

Interactions between respiratory viruses in US adults and children: A prospective cohort study



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Background

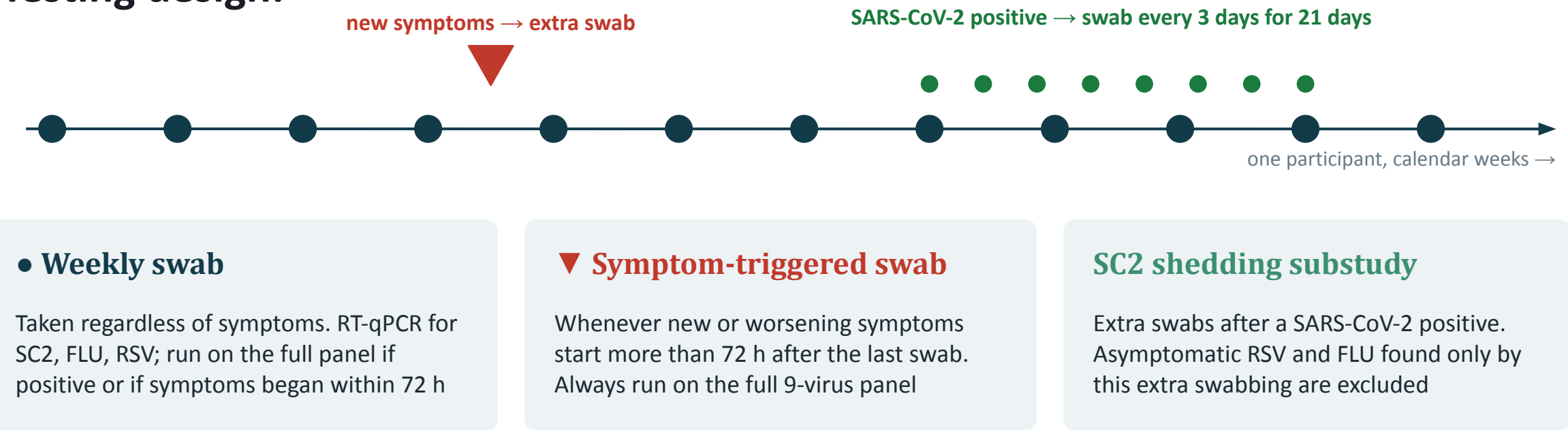
- Multiple respiratory viruses co-circulate each season; infection with one may transiently alter susceptibility to another (virus–virus interaction), e.g., through an innate interferon response (viral interference).
- Human evidence comes mostly from clinically indicated testing: it misses mild and asymptomatic infections, lacks an unexposed comparator, and usually studies one virus pair in one direction.

Objective: estimate the risk of symptomatic infection (illness) with each of 9 viruses after recent illness with another, in a prospective cohort of adults and children with weekly testing. *Secondary:* include asymptomatic infections and age-stratified results.

Methods

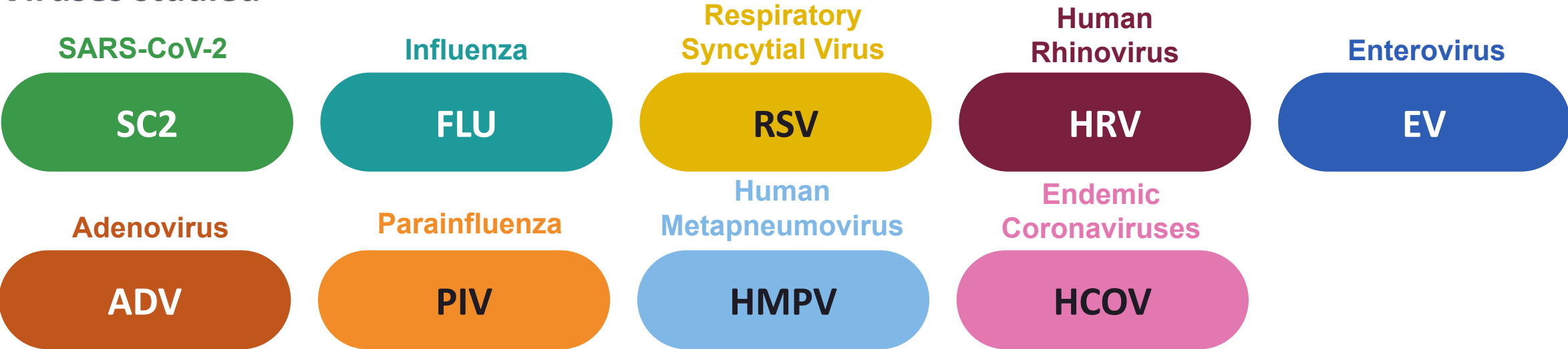
CASCADIA: community-based prospective household cohort, ages 6 mo–49 y, Washington and Oregon, June 2022 – March 2024.

