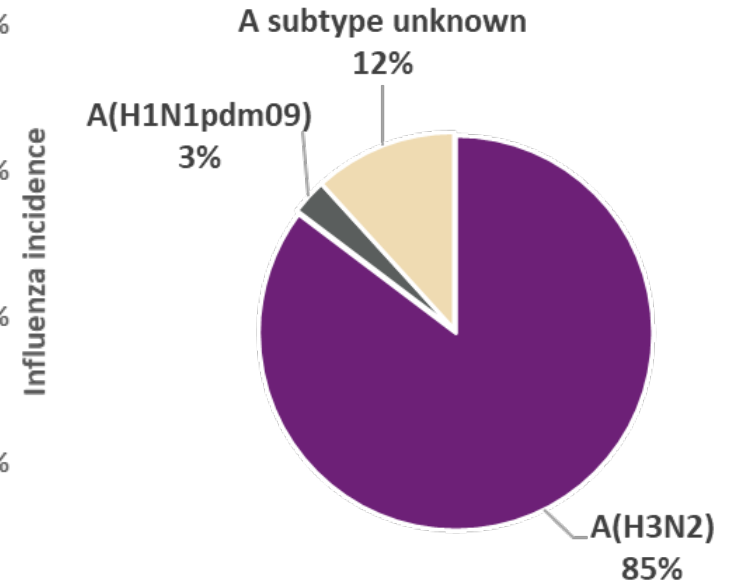
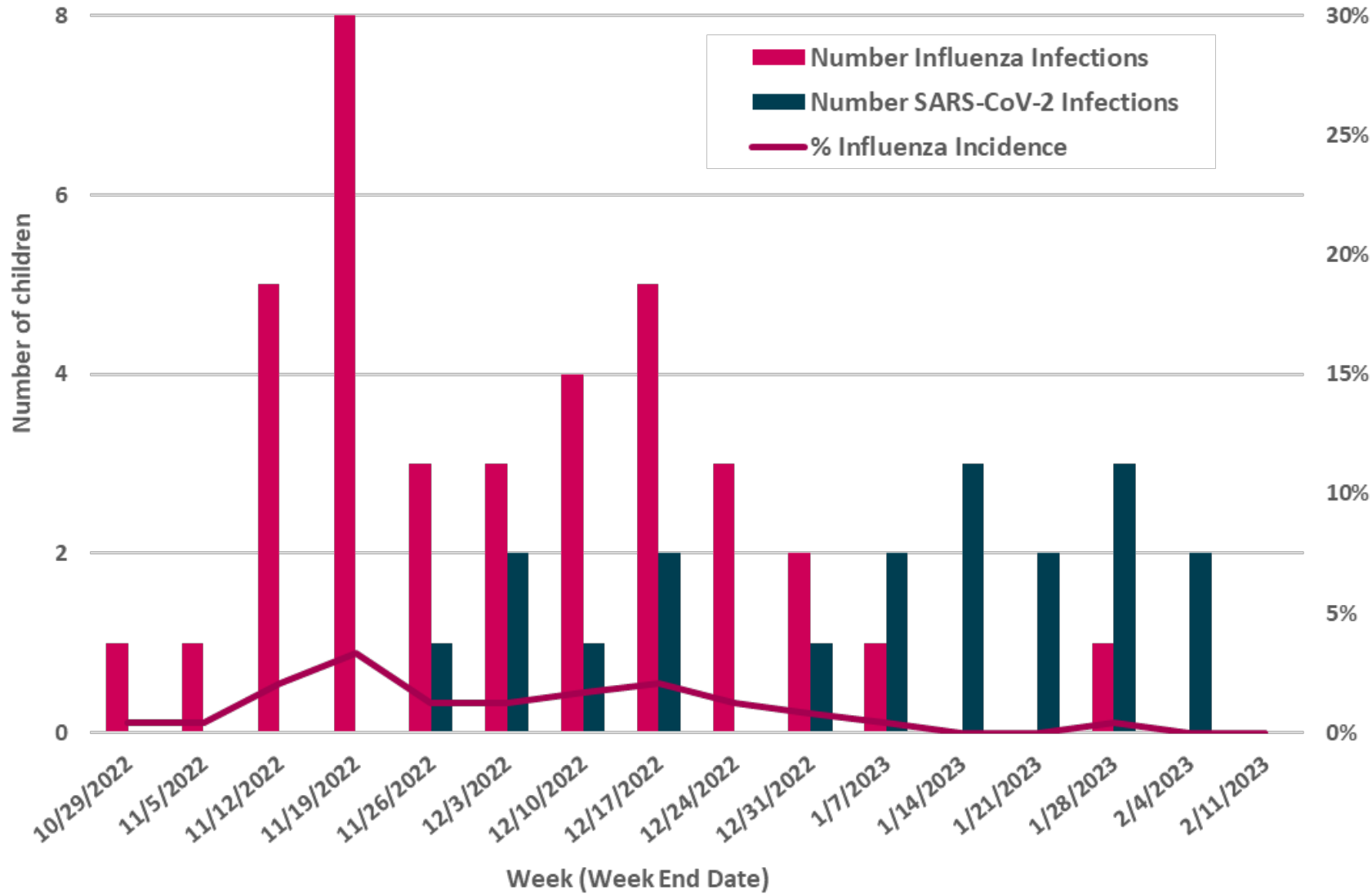
†84% received cell-culture based vaccine (ccIIIV4).

¶3 cases occurred ≤14 days from influenza vaccination and were censored at the time of vaccination.

§Based on self-report of asthma, immunocompromised state, serious heart condition, or other chronic lung disease.



Influenza and SARS-CoV-2 infections by week of onset



- 6/6 sequenced A(H3N2) viruses belonged to **subclade 2a2**



Vaccine effectiveness (VE) against symptomatic influenza among children

	No. of influenza infections*	No. of person-days	Incidence per 1,000 person-days	Adjusted VE [†] % (95% CI)
Vaccinated	6	7,292	0.82	71 (31 – 90)
Not Vaccinated	28	15,678	1.79	

Study period: October 23, 2022 – February 10, 2023.

*3 influenza infections were censored because onset occurred within 14 days of vaccination.

[†] VE was estimated from Cox proportional hazards model with time-varying influenza vaccination status, age, presence of at least one higher-risk condition (self-report of asthma, immunocompromised state, serious heart condition, or other chronic lung disease), and receipt of 2 or more COVID-19 vaccine doses before the analysis period.



Limitations

- **Single geographic area (central WI)**
 - **Predominant viruses similar in study population and across US**
- **Adults aged ≥ 65 years excluded**
 - **Generally have lower VE estimates against A(H3N2)**
- **Small sample sizes**
 - **Wide confidence intervals**
 - **Unable to estimate VE for A(H1N1)pdm09 or age groups**
- **Confounding and bias with observational studies**
 - **Comparable estimates across two study designs**



Summary

- **Interim results indicate substantial vaccine-induced protection against influenza A during 2022-23 season**
 - **VE 54% against medically attended influenza A in children and working aged adults**
 - **VE 71% against symptomatic influenza A in children**
- **All characterized viruses from the study population belonged to the same genetic subclade as the viruses included in the 2022–23 Northern Hemisphere influenza vaccine**



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*Coauthor

