ORCHARDS

Oregon CHild Absenteeism due to Respiratory Disease Study

# a Farewell to ORCHARDS:

## school-base respiratory virus epidemiology

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**School of Medicine and Public Health**

**April 18, 2024**

- CDC/NCZEID: Yenlik Zheteyeva, Amra Uzicanin
- WSLH: Pete Shult, Erik Residorf, Mary Wedig, Al Bateman, Rich Griesser, Erika Hanson, Kelsey Florek, CJ Jossart, etc…
- WDPH: Tom Haupt, Stephanie Schauer
- Quidel: John Tamerius, Sush Reddy, Kevin King
- OSD: Brian Busler, Leslie Bergstrom, Becky McCabe, John Tanner & Oregon/Brooklyn Families
- Coffee: Firefly Coffeehouse

OREGON SCHOOL DISTRICT

DEPARTMENT OF
Family Medicine and Community Health
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

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Oregon CHild Absentee due to Respiratory Disease Study


Department of Health Services
State of Wisconsin

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA
CDC

WSLH

QUIDEL

# Today’s Objectives

- Appreciate the value of K-12 school absenteeism monitoring as an early warning system for influenza in the community
- Understand how coupling individual level data coupled with molecular techniques can provide insights into repiratory virus epidemiology
- Identify factors associated with performance of rapid testing in community settings
- Apply concepts of microscale epidemiology for defining transmission, mitigation, and surveillance

Community-engaged public health research: microscale epidemiology

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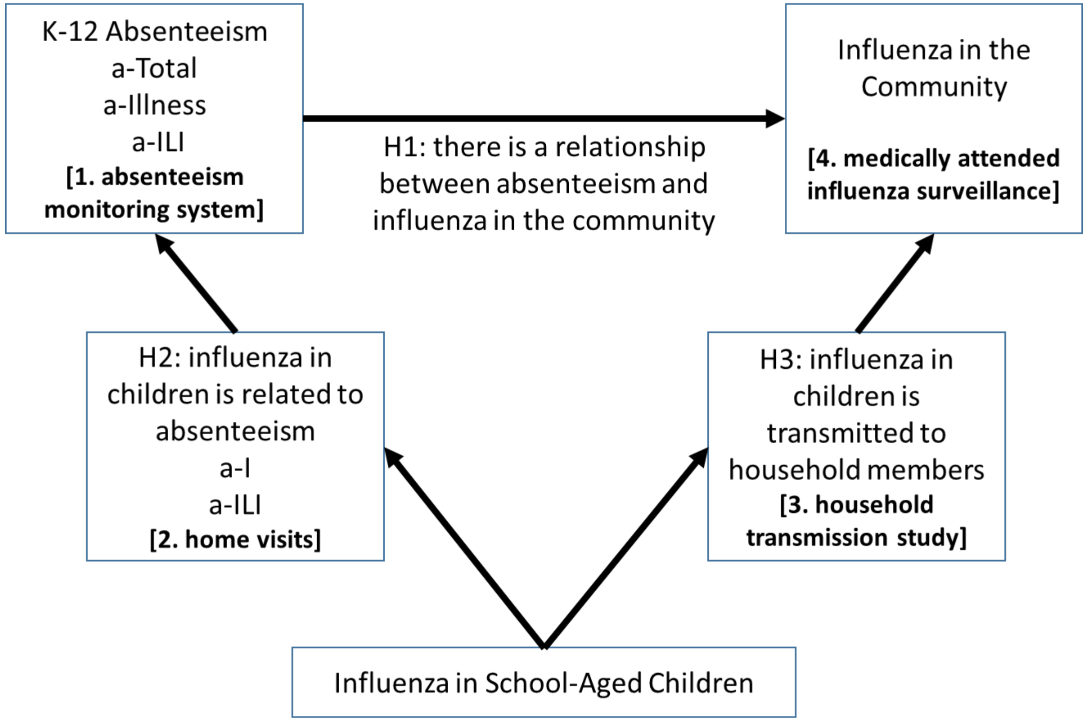
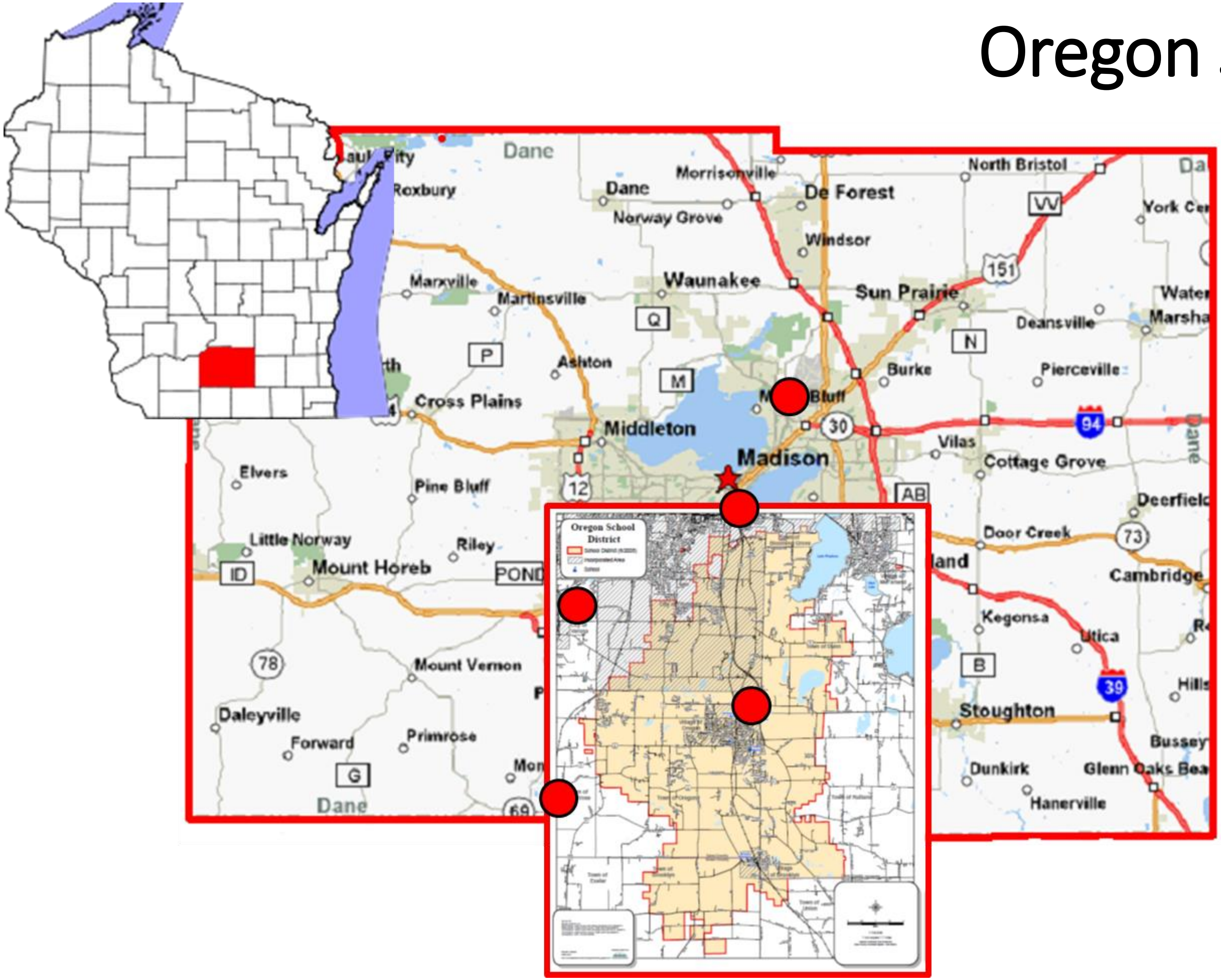
2013—2024

Funded by CDC/NCZEID

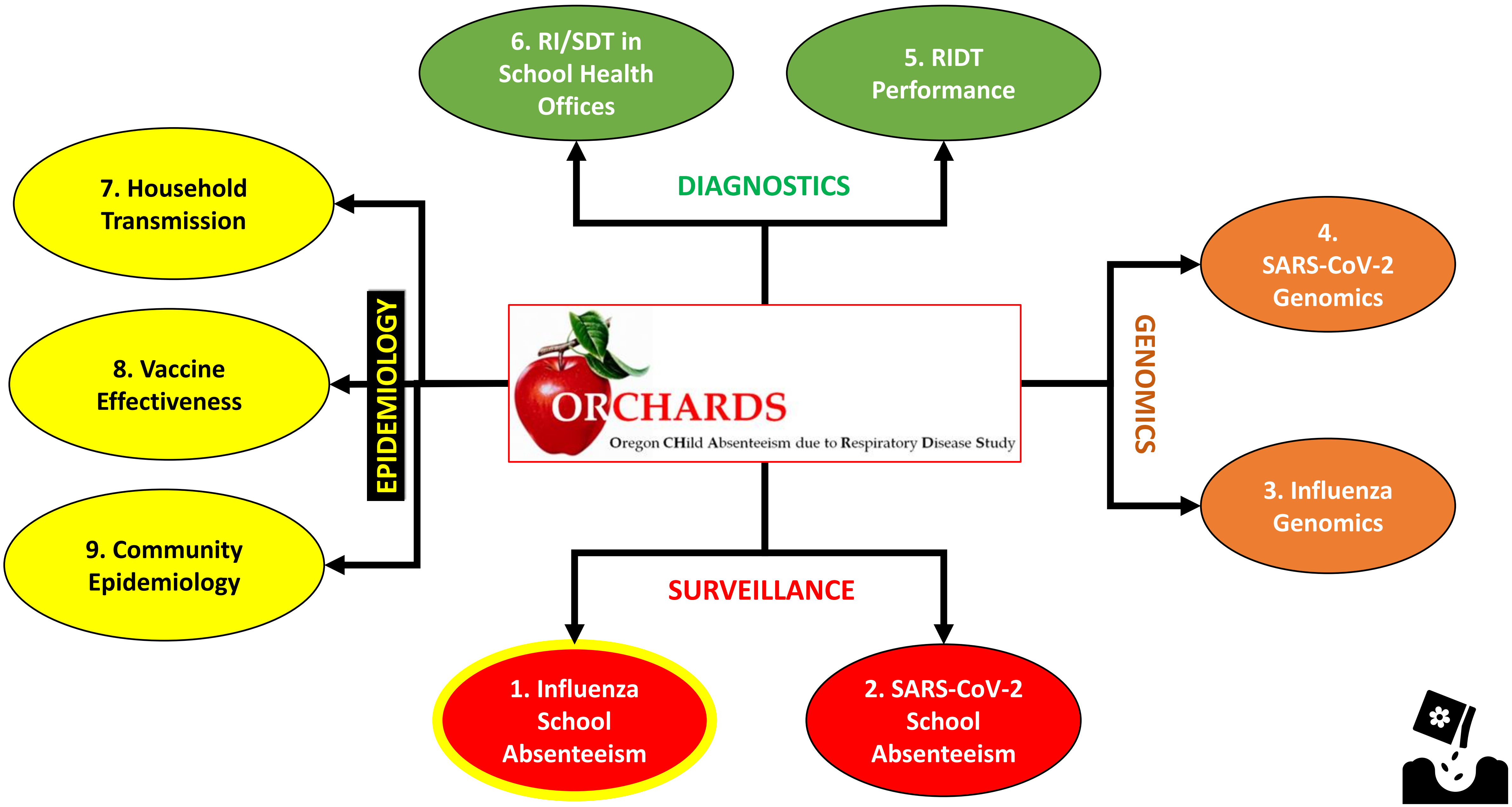
## Theoretical Design



# Oregon School District




= primary care surveillance clinic


6. RI/SDT in School Health Offices
5. RIDT Performance
DIAGNOSTICS
7. Household Transmission
8. Vaccine Effectiveness
9. Community Epidemiology
EPIDEMIOLOGY
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Oregon CHild Absenteeism due to Respiratory Disease Study
GENOMICS
4. SARS-CoV-2 Genomics
3. Influenza Genomics
SURVEILLANCE
1. Influenza School Absenteeism
2. SARS-CoV-2 School Absenteeism

**a-TOT**
**Absent for any Reason**

**a-I**
**Absent due to Illness**

**a-ILI**
**Absent for Influenza-like Illness**

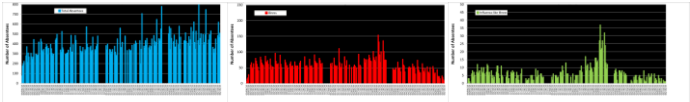
Parent/Guardian uses automated telephone absentee line

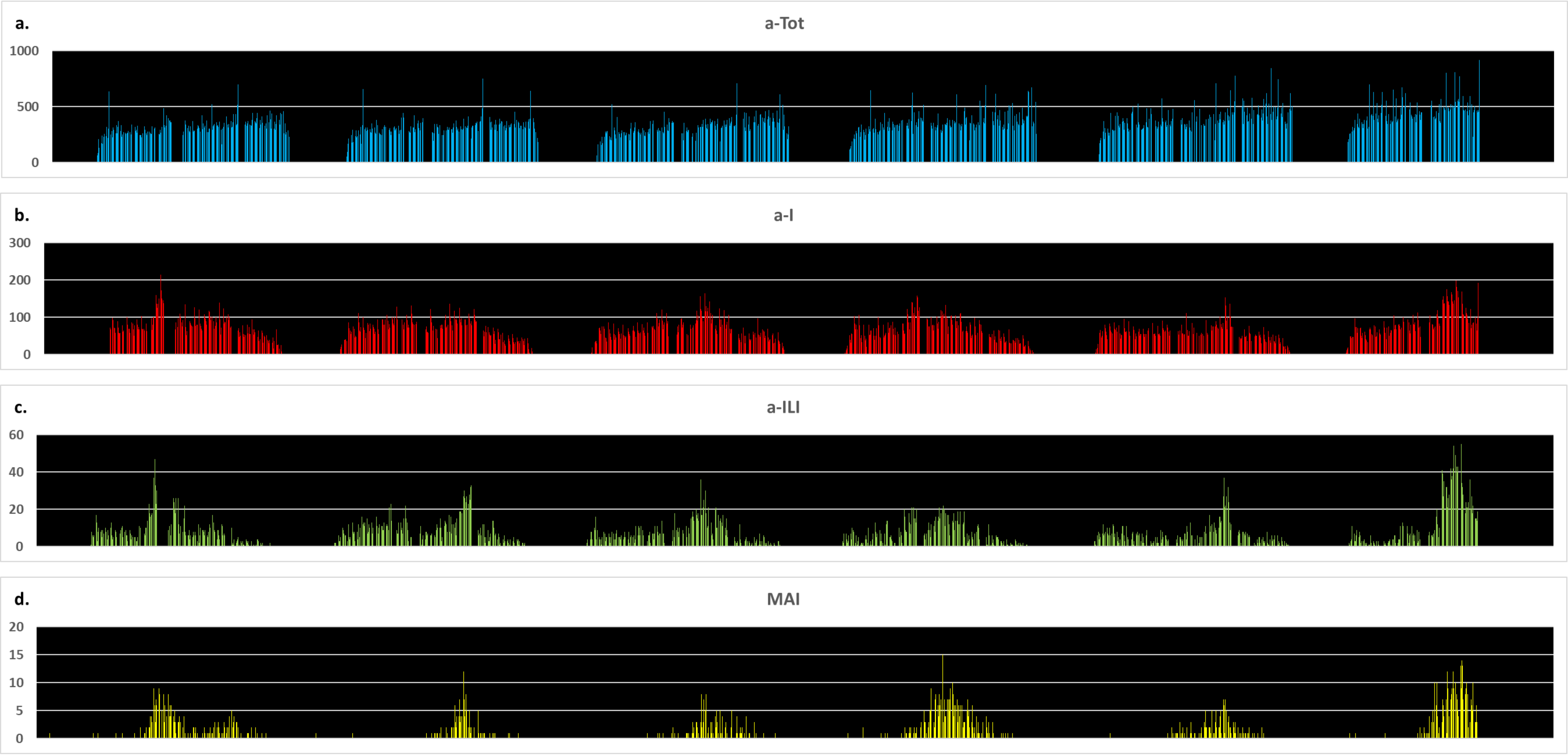
School Attendance Staff enters absenteeism data into school information system (SIS)

Anonymous data extraction through automated processes within SIS

Automated daily data transfer to secure ftp site

Data visualization, assessment and analysis




a.
a-Tot
1000
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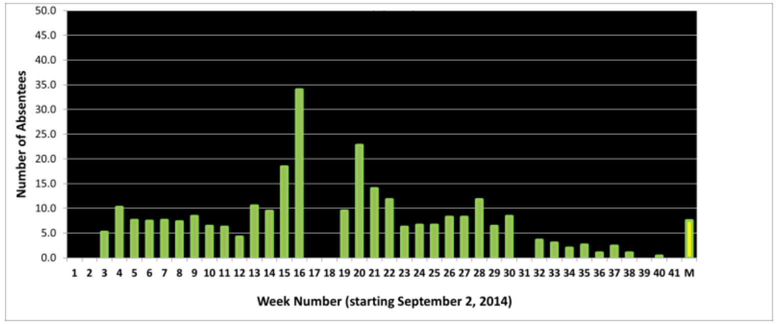
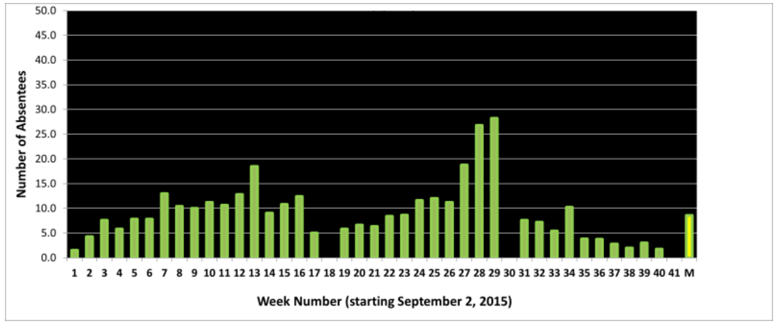
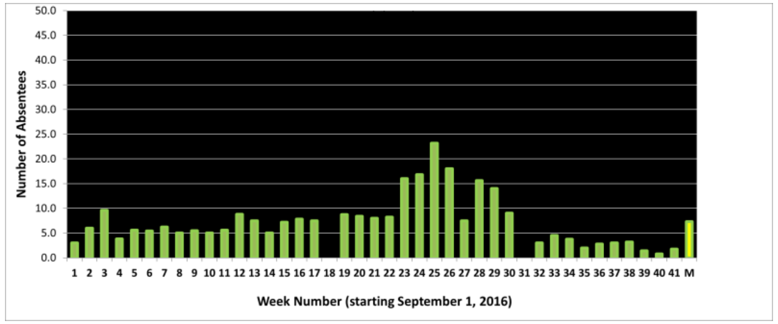


