



Influenza and SARS-CoV-2 from a School Perspective: the value of microscale epidemiology

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Wisconsin Virology Conference

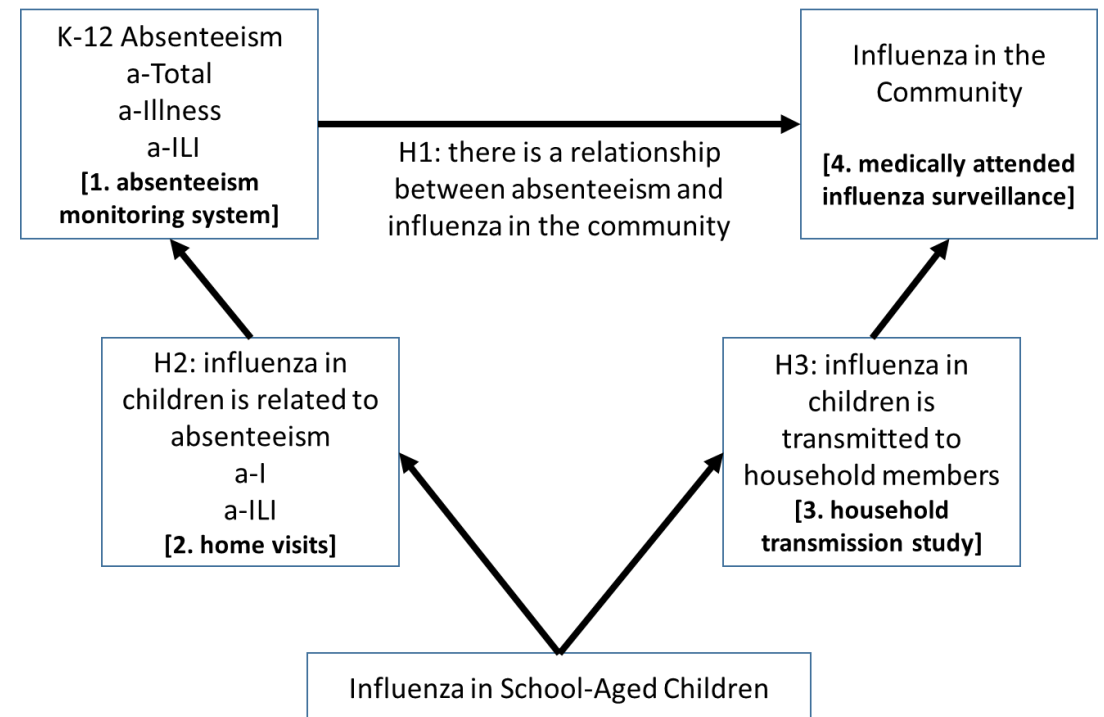
June 27, 2022



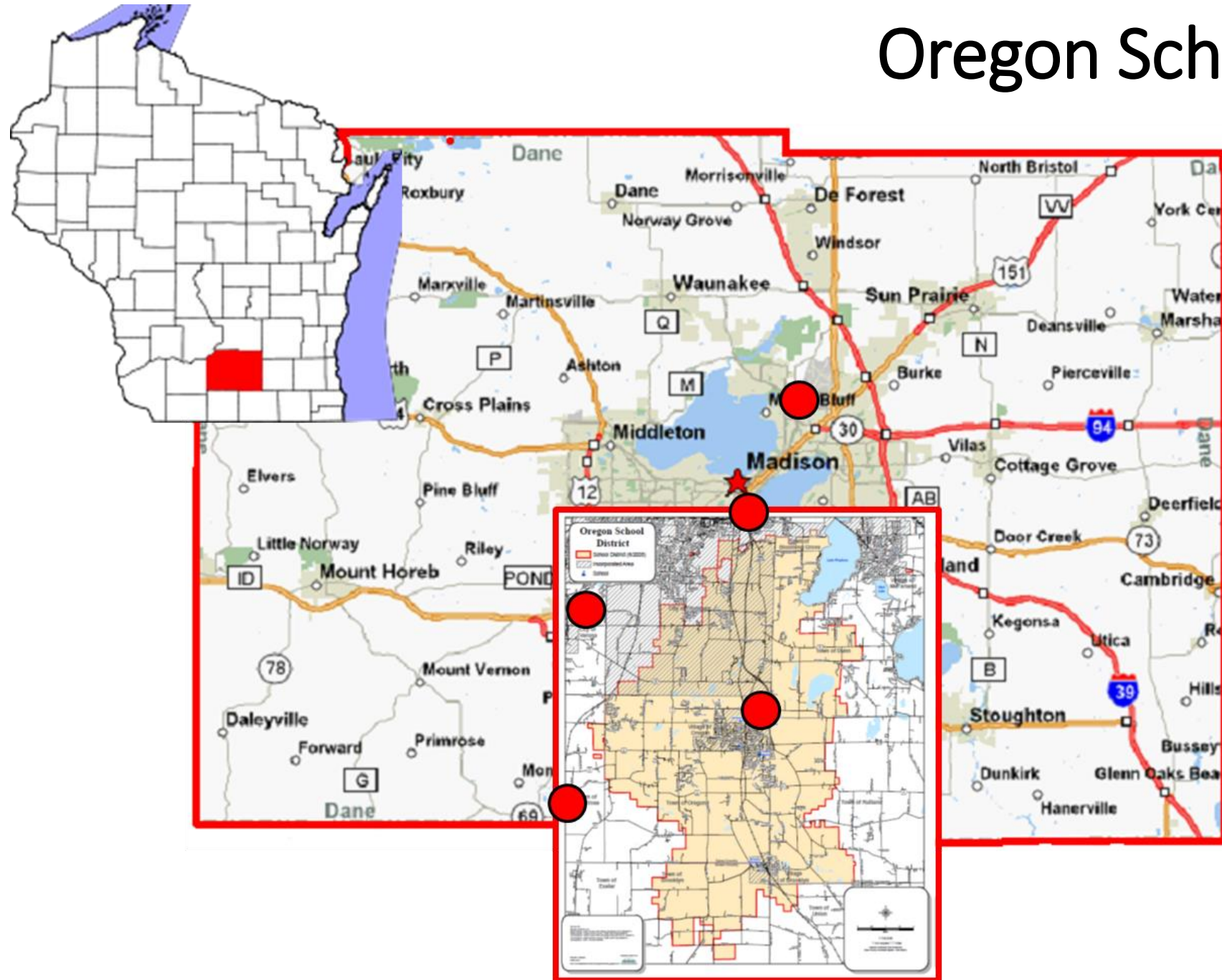


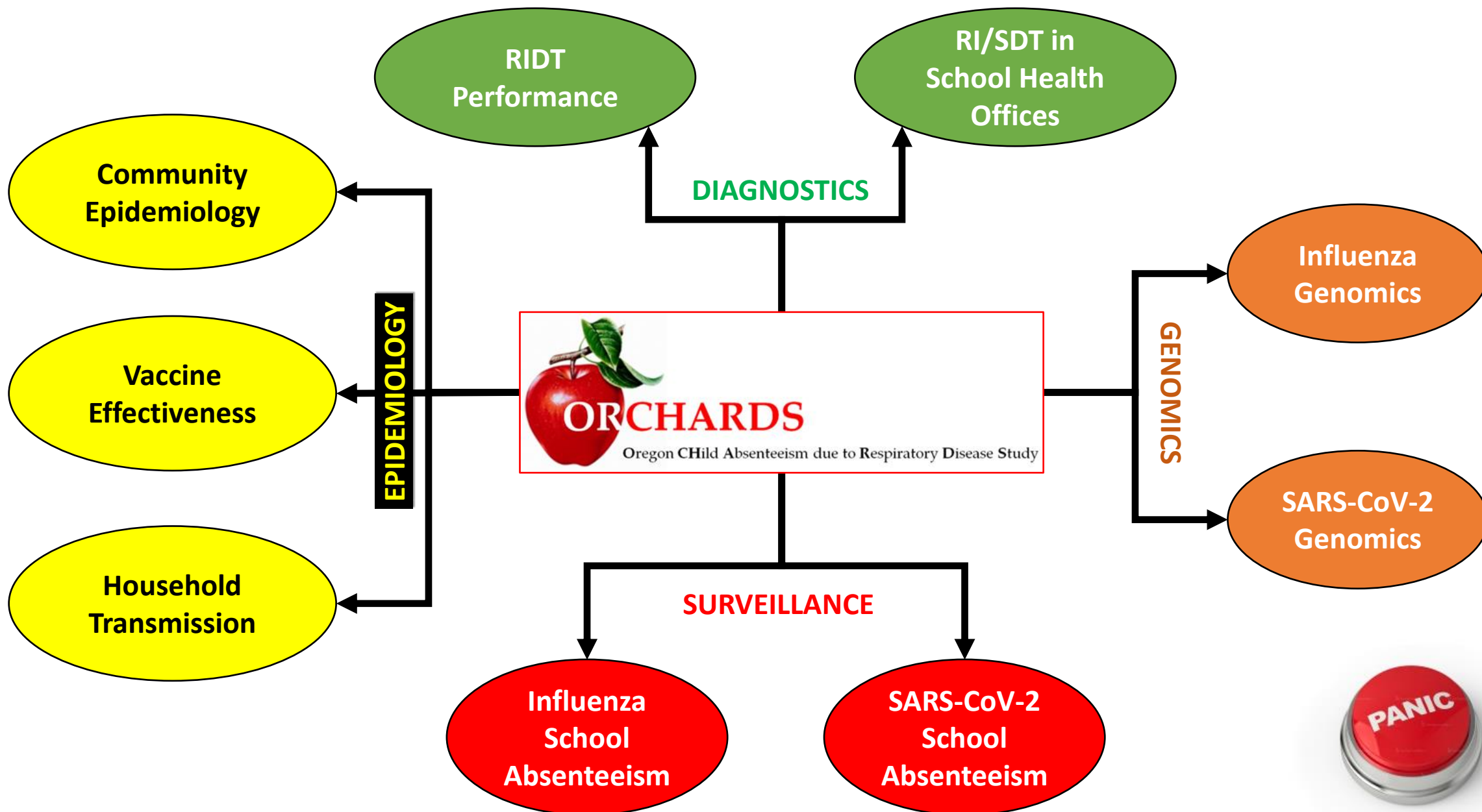
ORCHARDS

Oregon CHild Absenteeism due to Respiratory Disease Study



Oregon School District





Performance of Sofia FIA Influenza A+B in school-aged children in the community

ORCHARDS protocol from
January 2014—March 2020

Children with ARI visited at
home

- Demographic, epidemiologic, and clinical (symptom) data collected
- Sofia FIA tested within 2 hours of home visit by our staff
- RT-PCR for influenza at WSLH
- RPP for other respiratory pathogens

Results of Note



2,378 recruited students

2,368 (99.6%) had paired FIA and RT-PCR results

- Mean age = 10.2 years
- 58.8% met ILI case definition (fever plus ≥ 1 respiratory symptom).

Flu A and B were detected by RT-PCR in 447 (19%) and 363 (15%) children, respectively

Sensitivity was 76.1% (95% CI: 72.8—79.1)
with following associated factors:

- coryza (OR=3.0, $p<0.001$)
- nasal congestion (1.59, $p=0.045$)
- days from symptom onset (per day; 0.75; $p<0.001$)
- myalgia (0.61; $p=0.014$)
- age (per 5 years; 0.55; $p=0.001$)
- detection of another virus (0.50; $p=0.042$)

Specificity was 97.2% (96.2—97.9)

- No explored factors were associated with relative specificity

What would happen if rapid influenza/SARS-CoV-2 diagnostic test analyzers were placed in school health offices?