Testing design:



Illness = symptomatic detection (all 9 viruses); **infection** = symptomatic or asymptomatic detection (SARS-CoV-2, RSV, influenza only). An episode ends after 14 detection-free days.

Viruses studied



Exposure: indicator of prior symptomatic infection (illness) with each virus within the past ____ days

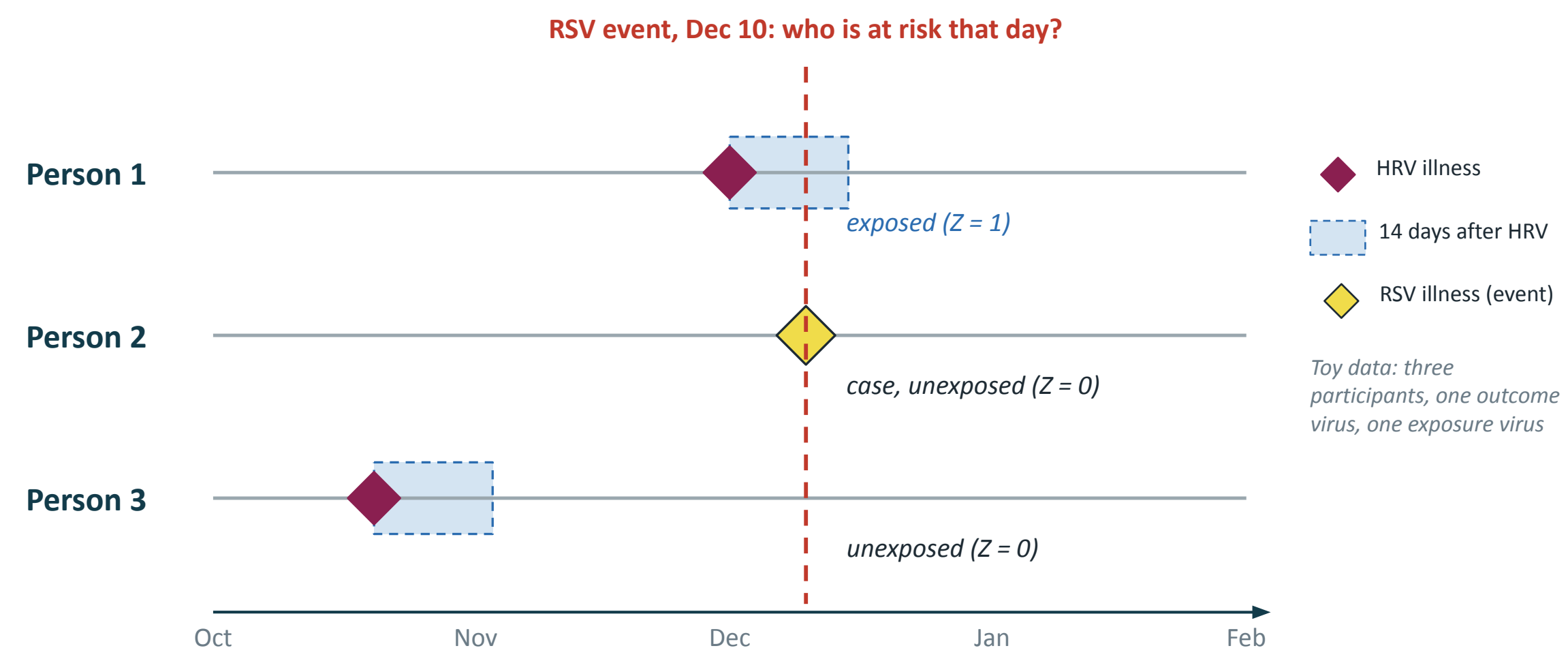


Short term (≤ 14 days) · Longer term (15–180 days) · Referent: no illness in prior 180 days

Cox models, one per outcome virus; calendar time scale (absorbs seasonality); left-truncated for delayed entry via enrollment; all 8 other viruses $\times$ 6 windows entered simultaneously.

Adjusted for age, sex, geographic region, household size, number of children in household, daycare/school/work. Household-clustered robust SEs; Benjamini–Hochberg False Discovery Rate controlled at 5% within each model.

Secondary analyses: infections instead of illnesses for SC2/FLU/RSV; exploratory age interactions; 21-/28-day episode definitions; full 180-day history.