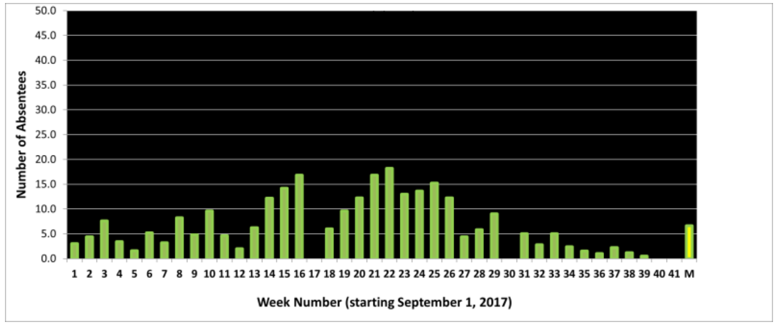

# 2014-2015



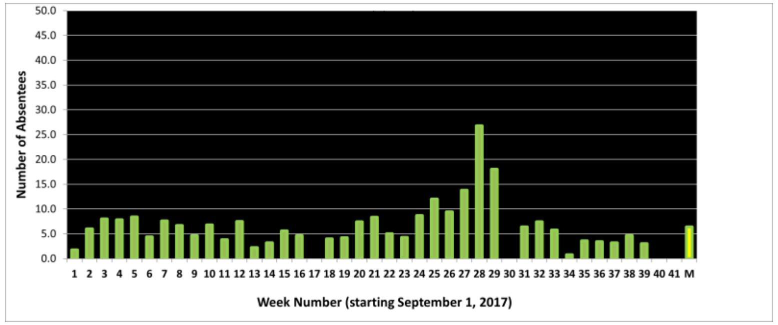

# 2015-2016



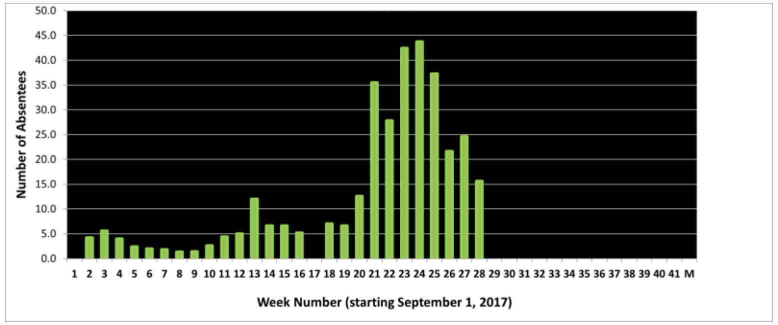

# 2016-2017



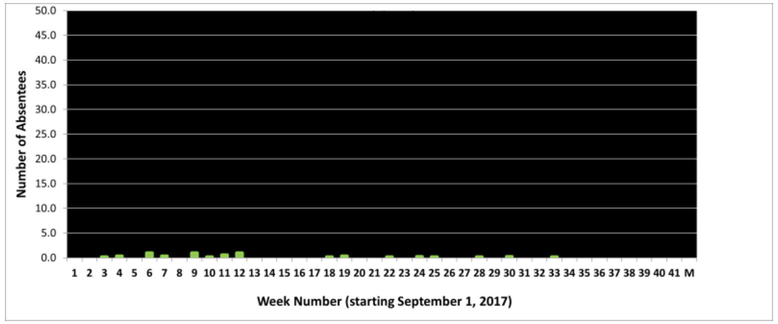

# 2017-2018



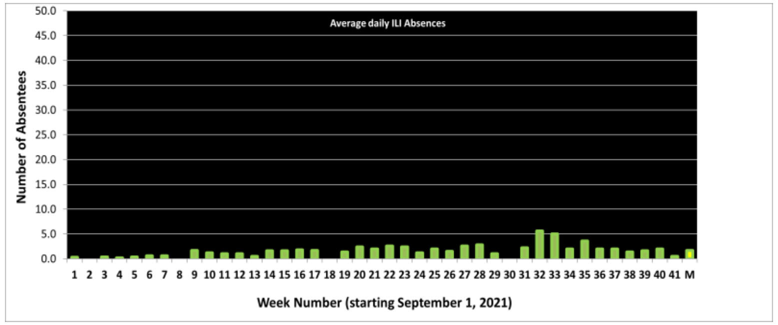

# 2018-2019



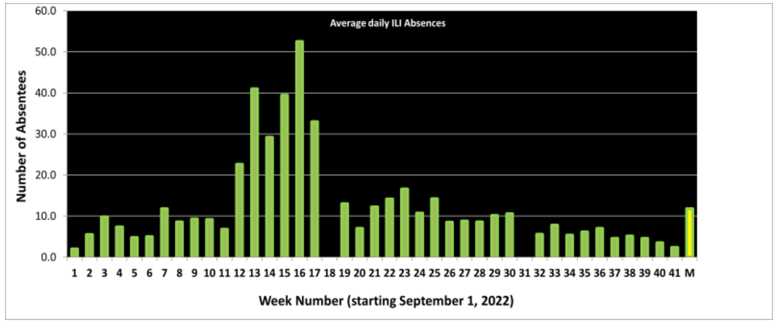

# 2019-2020



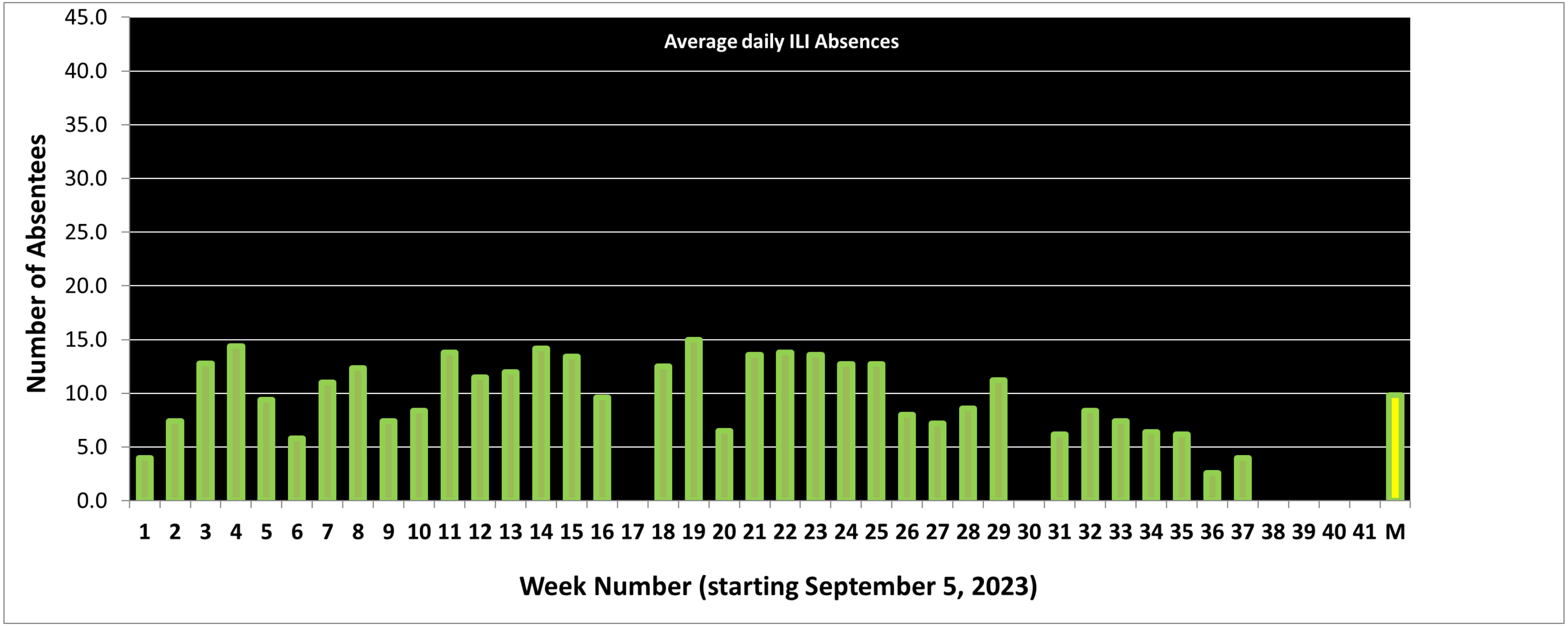

# 2020-2021




# 2021-2022




# 2022-2023



Average daily ILI Absences
Number of Absentees
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 M
Week Number (starting September 5, 2023)


# 2023-2024

# 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)**

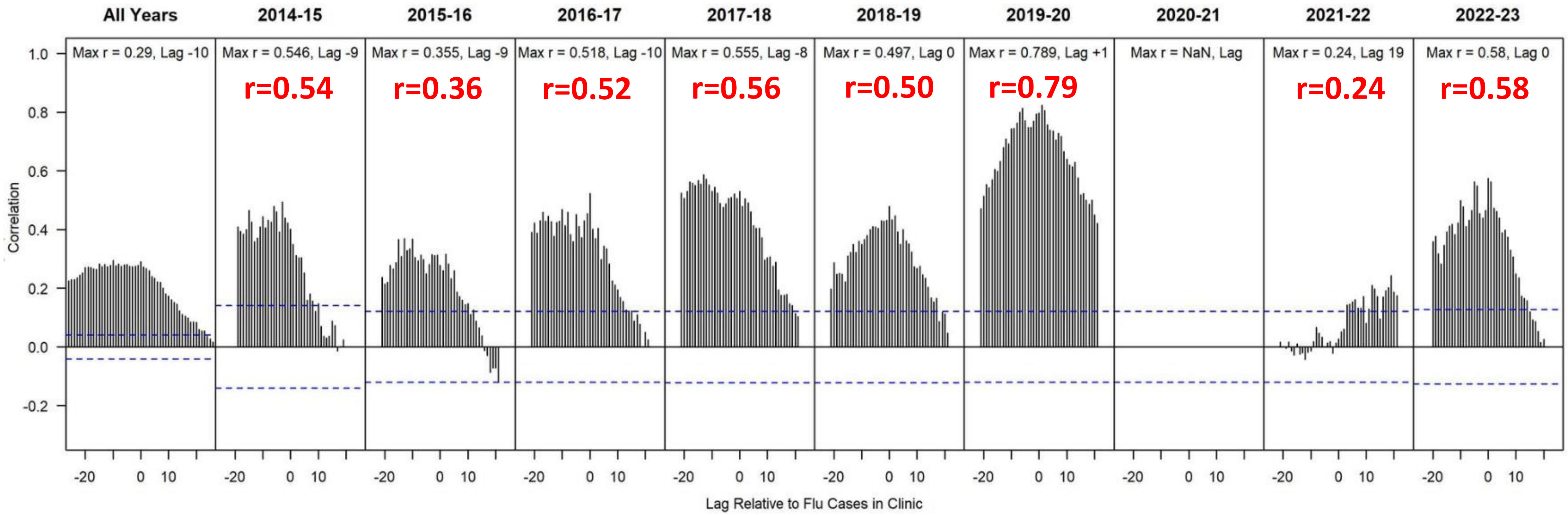
- with a 10-day lead time

**a-TOT (r = 0.27; 0.21—0.33)**

- following MAI by six days

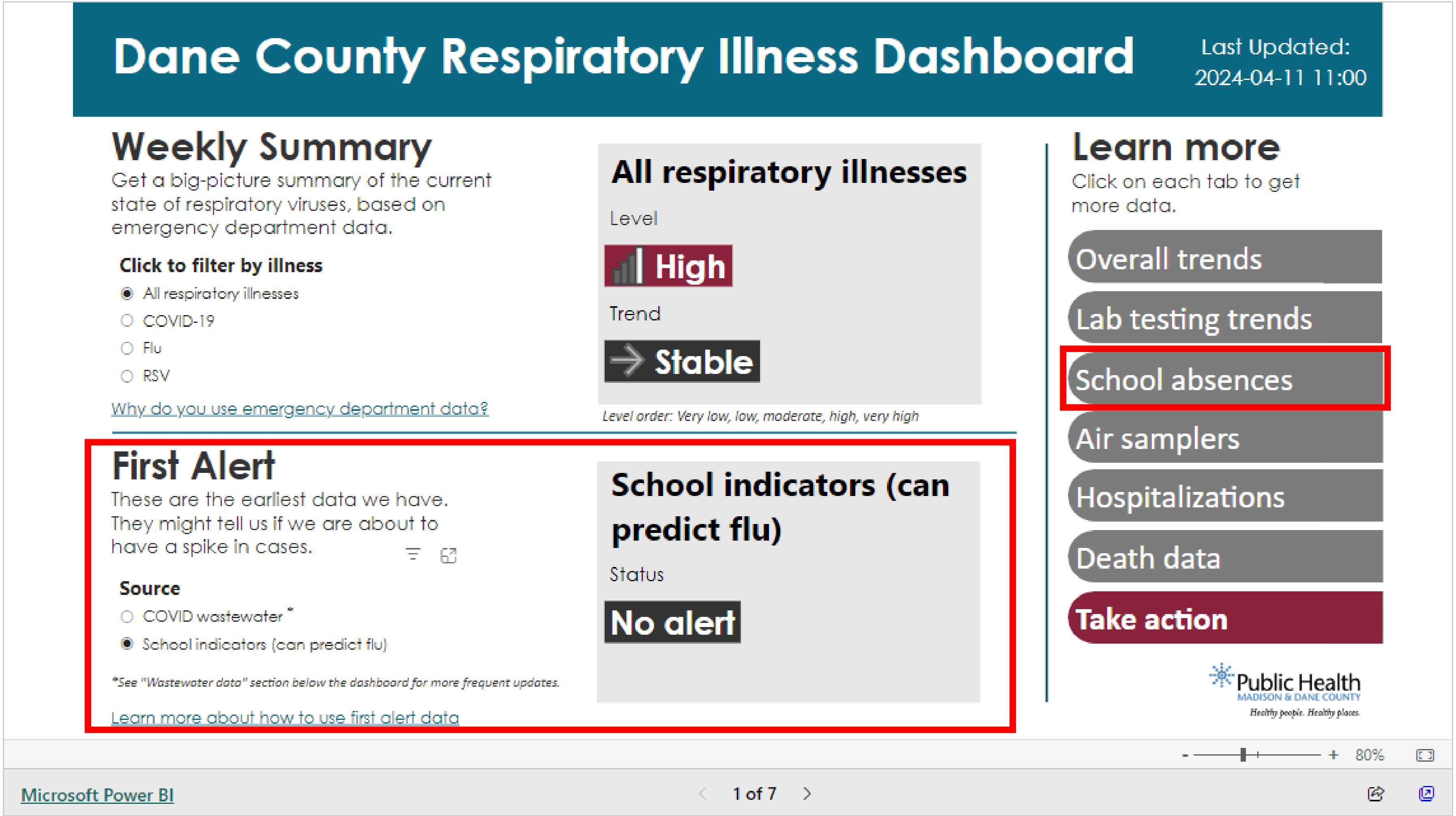
# Absenteeism due to Illness (a-I)

- strength of correlation tracks severity of influenza outbreak
- a-I peaks ~10 days before medically-attended influenza




Correlations between absenteeism due to illness (a-I) and medically attended influenza
2014—2023; Oregon School District – Dane County, Wisconsin

# Respiratory Illness Dashboard



# Feasibility/Generalizability

| Question | Yes n (%) |
|---|---|
| Do you document when a student is absent regardless of the reason? | 118 (100%) |
| When a student is absent, do you specify whether the absence was due to an illness | 116 (98%) |
| Are parents asked to provide a reason for the absence? | 113 (97%) |
| Do you document when teachers or staff members are absent? | 118 (100%) |
| Do you specify whether a teacher or staff member absence was due to an illness? | 26 (22%) |
| Would your district be interested in participating in a statewide illness surveillance program to help detect outbreaks of influenza and other respiratory viruses? | 33 (28%) |

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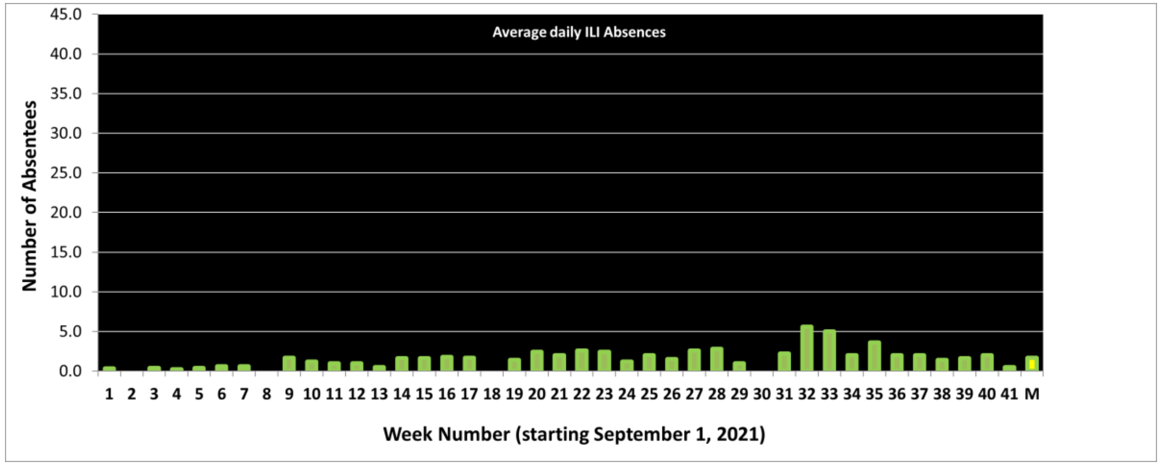
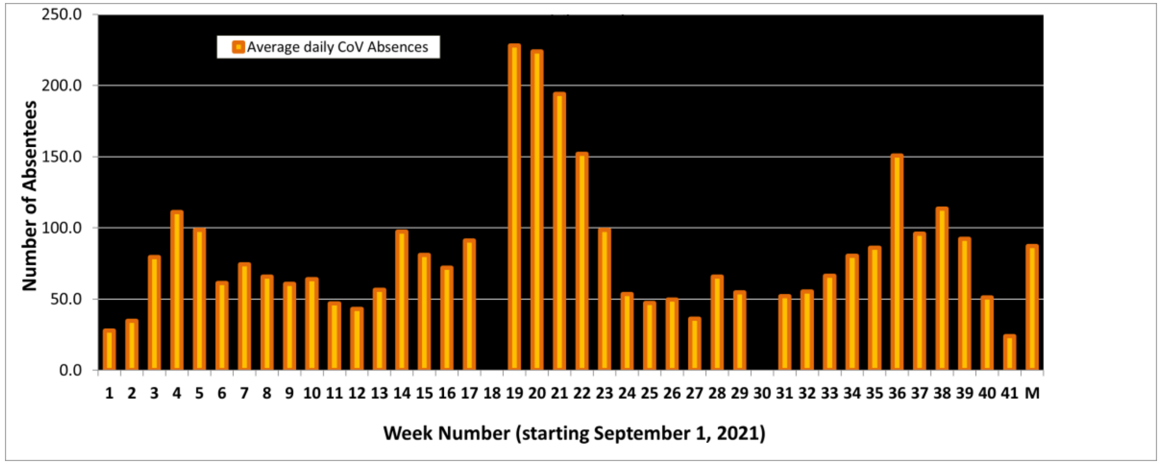
**Survey of Wisconsin School Districts:**
**N=339; response rate to date: 37%**