**Oregon School District
- 7 schools**

August 2021—June 2022

Minimal input

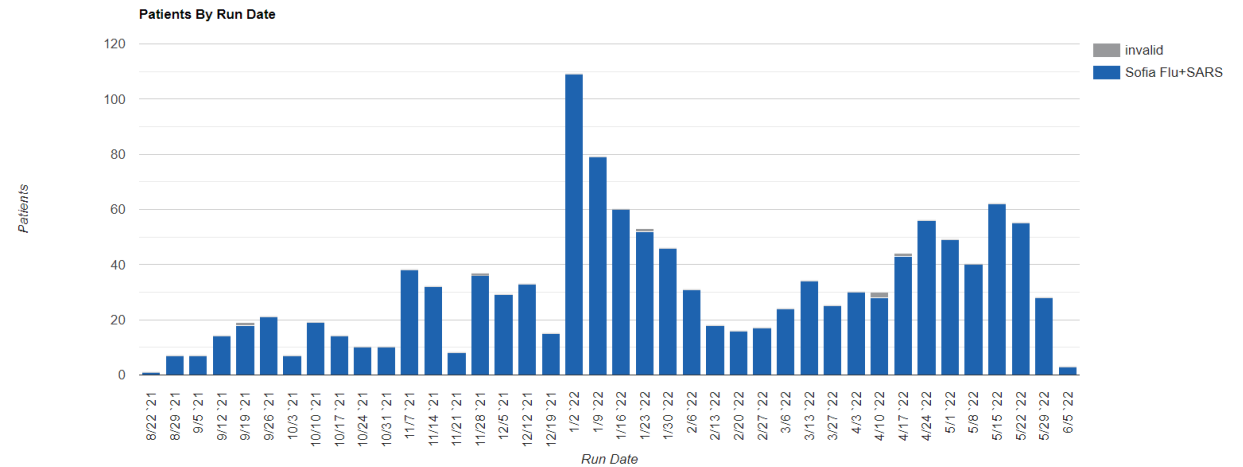
- Sofia set up and instructions
- Provision of supplies (courtesy of Quidel, Inc)
- Connectivity with COVID-Connect

Ability to monitor using My Virena

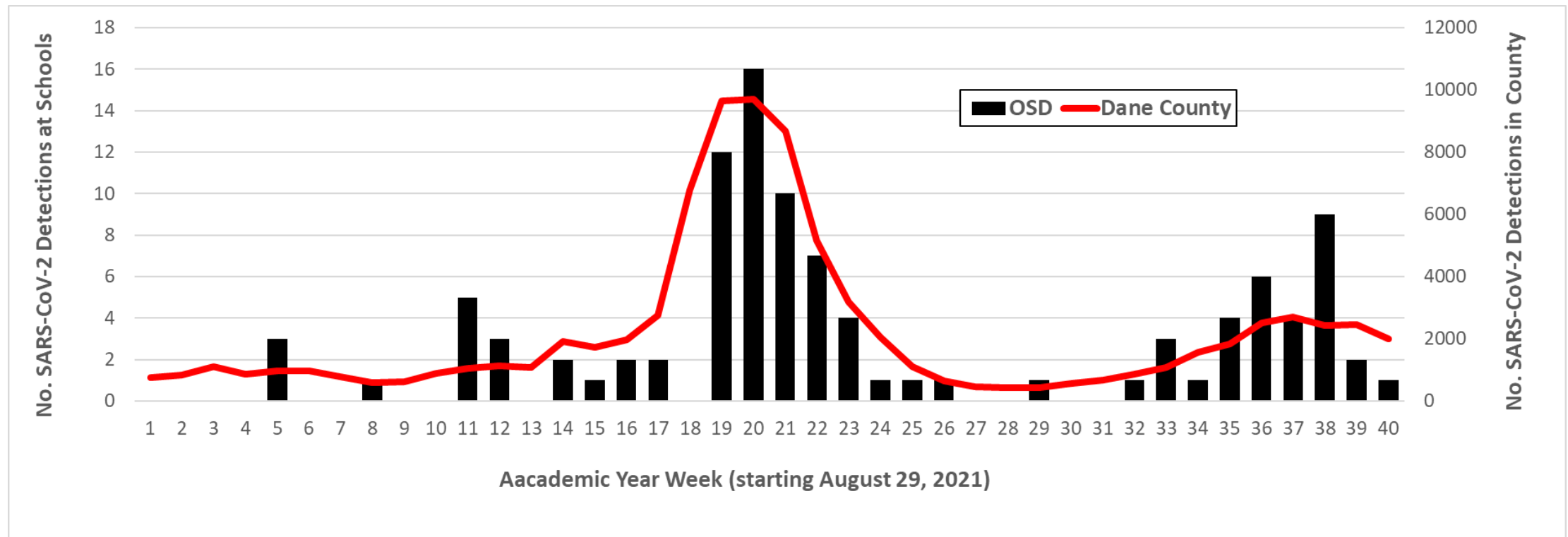
Rapid Testing was used – a lot!

- 1,230 tests performed by health office nurses and staff
 - 6 invalid tests (<0.5%)
- Used at all schools
- Results
 - 103 (+) for SARS-CoV-2
 - 35 (+) for influenza A
 - 20 (+) for influenza B
- Well liked by the staff

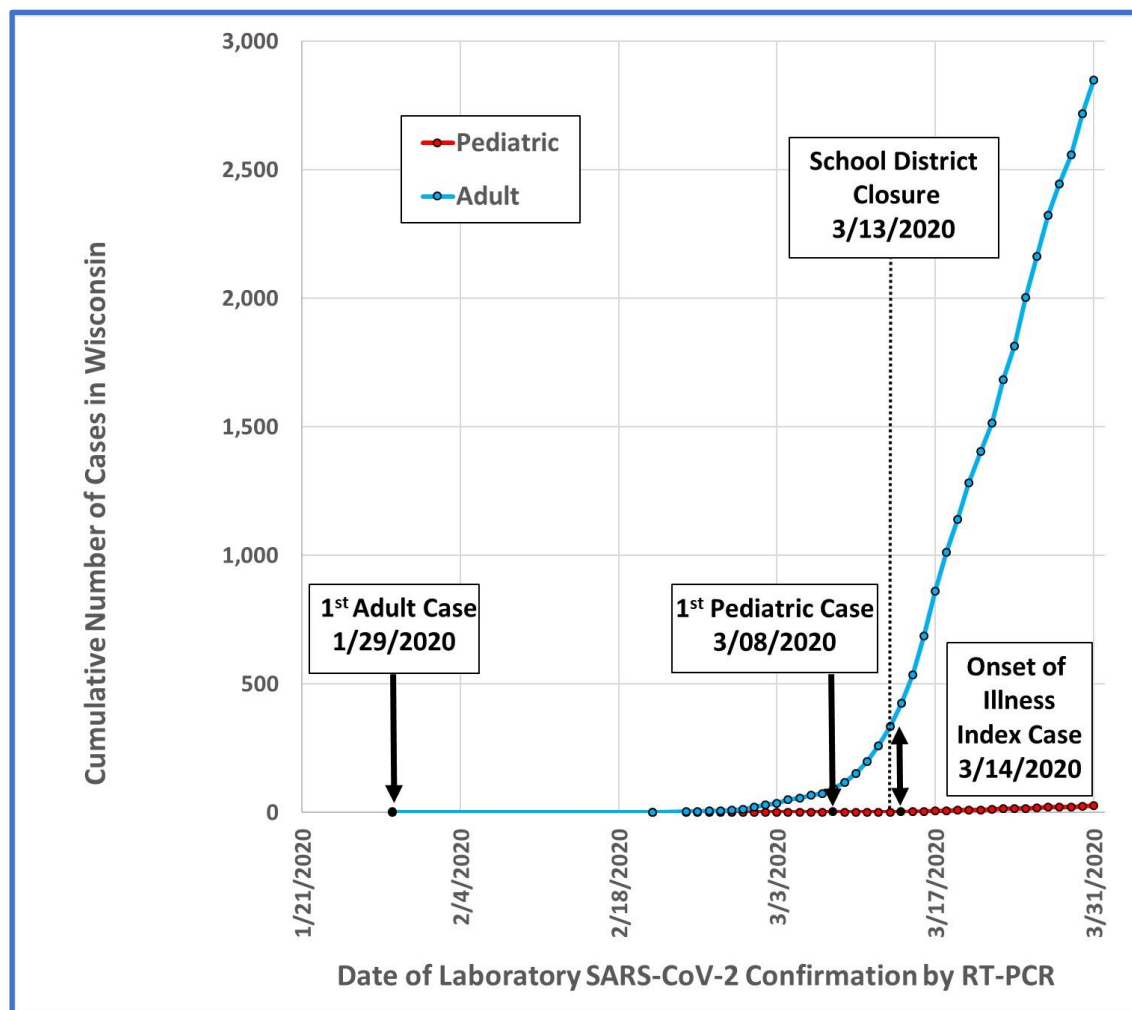
Number of tests per week



Comparability of School SARS-CoV-2 detections with county SARS-CoV-2 detections ($r=0.81$)