Cohort & surveillance

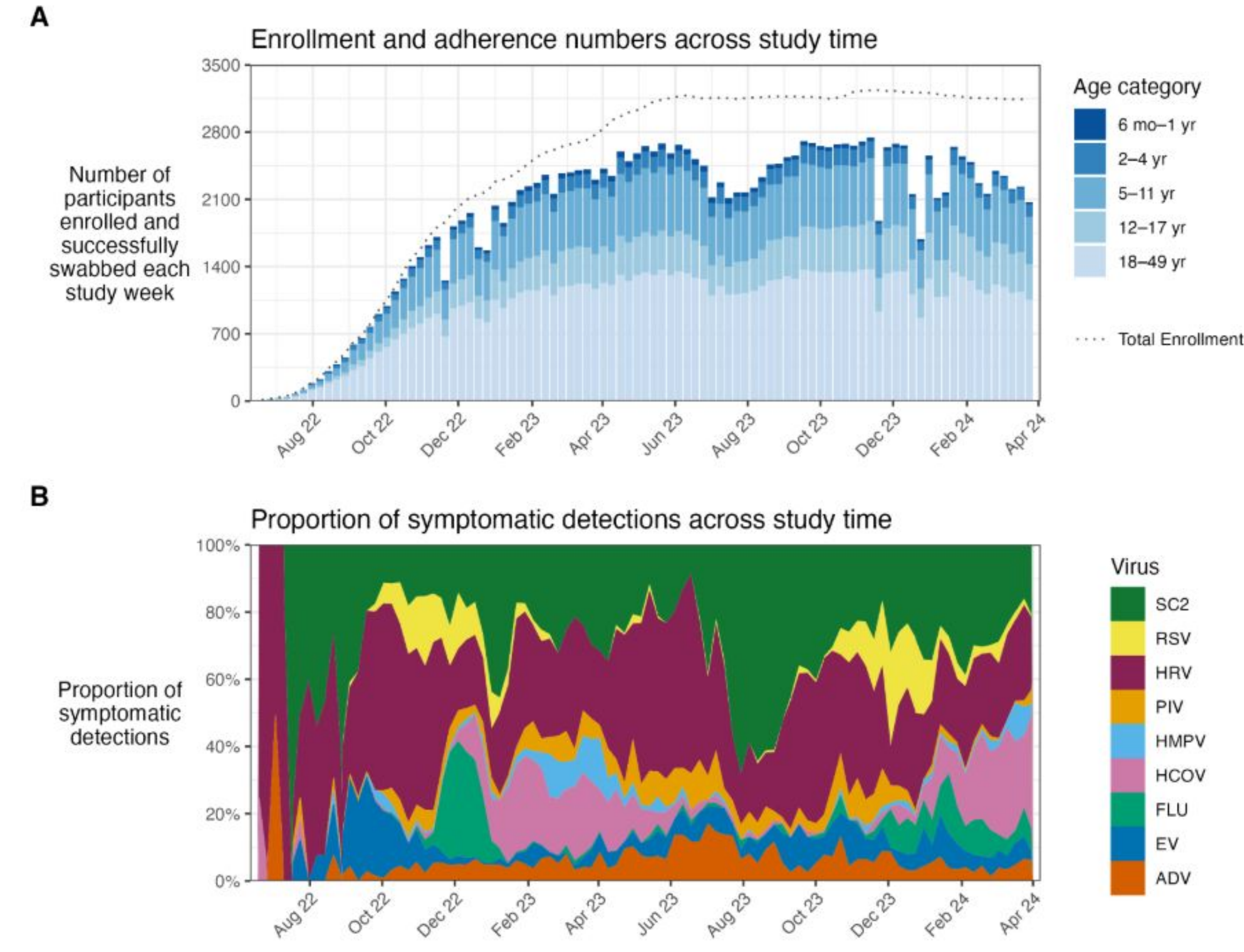
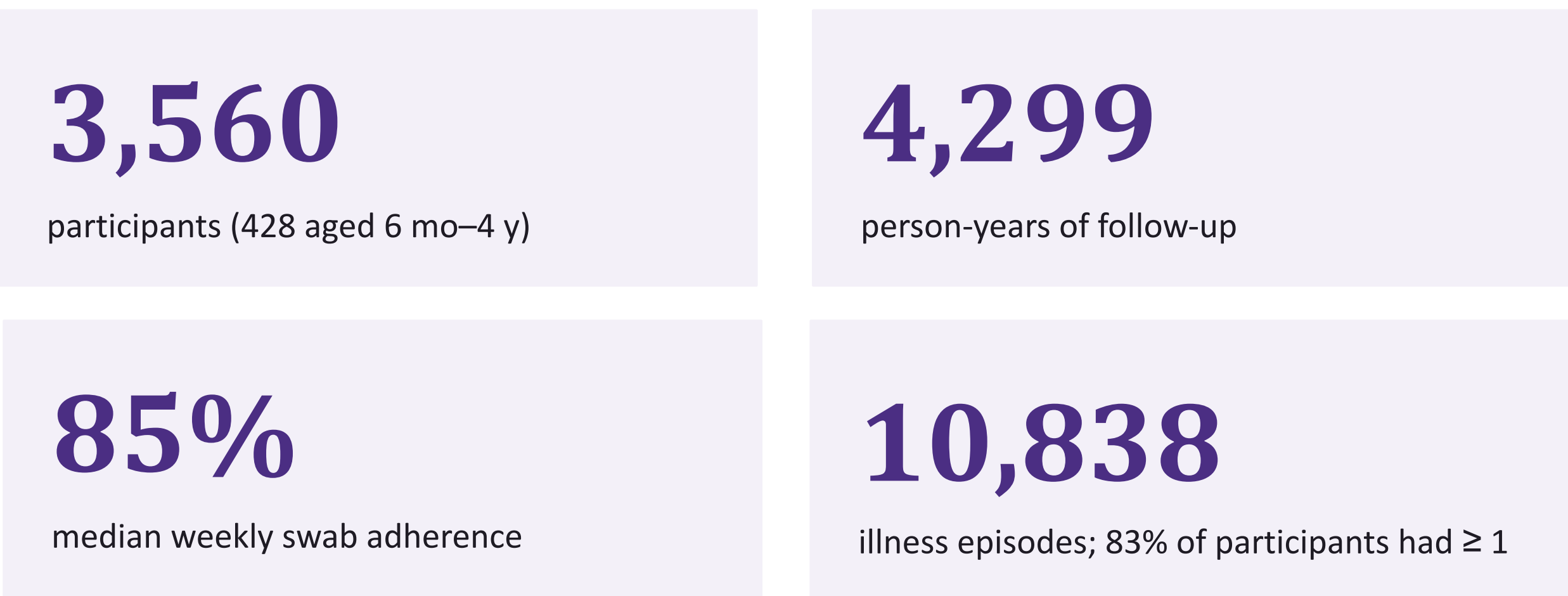


