Before and After: The Impact of the COVID-19 Pandemic on Influenza-like Illness in PAIVED

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Background

In early March 2020, influenza activity in the United States dropped precipitously and remained lower than typical for the rest of the 2019-20 and the 2020-21 influenza seasons[1]. Widespread interventions aimed at reducing the spread of COVID-19, e.g., social distancing, are thought to have led to these low influenza rates. However, other factors, such as limited access to care and decreased influenza testing, have also been postulated.

PAIVED, the Pragmatic Assessment of Influenza Vaccine Effectiveness in the Department of Defense (DoD), is a multicenter study assessing influenza vaccine effectiveness in active duty service members, retirees, and dependents[2]. Recently completing its third year, PAIVED offers a unique opportunity to examine influenza-like illness (ILI) trends before and during the COVID-19 pandemic in a well-defined cohort prospectively followed for ILI.

Methods

Objective
Describe ILI trends among DoD beneficiaries enrolled in PAIVED during the 2020-2021 influenza season compared to the previous two influenza seasons.

Study Locations
Annapolis, MD; Bethesda, MD; Portsmouth, VA; Fort Bragg, NC; San Antonio, TX; Fort Hood, TX; San Diego, CA; Tacoma, WA

Participants
- Adults eligible for medical care in DoD
  - Seeking influenza vaccination
  - Able to provide informed consent
- Exclusion criteria
  - Already received/plan to receive live attenuated influenza vaccine that season
  - Unable to receive standard dose influenza vaccine
  - Unable to return for follow up if ILI occurs

Study Procedures
- Randomized (1:1:1) to receive one of the following licensed, quadrivalent inactivated influenza vaccines:
  - Egg-based (*Afluria*®, *Fluarix*®, *FluLaval*®)
  - Cell-culture based (*Flucelvax*®)
  - Recombinant (*Flublok*®)
- Baseline demographic questionnaire
- Weekly surveillance for ILI symptoms (email or text)
  - Exception: recruits presenting to sick-call for ILI

Methods (cont.)

- ILI defined *a priori* as having a cough or sore throat AND
  - Fever/feeling feverish or having chills/night sweats, OR
  - Having muscle/body aches or fatigue

Participants with Confirmed ILI
- Online symptom questionnaire (Flu-PRO) x 7 days
- 2 study visits: in-person or virtual as needed during pandemic (per infection control procedures)
  - Visit 1 (0-14d): interview & nasal swab ± *vital signs (VS) & blood draw (in-person only)*
  - Visit 2 (28 ± 7d): interview ± *VS & blood draw*

Statistical Analysis
- Descriptive statistics exclude those who dropped out prior to completing any ILI surveillance
- Tested for differences in demographics & ILI experience using chi-squared or Kruskal-Wallis tests as appropriate

Results

- 10,656 total PAIVED participants over 3 three seasons (Table 1)
- Mean age: 34±14.8 years at enrollment
- Majority male (70%) and active duty military (75.5%)

Table 1. Self-reported demographics for PAIVED cohort at enrollment, by year of enrollment

	2018-19 (N=1514)	2019-20 (N=5876)	2020-21 (N=3266)
Age			
Mean (SD)	36.5 (19.3)	33.6 (14.6)	33.6 (12.5)
Range	18.0 - 87.9	17.9 - 91.6	18.1 - 90.6
Missing (N)	0	29	29
Sex			
Female	409 (27.0%)	1817 (30.9%)	1034 (31.7%)
Male	1105 (73.0%)	4058 (69.1%)	2221 (68.0%)
Not reported	0 (0.0%)	1 (0.0%)	11 (0.3%)
Race/ethnicity			
Asian	71 (4.7%)	363 (6.2%)	256 (7.8%)
Black	132 (8.7%)	666 (11.3%)	374 (11.5%)
Hispanic	429 (28.3%)	1114 (19.0%)	599 (18.3%)
Multiple races	54 (3.6%)	213 (3.6%)	134 (4.1%)
Unknown/Other	15 (1.0%)	59 (1.0%)	69 (2.1%)
White	813 (53.7%)	3461 (58.9%)	1834 (56.2%)
Military status			
Active duty	881 (58.2%)	4465 (76.0%)	2701 (82.7%)
Dependent	327 (21.6%)	696 (11.8%)	230 (7.0%)
Retiree	306 (20.2%)	715 (12.2%)	318 (9.7%)
Missing	0 (0.0%)	0 (0.0%)	17 (0.5%)
Education level			
High school	841 (55.5%)	2769 (47.1%)	1297 (39.7%)
Associate's degree	209 (13.8%)	861 (14.7%)	471 (14.4%)
Bachelor's degree	210 (13.9%)	1006 (17.1%)	646 (19.8%)
Higher degree	253 (16.7%)	1219 (20.7%)	838 (25.7%)
Missing	1 (0.1%)	21 (0.4%)	14 (0.4%)

Results (cont.)