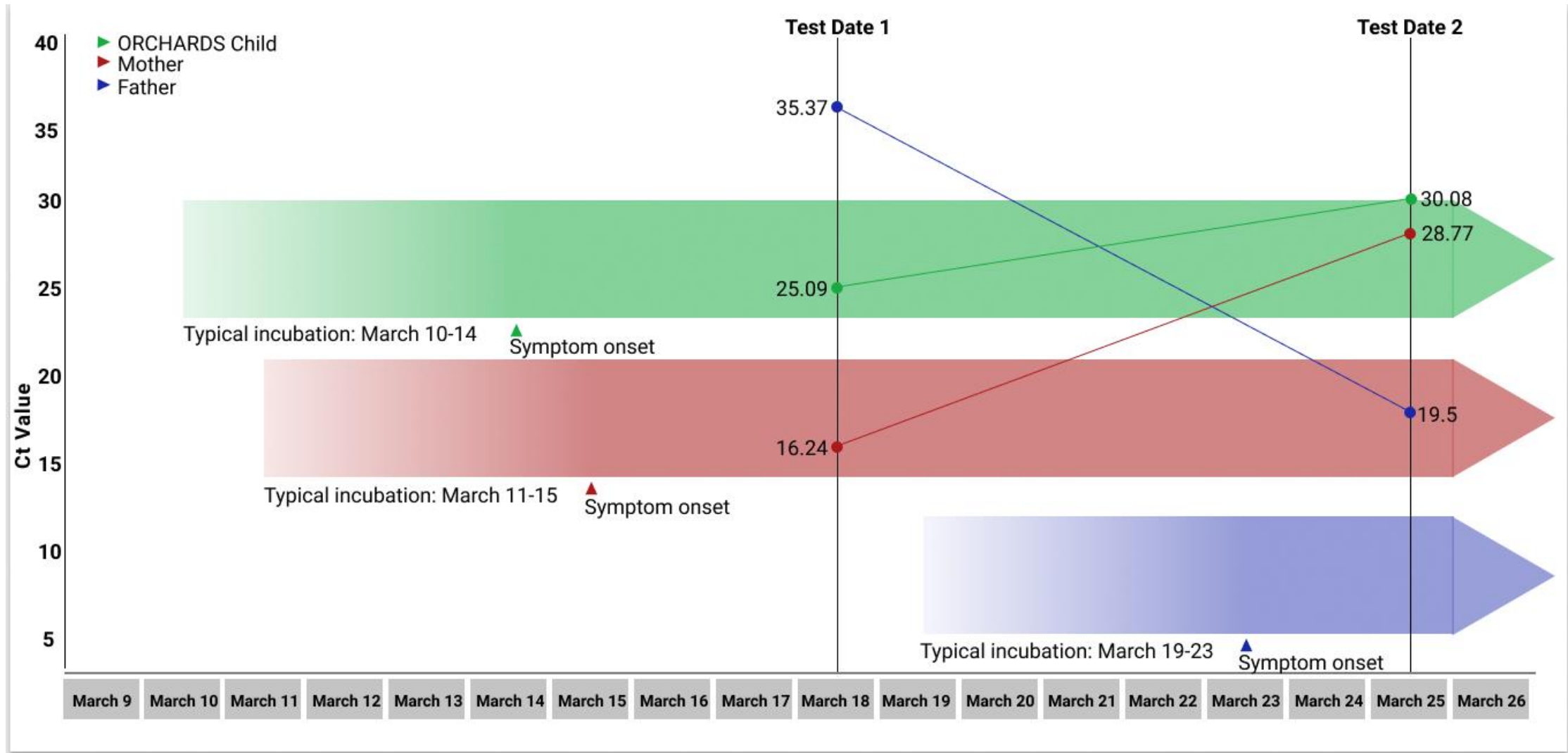


Evidence of Early SARS-CoV-2 Activity in Wisconsin



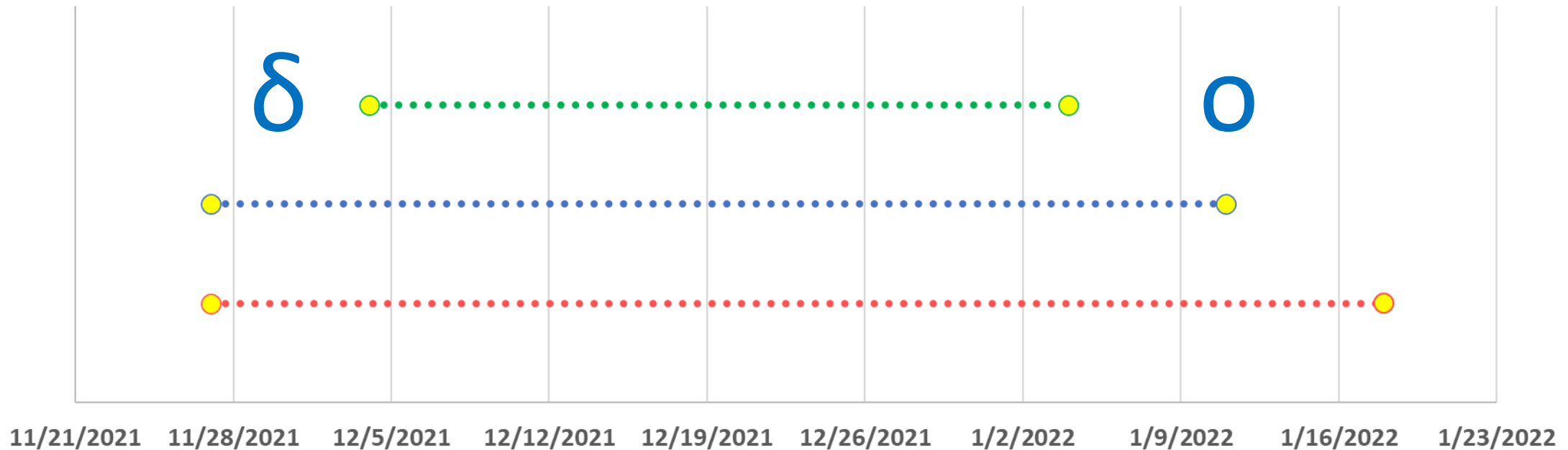
Specimen Collection Period	Specimens Available	SARS-CoV-2 (+) (%)
September 2019	38	0 (0)
October 2019	38	0 (0)
November 2019	27	0 (0)
December 2019	63	0 (0)
January 2020	191	0 (0)
February 2020	237	0 (0)
Early-March 2020*	57	0 (0)
Late-March 2020*	18	1 (5.6%)
April 2020	2	0 (0)
May 2020	2	0 (0)
June 2020	2	0 (0)
Total: September–June	670	1 (0.15)

First known household transmission in Wisconsin



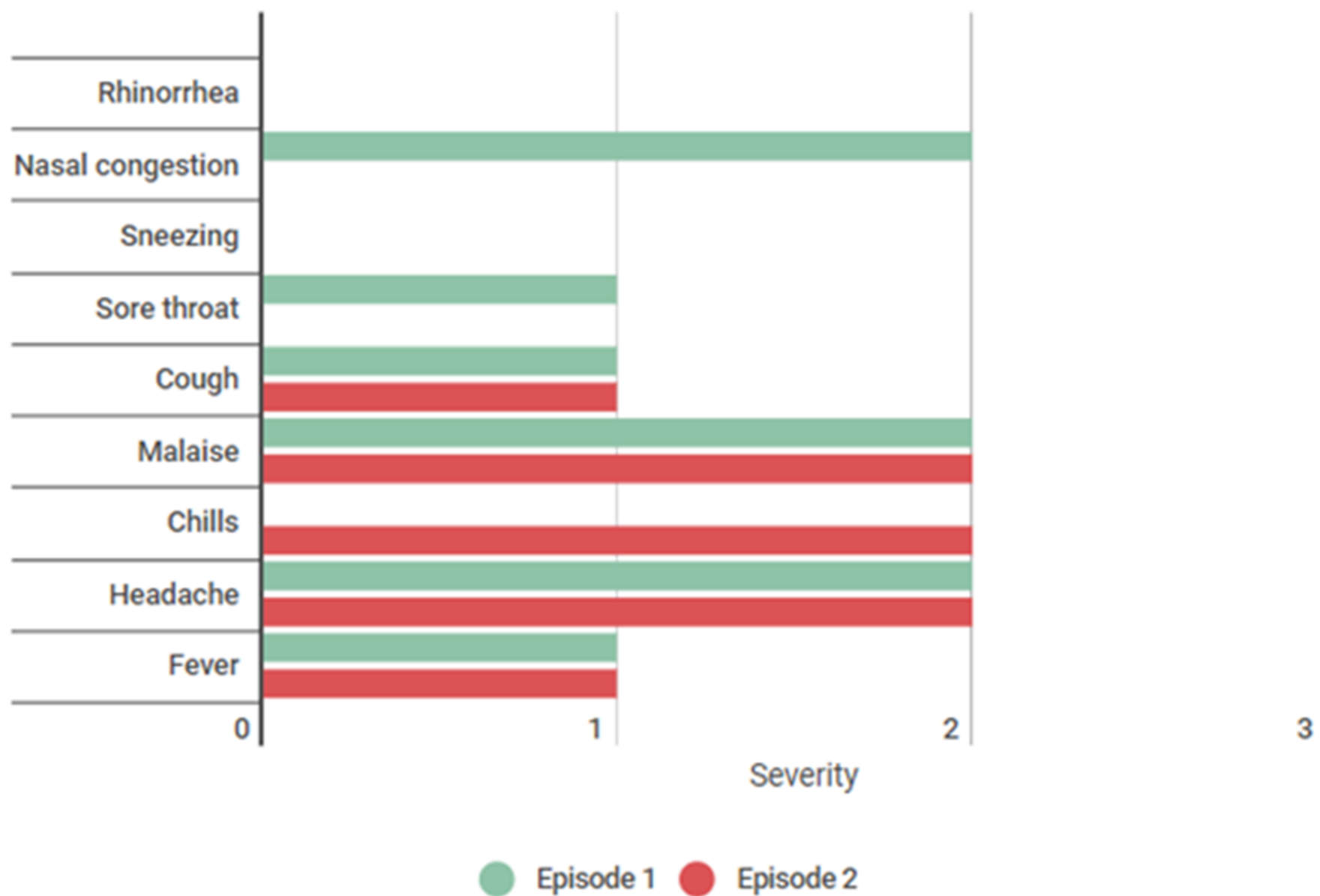
Early Reinfection with Omicron following Delta

- Child 1: age 8 (ill, recovered, ill again 53 days later)
- Child 2: age 11 (ill, recovered, ill again 46 days later)
- Child 3: age 5 (ill, recovered, ill again 31 days later)