Figure 1. Swab adherence and seasonality of symptomatic detections, June 2022 – March 2024.

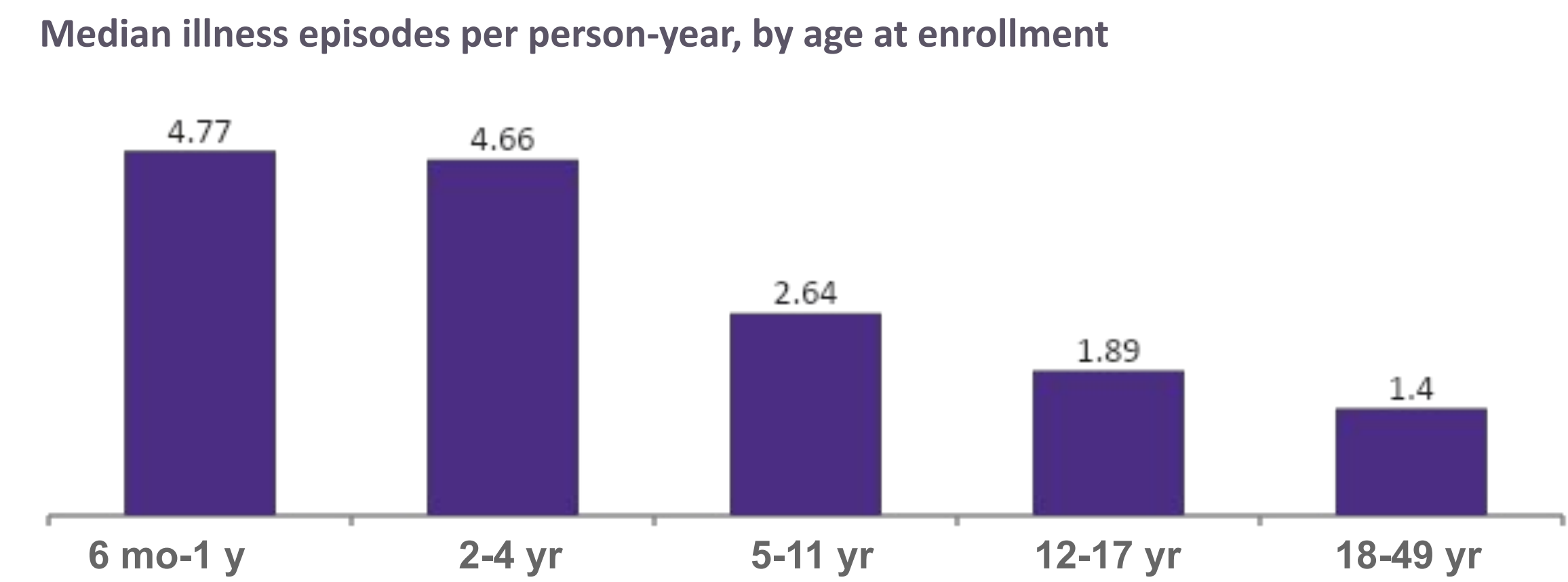


Figure 2. Number of illnesses per year of follow-up by age group. 83% of participants had ≥ 1 illness; young children $\sim 3\times$ the adult rate.