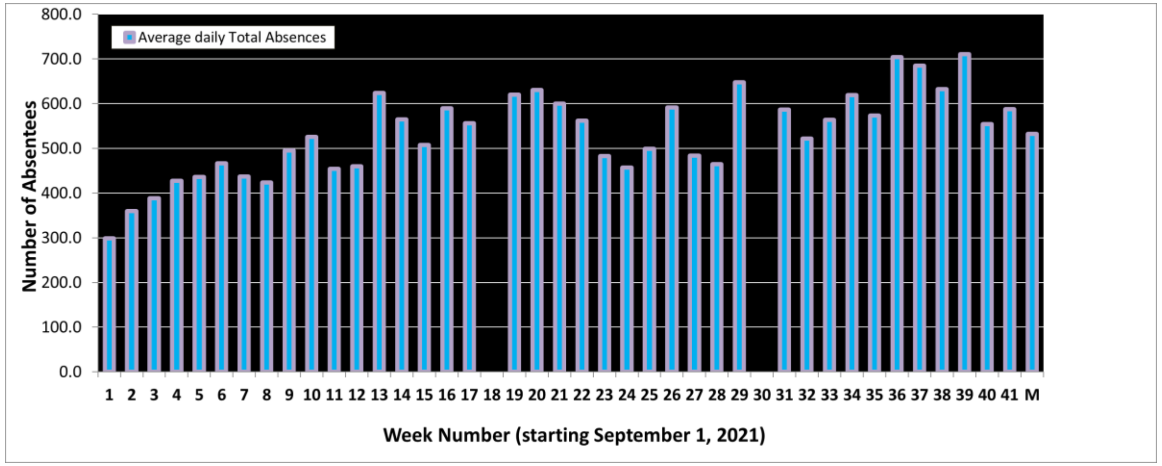
# Absenteeism in the Pandemic (2021-2022)



