

Adapting COVID-19 research infrastructure to capture influenza and respiratory syncytial virus alongside SARS-CoV-2 in UK healthcare workers winter 2022/23: Results of a pilot study in the SIREN cohort

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NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.

ABSTRACT

Introduction

The combination of patient illness and staff absence driven by seasonal viruses culminates in annual “winter pressures” on UK healthcare systems and has been exacerbated by COVID-19. In winter 2022/23 we ran a pilot study aiming to introduce multiplex testing to determine the incidence and burden of SARS-CoV-2, influenza and respiratory syncytial virus (RSV) in our cohort of UK healthcare workers (HCWs).

Methods

The pilot study was conducted from 28/11/2022-31/03/2023 within the SIREN prospective cohort study. Participants completed fortnightly questionnaires, capturing symptoms and sick leave, and multiplex PCR testing for SARS-CoV-2, influenza and RSV, regardless of symptoms. PCR-positivity rates by virus were calculated over time, and viruses were compared by symptoms and severity. Self-reported symptoms and associated sick leave were described. Sick leave rates were compared by vaccination status and demographics.

Results

5,863 participants were included, 84.6% female, 70.3% ≥45-years, and 33.4% were nurses. PCR-positivity peaked in early December for all three viruses (4.6 positives per 100 tests (95%CI 3.5, 5.7) SARS-CoV-2, 3.9 (95%CI 2.2, 5.6) influenza, 1.4 (95%CI 0.4, 2.4) RSV), declining to <0.3/100 tests after January for influenza/RSV, and around 2.5/100 tests for SARS-CoV-2. Over one-third of all infections were asymptomatic, and symptoms were similar for all viruses. 1,368 (23.3%) participants reported taking sick leave, median 4 days (range 1-59). Rates of sick leave were higher in participants with co-morbidities, working in clinical settings, and who had not been vaccinated (COVID-19 booster or seasonal influenza vaccine) versus those who had received neither vaccine (2.04 vs 1.41 sick days/100 days, adjusted Incidence Rate Ratio 1.47 (95%CI 1.38, 1.56).

Conclusion

This pilot demonstrated the use of multiplex testing allowed better understanding of the impact of seasonal respiratory viruses and respective vaccines on the HCW workforce. This highlights the important information on asymptomatic infection and persisting levels of SARS-CoV-2 infection.

INTRODUCTION

UK healthcare systems experience significant challenges each winter, due to the impact of seasonal surges in respiratory viruses, including influenza and respiratory syncytial virus (RSV), which combined are often described as “winter pressures” (1, 2). Respiratory illness increases patient attendance but also causes significant staff absence, with respiratory illness the second most common cause of sick leave within the NHS (3). Reduction in staff sickness absence and preventing nosocomial transmission are the rationale for the annual NHS winter flu vaccine campaign for healthcare workers (HCW) and the prioritisation of HCW for COVID-19 vaccine boosters (4, 5).

As a result of the pandemic, COVID-19 has been well characterised in relation to key scientific and clinical questions including the role of antibodies as correlates of protection, rates of asymptomatic disease and real-world vaccine effectiveness (6-11). However, this is not the case for the other principle seasonal viruses, influenza and RSV, where the focus has been on symptomatic disease and in populations most at risk, including children and the elderly (12, 13). HCWs are an important population to study given the impact of respiratory illnesses on the workforce and their high exposure (14, 15), offering insights into the natural history, epidemiology and burden of influenza and RSV in working aged populations.

The SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study is a prospective cohort study of HCWs across the UK, with participants completing regular SARS-CoV-2 PCR testing and antibody testing continuously since June 2020 (16). It was set up at the start of the pandemic to assess the risk of re-infection with SARS-CoV-2 and has continued to adapt to address key scientific questions.