Recurrent Influenza

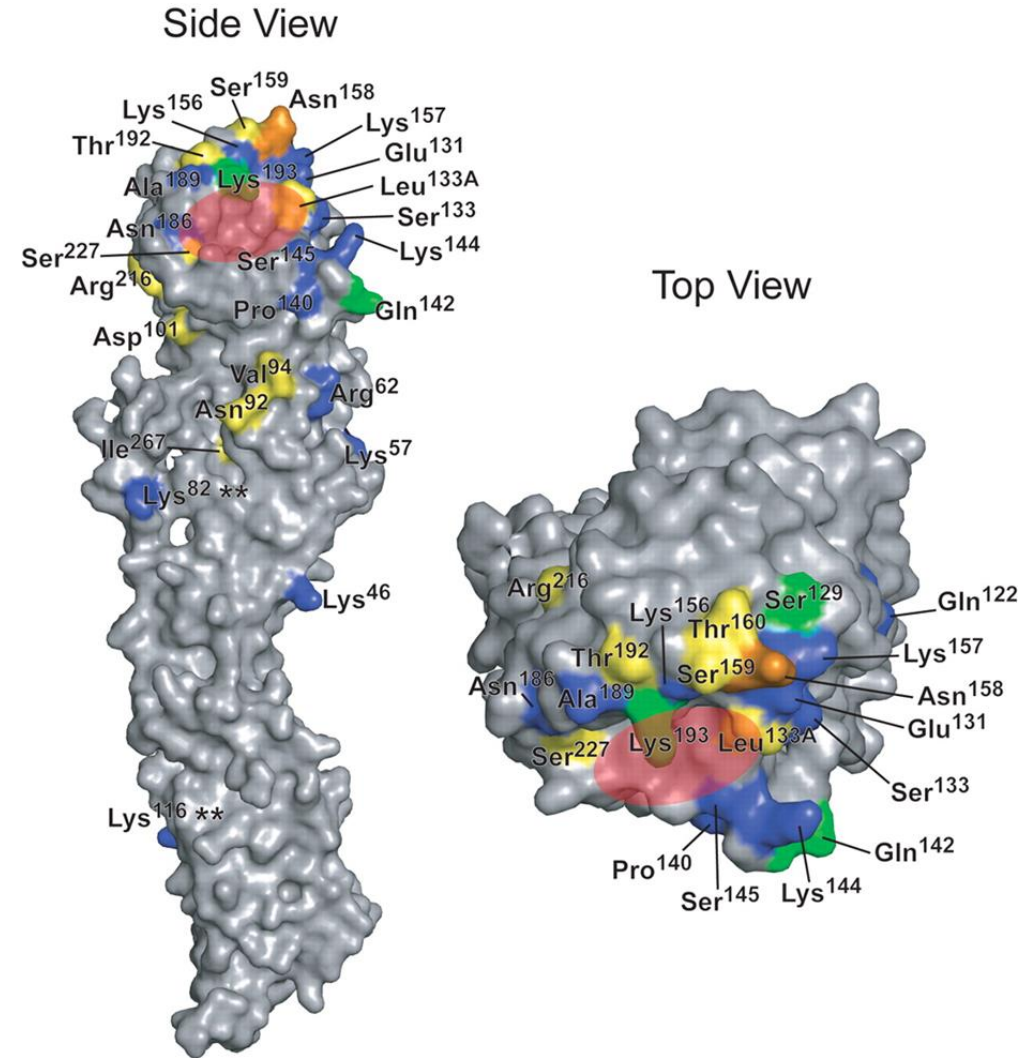


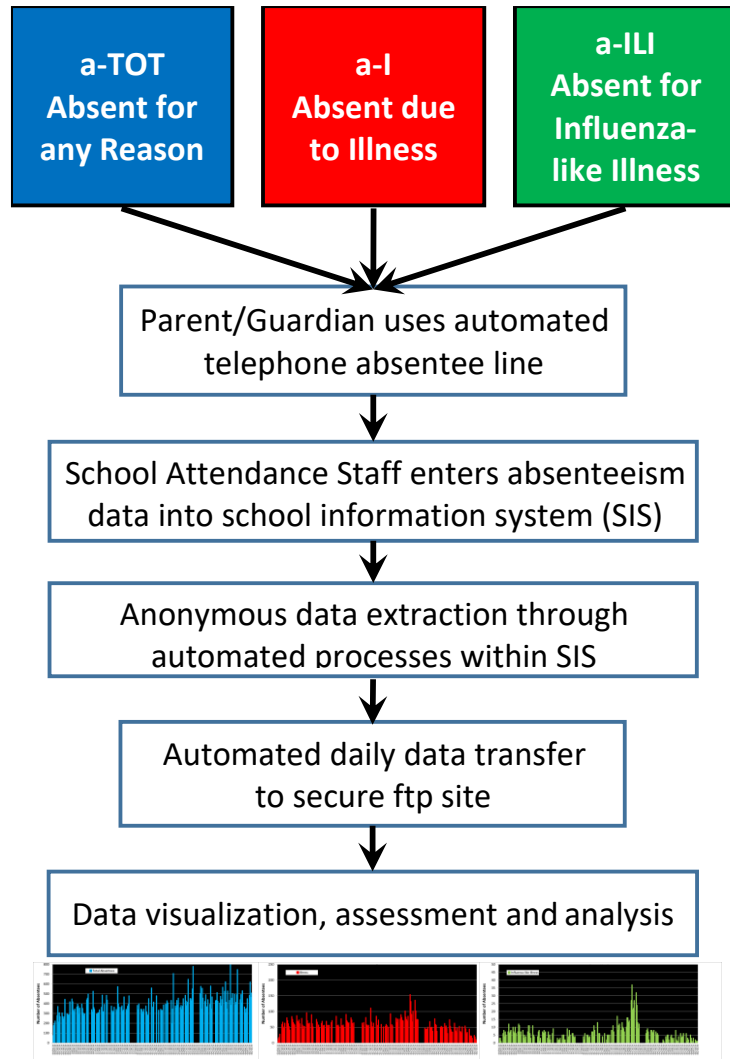


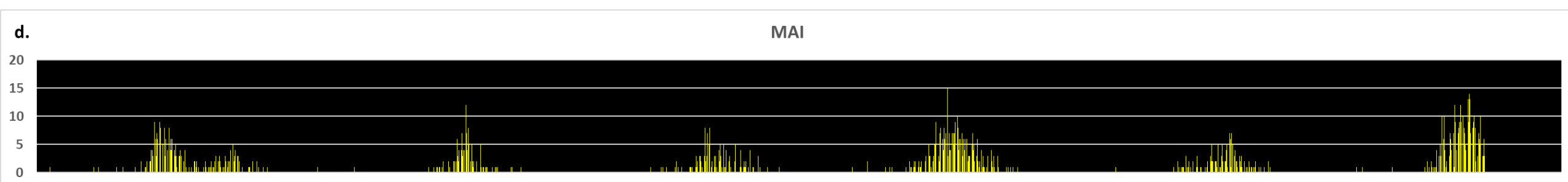
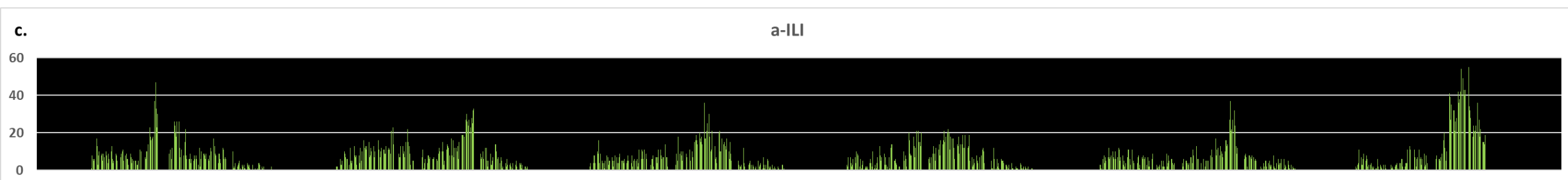
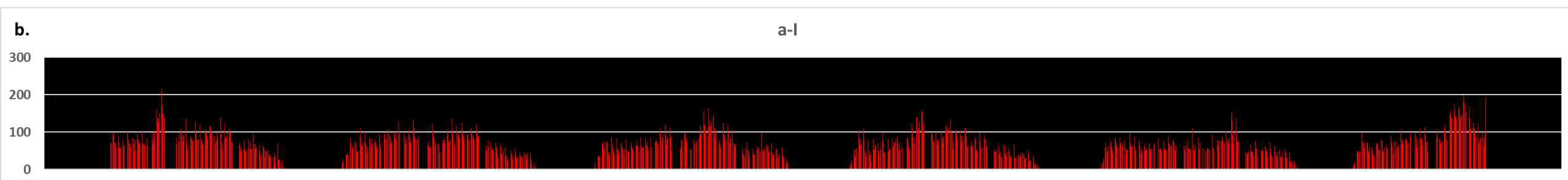
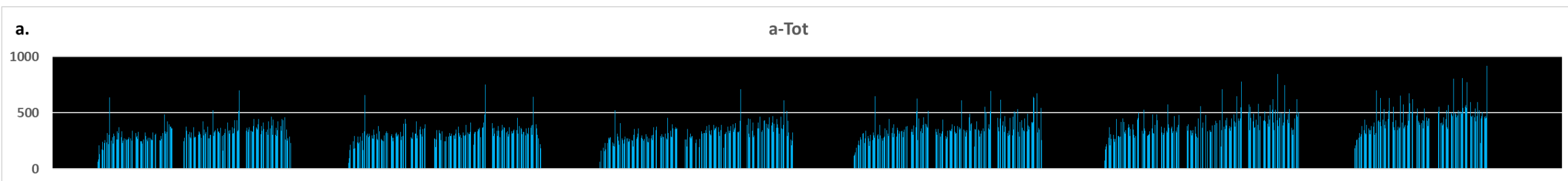
So...

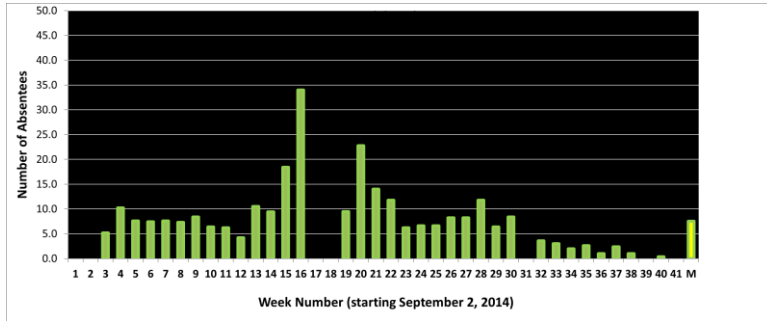
What Happened?

- First known case of recurrent, in-season infection with influenza A(H3N2)
- Whole genome sequencing revealed clade 3C.2a for both episodes
- 3 single nucleotide polymorphisms identified, all in the coding region of the HA protein
 - One resulted in an amino acid change
 - isoleucine to leucine
 - Located 4 amino acids away from an established antibody epitope site