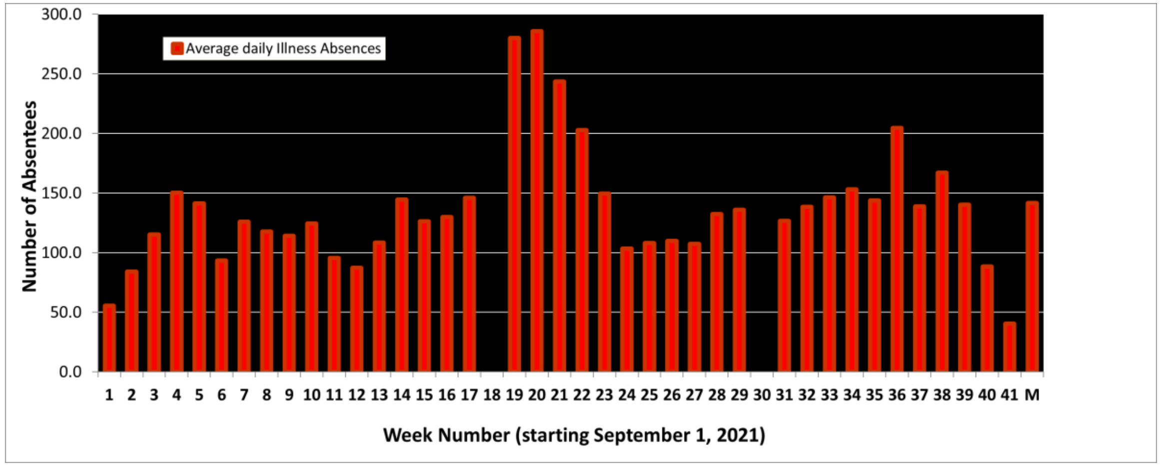

a-ILI




a-COV



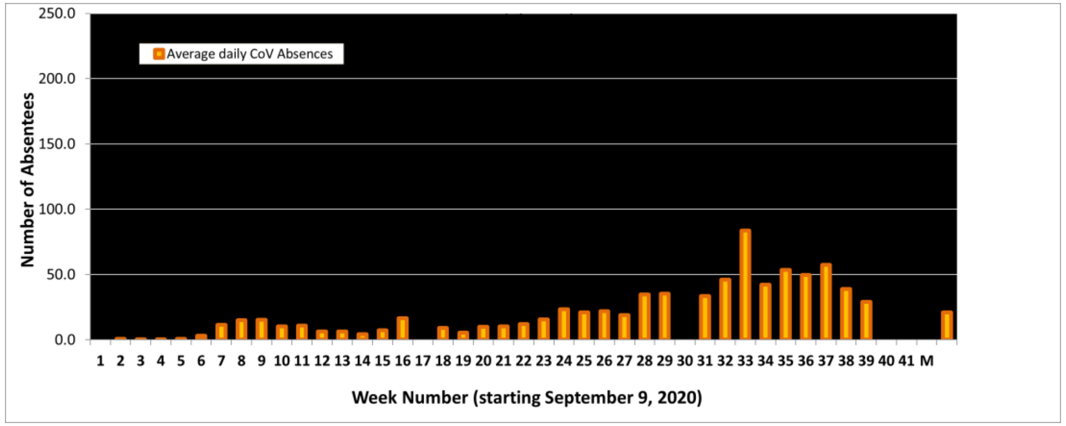

a-TOT



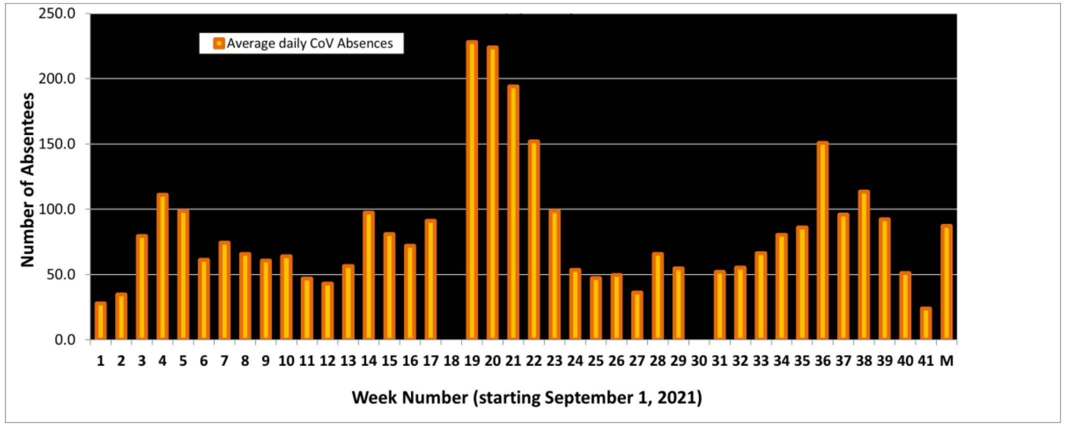

a-I

# Absenteeism due to COVID-19 (a-CoV)

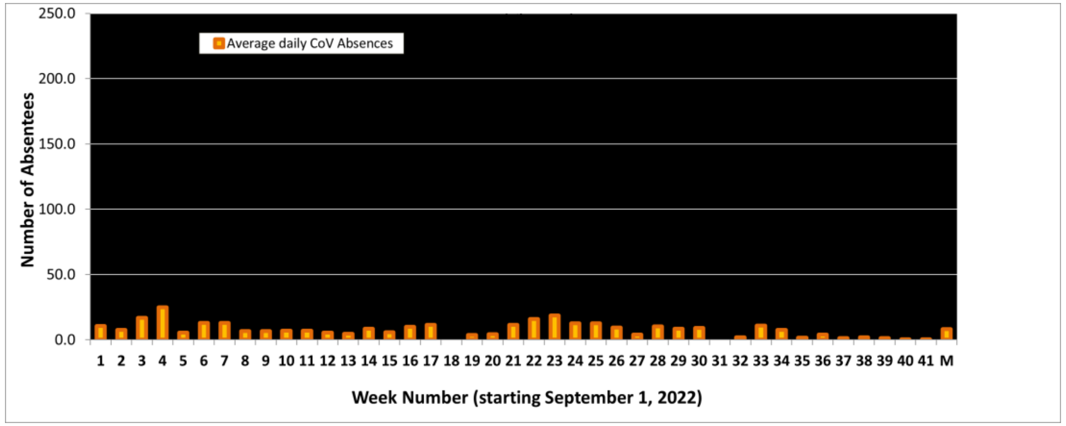
## was behavioral, not biological



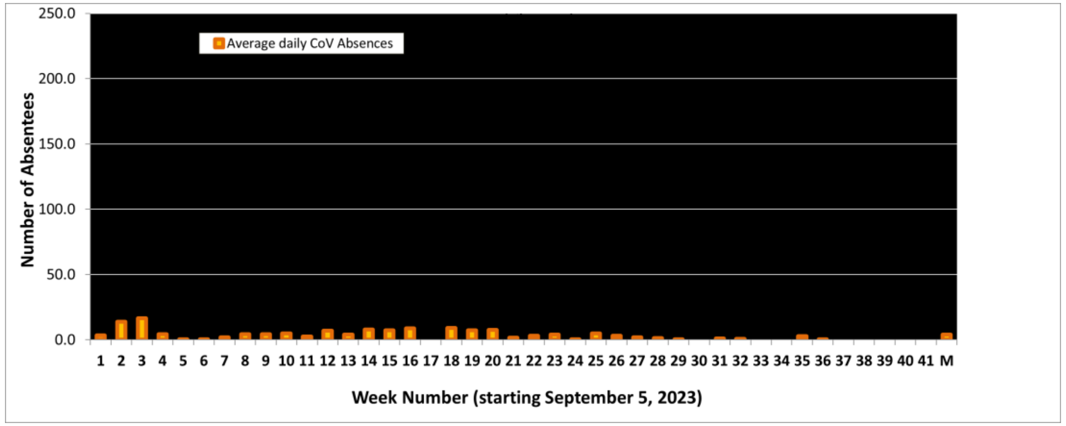

**2020-2021**




**2021-2022**

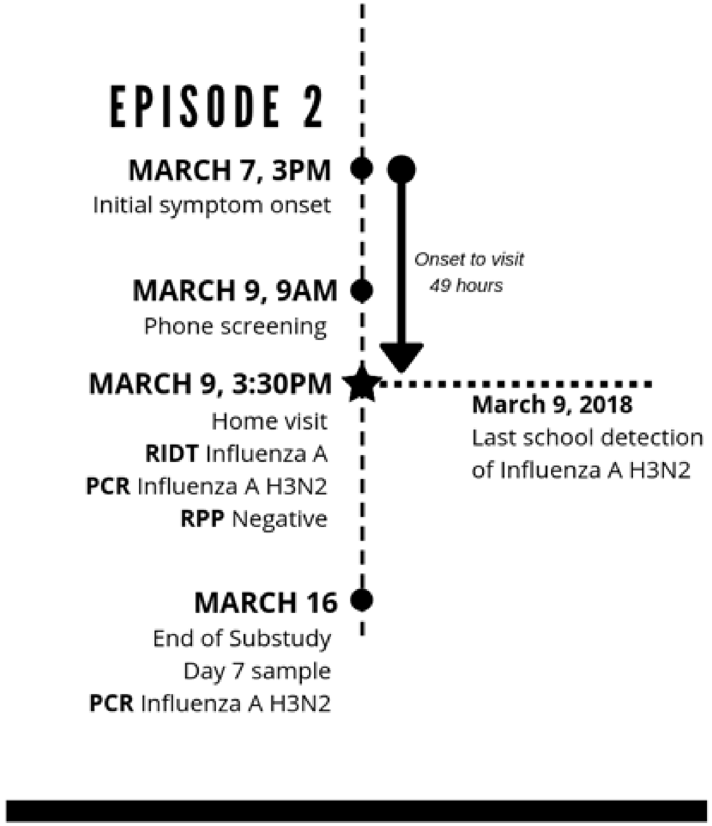


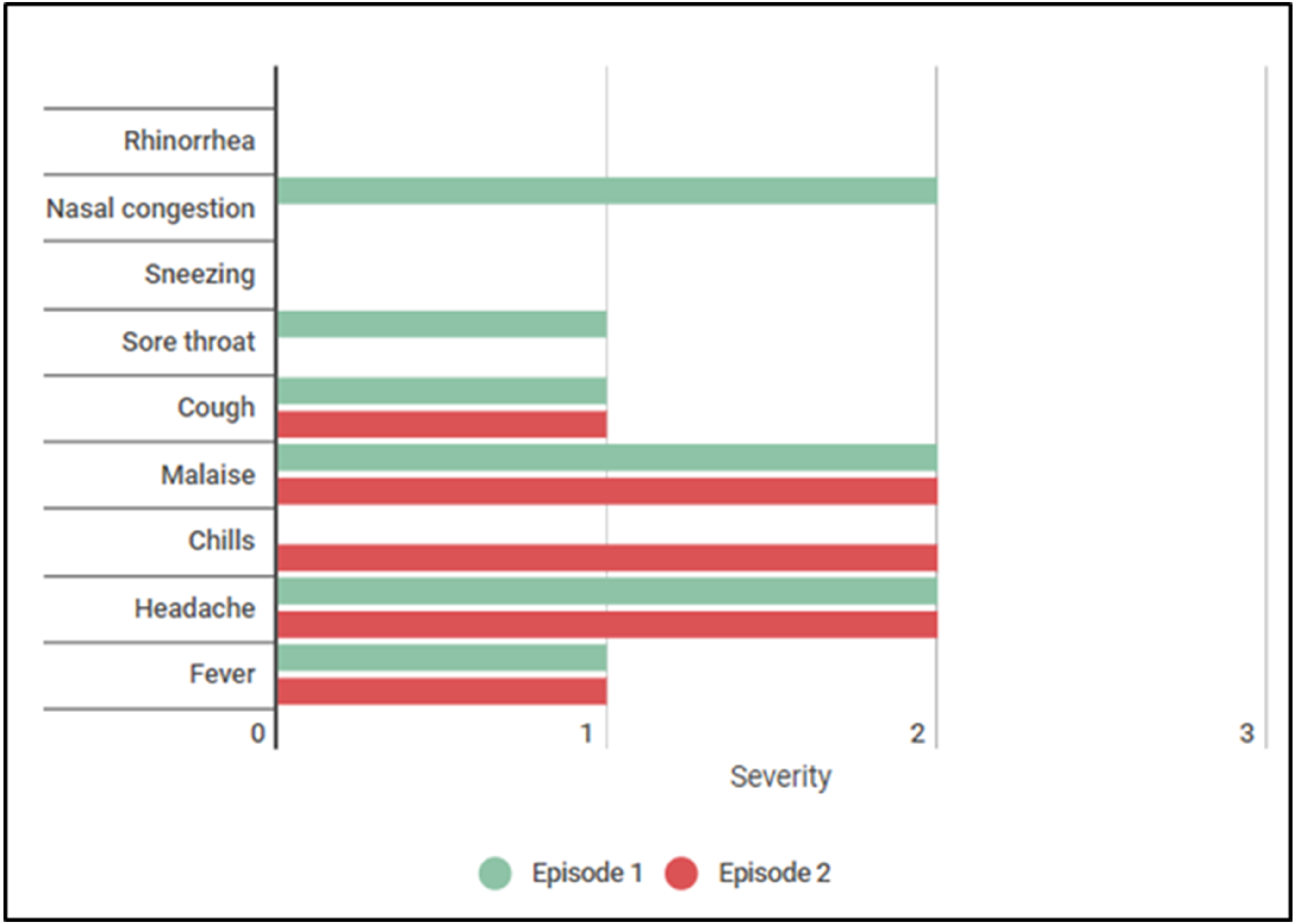

**2022-2023**




**2023-2024**

# Recurrent Influenza

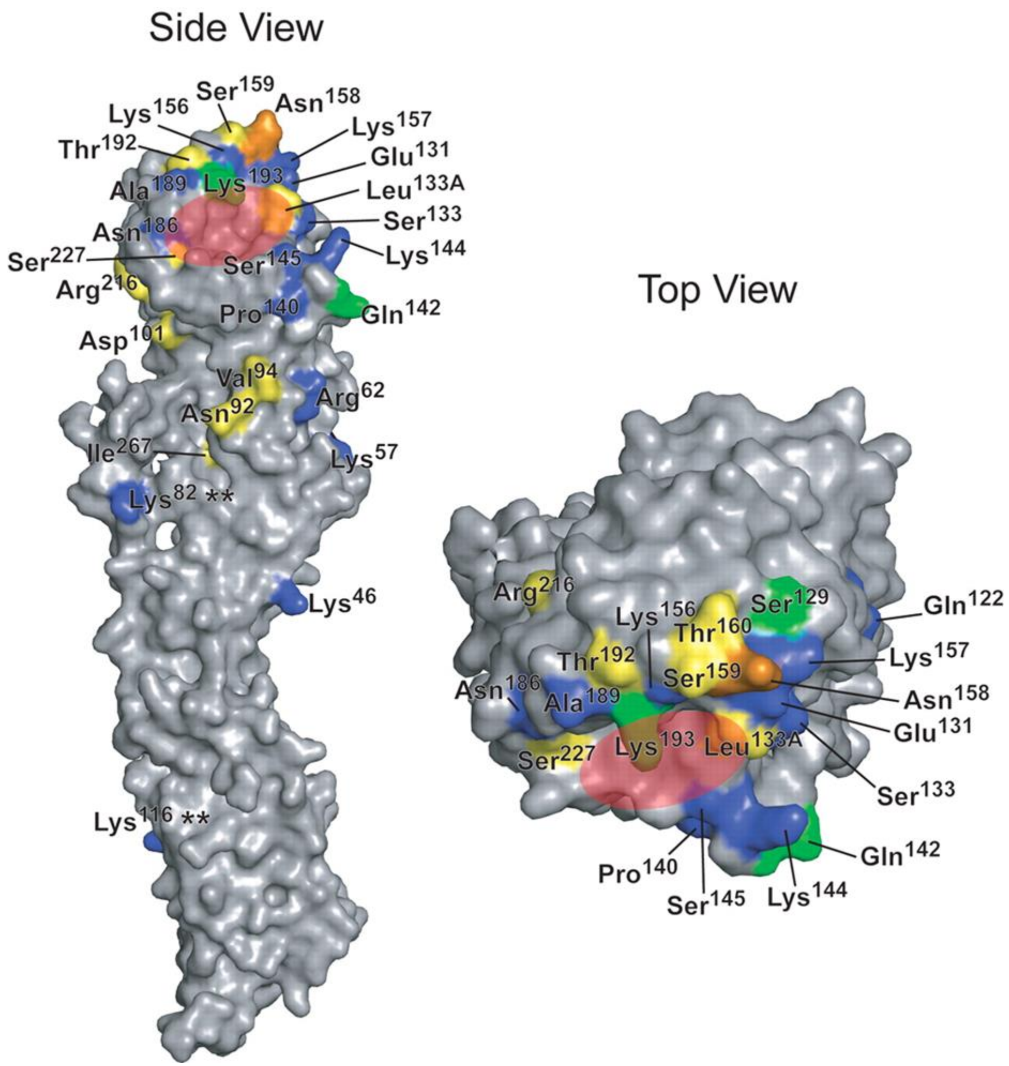





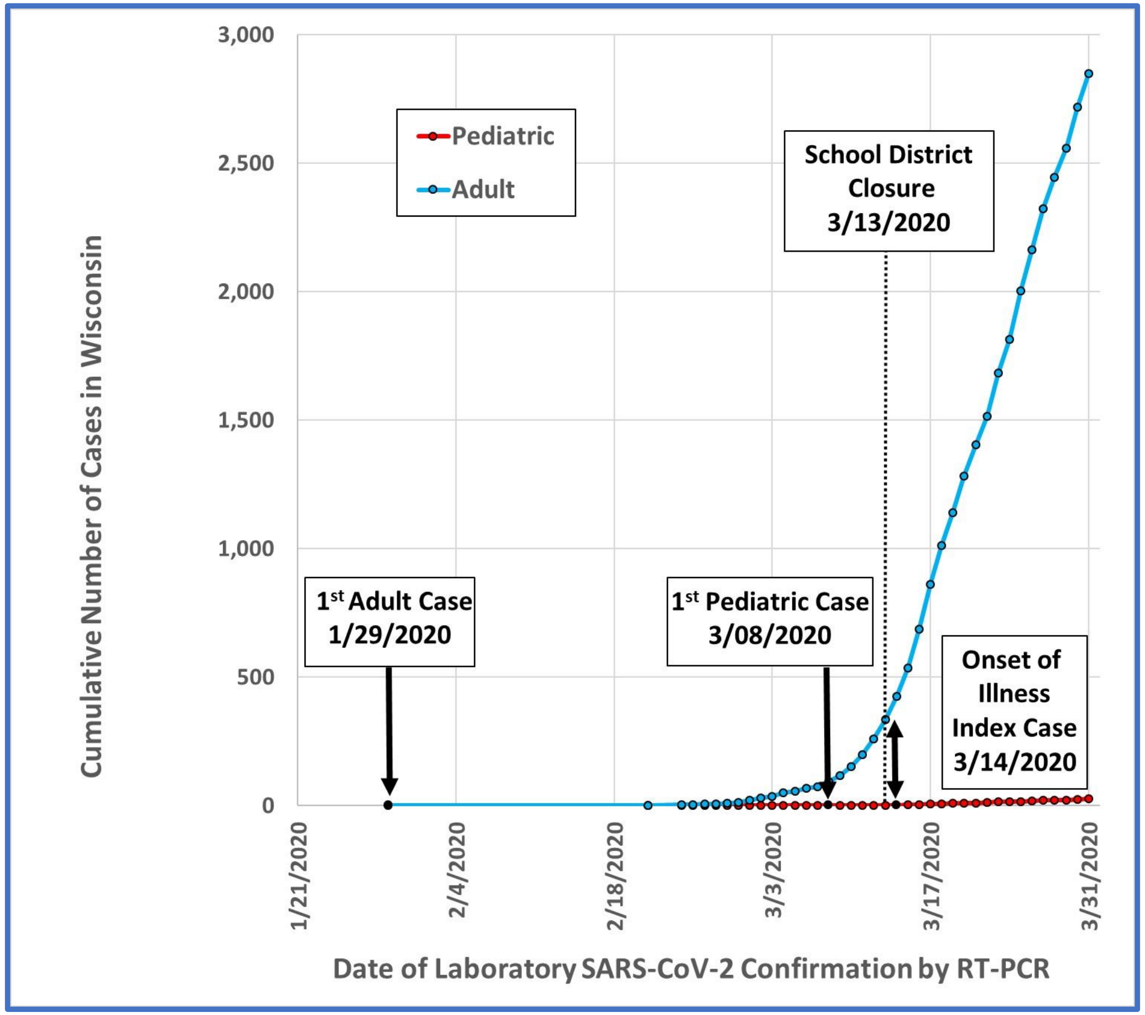
Rhinorrhea
Nasal congestion
Sneezing
Sore throat
Cough
Malaise
Chills
Headache
Fever
0
1
2
3
Severity
Episode 1
Episode 2

# So…
# What Happened?

- First know 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

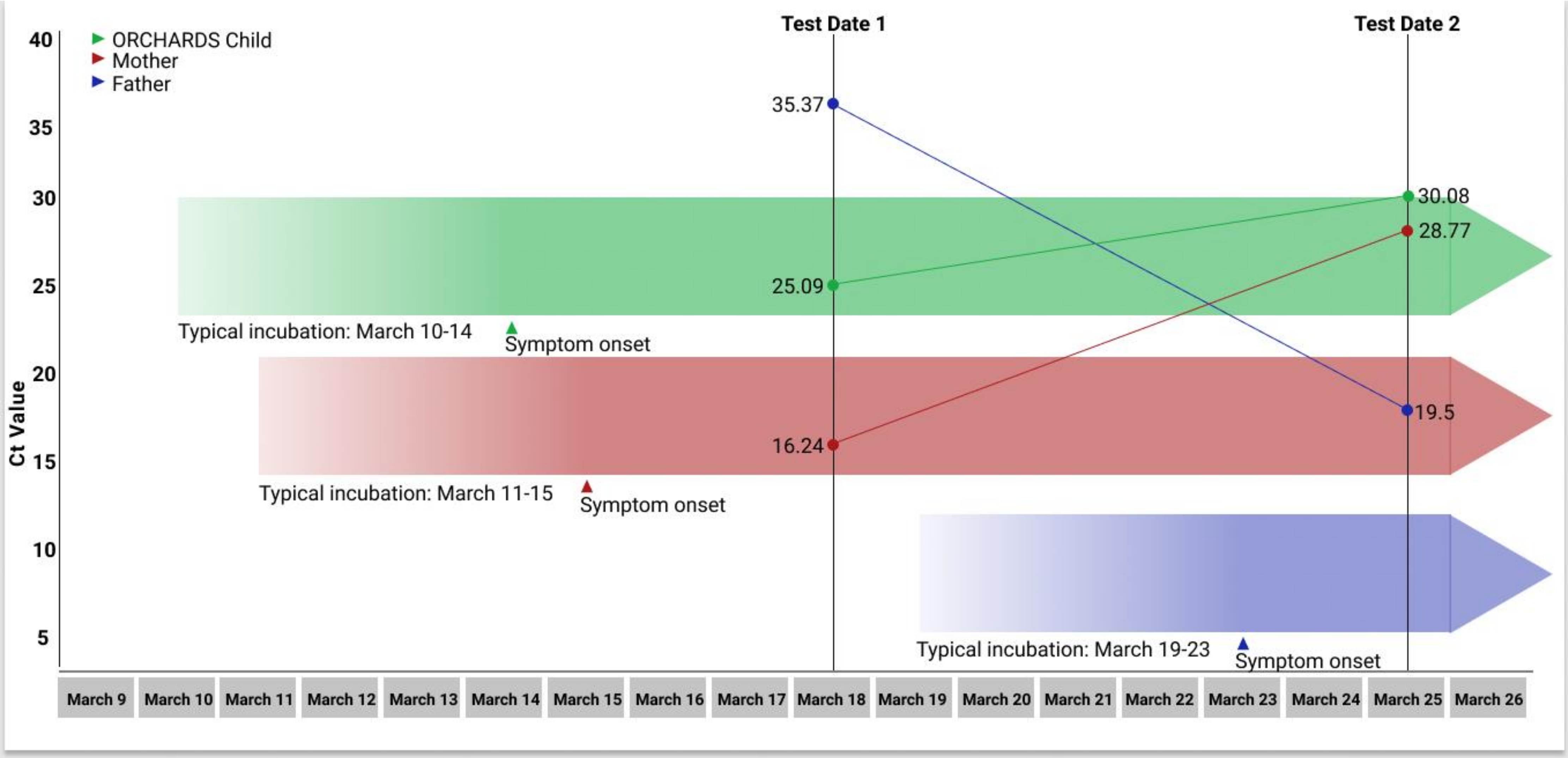


# Evidence of Early SARS-CoV-2 Activity in Wisconsin



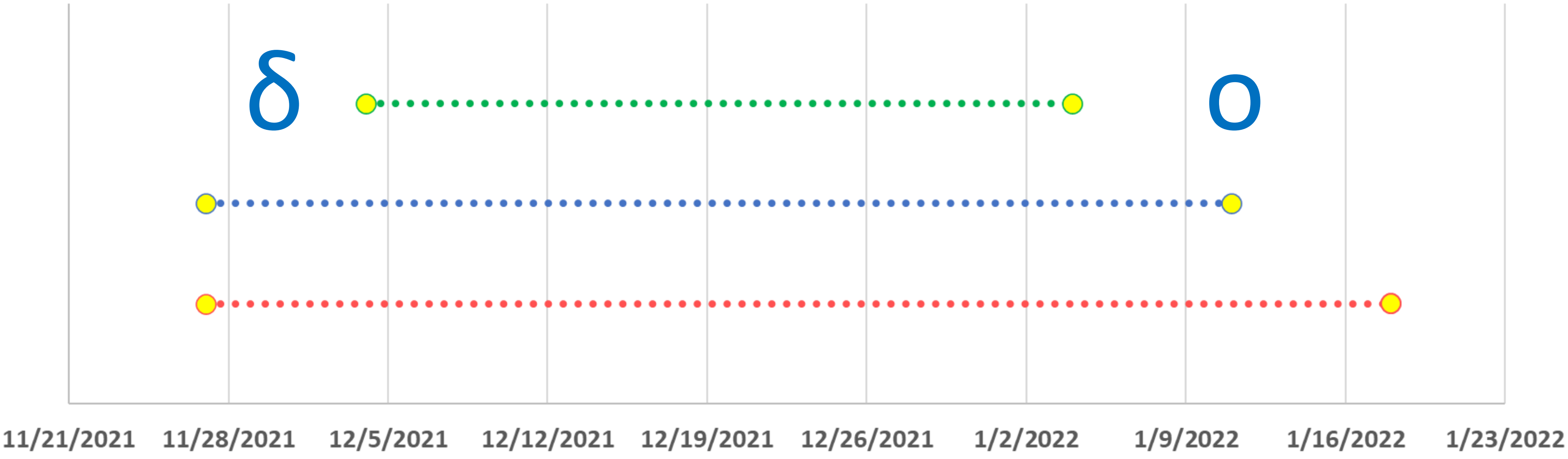

| Specimen Collection Period | Specimens Available | SARS-CoV-2 (+) (%) |
|---|---|---|
| September 2019 | 38 | 0 (0) |
| October 2019 | 38 | 0 (0) |
| November 2019 | 27 | 0 (0) |
| December 2019 | 63 | 0 (0) |
| January 2020 | 191 | 0 (0) |
| February 2020 | 237 | 0 (0) |
| Early-March 2020* | 57 | 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)



# 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**

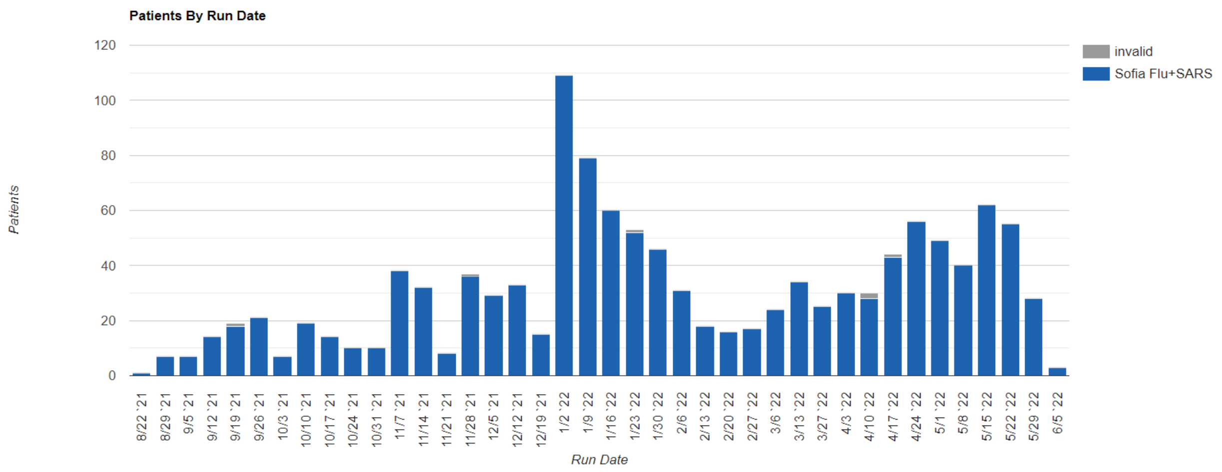
- Sofia set up and instructions
- Provision of  supplies (courtesy of Quidel Corp.)
- Connectivity with COVID-Connect

**Ability to monitor using My Virena**

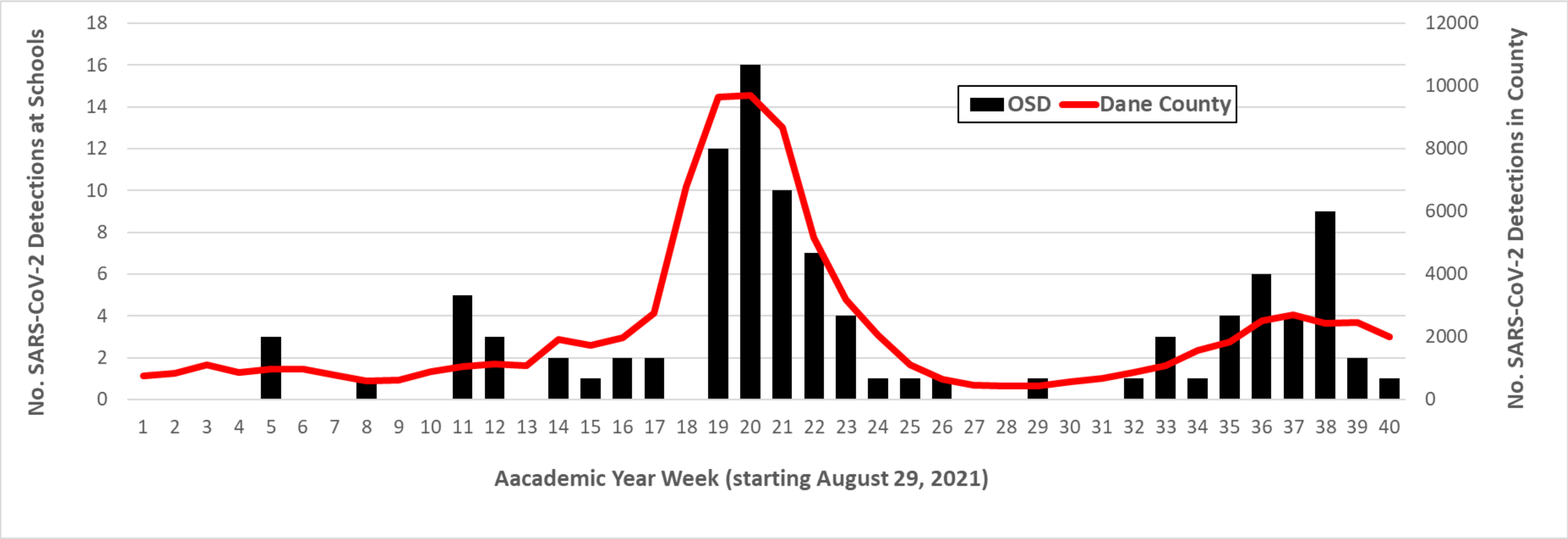
# Rapid Testing was used – a lot!