During the COVID-19 pandemic, the introduction of non-pharmaceutical measures, including universal masking and social distancing, was found to reduce the rates of other respiratory viruses (4, 17). However, following the removal of these interventions, the winter of 2022/23 was the first opportunity to understand the impact of circulating seasonal viruses on the NHS

workforce. Therefore, in winter 2022/23 the SIREN study piloted a “Winter Pressures sub-study” that included multiplex PCR testing for influenza and RSV alongside SARS-CoV-2 (18).

This paper outlines the results of the SIREN Winter Pressures Pilot study 2022/23, with the aim of a) describing the burden of influenza (A and B), RSV, and SARS-CoV-2, b) characterisation of SIREN HCW symptom profile, and c) understanding time off work due to being symptomatic in the context of HCW vaccination.

METHODS

Study design

The SIREN Winter Pressures sub-study is a prospective cohort study nested within the SIREN UK multicentre HCW cohort study (16, 18).

Participants

Participants were recruited into the sub-study via two routes: 1) participants previously completing monoplex testing (for SARS-CoV-2 only) were informed, in writing, before the sub-study start date (28 November 2022) that testing would move to multiplex testing (SARS-CoV-2, Influenza and RSV), and were given the opportunity to withdraw from the study; 2) additional participants were re-recruited (from participants who were not currently testing) and consented directly into the winter pressures postal testing pathway, between 13 December 2022 and 24 January 2023 (18).

Participants undergoing PCR testing between 28 November 2022 and 31 March 2023 were included in the sub-study. Participants contributed different lengths of time to the analysis period, due to completing study follow-up time or withdrawing from the study.

Data collection

Participants completed fortnightly questionnaires on symptoms (onset date, type and duration) and related time taken-off work due to reported symptoms, in addition to an enrolment survey at the start of the SIREN study, detailing the participant's demographics, occupation, underlying medical conditions and household composition. Vaccination data (COVID-19 and seasonal influenza vaccination) was obtained both from the fortnightly questionnaire and linkage to national vaccination registries.

Participants completed swabs for either multiplex PCR (SARS-CoV-2, influenza and where available RSV) or monoplex PCR (SARS-CoV-2 only), fortnightly regardless of symptoms. PCR testing, symptoms and sociodemographic data were linked via a unique study ID.

Variables

We defined participants who reported at least one of any of the following symptoms as being symptomatic: cough, fever, shortness of breath, sore throat, runny nose, headache, muscle aches, altered sense of smell or taste, fatigue, diarrhoea, nausea or vomiting, itchy red patches on fingers or toes, rash, swollen glands (19). Influenza-like illness (ILI) was defined as participants reporting fever and at least one of following: cough, sore throat, shortness of breath, headache, muscle ache or fatigue. For this analysis, COVID-19 vaccination refers to receiving the second booster dose of the COVID-19 vaccine, and influenza vaccination refers to receiving the 2022/23 seasonal influenza vaccine between 01 September 2022 and 31 March 2023. Sick leave was defined as any self-reported days off work due to being symptomatic.

Outcomes

The co-primary outcomes were a) a PCR-positive test for either SARS-CoV-2, influenza or RSV; b) proportion of participants reporting ILI symptoms; and c) the number of days taken off work due to being symptomatic.

Inclusion criteria

Participants who completed at least one fortnightly questionnaire and at least one PCR test during the analysis period were included.

Statistical analysis

Participants' sociodemographic and occupational characteristics were described.

Infection rates by pathogen were calculated over time. Samples were initially de-duplicated resulting in one test per fortnight per participant, prioritising a positive sample over a negative sample in the same fortnight. Samples which were positive for multiple viruses were excluded from the analysis. Further de-duplication by infection episode meant that for SARS-CoV-2, participants could only have one positive sample per 90 days. For influenza and RSV, participants could only have one positive sample per 30 days.

For the infection analysis, participants were considered vaccinated if they had received the seasonal vaccine dose at least 14 days before the first positive PCR sample of the infection episode.

An infection was considered symptomatic if the participant had reported a symptom onset date seven days pre or post the date of first positive PCR sample for each infection episode.