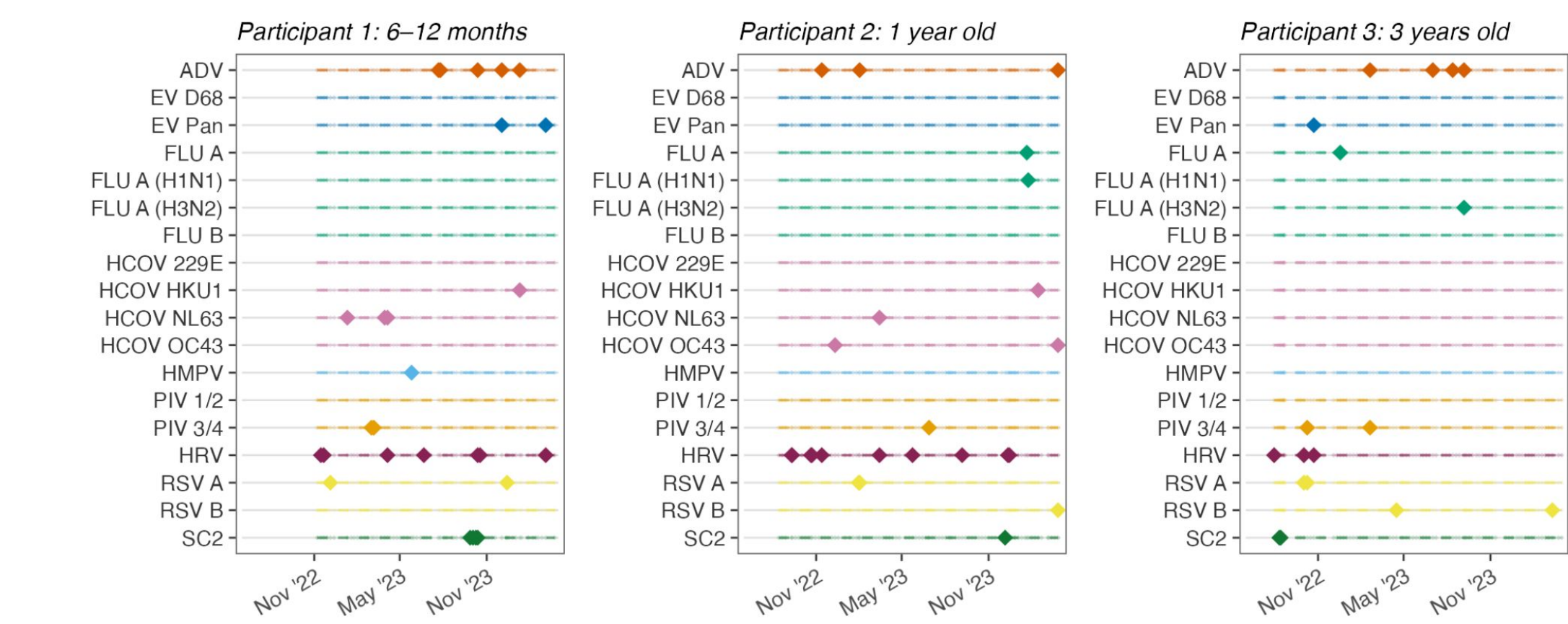


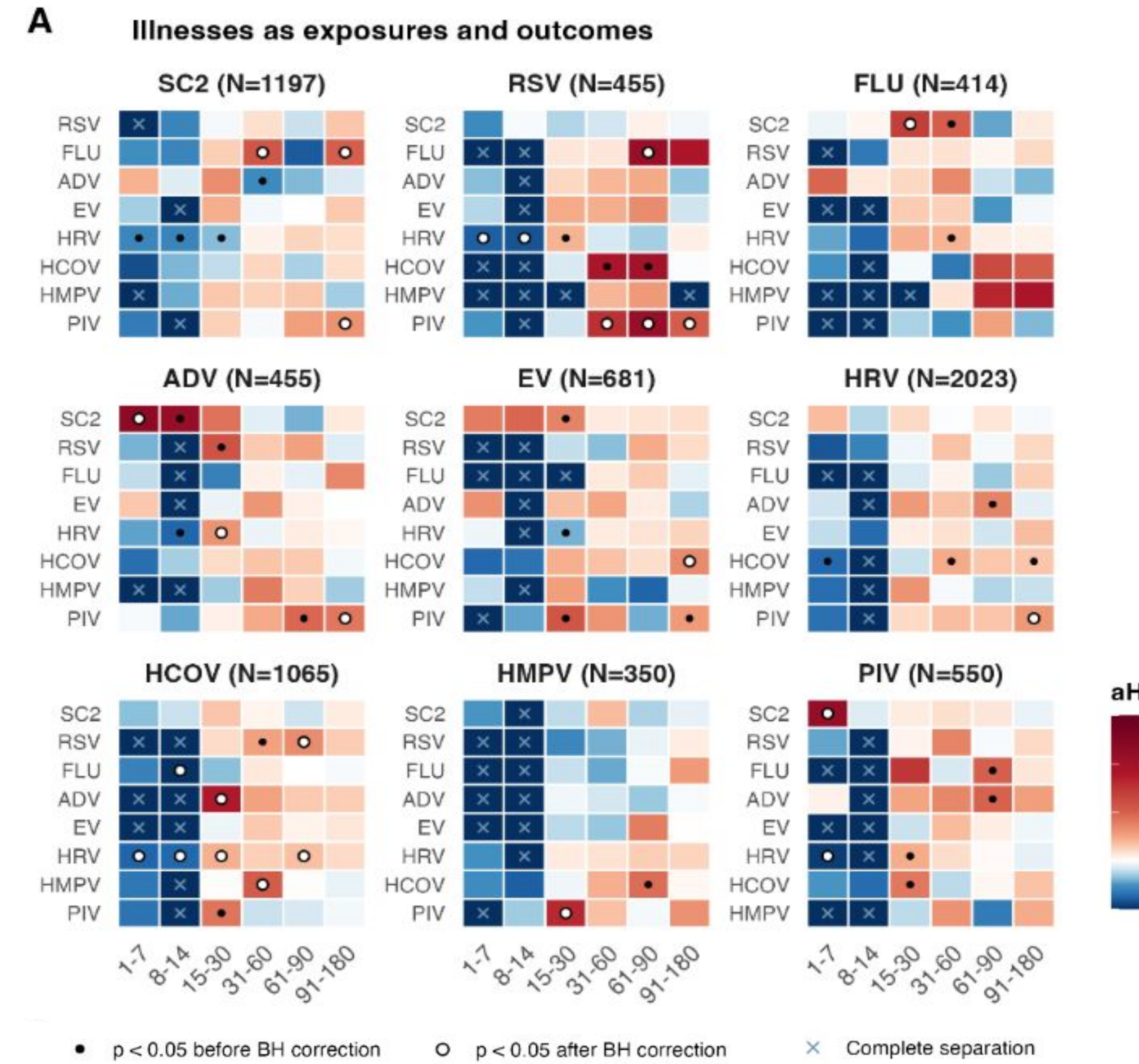
Figure 3. Young children often tested positive for many viruses in overlapping intervals.