ILI Surveillance
- 2268 participants reported a total of 2673 unique ILIs
  - 2018-19: 19.7% participants with at least 1 ILI
  - 2019-20: 28.2%
  - 2020-21: 9.6%

Table 2: Key characteristics of participants who reported ILI, by season

	2018-19 (N=298)	2019-20 (N=1656)	2020-21 (N=314)
Age			
Mean (SD)	34.5 (18.2)	34.2 (13.5)	34.8 (11.8)
Range	18.0 - 84.9	17.9 - 85.3	18.3 - 78.0
Male	218 (73.2%)	973 (58.8%)	178 (56.7%)
Race			
Asian	10 (3.4%)	115 (6.9%)	22 (7.0%)
Black	27 (9.1%)	186 (11.2%)	36 (11.5%)
Hispanic	91 (30.5%)	298 (18.0%)	64 (20.4%)
Multiple races	18 (6.0%)	67 (4.0%)	18 (5.7%)
Unknown/Other	2 (0.7%)	16 (1.0%)	8 (2.5%)
White	150 (50.3%)	974 (58.8%)	166 (52.9%)
Military status			
Active duty	188 (63.1%)	1241 (88.7%)	247 (78.7%)
Dependent	56 (18.8%)	220 (13.3%)	35 (11.1%)
Retired military	54 (18.1%)	195 (11.8%)	32 (10.2%)