The proportion of participants with each infection was summarised by sociodemographic characteristics and vaccination status. Symptom type, number, duration, hospital attendance and time off work were compared by infection and vaccination status (SARS-CoV-2 and influenza only) using proportions.

The proportion of participants reporting ILI symptoms was calculated over time, by dividing the number of surveys where ILI was reported by the total number of surveys in each time period.

Sick leave rate was calculated by fortnight, using the number of days taken off work divided by the number of days participants contributed to the analysis period, per 100 days, with

95% confidence interval. Incidence rate ratio were calculated to estimate demographic factors associated with taking time off work, unadjusted and adjusted (vaccination status, age, occupational setting and co-morbidities).

For sick leave rate by vaccination status, participants contributed days to the vaccinated state (COVID-19 and influenza separately or simultaneously) if they had received the vaccine at least 14 days before the start of the fortnightly survey period. Participants contributed days to the unvaccinated state if they had not received the seasonal dose or had received the dose after the end of the survey period. For participants who received either vaccine within a survey period, or within the 14 days prior to the survey start date, this survey period did not count towards the rate analysis.

RESULTS

A total of 7,774 participants consented to the SIREN Winter Pressures pilot sub-study from 28 November 2022 to 31 March 2023. Of these, 5,863 (75.4%) participants had both survey and testing data and were included in the analysis (Fig 1). Most participants were female (84.6%), of white ethnicity (91.4%), over 45-years of age (70.3%); nursing was the largest staff group (33.4%). Study participants were highly vaccinated, with 74.2% receiving both COVID-19 and the seasonal influenza vaccine (Table 1).

Fig 1: Flow diagram describing participants included in the SIREN Winter Pressures pilot sub-study

Table 1: Demographics of participants included in the analysis, overall and by infection (SARS-CoV-2, Influenza and RSV), 28 November 2022 to 31 March 2023