- 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-CoC-2 detections with county SARS-CoV-2 detections (r=0.81)



# 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 (added in fall 2020)
- ORCHARDS children are tested for SARS-CoV-2 and influenza A/B
  - plus many other viruses using a multiplexed respiratory pathogen panel
- Other household members are tested for SARS-CoV-2 and influenza A/B

# 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

# Secondary Infection Rates (SIR) of SARS-CoV-2

Overall SIR was **47%** (95% CI: 42—51)

- pre-Delta 72% (58—83)
- Delta 51% (40—63)
- Omicron 41% (36—47)

Greater household density associated with increased transmission overall

- OR: 5.13 for each increase of one person/bedroom, CI: 1.97 – 13.35, p=0.0008

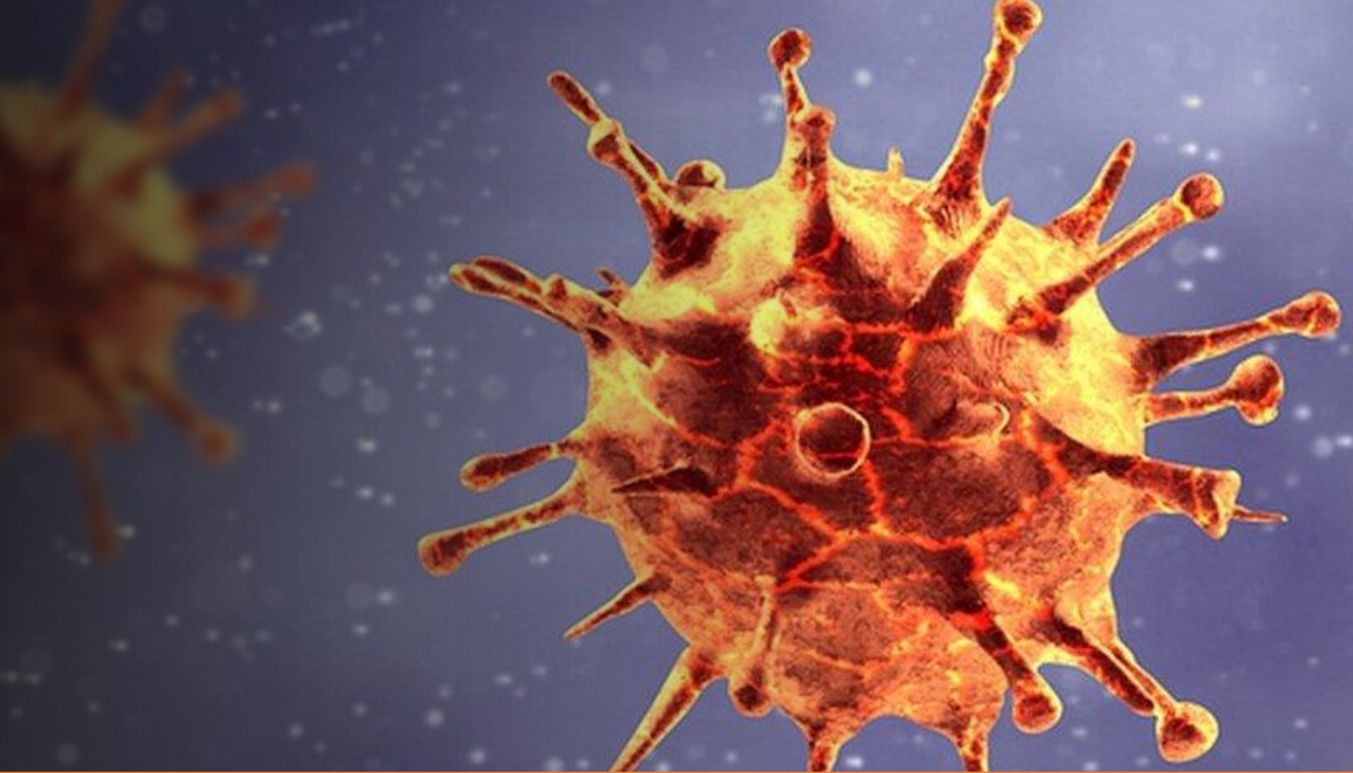
Presence of a household cat was not significantly associated with household SARS-CoV-2 transmission

Exclusion of 13 households (10%) with evidence of discordant detections of SARS-CoV-2 resulted in modest reductions in the estimated SIR

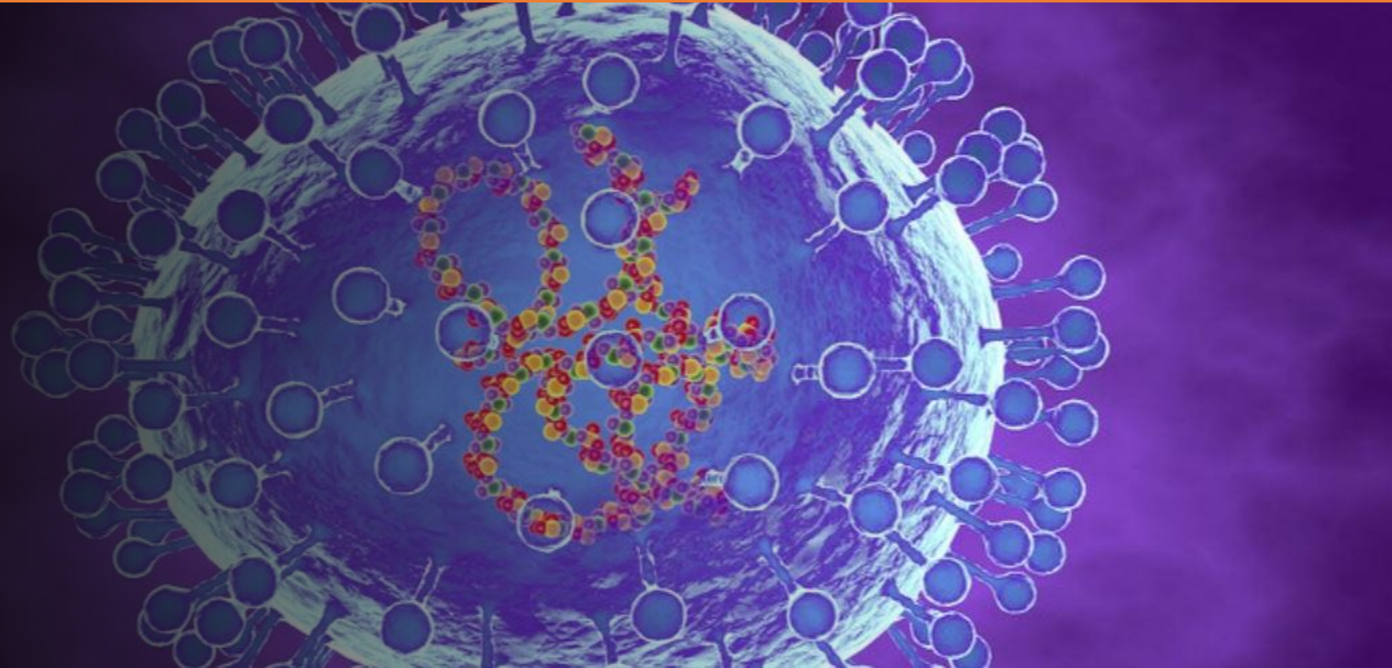
- entire study period: 47% vs. 43%
- Delta period: 51% vs. 47%
- Omicron period: 41% vs 36%

Significant difference in self-reported vaccination proportion between households with concordant (65.2%) and discordant (91.4%) virus identification (P<0.001).

# Secondary Infection Rates:



ß-coronaviruses (OC43 and HKU1)
19.2% (95% CI: 13.8%-25.7%)



human metapneumovirus
12.2% (95% CI: 8.1%-17.4%)

Bell C, He C, Norton D, Goss M, Chen G, Temte J. Household transmission of human metapneumovirus and seasonal coronavirus. Epidemiology and Infection [in press]

# 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

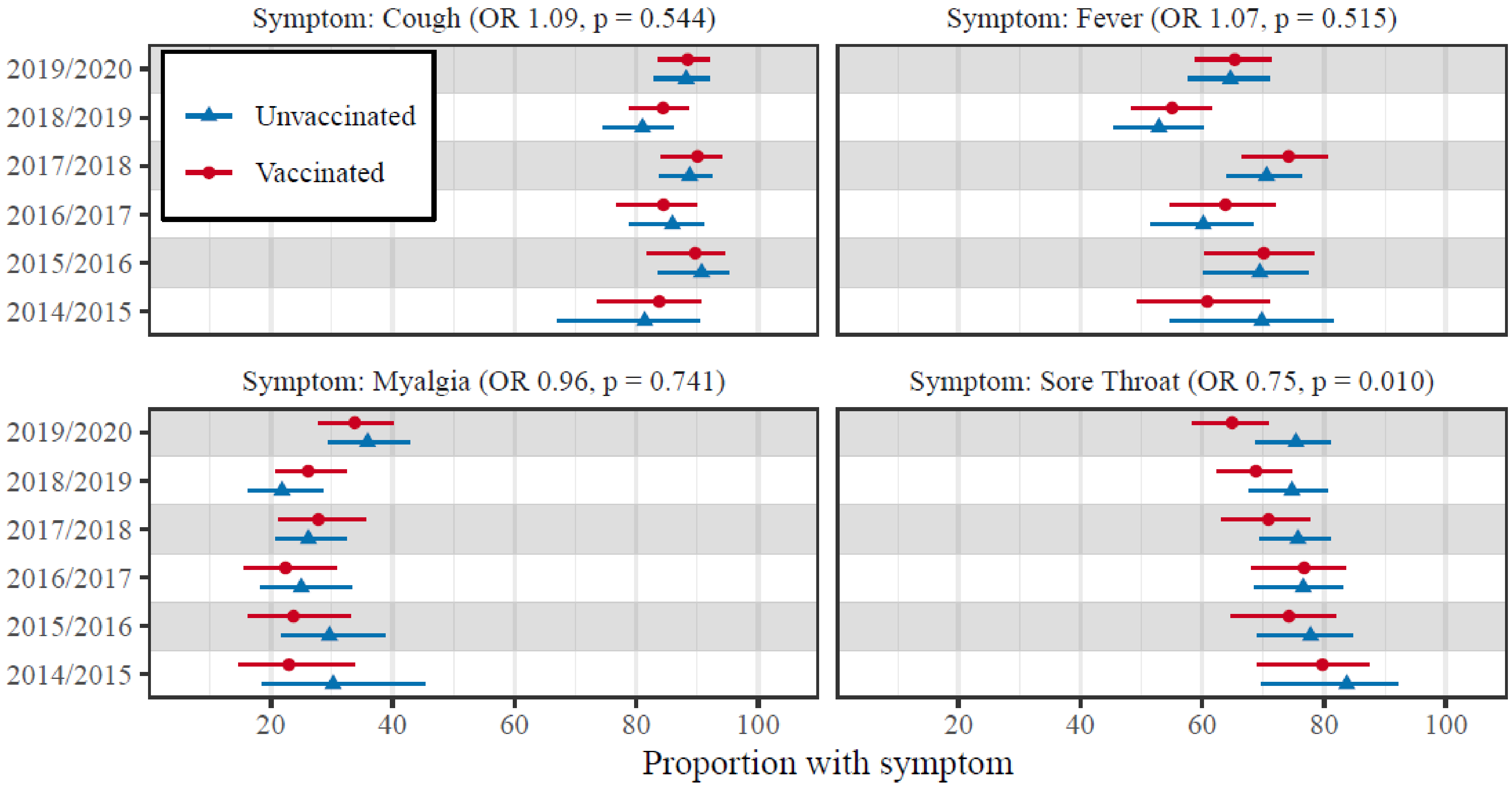
# Evaluation over 6 years (2014—2020)

- 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 (-)

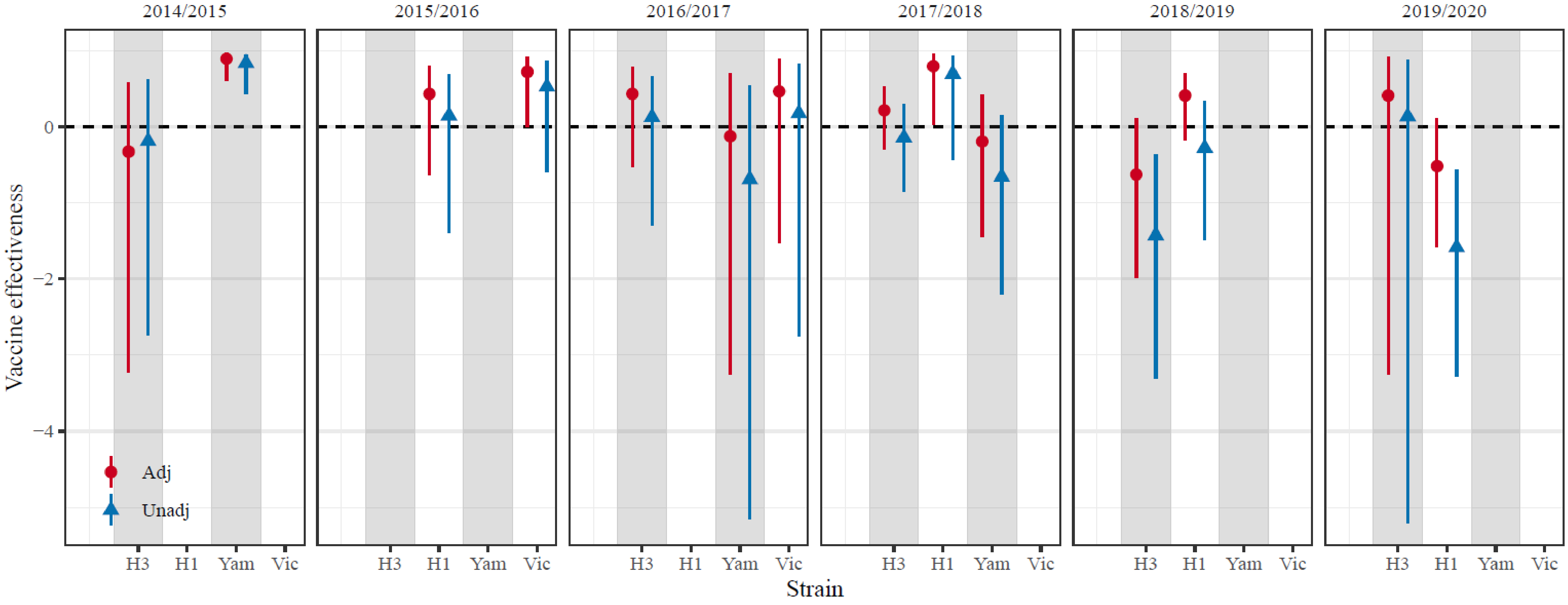
and the estimate effectiveness is:

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

# Effect of vaccine status on symptoms (PCR+)



# Vaccine effectiveness by year and strain



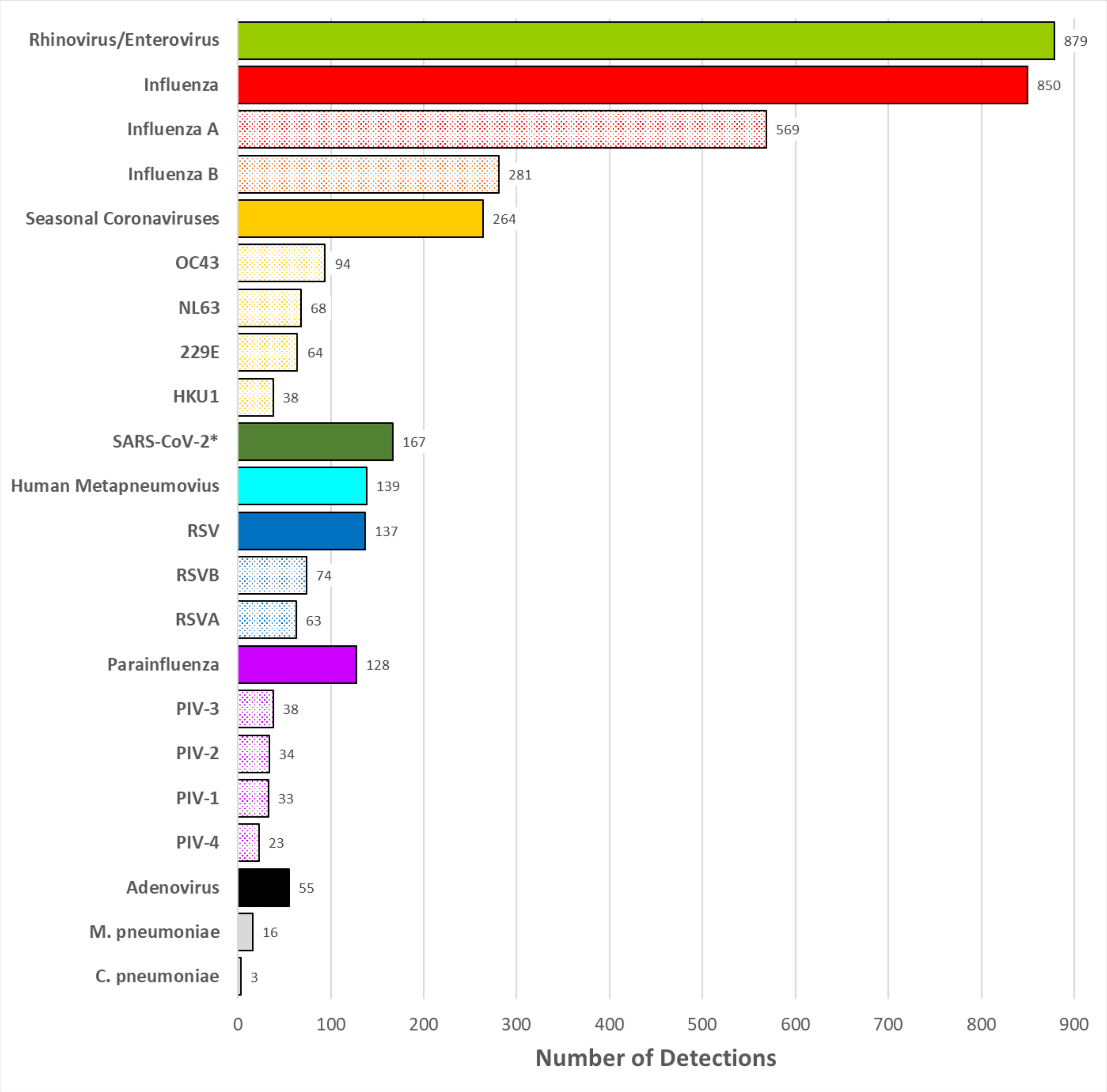
# Part 1. Community-engaged epidemiology