Figure 1. Percentage of PAIVED participants reporting ILI by week of year, according to ILI season
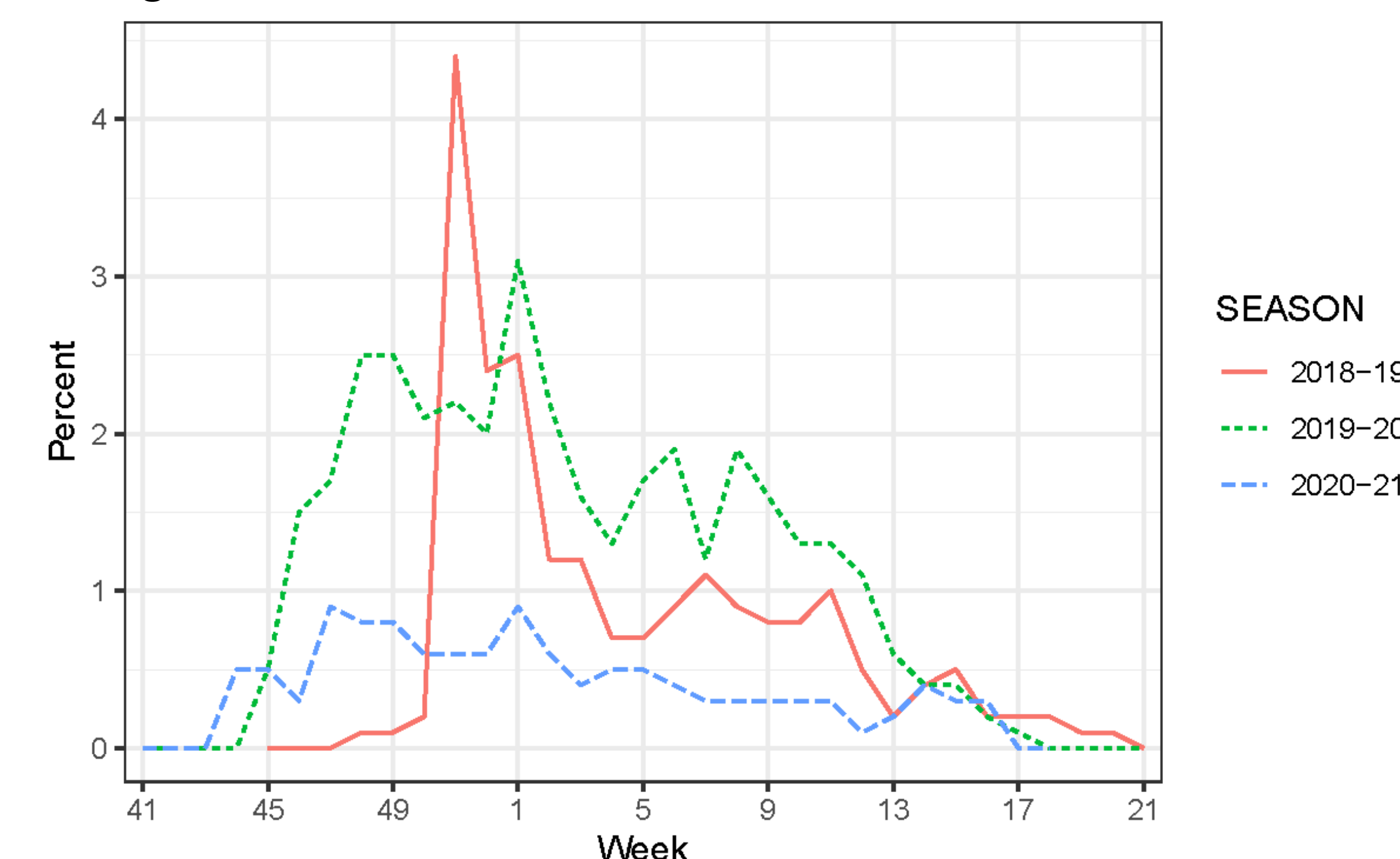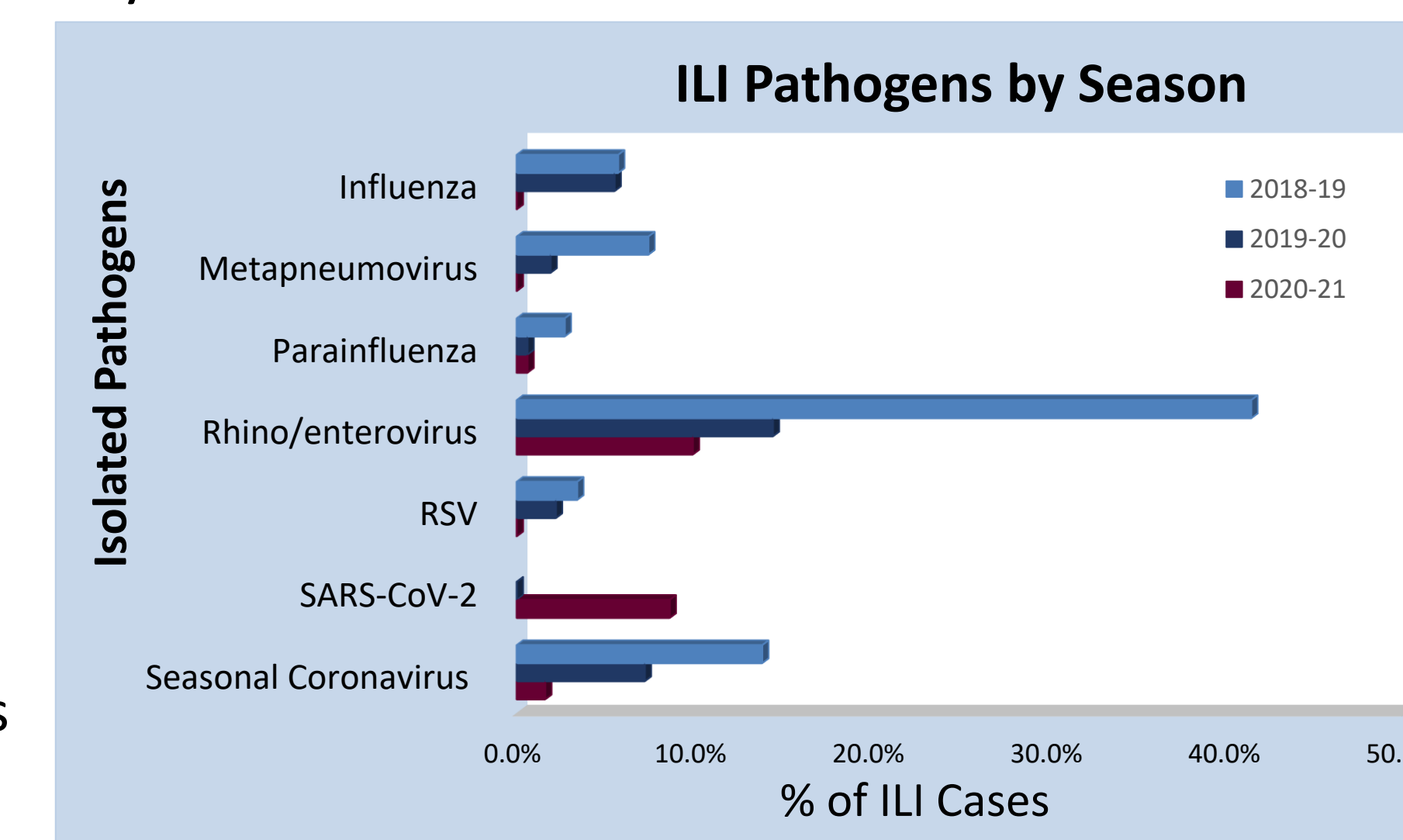

Figure 2. Distribution of pathogens isolated in participants meeting ILI criteria, categorized by season

- Nasal sample collected in 73% cases overall
  - 2018-19: 95%
  - 2019-20: 69%
  - 2020-21: 71%
- No pathogen isolated in majority of cases

ILI Pathogens by Season

Results (cont.)