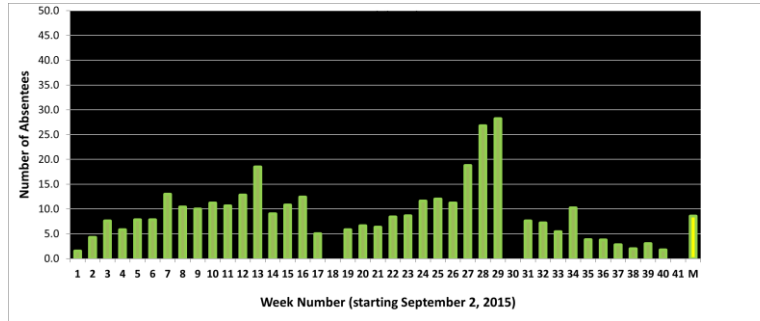




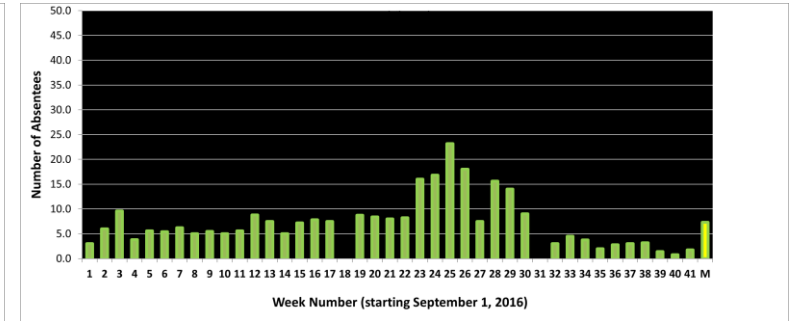




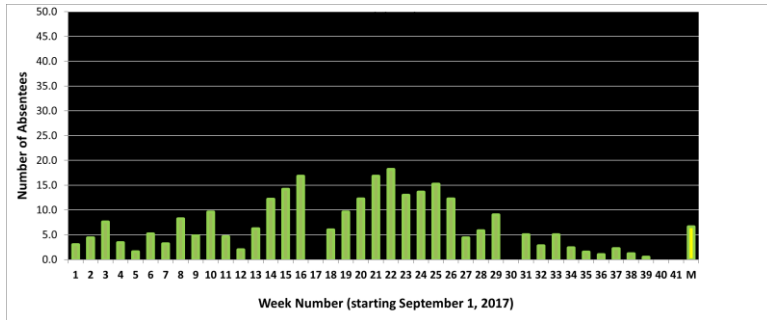
2014-2015



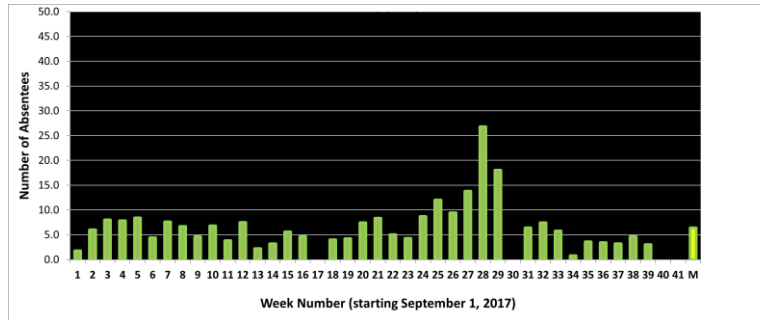
2015-2016



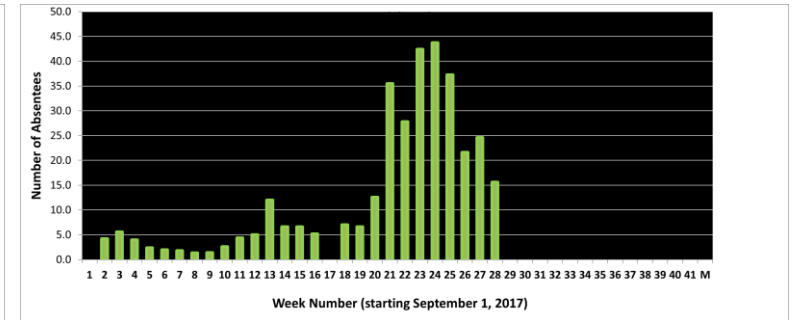
2016-2017



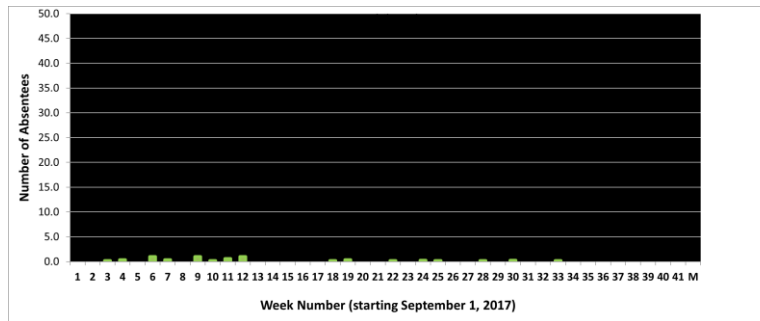
2017-2018



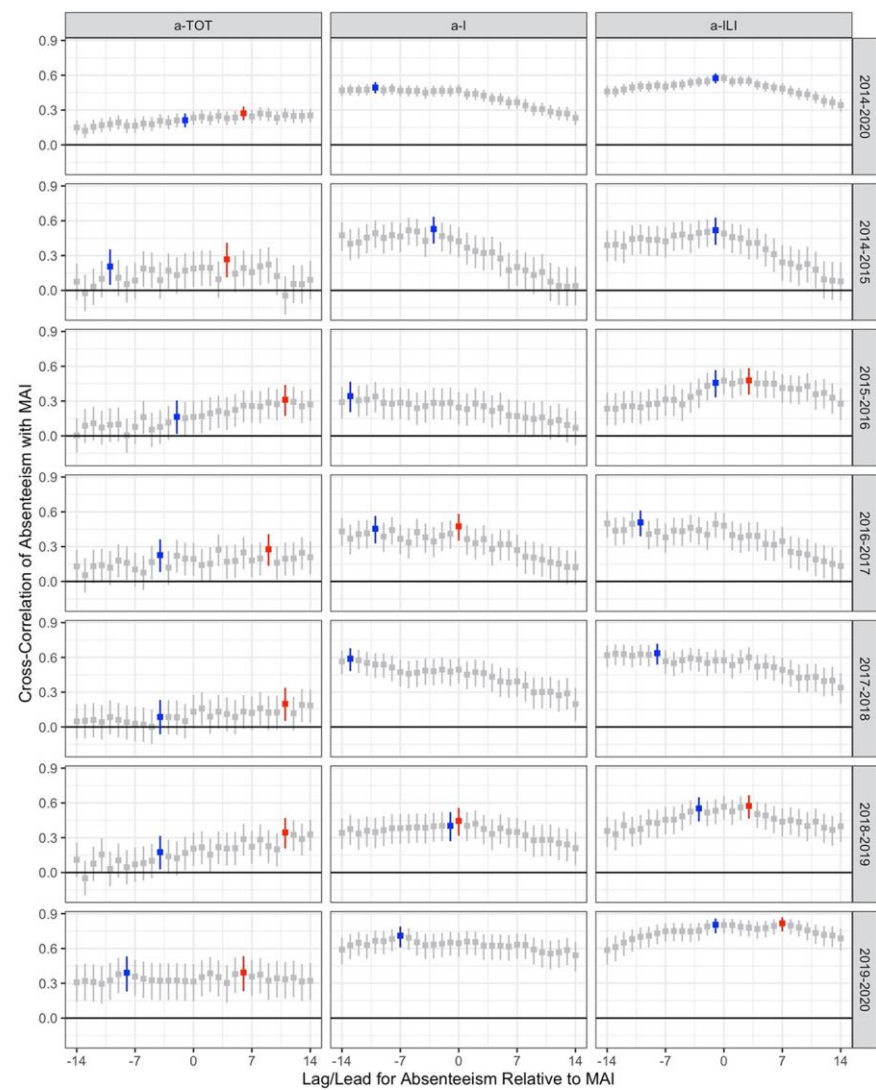
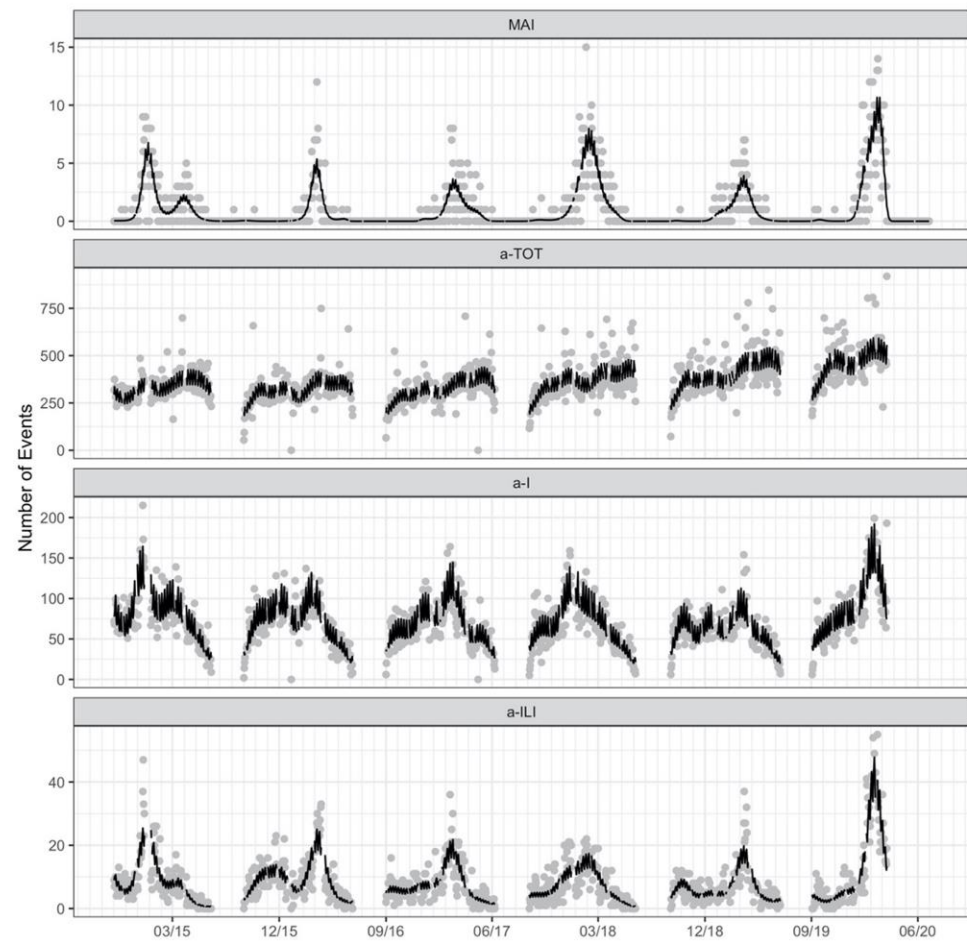
2018-2019



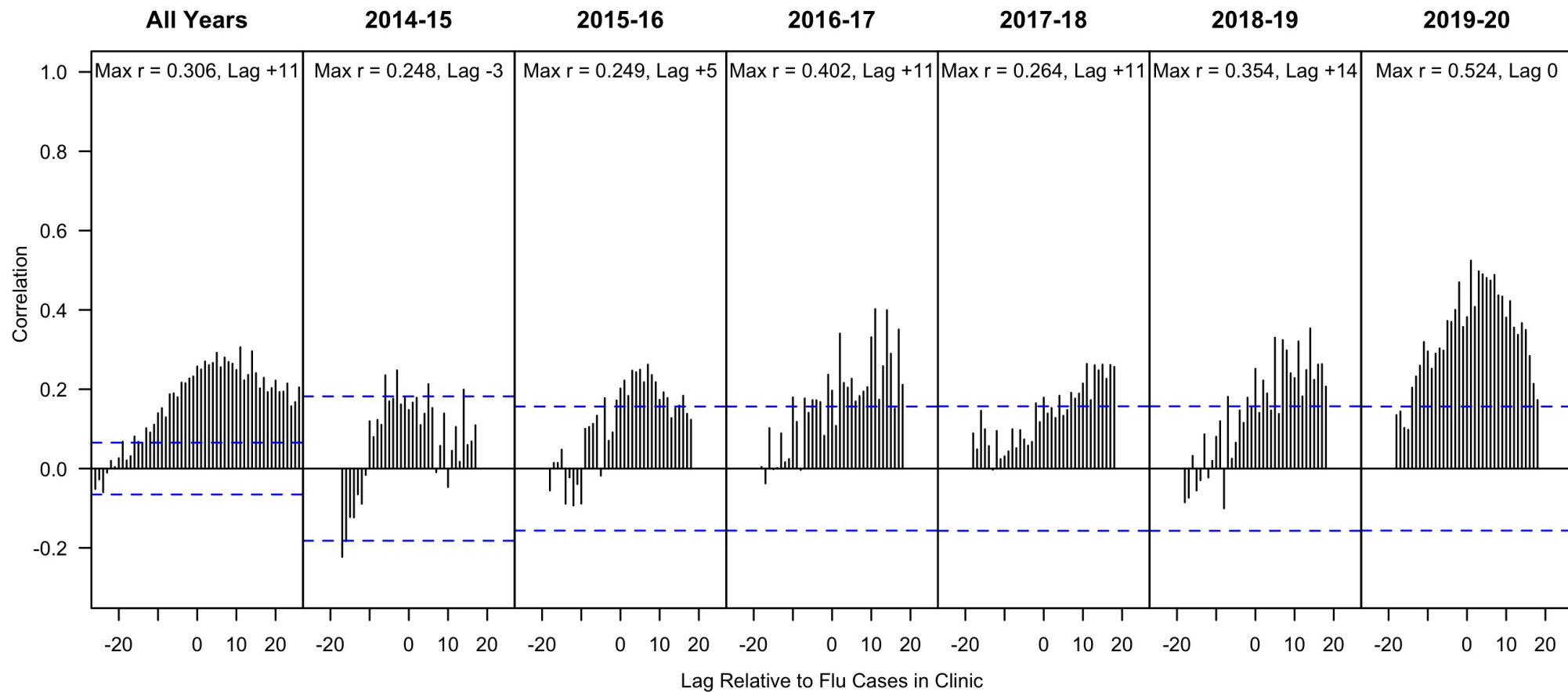
2019-2020



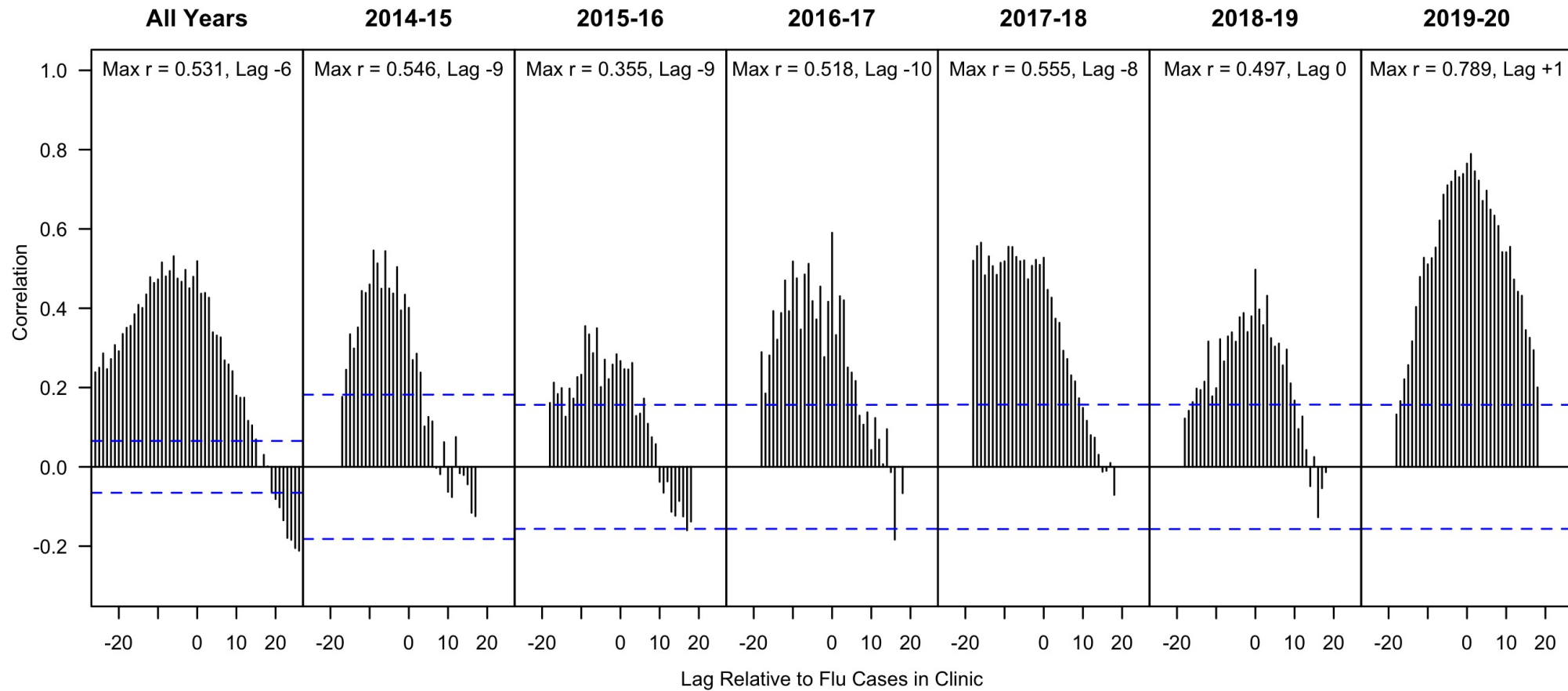
2020-2021



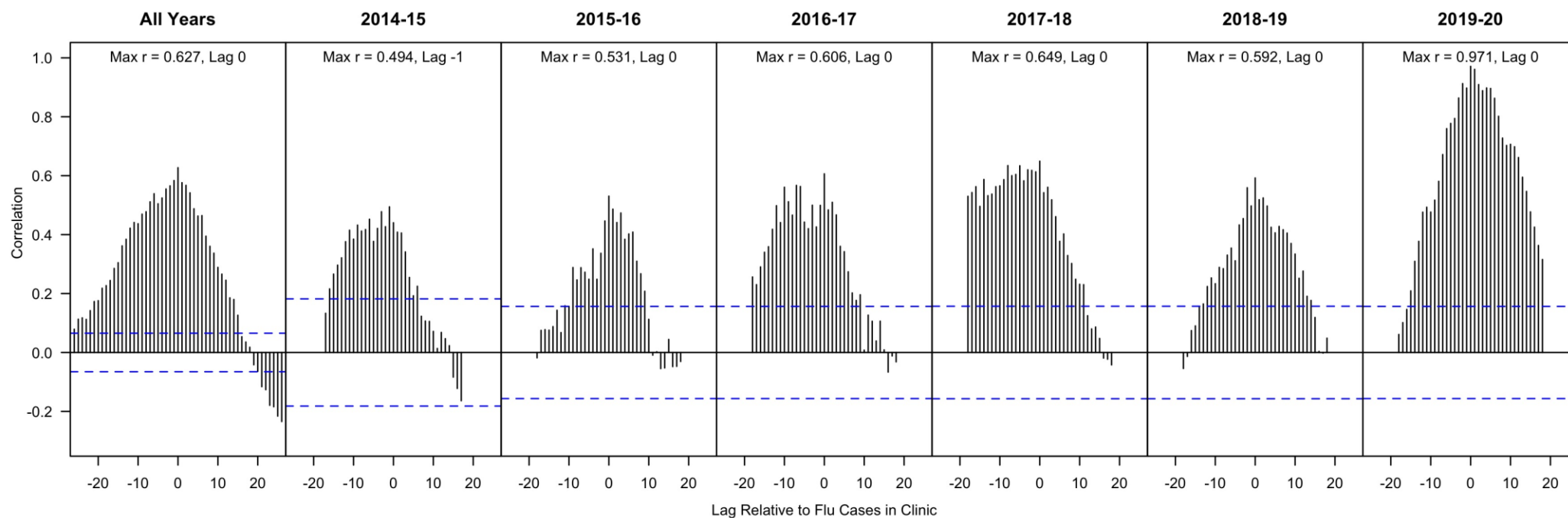
Correlations: a-TOT and MAI



Correlations: a-I and MAI



Correlations: a-ILI and MAI



Absenteeism monitoring can be used to Identify Influenza in the Community

Over six influenza seasons, absenteeism was significantly correlated with MAI in the community

a-ILI ($r = 0.57$; 95% CI: 0.53—0.63)