## Basic Epidemiology of Respiratory Viruses in Children

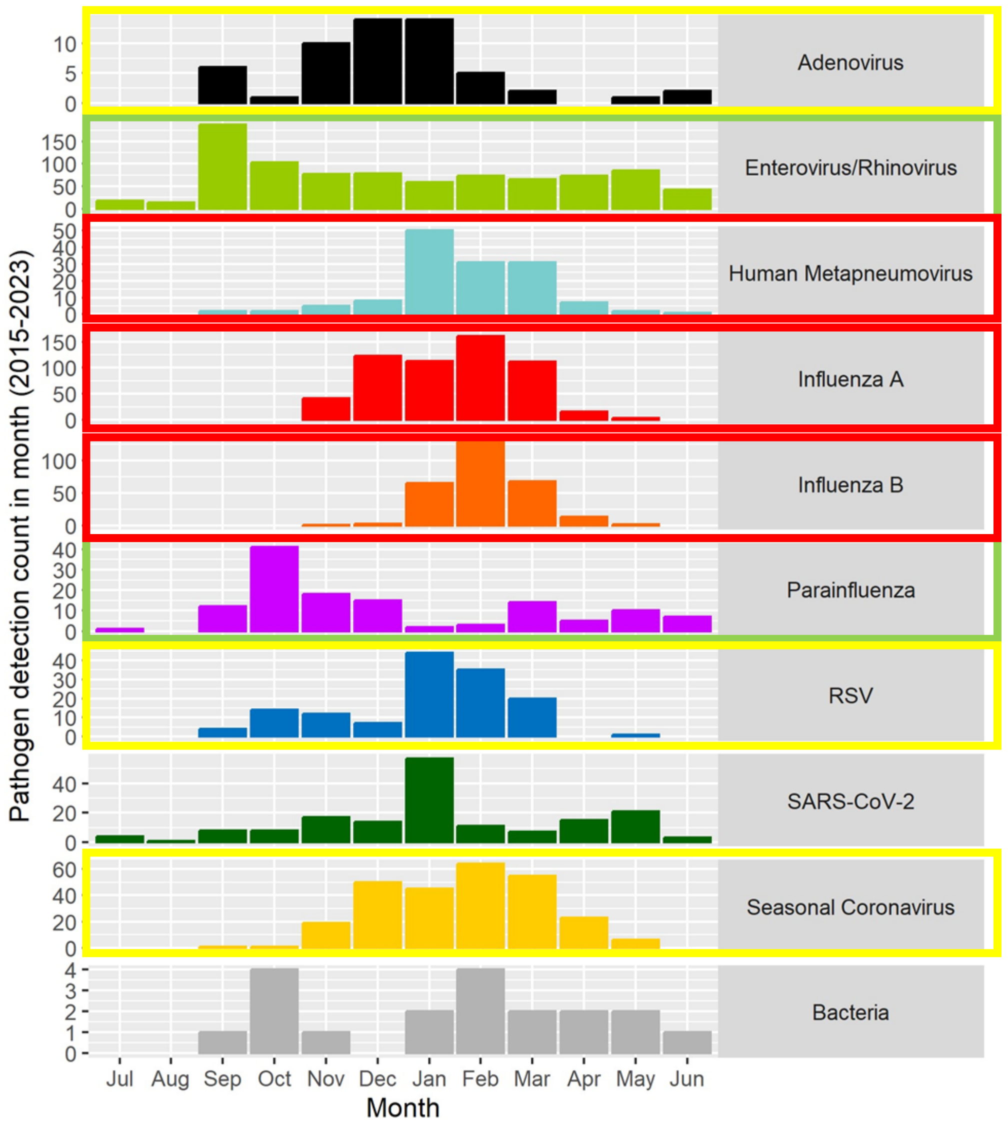
- **Community-based, laboratory-supported, longitudinal study in one school district**
- **January 2015 through May 2023**
- **Recruitment of K-12 children with acute respiratory infections**
- **Basic demographic, epidemiological, and symptom data**
- **Specimens collected for RT-PCR for a wide range of viruses**

# Wide Variety of Viruses

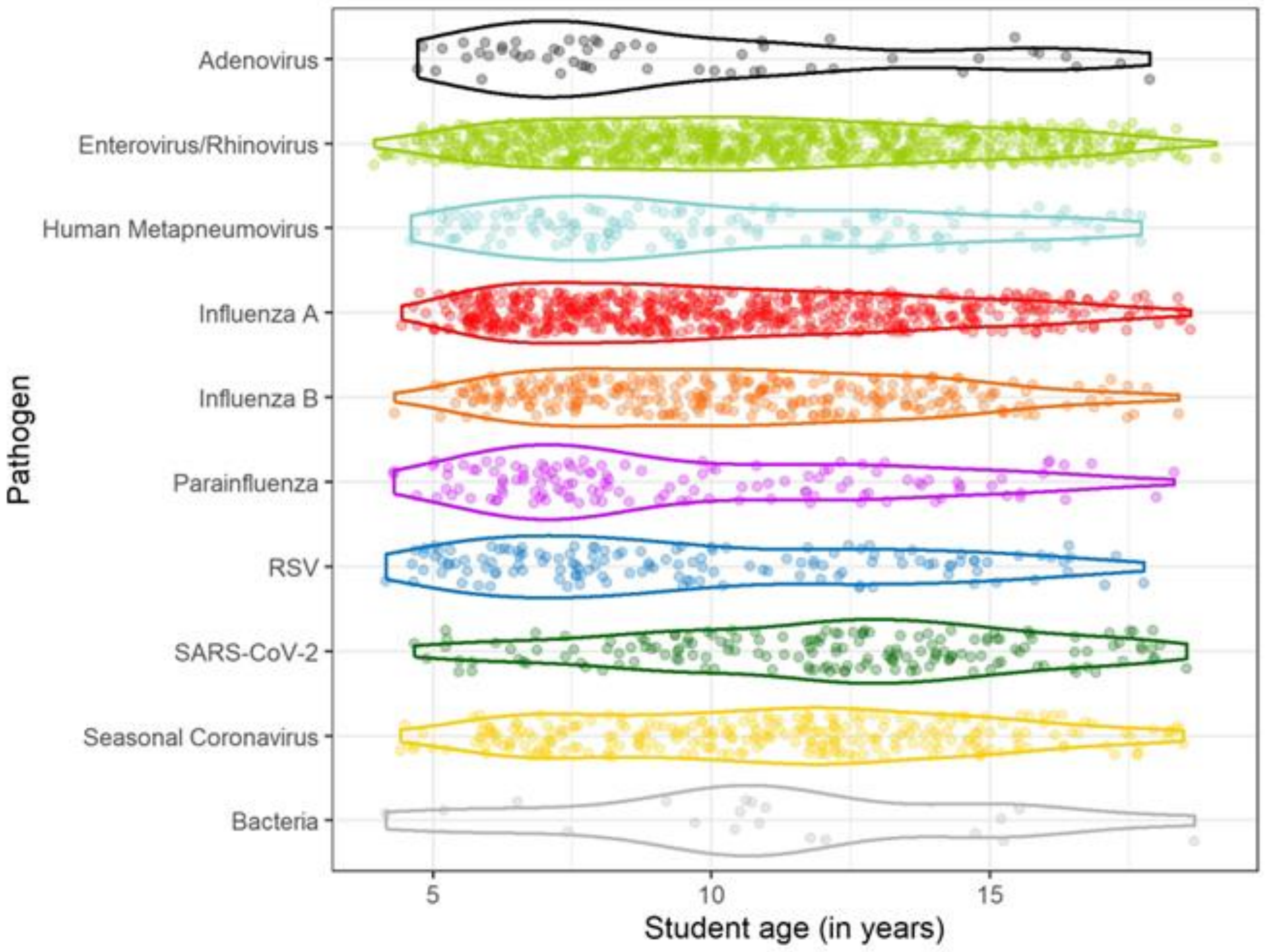
- 3,498 children
- 70.3% of specimens (+) for at least one pathogen
- Lots of rhinoviruses and influenza
- Few bacterial infections



# Seasonality




# Age Distribution

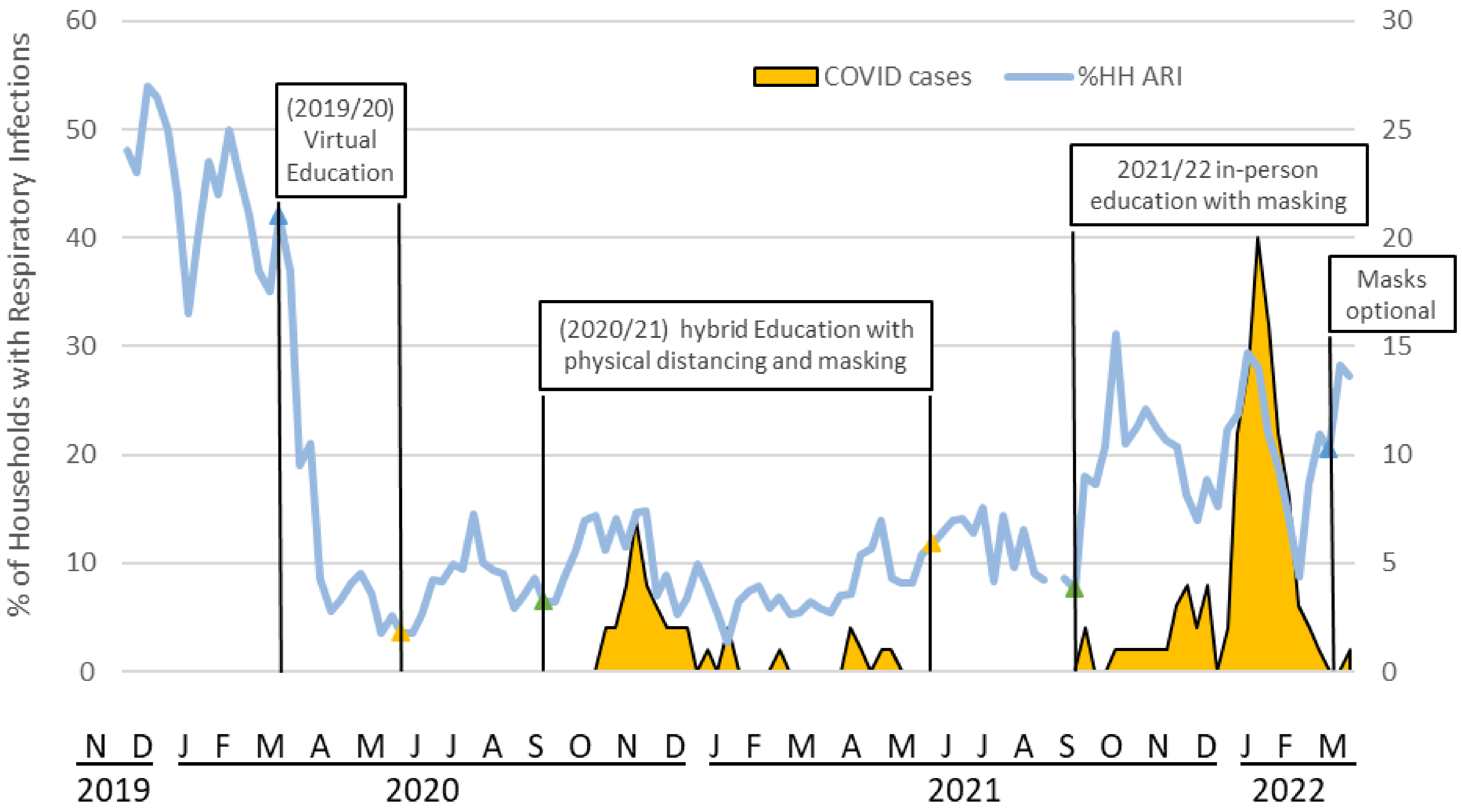


# Part 2. Community-engaged epidemiology

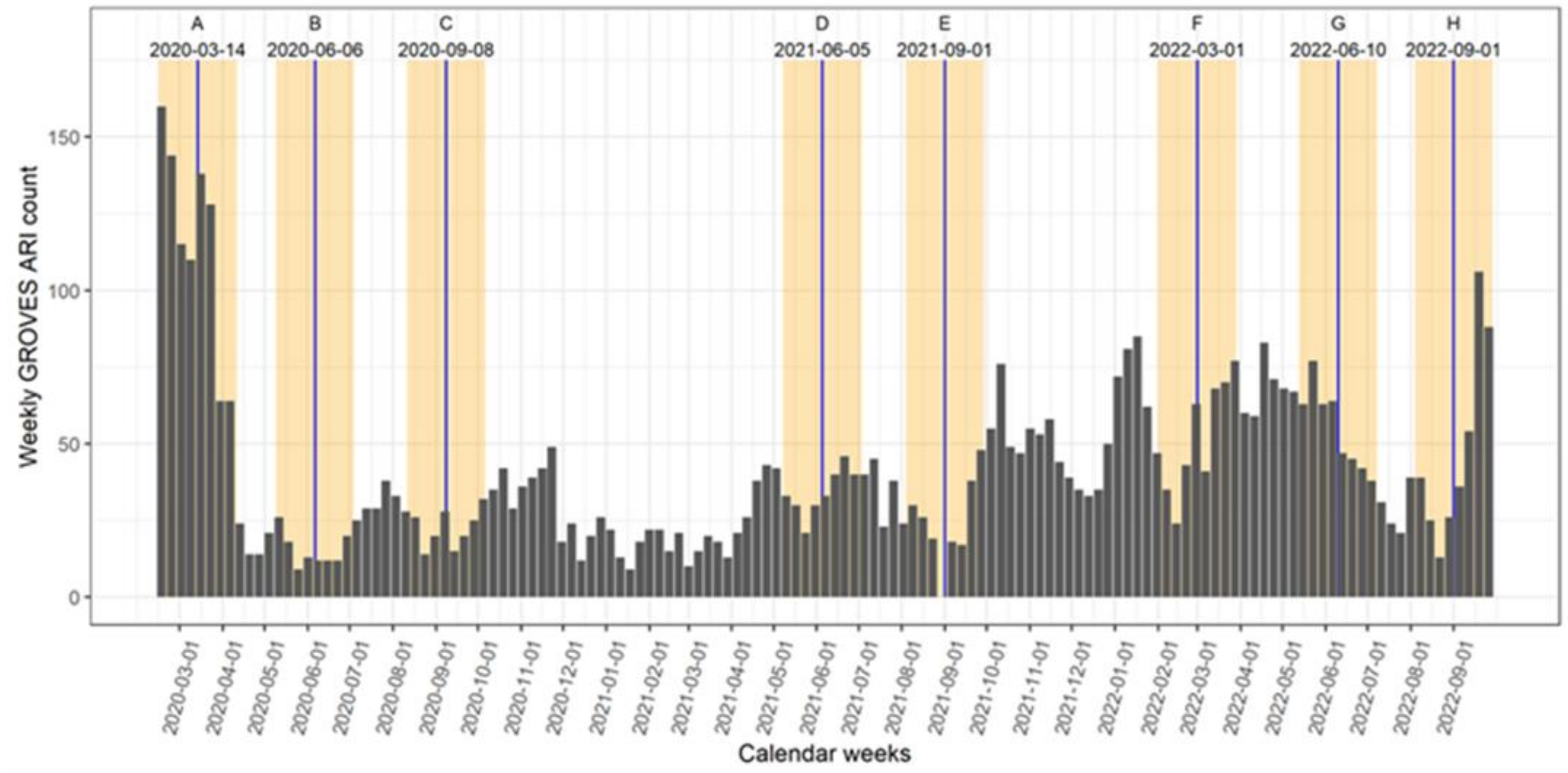
# GROVES: Great Oregon Vaccine Effectiveness Study

- **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**

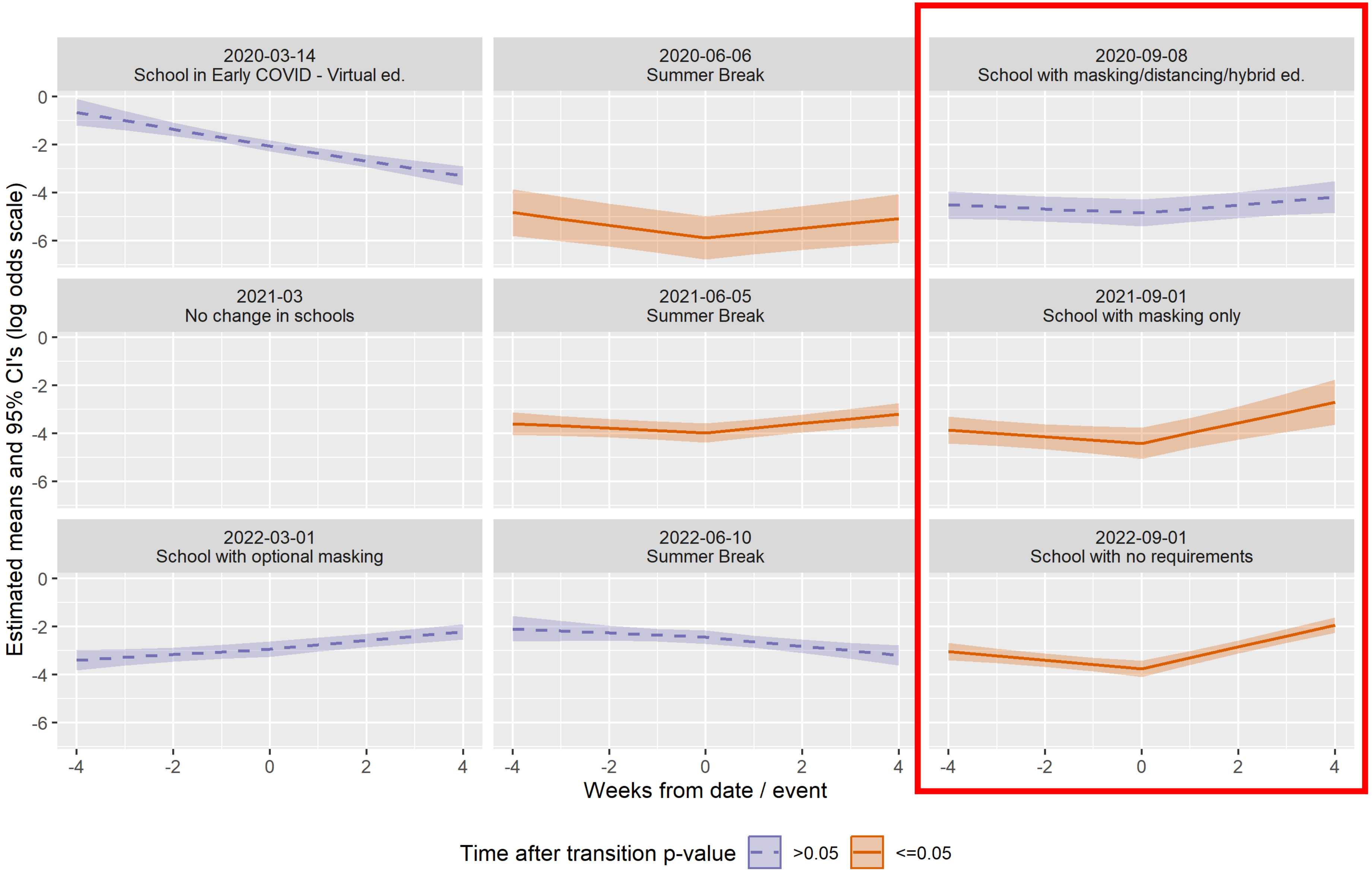
# Respiratory infections and COVID-19 in households