Characteristic	All participants n (%)	SARS-CoV-2 positive N (%)	Influenza positive n (%)	RSV positive n (%)
Total	5,863	643	91	74
Age group				
Under 25	39 (0.7)	1 (0.2)	1 (1.1)	3 (4.1)
25 to 34	447 (7.6)	56 (8.7)	11 (12.1)	2 (2.7)
35 to 44	1,257 (21.4)	151 (23.5)	24 (26.4)	13 (17.6)
45 to 54	2,280 (38.9)	244 (37.9)	30 (33.0)	36 (48.6)
55 to 64	1,690 (28.8)	173 (26.9)	23 (25.3)	20 (27.0)
Over 65	150 (2.6)	18 (2.8)	2 (2.2)	0 (0.0)
Gender				
Female	4,960 (84.6)	541 (84.1)	67 (73.6)	64 (86.5)
Male	896 (15.3)	101 (15.7)	24 (26.4)	9 (12.2)
Non-binary	4 (0.1)	1 (0.2)	0 (0.0)	1 (1.4)
Prefer not to say	3 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Ethnicity				
White	5,359 (91.4)	594 (92.4)	85 (93.4)	70 (94.6)
Asian	272 (4.6)	30 (4.7)	4 (4.4)	3 (4.1)
Black	94 (1.6)	5 (0.8)	0 (0.0)	0 (0.0)
Mixed Race	70 (1.2)	6 (0.9)	1 (1.1)	1 (1.4)
Other Ethnic Group	52 (0.9)	4 (0.6)	1 (1.1)	0 (0.0)
Prefer not to say	16 (0.3)	4 (0.6)	0 (0.0)	0 (0.0)
Medical condition				
Chronic respiratory conditions	738 (12.6)	75 (11.7)	13 (14.3)	8 (10.8)
Chronic non-respiratory conditions	679 (11.6)	76 (11.8)	8 (8.8)	13 (17.6)
Immunosuppression	128 (2.2)	16 (2.5)	2 (2.2)	1 (1.4)
No medical condition	4,318 (73.6)	476 (74.0)	68 (74.7)	52 (70.3)
Household				
Lives alone	683 (11.6)	82 (12.8)	11 (12.1)	9 (12.2)
Lives with adults	3,010 (51.3)	325 (50.5)	42 (46.2)	30 (40.5)
Lives with children	2,170 (37.0)	236 (36.7)	38 (41.8)	35 (47.3)
Staff type				
Nursing	1,957 (33.4)	221 (34.4)	22 (24.2)	21 (28.4)
Administrative/Executive	1,014 (17.3)	95 (14.8)	14 (15.4)	11 (14.9)
Doctor	670 (11.4)	67 (10.4)	12 (13.2)	14 (18.9)
Healthcare Assistant	360 (6.1)	53 (8.2)	3 (3.3)	2 (2.7)
Healthcare Scientist	279 (4.8)	32 (5.0)	7 (7.7)	5 (6.8)
Student	175 (3.0)	25 (3.9)	3 (3.3)	1 (1.4)
Physiotherapist/Occupational Therapist/SALT	228 (3.9)	33 (5.1)	10 (11.0)	4 (5.4)
Midwife	133 (2.3)	12 (1.9)	3 (3.3)	1 (1.4)
Pharmacist	129 (2.2)	16 (2.5)	3 (3.3)	2 (2.7)
Estates/Porters/Security	113 (1.9)	8 (1.2)	3 (3.3)	1 (1.4)
Other	805 (13.7)	81 (12.6)	11 (12.1)	12 (16.2)
Occupation setting				
Office	1,333 (22.7)	135 (21.0)	26 (28.6)	11 (14.9)
Outpatient	1,213 (20.7)	135 (21.0)	19 (20.9)	18 (24.3)
Inpatient Wards	671 (11.4)	89 (13.8)	9 (9.9)	13 (17.6)
Patient facing (non-clinical)	273 (4.7)	29 (4.5)	2 (2.2)	8 (10.8)
Intensive Care	208 (3.5)	30 (4.7)	4 (4.4)	4 (5.4)
Theatres	152 (2.6)	22 (3.4)	2 (2.2)	5 (6.8)
Ambulance/Emergency Department	108 (1.8)	12 (1.9)	4 (4.4)	2 (2.7)
Maternity/Labour Ward	82 (1.4)	7 (1.1)	1 (1.1)	1 (1.4)
Other	1,823 (31.1)	184 (28.6)	24 (26.4)	12 (16.2)

Characteristic	All participants n (%)	SARS-CoV-2 positive N (%)	Influenza positive n (%)	RSV positive n (%)
Patient contact				
Yes	4,841 (82.6)	535 (83.2)	75 (82.4)	71 (95.9)
No	1,022 (17.4)	108 (16.8)	16 (17.6)	3 (4.1)
Vaccination status				
Both	4,349 (74.2)	481 (74.8)	62 (68.1)	54 (73.0)
Influenza 2022/23 vaccine only	499 (8.5)	53 (8.2)	8 (8.8)	5 (6.8)
COVID-19 second booster dose only	354 (6.0)	28 (4.4)	10 (11.0)	5 (6.8)
Neither	661 (11.3)	81 (12.6)	11 (12.1)	10 (13.5)

Note: Eight participants had multiple infections during the analysis period – four participants had a SARS-CoV-2 and an influenza infection, three had influenza and RSV, and one had SARS-CoV-2 and RSV.

SARS-CoV-2, influenza and RSV infection rates over winter 2022/23

All 5,863 participants were tested for SARS-CoV-2, 4,689 (80.0%) for influenza and 4,695 (80.0%) for RSV. Of these, 643/5,863 (11.0%) participants had a positive SARS-CoV-2 result, 93/4,689 (2.0%) had a positive influenza result and 74/4,695 (1.6%) had a positive RSV result.