Figure 3. Timing of pathogen isolation by week of year, categorized by ILI season
   a. Influenza
   b. Rhinovirus/enterovirus
   c. Seasonal coronavirus
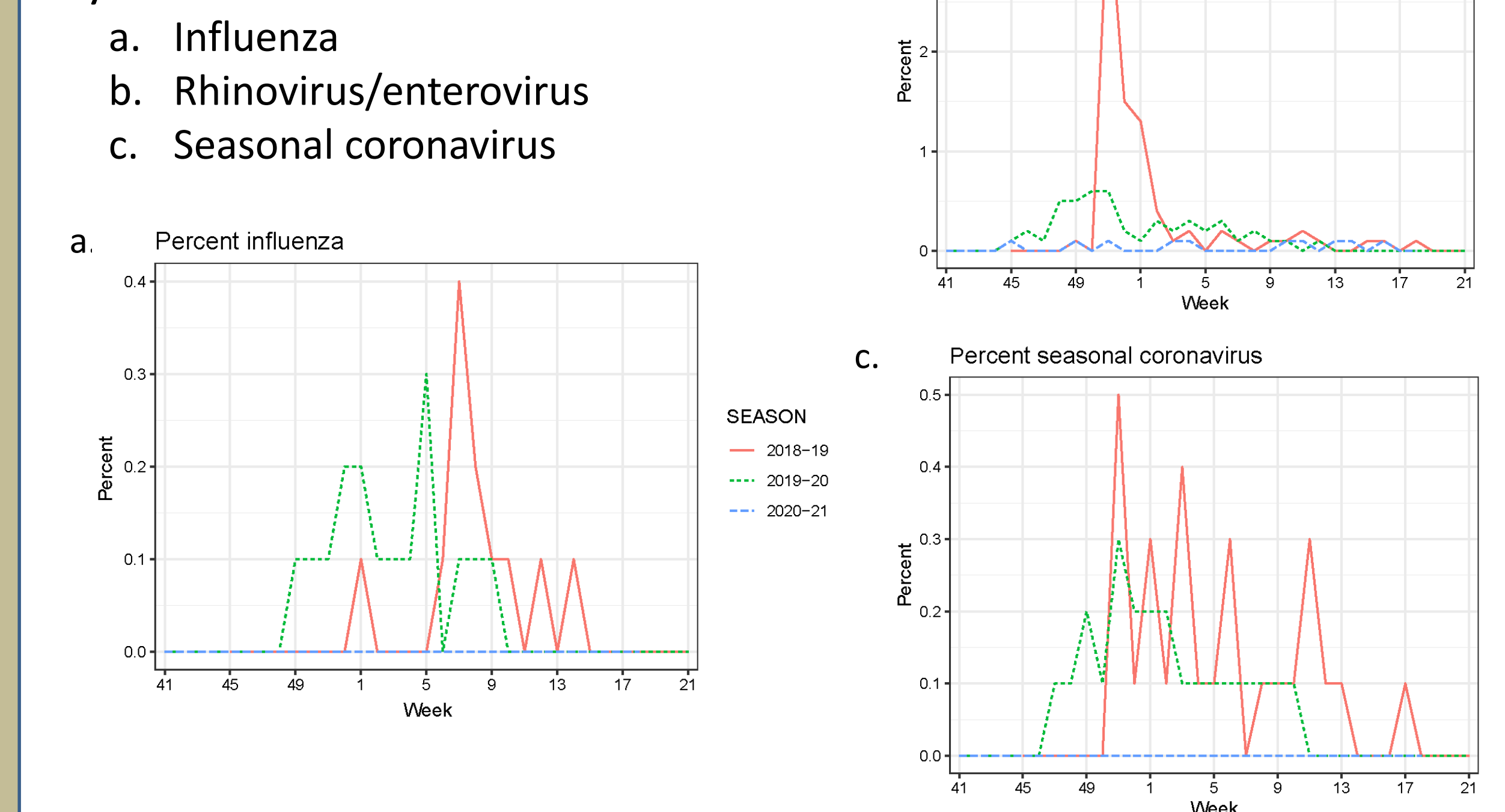
Conclusions

The low incidence of reported ILI, and lack of any detected influenza, in PAIVED participants undergoing active surveillance during the COVID-19 pandemic is consistent with national influenza and ILI surveillance reports. These findings suggest that mitigation measures to reduce transmission of SARS-CoV-2 decreased the spread of other respiratory viruses, notably influenza, RSV, and seasonal coronaviruses. Continued evaluation of ILI trends in 2021-22, as the pandemic and associated societal behaviors evolve, may help inform future ILI prevention strategies.

References

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Disclaimers

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