A descriptive analysis of secondary pathogens

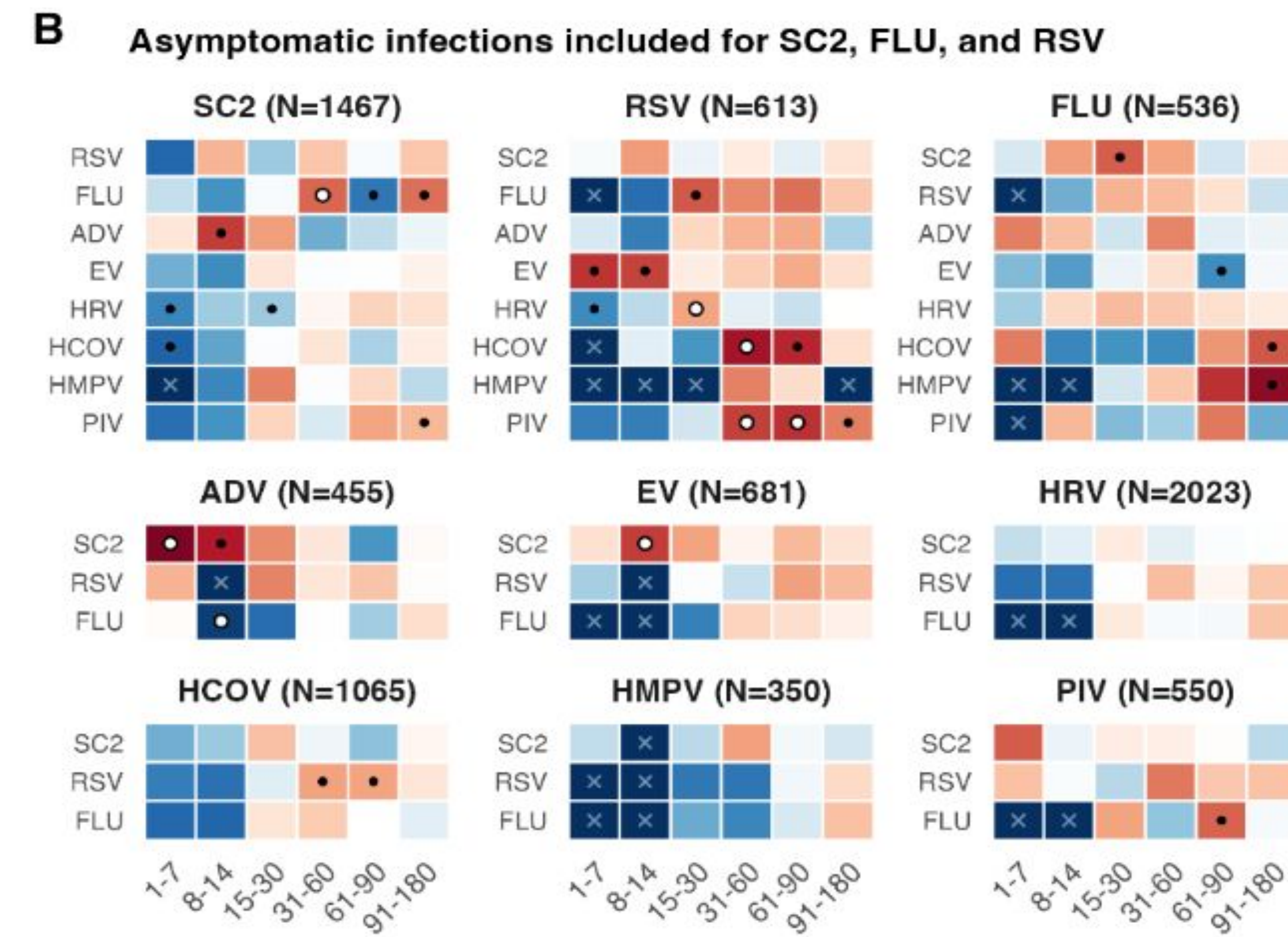
		Secondary pathogen detected within 180 days, n (%)									
		N	SC2	FLU	RSV	HCOV	ADV	HMPV	PIV	HRV	EV
Primary and secondary illnesses											
SC2	1375	60 (4.4%)	62 (4.5%)	44 (3.2%)	172 (12.5%)	87 (6.3%)	39 (2.8%)	75 (5.5%)	422 (30.7%)	127 (9.2%)	
FLU	468	71 (15.2%)	25 (5.3%)	16 (3.4%)	92 (19.7%)	36 (7.7%)	33 (7.1%)	37 (7.9%)	144 (30.8%)	23 (4.9%)	
RSV	497	59 (11.9%)	30 (6.0%)	17 (3.4%)	143 (28.8%)	60 (12.1%)	38 (7.6%)	54 (10.9%)	207 (41.6%)	43 (8.7%)	
HCOV	1339	129 (9.6%)	15 (1.1%)	20 (1.5%)	114 (8.5%)	115 (8.6%)	78 (5.8%)	110 (8.2%)	417 (31.1%)	96 (7.2%)	
ADV	758	75 (9.9%)	31 (4.1%)	55 (7.3%)	140 (18.5%)	231 (30.5%)	35 (4.6%)	122 (16.1%)	359 (47.4%)	103 (13.6%)	
HMPV	364	36 (9.9%)	10 (2.7%)	5 (1.4%)	42 (11.5%)	32 (8.8%)	2 (0.5%)	33 (9.1%)	128 (35.2%)	22 (6.0%)	
PIV	663	100 (15.1%)	18 (2.7%)	54 (8.1%)	101 (15.2%)	115 (17.3%)	43 (6.5%)	56 (8.4%)	311 (46.9%)	86 (13.0%)	
HRV	4454	551 (12.4%)	215 (4.8%)	273 (6.1%)	776 (17.4%)	462 (10.4%)	231 (5.2%)	413 (9.3%)	1767 (39.7%)	424 (9.5%)	
EV	920	120 (13.0%)	46 (5.0%)	86 (9.3%)	161 (17.5%)	100 (10.9%)	46 (5.0%)	78 (8.5%)	346 (37.6%)	89 (9.7%)	
Primary and secondary infections for SC2, FLU, and RSV											
SC2*	1762	107 (6.1%)*	101 (5.7%)*	102 (5.8%)*	209 (11.9%)*	108 (6.1%)	54 (3.1%)	86 (4.9%)	521 (29.6%)*	154 (8.7%)	
FLU*	652	114 (17.5%)*	74 (11.3%)*	35 (5.4%)*	132 (20.2%)*	44 (6.7%)	39 (6.0%)	45 (6.9%)	205 (31.4%)*	35 (5.4%)	
RSV*	691	102 (14.8%)*	61 (8.8%)*	26 (3.8%)*	176 (25.5%)*	77 (11.1%)	46 (6.7%)	71 (10.3%)	268 (38.8%)*	69 (10.0%)	

Table 1. Breakdown of secondary illnesses and infections, conditional on a primary illness or infection.