PCR positivity rates for all three viruses peaked in early December 2022 (peak positive PCR per 100 tests: 4.6 (95% CI 3.5, 5.7) for SARS-CoV-2, 3.9 (95% CI 2.2, 5.6) influenza, 1.4 (95% CI 0.4, 2.4) RSV), with influenza and RSV decreasing to low levels after January 2023 (for influenza ≤ 0.2 and RSV ≤ 0.3 positives per 100 tests), whereas SARS-CoV-2 maintained rates around 2.5 per 100 tests until March 2023 (Fi 2).

Fig 2: PCR positivity rate (per 100 tests) by fortnight and infection, 28 November 2022 to 31 March 2023

Note: shaded areas represent 95% confidence intervals

Influenza-like illness symptoms over winter 2022/23

There were 4,003 (68.3%) participants who reported symptoms over the analysis period, with 1,054 (18.0%) reporting ILI symptoms. The proportion of participants reporting ILI symptoms by fortnight peaked in early December 2022 (peak fortnight was 7.5% (95% CI 6.8, 8.3) (368/4,893 surveys) (Fig 3).

Fig 3: Proportion of participants reporting influenza-like illness symptoms by fortnight, 28 November 2022 to 31 March 2023

Shaded areas represent 95% confidence intervals

Symptom profile by SARS-CoV-2, influenza and RSV

The proportion of asymptomatic infections were similar among the three viruses – influenza (45.6%), SARS-CoV-2 (41.7%) and RSV (37.5%). Symptom profiles were similar for all three viruses. Although, loss of sense of smell and taste were more common among those with an SARS-CoV-2 infection and fever more common with a influenza infection. Hospital attendance was low for all viruses (Table 2).

Table 2: Description of the symptom profile and severity of SARS-CoV-2, influenza and RSV PCR positive infections, 28 November 2022 to 31 March 2023

	SARS-CoV-2 n (%)	Influenza n (%)	RSV n (%)	<i>p-value (SARS-CoV-2 vs influenza)</i>	<i>p-value (SARS-CoV-2 vs RSV)</i>	<i>p-value (RSV vs influenza)</i>
Total	643	93	74			
Symptoms				<i>0.494</i>	<i>0.594</i>	<i>0.327</i>
Any symptoms	346 (58.3)	49 (54.4)	40 (62.5)			
Asymptomatic	247 (41.7)	41 (45.6)	24 (37.5)			
Symptoms type						
Loss of smell	67 (11.3)	3 (3.3)	4 (6.3)	<i>0.015</i>	<i>0.289</i>	<i>0.45</i>
Cough	182 (30.7)	33 (36.7)	17 (26.6)	<i>0.274</i>	<i>0.568</i>	<i>0.223</i>
Diarrhoea	37 (6.2)	5 (5.6)	2 (3.1)	<i>>0.999</i>	<i>0.414</i>	<i>0.7</i>
Loss of taste	80 (13.5)	3 (3.3)	4 (6.3)	<i>0.005</i>	<i>0.116</i>	<i>0.45</i>
Fatigue	160 (27.0)	24 (26.7)	13 (20.3)	<i>>0.999</i>	<i>0.297</i>	<i>0.445</i>
Fever	105 (17.7)	25 (27.8)	9 (14.1)	<i>0.03</i>	<i>0.602</i>	<i>0.05</i>
Swollen glands	45 (7.6)	6 (6.7)	1 (1.6)	<i>>0.999</i>	<i>0.074</i>	<i>0.24</i>
Headache	228 (38.4)	29 (32.2)	24 (37.5)	<i>0.294</i>	<i>>0.999</i>	<i>0.606</i>
Muscle aches	179 (30.2)	24 (26.7)	13 (20.3)	<i>0.538</i>	<i>0.112</i>	<i>0.445</i>
Runny nose	258 (43.5)	33 (36.7)	28 (43.8)	<i>0.253</i>	<i>>0.999</i>	<i>0.406</i>
Shortness of breath	87 (14.7)	12 (13.3)	13 (20.3)	<i>0.873</i>	<i>0.27</i>	<i>0.273</i>
Sore throat	231 (39.0)	39 (43.3)	29 (45.3)	<i>0.488</i>	<i>0.348</i>	<i>0.87</i>
Vomiting	38 (6.4)	8 (8.9)	5 (7.8)	<i>0.368</i>	<i>0.598</i>	<i>>0.999</i>
Duration of symptoms				<i>0.09</i>	<i>0.405</i>	<i>0.729</i>
1-3	43 (12.6)	1 (2.0)	2 (5.0)			
4-6	79 (23.2)	10 (20.4)	8 (20.0)			
7-14	54 (15.9)	8 (16.3)	9 (22.5)			
>14	164 (48.2)	30 (61.2)	21 (52.5)			
Sick leave				<i>0.002</i>	<i>0.868</i>	<i>0.049</i>
Taken	180 (52.2)	14 (28.6)	20 (50.0)			
Not taken	165 (47.8)	35 (71.4)	20 (50.0)			
Number of sick leave taken (days)				<i>0.015</i>	<i>0.484</i>	<i>0.079</i>
1-3	67 (37.2)	9 (64.3)	10 (50.0)			
4-6	56 (31.1)	5 (35.7)	4 (20.0)			
7-14	57 (31.7)	0 (0.0)	6 (30.0)			
Hospital attendance				<i>0.358</i>	<i>0.095</i>	<i>0.654</i>
Yes	8 (2.3)	2 (4.1)	3 (7.5)			
No	338 (97.7)	47 (95.9)	37 (92.5)			