- with a 1-day lead time

a-I ($r = 0.49$; 0.44-0.54)

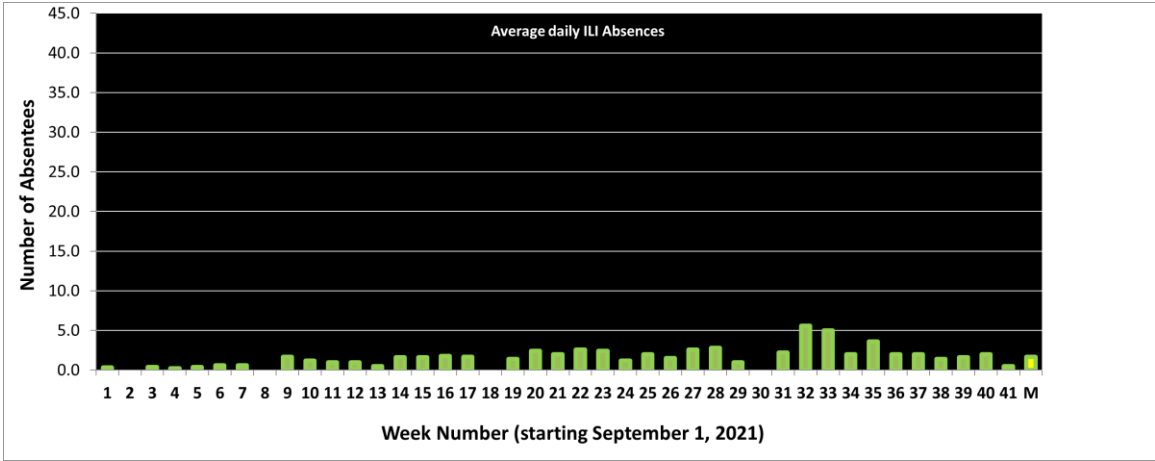
- with a 10-day lead time

a-TOT ($r = 0.27$; 0.21—0.33)

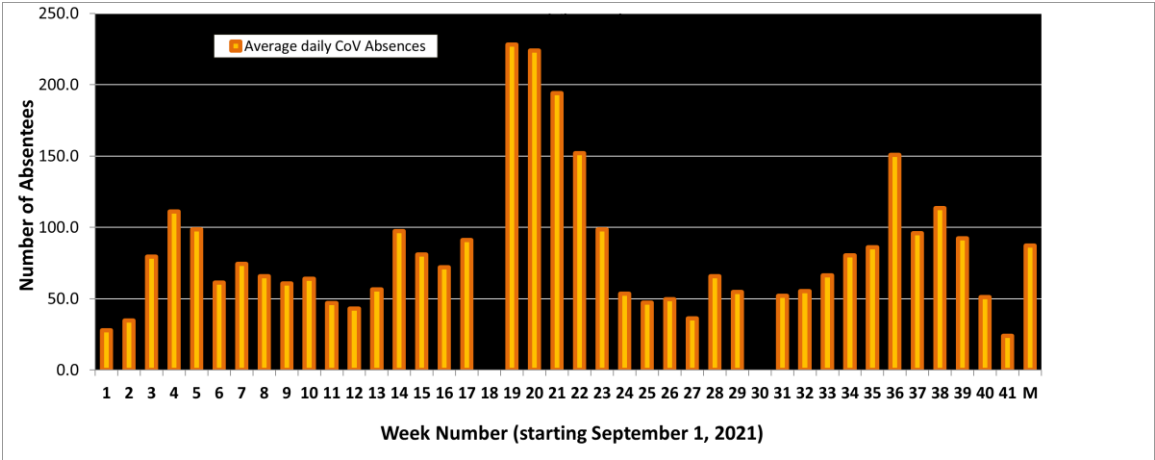
- following MAI by six days



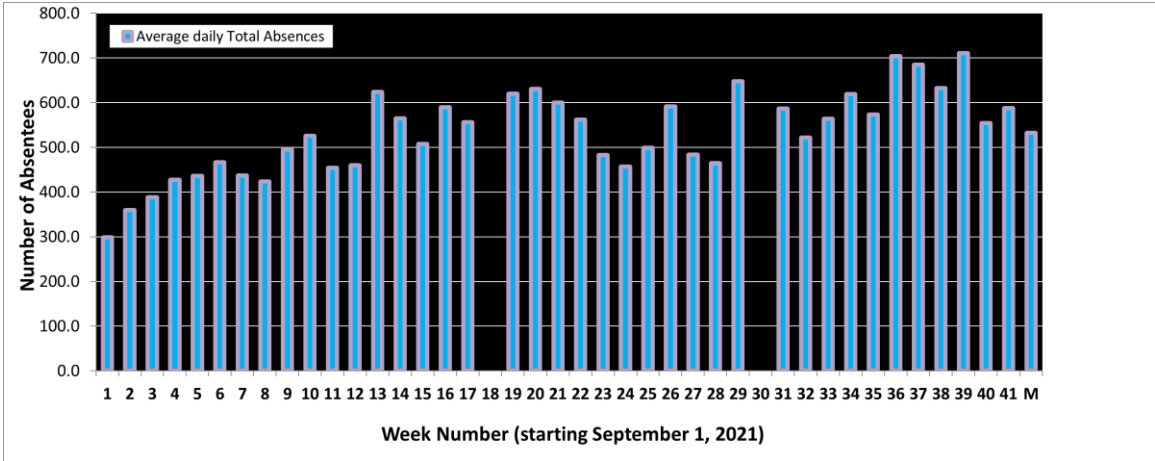
Absenteeism in the Pandemic



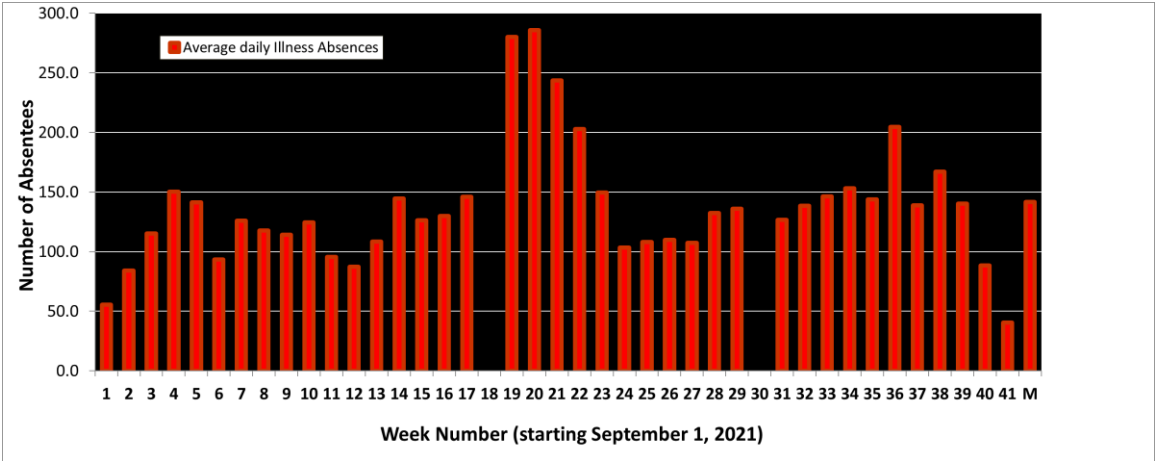
a-ILI



a-COV



a-TOT



a-I

ORCHARDS Household Transmission

- Data collection has been ongoing since January 2015
- No pause with onset of the pandemic
 - Modified protocol
- Recruitment is triggered by a child with ILI or CLI
- All household members self-collect nasal swab specimens
 - Day 0
 - Day 7
 - Day 14
- ORCHARDS children are tested for SARS-CoV-2, influenza A/B
 - Plus a respiratory pathogen panel
- Other household members are tested for SARS-CoV-2 and influenza A/B

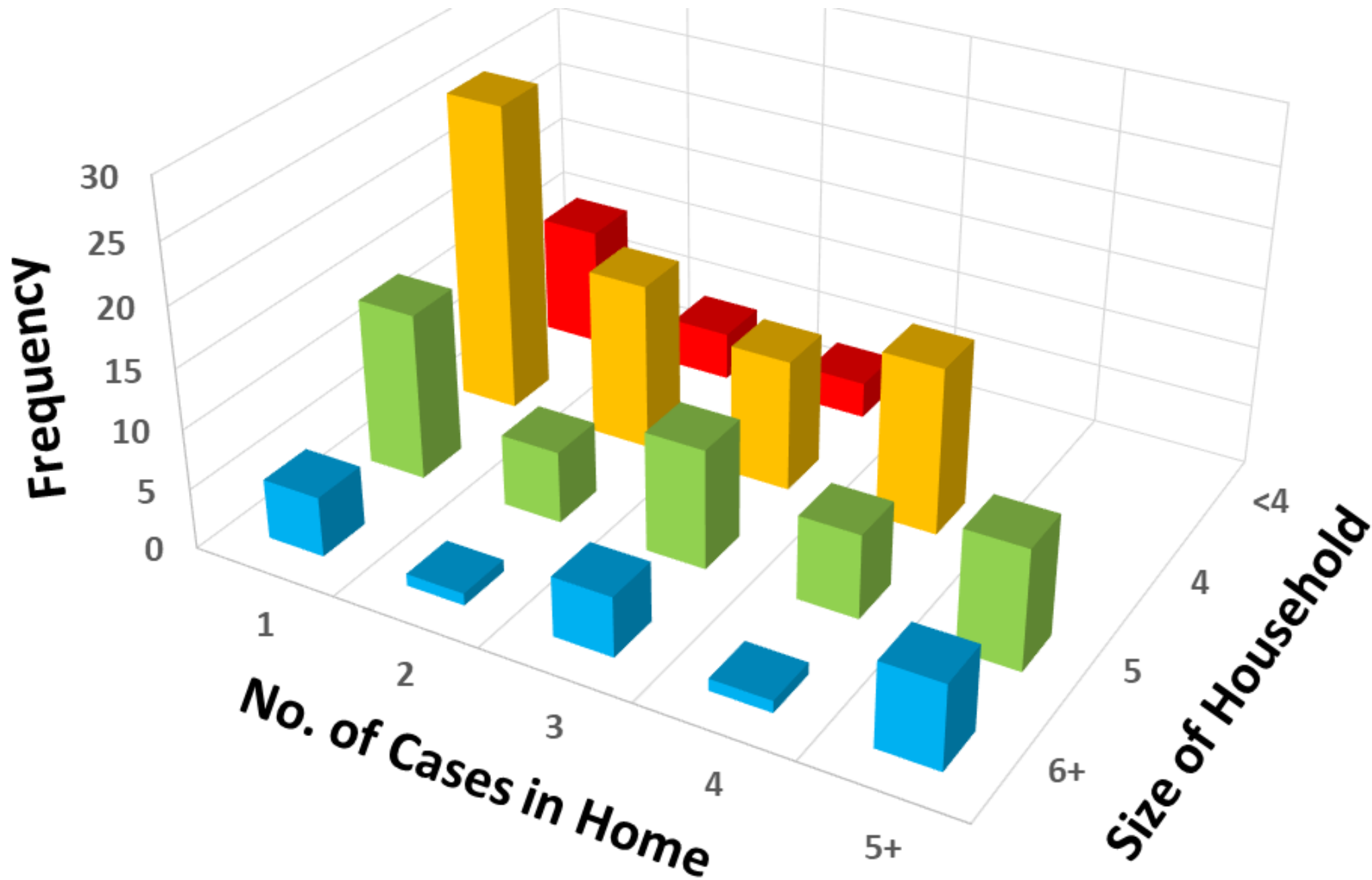
Abundant Data from Households

	Total	SARS-CoV-2 (+)
Specimens	7,599	644 (8.5%)
Individuals	2,614	378 (14.5%)
Families with ≥ 1 SARS-CoV-2	608	152 (25.0%)
Families with ≥ 2 SARS-CoV-2	94	94 (15.5%)