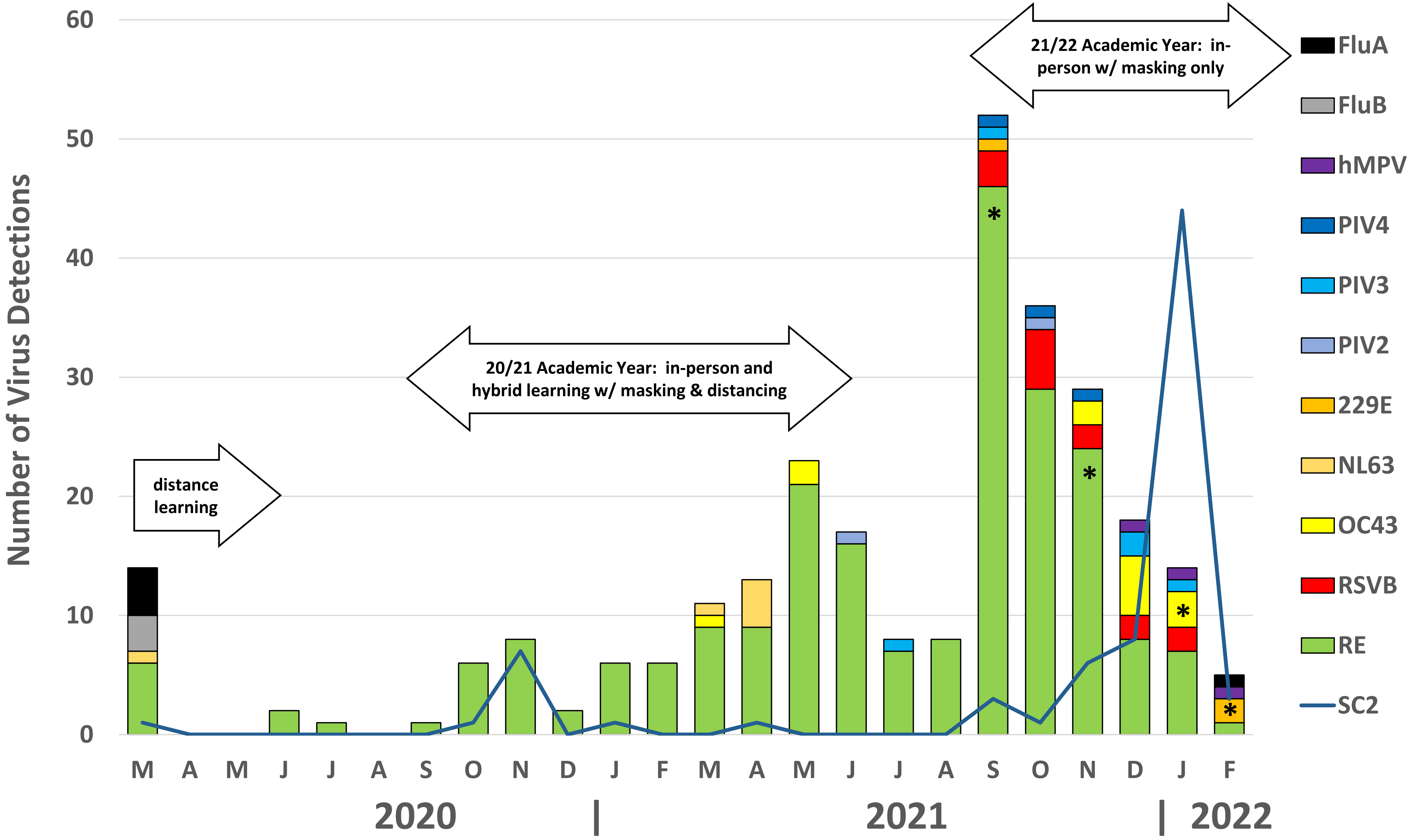


# Comparison of ARI patterns to school district mitigation efforts



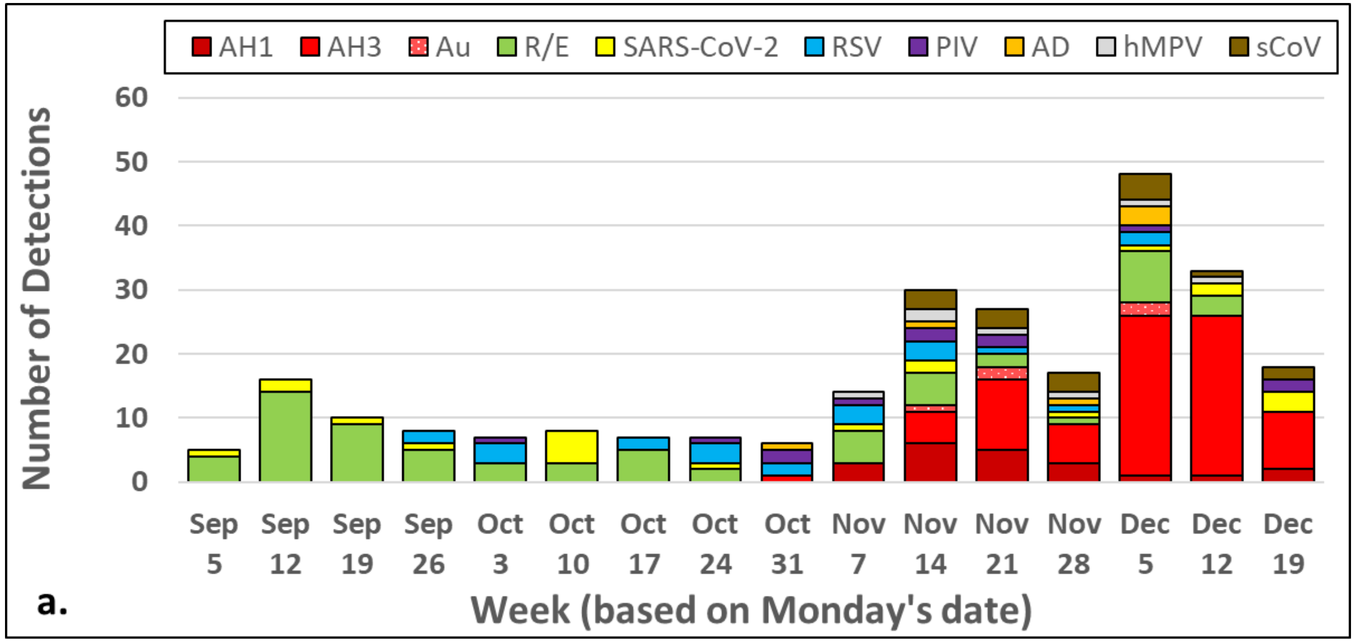
# Statistical analysis of mitigation efforts for COVID-19

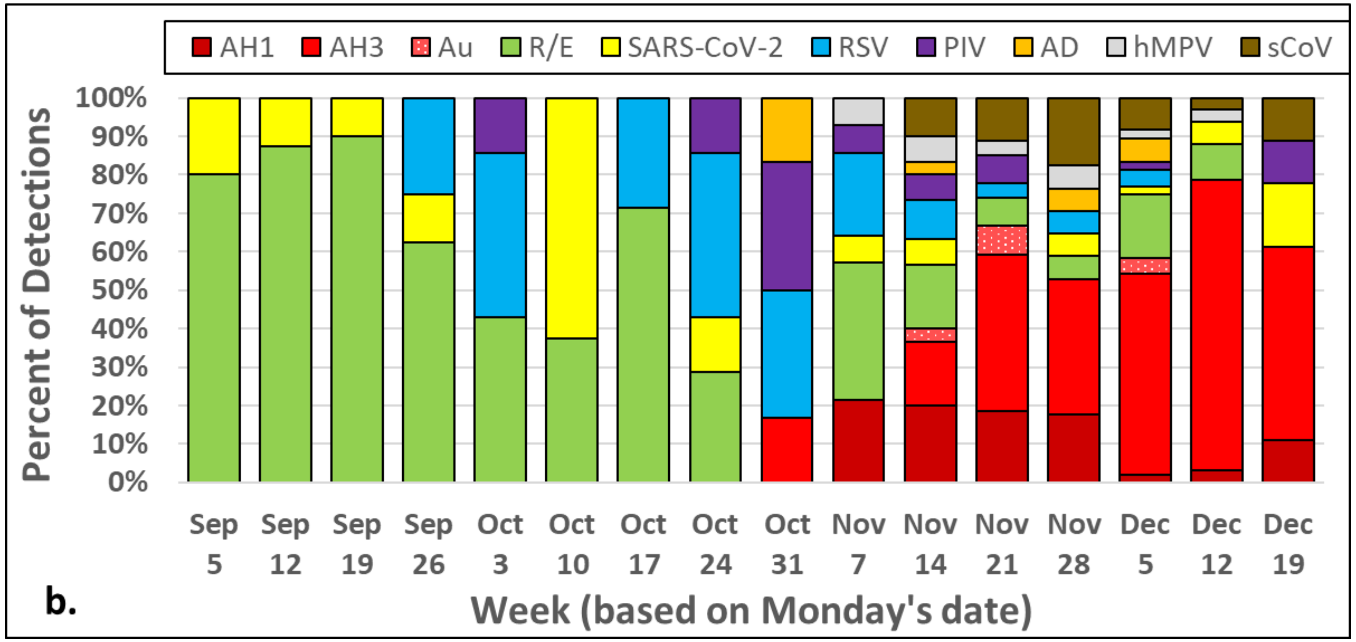




Number of Virus Detections
60
50
40
30
20
10
0
distance learning
20/21 Academic Year: in-person and hybrid learning w/ masking & distancing
21/22 Academic Year: in-person w/ masking only
FluA
FluB
hMPV
PIV4
PIV3
PIV2
229E
NL63
OC43
RSVB
RE
SC2
*
*
*
*
M
A
M
J
J
A
S
O
N
D
J
F
M
A
M
J
J
A
S
O
N
D
J
F
2020
|
2021
|
2022

# Oregon School District
# Autumn 2022

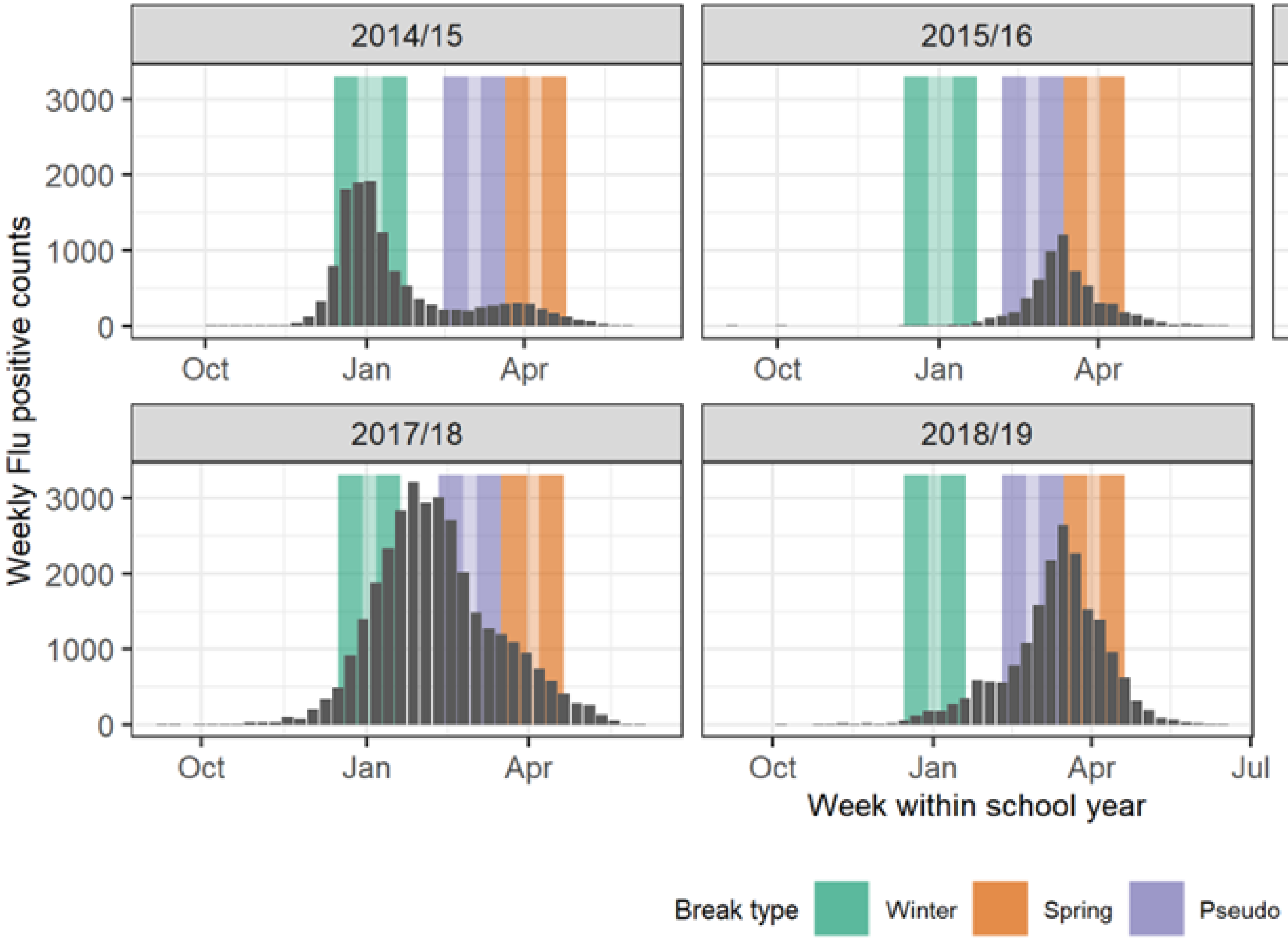


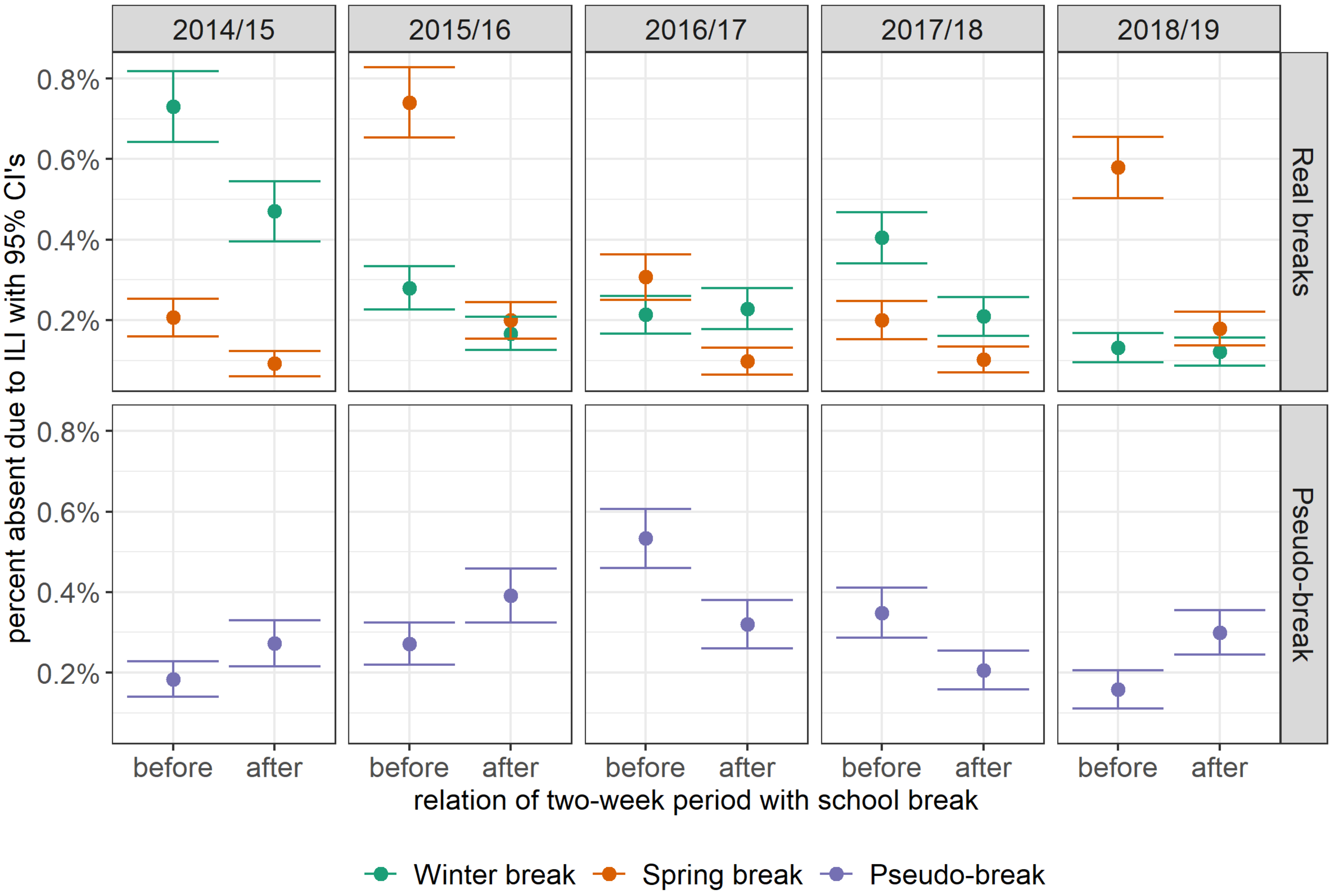
# Part 3. Community-engaged epidemiology

# Effect of planned school breaks on influenza-like illness

- **Interest in effect of planned school breaks**
  - Winter break (10-16 days)
  - Spring Break (9 days)
- **ORCHARDS**
  - Absenteeism due to ILI used as “proxy” for influenza like illness
- **Challenge**
  - Observational study – no ability to control for influenza occurrence vs. timing of break
- **Solution**
  - Evaluation of effect of “pseudo-break”



2014/15
2015/16
2016/17
2017/18
2018/19
3000
2000
1000
0
Oct
Jan
Apr
Jul
Weekly Flu positive counts
Week within school year
Break type
Winter
Spring
Pseudo


2014/15
2015/16
2016/17
2017/18
2018/19
Real breaks
Pseudo-break
0.8%
0.6%
0.4%
0.2%
percent absent due to ILI with 95% CI's
before
after
relation of two-week period with school break
Winter break
Spring break
Pseudo-break

# Part 4. Community-engaged epidemiology

## Comparability of multiple methods of respiratory virus surveillance

influenza

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### Four Methods for Monitoring SARS-CoV-2 and Influenza A Virus Activity in Schools

Jonathan Temte, MD, PhD; Maureen Goss, MPH; Shari Barlow, BA; David H. O'Connor, PhD; Shelby L. O'Connor, PhD;
Mitchell D. Ramuta, PhD, MS; Amra Uzicanin, MD, MPH