Time off work due to being symptomatic over winter 2022/23

Of participants testing positive for SARS-CoV-2 and RSV, ≥50% of participants reported taking time off work for being symptomatic (52.2% and 50.0%, respectively), compared to 28.6% for influenza infections (Table 2). The median number of days taken off work for a SARS-CoV-2 infection was 5 (IQR: 2-7); 3 days (IQR: 2.25-5) for influenza and 4 days (IQR: 2-7) for RSV.

Over the analysis period, a total of 1,368/5,863 (23.3%) participants reported taking time off work due to being symptomatic; taking a median of 4 days off over the analysis period (range: 1-59 days). Of participants reporting ILI symptoms, 616/1,054 (58.4%) reported taking time off work; taking a median of 5 days; range: 1-59 days.

The 5,863 participants included contributed to a total of 507,388 follow-up days during the winter period. The rate of sick leave over this period was 1.48 days per 100 days of follow-up, with the peak seen in early December 2022 (2.4 days per 100 days) (Fig 4).

Fig 4: Rate of sick leave taken (per 100 days) by fortnight, 28 November 2022 to 31 March 2023

Note: Sick leave rate was calculated as number of sick leave days taken divided by the number of days participants contributed to the analysis period, per 100 days; Shaded areas represent 95% confidence intervals

Factors associated with taking time off work

Participants who took time off work due to being symptomatic between November 2022 and March 2023 appeared to differ by occupational setting, long-term medical conditions and vaccination status (Table 3).

Table 3: Factors associated with time off work due to being symptomatic, 28 November 2022 to 31 March 2023

Characteristic	Sick leave rate ^b (95% CI)	IRR (95% CI)	Adjusted IRR (95% CI)
Vaccination status ^a			
Both COVID-19 second booster and Influenza 2022/23 vaccine	1.41 (1.37, 1.45)	Ref	Ref
Influenza 2022/23 Vaccine	1.52 (1.40, 1.65)	1.08 (0.99, 1.17)	1.04 (0.95, 1.13)
COVID-19 second booster dose	1.26 (1.14, 1.40)	0.90 (0.81, 1.0)	0.91 (0.82, 1.02)
Neither vaccine	2.04 (1.93, 2.16)	1.45 (1.36, 1.54)	1.47 (1.38, 1.56)