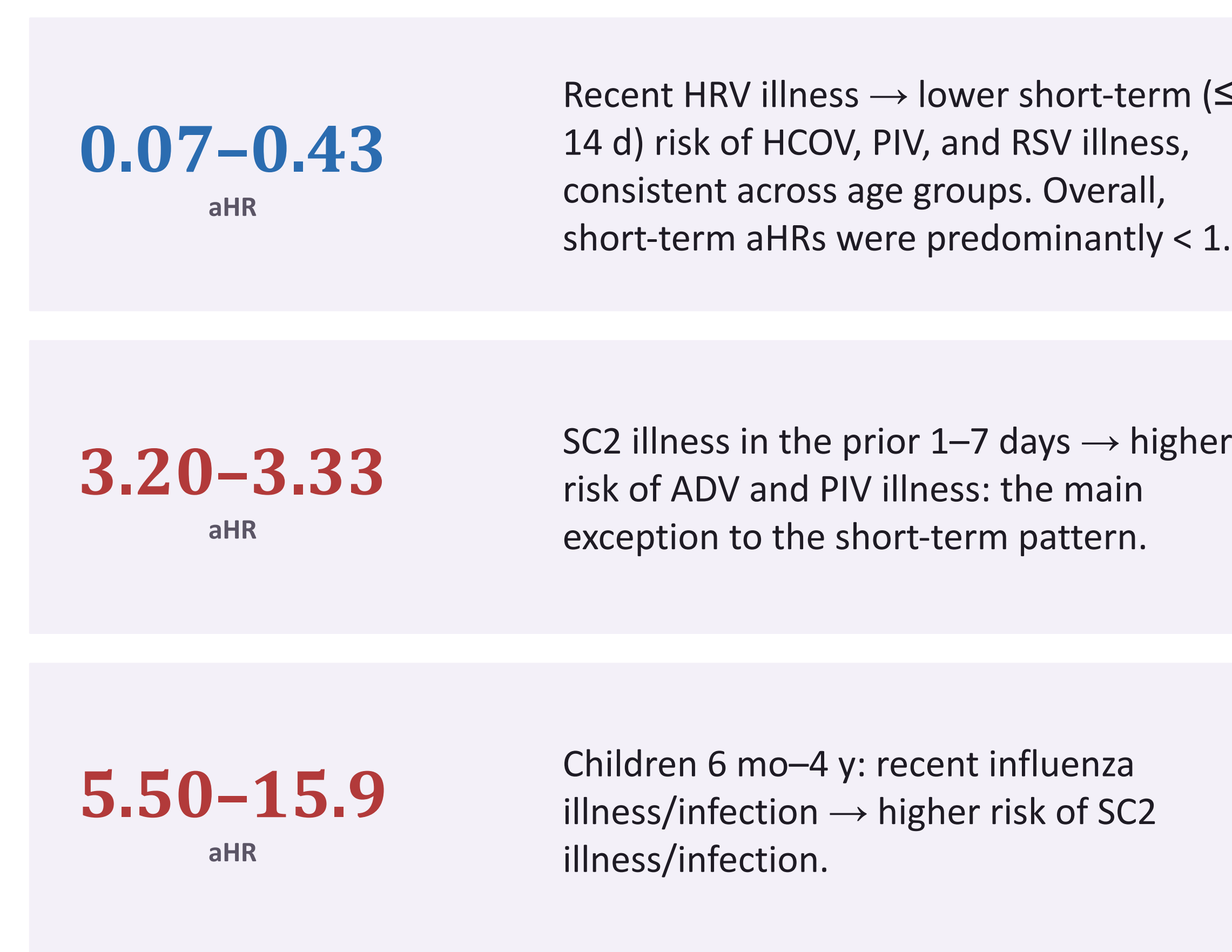
Recent illness, subsequent risk: adjusted hazard ratios



Including asymptomatic infections



Key findings



Discussion

- The risk of a viral illness tends to be lower for those with vs without a recent different viral illness, most strongly after rhinovirus.
 - Exception: higher risk after SARS-CoV-2 illness or infection, but participants also reported new and worsening symptoms at higher rates.
- Differential risk patterns may exist for children; biologically plausible because of their less mature immune system.
- Including asymptomatic infections attenuated associations, suggesting there may be an inflammatory response threshold for protection, and/or symptoms of a secondary infection are masked by the first.
- Limitations: (1) Post-illness behavior (staying home, masking) and residual confounding, (2) Detection times are not infection times, (3) Asymptomatic data for 3 of 9 viruses only, (4) Complete separation: many short-window aHRs not estimable, (5) First event per outcome only, (6) Mostly higher-income Pacific Northwest households; no adults ≥ 50 .