Ability to measure household transmission within a community and across time, paying attention to age of index case, age of secondary cases, size of household and other factors

- Pre-Delta
- Delta
- Omicron





Influenza Vaccine Effectiveness

- ORCHARDS provides a unique platform to measure vaccine effectiveness
- Participants are recruited from the community, not from health care settings
- Removes some biases associated with healthcare seeking behavior



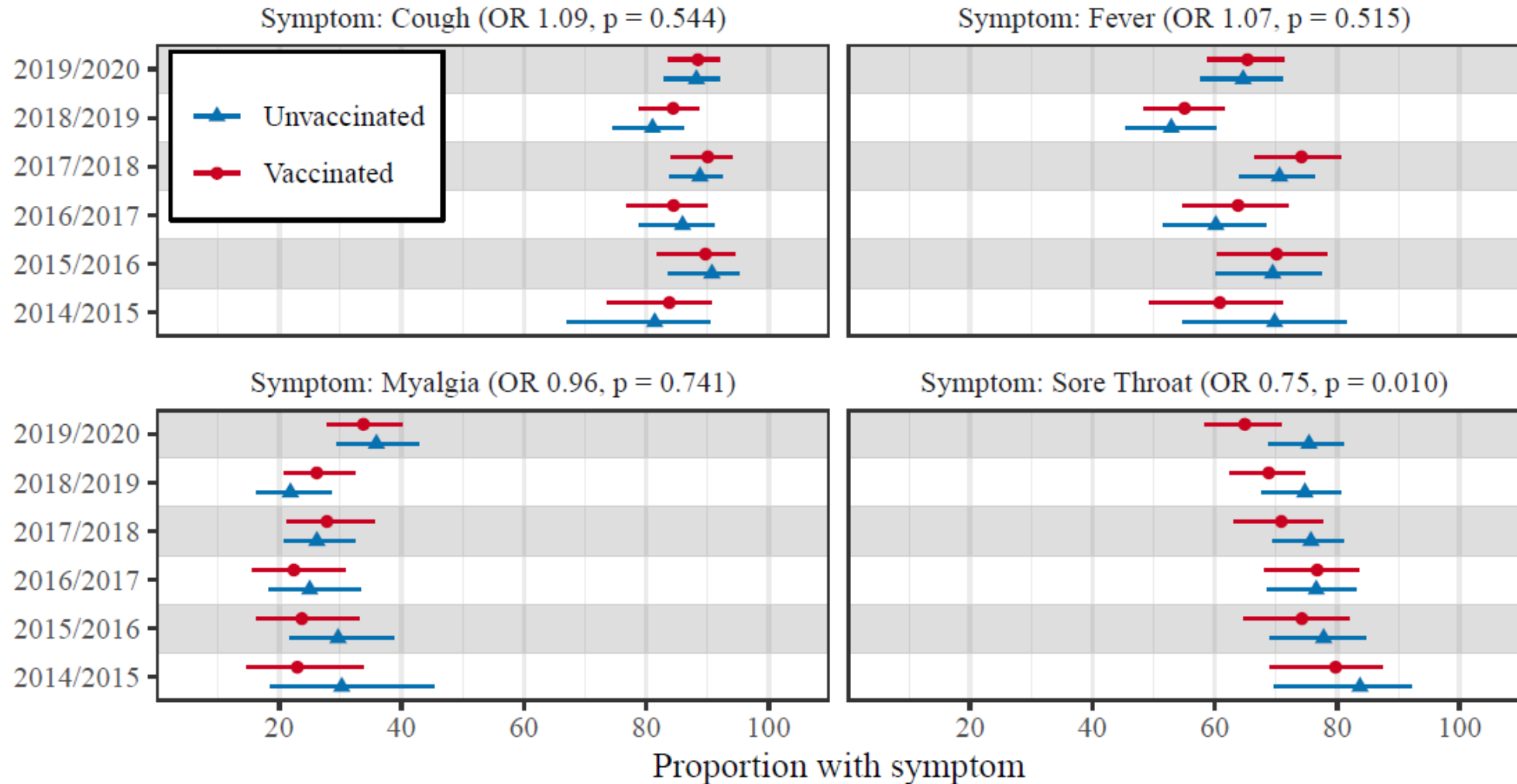
Evaluation over 6 years (2014—2020)

- All participants with RT-PCR for influenza
- Vaccination status confirmed via Wisconsin Immunization Registry
- Additional data on symptoms, absenteeism
- Sample = 1,743 children (5-18 years)
 - 50.6% vaccinated; 49.4% unvaccinated
- Influenza status
 - 31.9% PCR (+); 68.1% PCR (-)

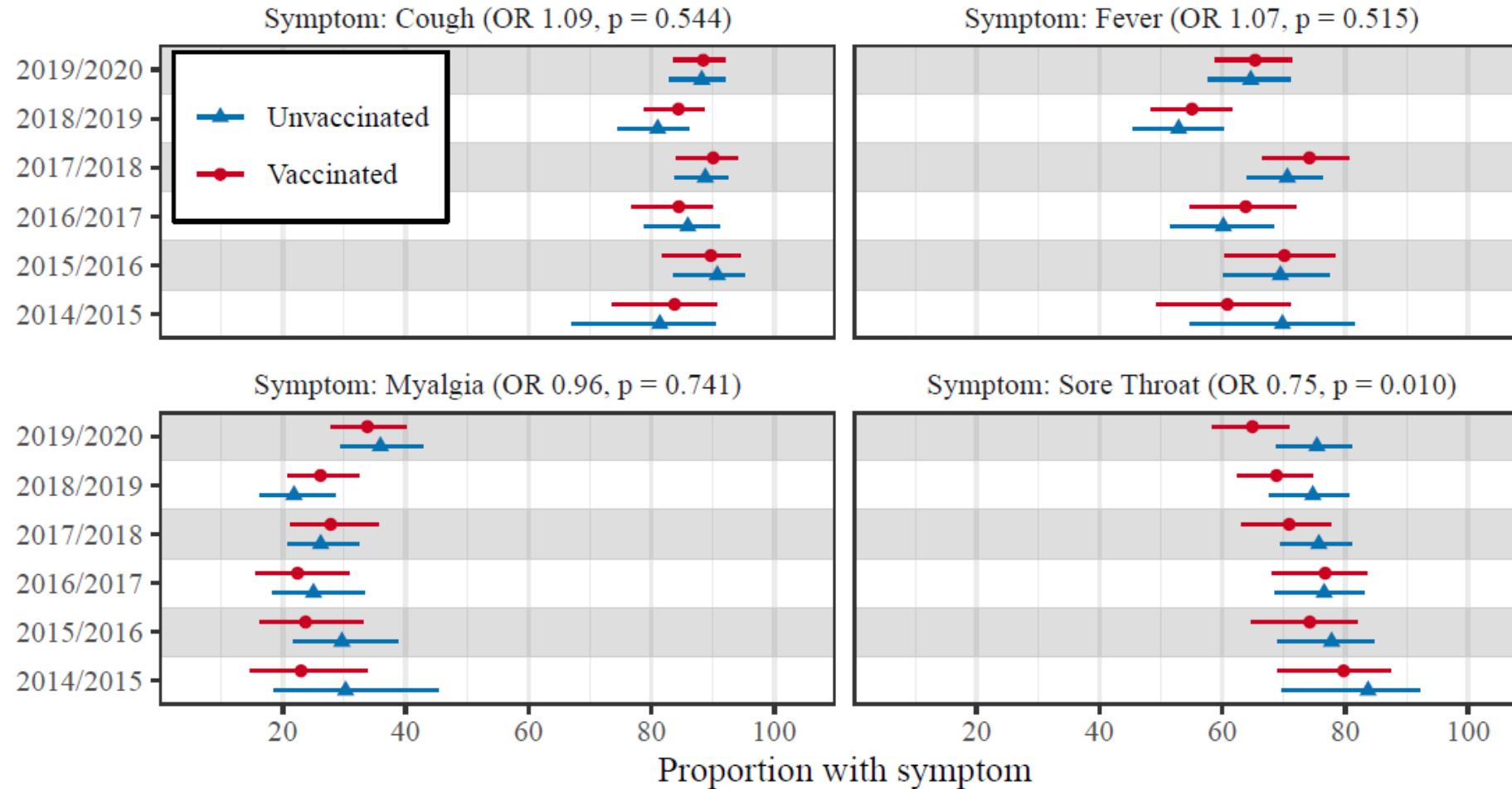
and the estimate effectiveness is:

Adjusted for year, season, healthcare, and age:
0.32 (CI: 0.13 to 0.46, $p = 0.002$)

Effect of vaccine status on symptoms (all)

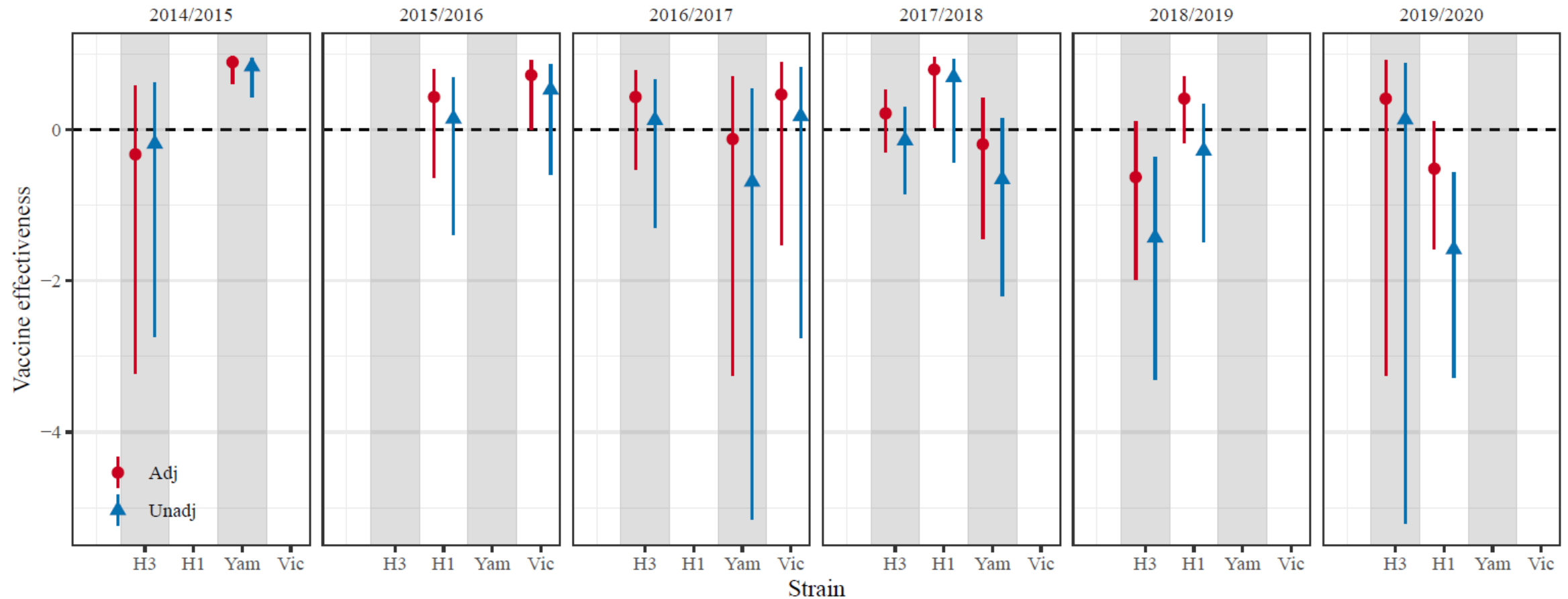


Effect of vaccine status on symptoms (PCR+)