Figure. Comparisons of In-School Disease Surveillance Methods

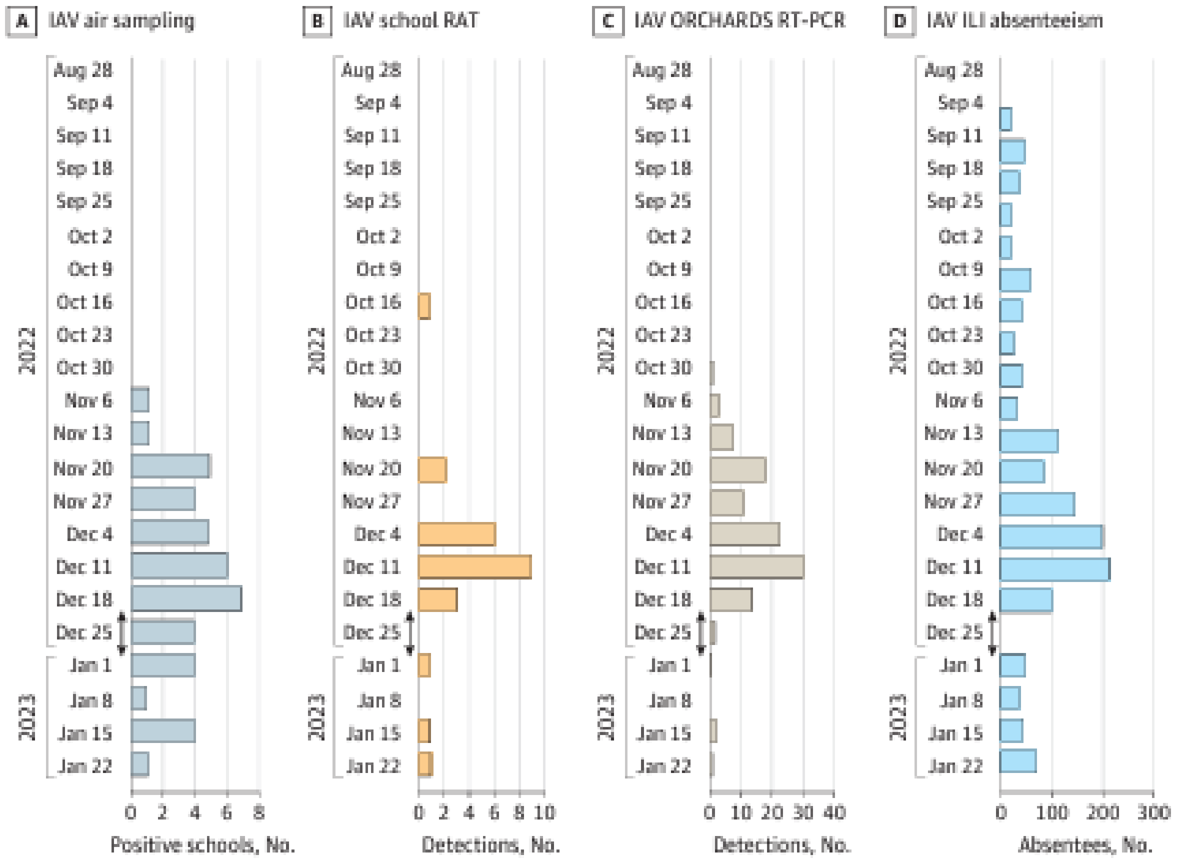
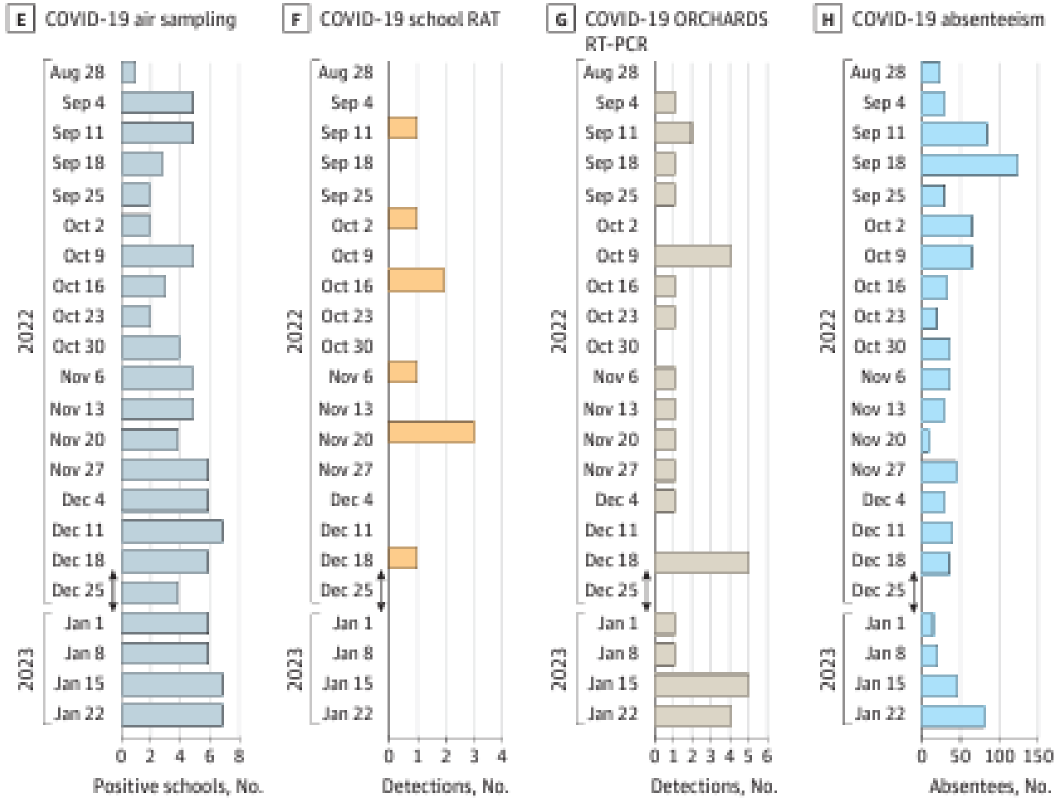


**Table. Comparisons of Surveillance Platforms Showing Maximal Cross-Correlations With Associated Lags for Influenza A Virus and SARS-CoV-2 Detections per Week in the Oregon School District, Dane County, Wisconsin, Between September 1, 2022, and January 28, 2023**

| Surveillance platform | Cross-correlations for data series maximal correlation (lag, wk)[a] | | |
|---|---|---|---|
| | Air sampling[b] | RAT | RT-PCR |
| **Influenza A** | | | |
| School-based RAT (n = 200; median [range] age, 15 [5-65] y)[c] | 0.681 (0) | NA | NA |
| ORCHARDS respiratory samples tested by RT-PCR (n = 334; median [range] age, 12 [4-18] y;)[d] | 0.823 (1) | 0.891 (0) | NA |
| Influenza-like illness absenteeism | 0.860 (1) | 0.814 (0) | 0.908 (0) |
| **SARS-CoV-2** | | | |
| School-based RAT[c] | −0.424 (−7) | NA | NA |
| ORCHARDS respiratory samples tested by RT-PCR[d] | 0.494 (0) | 0.503 (−4) | NA |
| COVID-19 absenteeism | −0.625 (2) | 0.446 (9) | 0.319 (0) |

# Influenza - epidemic
# SARS-CoV-2 - endemic

## SARS-CoV-2




Great correlations between a-ILI and:

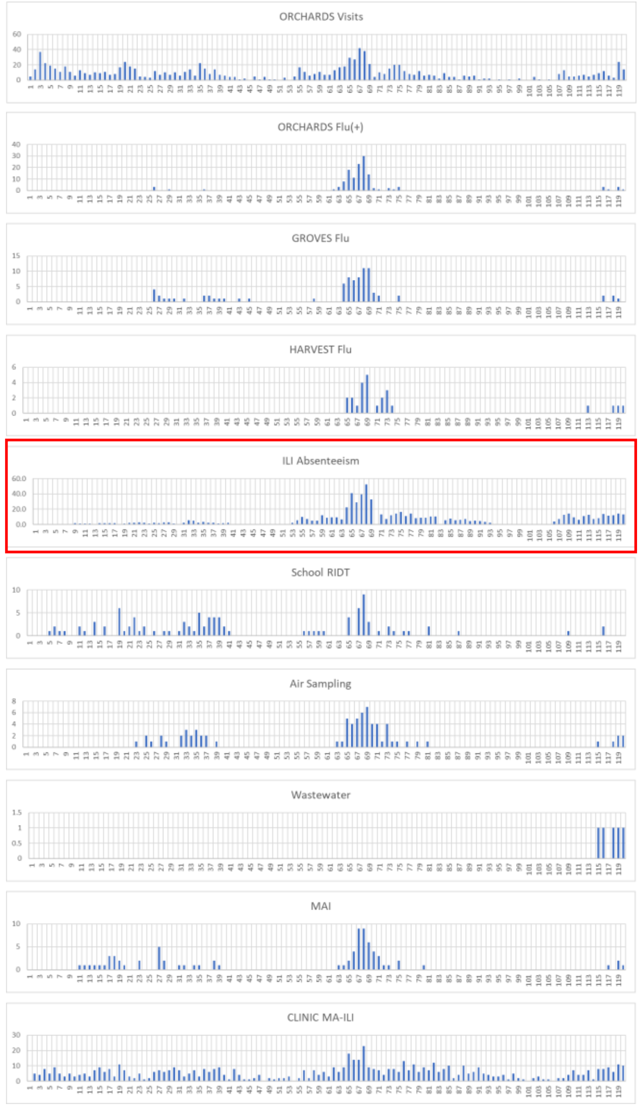
- Air sampling: r = 0.86 (1 week lag)
- Rapid testing in school health office: r = 0.81 (no lead/lag)
- ORCHARDS RT-PCR: r=0.91 (no lead/lag)

No so great correlations between a-CoV and:

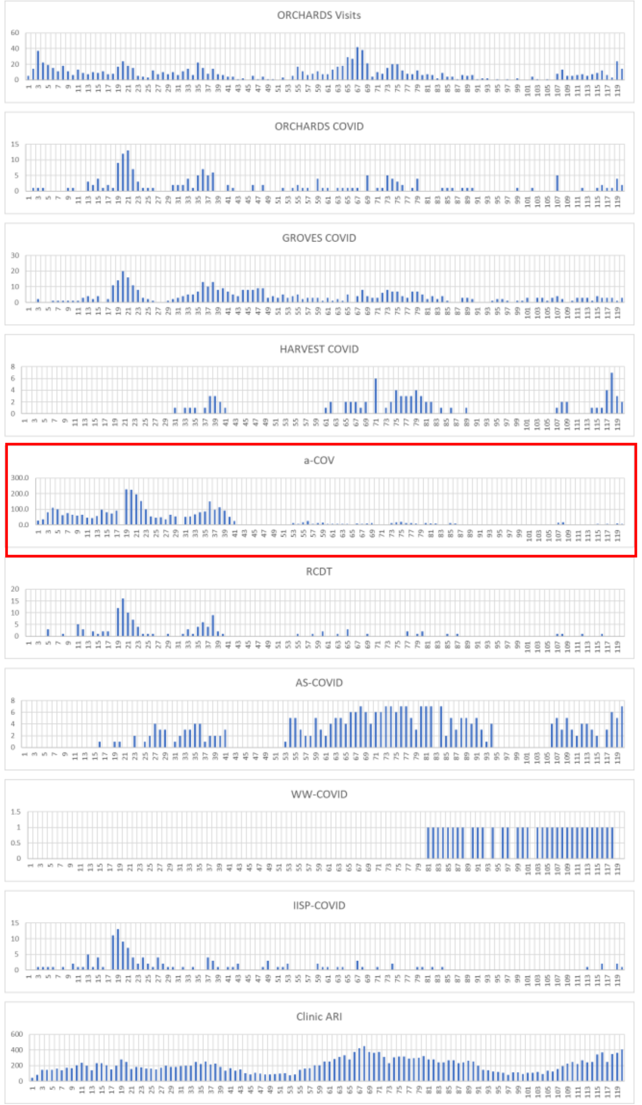
- Air sampling: r = -0.63 (2-week lag)
- Rapid testing in school health office: r = 0.45 (9-week lag)
- ORCHARDS RT-PCR: r=0.32 (no lead/lag)

# Comparability

Influenza




SARS-CoV-2




Comparisons of 10 methods of infectious disease monitoring for influenza and COVID-19

- Oregon School District
- Dane County, WI
- 8/29/2021 - 12/16/2023

See: Temte J, et al. Four Methods for Monitoring SARS-CoV-2 and Influenza A Virus Activity in Schools. JAMA Netw Open. 2023 Dec 1;6(12):e2346329. doi: 10.1001/jamanetworkopen.2023.46329.

# Some final thoughts…

## Big studies in small communities create a great deal of insight

- Connections
- Familiarity
- Intimacy

## Longitudinal approaches are awesome

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

## Partnerships are essential (and fun!)

- Research, primary care, public health, and laboratory science

# ORCHARDS References

Influenza and other respiratory viruses | Open Access | isirv

SHORT COMMUNICATION | Open Access

## Changing pattern of respiratory virus detections among school-aged children in a small community – Dane County, Wisconsin, September to December 2022

Jonathan L. Temte, Maureen Goss, Cristalyne Bell, Shari Barlow, Emily Temte, Allen Bateman, Amra Uzicanin

First published: 28 June 2023 | https://doi.org/10.1111/irv.13171

Case Reports > WMJ. 2021 Oct;120(3):233-236.

## Evidence of Early Household Transmission of SARS-CoV-2 Involving a School-aged Child

Jonathan L Temte [1], Shari Barlow [2], Emily Temte [2], Maureen Goss [2], Kelsey Florek [3], Katarina M Braun [4], Thomas C Friedrich [4], Erik Reisdorf [3], Allen C Bateman [3], Amra Uzicanin [5]

Affiliations + expand

PMID: 34710308 PMCID: PMC8721881

Free PMC article

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## Four Methods for Monitoring SARS-CoV-2 and Influenza A Virus Activity in Schools

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Influenza and other respiratory viruses | Open Access | isirv

SHORT ARTICLE | Open Access

## Sequential, within-season infection with influenza A (H3N2) in a usually healthy vaccinated child

Jonathan L. Temte, Amra Uzicanin, Maureen Goss, Lily Comp, Emily Temte, Shari Barlow, Erik Reisdorf, Peter Shult, Mary Wedig, Kelsey Florek

First published: 26 June 2019 | https://doi.org/10.1111/irv.12668 | Citations: 1

Influenza and other respiratory viruses | Open Access | isirv

SHORT COMMUNICATION | Open Access

## Factors influencing sensitivity of a rapid influenza diagnostic test in a community-based population of kindergarten through 12th-grade students: Wisconsin 2015–2020

Cristalyne Bell, Jennifer Birstler, Maureen D. Goss, Emily Temte, Shari Barlow, Guanhua Chen, Amra Uzicanin, Jonathan Temte

First published: 31 October 2022 | https://doi.org/10.1111/irv.13064

> MMWR Morb Mortal Wkly Rep. 2022 Apr 8;71(14):524-526. doi: 10.15585/mmwr.mm7114a2.

## Notes from the Field: SARS-CoV-2 Omicron Variant Infection in 10 Persons Within 90 Days of Previous SARS-CoV-2 Delta Variant Infection - Four States, October 2021-January 2022

Mellisa Roskosky, Brian F Borah, Peter M DeJonge, Catherine V Donovan, Lynn Zanardi Blevins, Allison G Lafferty, Julia C Pringle, Patsy Kelso, Jonathan L Temte, Emily Temte, Shari Barlow, Maureen Goss, Amra Uzicanin, Allen Bateman, Kelsey Florek, Vance Kawakami, James Lewis, Julie Loughran, Sargis Pogosjans, Meagan Kay, Jeff Duchin, Stephanie Lunn, Hannah Schnitzler, Shivani Arora, Jacqueline Tate, Jessica Ricaldi, Hannah Kirking

PMID: 35389976 PMCID: PMC8989372 DOI: 10.15585/mmwr.mm7114a2

Comparative Study > PLoS One. 2020 Oct 7;15(10):e0239000. doi: 10.1371/journal.pone.0239000. eCollection 2020.

## Comparison of participant-collected nasal and staff-collected oropharyngeal specimens for human ribonuclease P detection with RT-PCR during a community-based study

Mitchell T Arnold [1], Jonathan L Temte [1], Shari K Barlow [1], Cristalyne J Bell [1], Maureen D Goss [1], Emily G Temte [1], Mary M Checovich [1], Erik Reisdorf [2], Samantha Scott [2], Kyley Guenther [2], Mary Wedig [2], Peter Shult [2], Amra Uzicanin [3]

Provided to the PMC COVID-19 Collection by Oxford University Press

Clin Infect Dis. 2022 Jun 23 : ciac487. PMCID: PMC9278263
Published online 2022 Jun 23. doi: 10.1093/cid/ciac487 PMID: 35737942

## SARS-CoV-2 co-detection with influenza A and other respiratory viruses among school-aged children and their household members— March 12, 2020, to February 22, 2022, Dane County, Wisconsin

Jonathan L Temte, MD/PhD, Shari Barlow, BA, Emily Temte, BA, Maureen Goss, MPH, Allen Bateman, MPH/PhD, Kelsey Florek, PhD, and Amra Uzicanin, MD/MPH

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RESEARCH ARTICLE

## Cause-specific student absenteeism monitoring in K-12 schools for detection of increased influenza activity in the surrounding community—Dane County, Wisconsin, 2014–2020

Jonathan L. Temte, Shari Barlow, Maureen Goss, Emily Temte, Amber Schemmel, Cristalyne Bell, Erik Reisdorf, Peter Shult, Mary Wedig, Thomas Haupt, James H. Conway, Ronald Gangnon, Amra Uzicanin

Published: April 19, 2022 • https://doi.org/10.1371/journal.pone.0267111 See the preprint

Influenza and other respiratory viruses | Open Access | isirv

ORIGINAL ARTICLE | Open Access

## The Oregon Child Absenteeism Due to Respiratory Disease Study (ORCHARDS): Rationale, objectives, and design

Jonathan L. Temte, Shari Barlow, Maureen Goss, Emily Temte, Cristalyne Bell, Cecilia He, Caroline Hamer, Amber Schemmel, Bradley Maerz, Lily Comp, Mitchell Arnold ... See all authors

First published: 08 October 2021 | https://doi.org/10.1111/irv.12920 | Citations: 5

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**Funding information:** Centers for Disease Control and Prevention, Grant/Award Number: 5U01CK000542-02-00

ORCHARDS
Oregon CHild Absenteeism due to Respiratory Disease Study

*we combine primary care clinical medicine,*
*advanced molecular laboratory science,*
*innovative technology,*
*community connections,*
*and public health practice*
*to create information that transforms care*


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