Vaccine effectiveness by year and strain

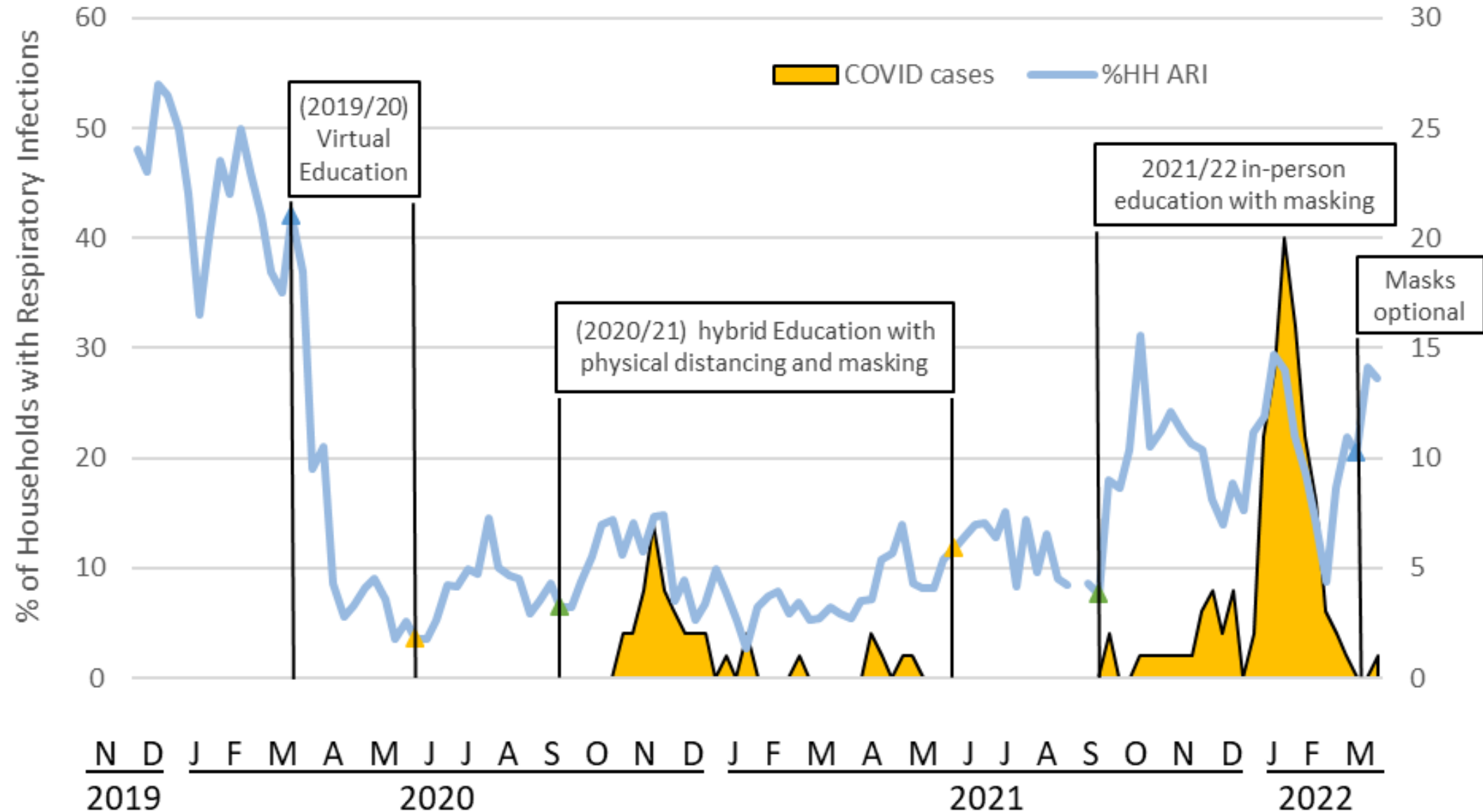


Community- engaged epidemiology

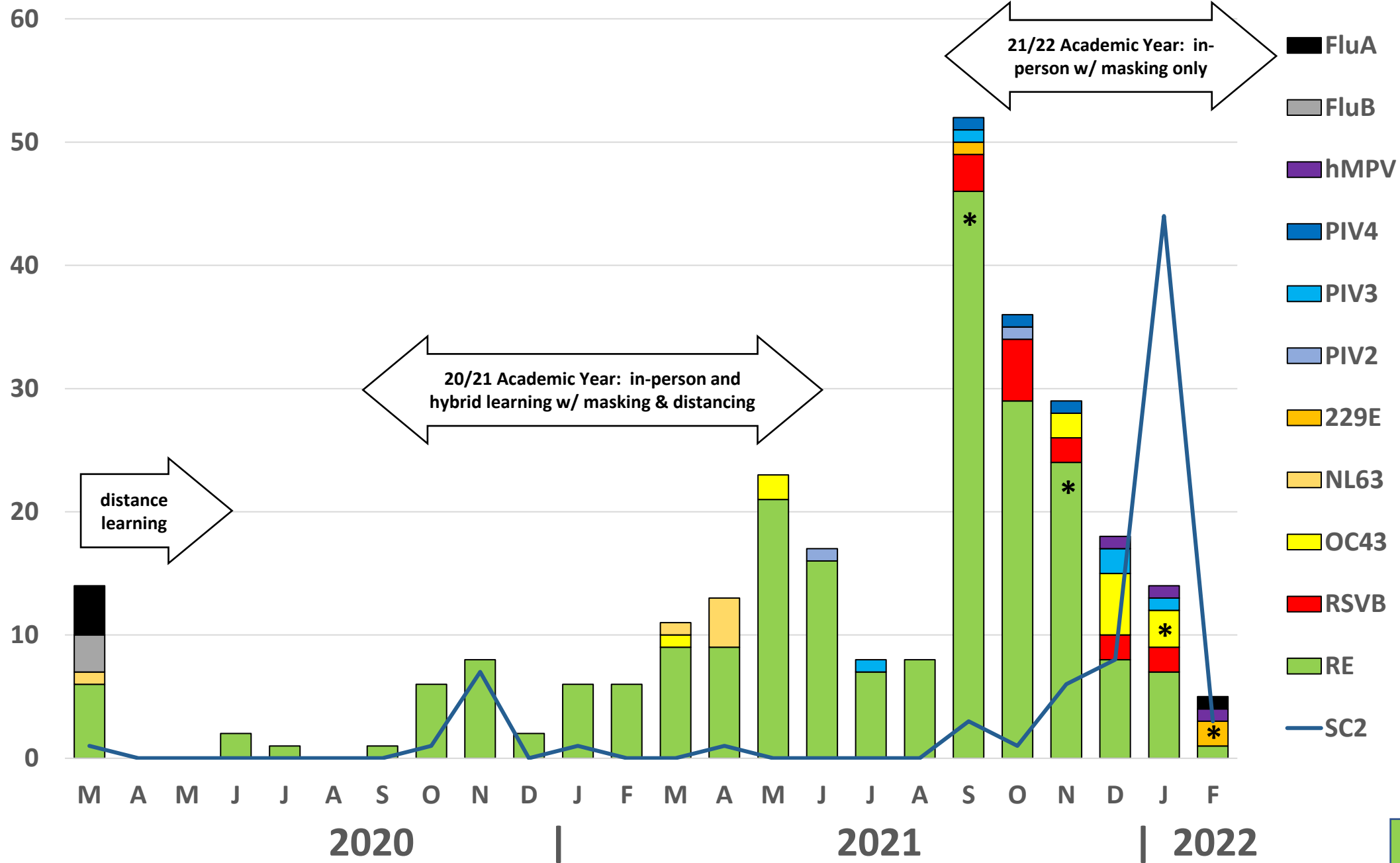
GROVES: Great Oregon Vaccine Effectiveness Study

- **Longitudinal cohort of about 200 households**
 - Recruited in November 2019 (remember how normal things were then???)
- **Respond to weekly web-based surveys**
 - text messages
 - Email
- **Reporting the presence and count of new ARIs in the household**
- **Reporting presence of influenza**
- **Reporting presence of COVID**

Respiratory infections and COVID-19 in households



Number of Virus Detections



Some final thoughts...

Big studies in a small community create a great deal of insight

- Connections
- Familiarity
- intimacy

Longitudinal approaches are awesome

- ORCHARDS has been funded from 2013—2024
- Thanks CDC

Partnerships are essential

- Research, primary care, public health and laboratory science

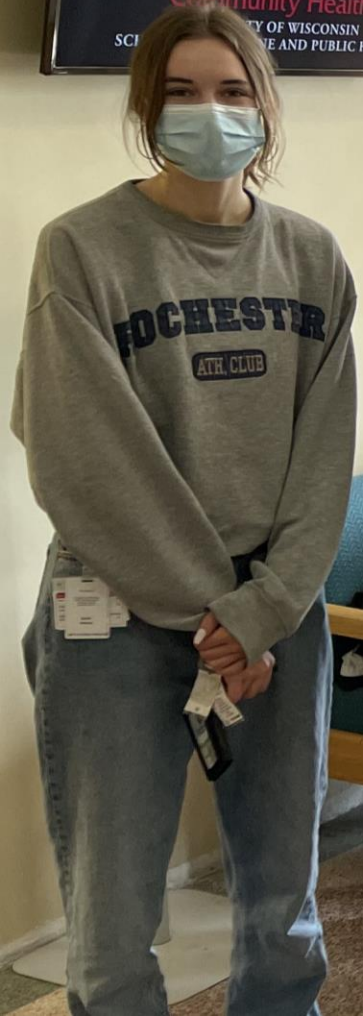
ORCHARDS References

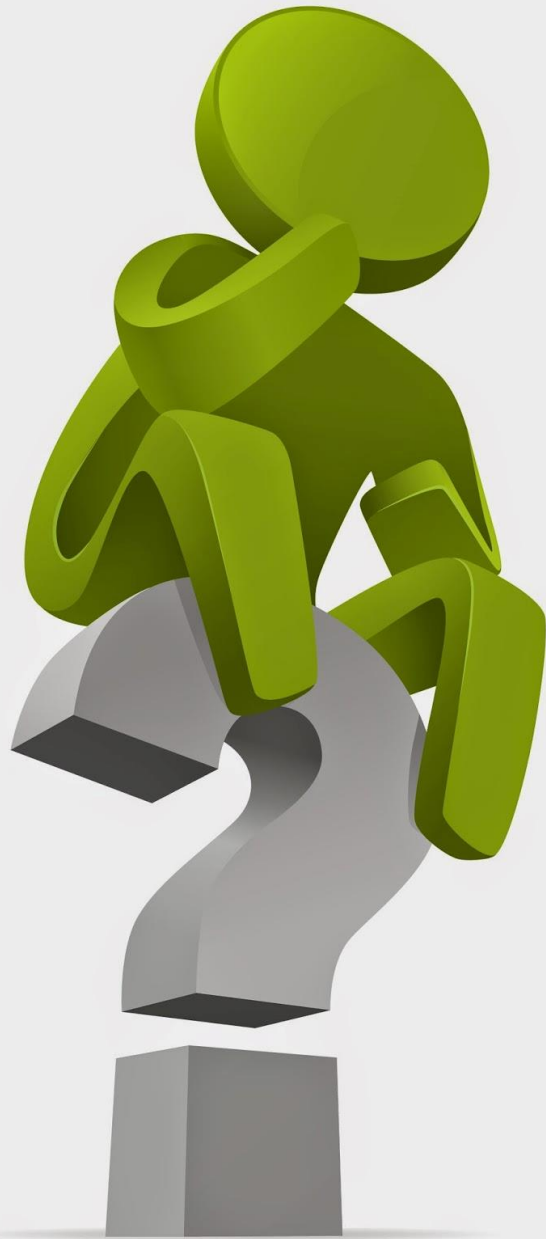
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- Temte JL, et al. Sequential, within-season infection with influenza A (H3N2) in a usually healthy vaccinated child. Influenza Other Respir Viruses. 2019 Sep;13(5):528-531. doi: 10.1111/irv.12668. Epub 2019 Jun 26. PMID: 32744798; PMCID: PMC6692547.



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