Age group			
Under 25	1.55 (1.10, 2.16)	Ref	Ref
25 to 34	1.84 (1.69, 1.99)	1.19 (0.85, 1.66)	1.16 (0.83, 1.63)
35 to 44	1.51 (1.44, 1.59)	0.98 (0.70, 1.36)	0.92 (0.66, 1.28)
45 to 54	1.49 (1.43, 1.54)	0.96 (0.69, 1.33)	0.91 (0.65, 1.26)
55 to 64	1.44 (1.38, 1.50)	0.93 (0.67, 1.29)	0.89 (0.64, 1.24)
Over 65	0.69 (0.56, 0.84)	0.44 (0.30, 0.65)	0.45 (0.30, 0.66)
Occupation setting			
Theatres	2.13 (1.89, 2.40)	1.91 (1.68, 2.18)	1.89 (1.66, 2.15)
Intensive Care	1.91 (1.72, 2.13)	1.72 (1.52, 1.94)	1.74 (1.54, 1.96)
Outpatient	1.62 (1.55, 1.70)	1.45 (1.35, 1.56)	1.49 (1.39, 1.60)
Ambulance/Emergency Department	1.58 (1.33, 1.86)	1.42 (1.19, 1.69)	1.36 (1.14, 1.62)
Maternity/Labour Ward	1.58 (1.30, 1.92)	1.42 (1.16, 1.73)	1.38 (1.13, 1.68)
Inpatient Wards	1.57 (1.47, 1.67)	1.41 (1.29, 1.53)	1.36 (1.25, 1.49)
Patient facing (non-clinical)	1.53 (1.38, 1.70)	1.38 (1.23, 1.55)	1.40 (1.25, 1.57)
Other	1.50 (1.44, 1.56)	1.35 (1.26, 1.44)	1.38 (1.29, 1.47)
Office	1.11 (1.05, 1.18)	Ref	Ref
Medical group			
No medical condition	1.29 (1.26, 1.33)	Ref	Ref
Immunosuppression	2.71 (2.42, 3.03)	2.09 (1.86, 2.35)	2.19 (1.95, 2.46)
Chronic Respiratory conditions	2.01 (1.90, 2.12)	1.55 (1.46, 1.65)	1.60 (1.50, 1.70)
Chronic Non-Respiratory conditions	1.87 (1.77, 1.99)	1.45 (1.36, 1.55)	1.52 (1.42, 1.63)

^a Participants were excluded if they were vaccinated in one survey period and unvaccinated in another survey period. Surveys were excluded from the analysis if the participant was vaccinated within the survey date range. ^b Sick leave rate was calculated as number of sick leave days taken divided by the number of days participants contributed to the analysis period, per 100 days. IRR = Incidence rate ratio. CI = Confidence interval

Participants in office-based roles took less time off work (1.11 days per 100 days) when compared to clinical roles such as theatres and intensive care units (2.13 and 1.91 days per 100 days, respectively). Estimated from adjusted Incidence Rate Ratios (IRR) also show this; theatres (1.89; 95% CI 1.66, 2.15) and intensive care units (1.74; 95% CI 1.54, 1.96) verses office-based participants. Participants with immunosuppressive, chronic respiratory and chronic non-respiratory conditions took more time off work than participants with no reported comorbidities (who took off 1.29 days per 100 days): immunosuppressive conditions 2.71 days per 100, adjusted IRR 2.19 (95% CI 1.95, 12.46); chronic respiratory 2.01/100 days,

adjusted IRR 1.60 (95% CI 1.50, 1.70); and chronic non-respiratory conditions 1.87/100 days, adjusted IRR 1.52 (95% CI 1.42, 1.63).

Those who were vaccinated against both influenza and COVID-19 took less time off work (1.41 days per 100 days) than those who did not receive either vaccine (2.04 days per 100 days) (Table 3). After controlling for age, occupational setting and co-morbidities, we estimated that those who received neither vaccine had a 47% higher rate of sick leave than those vaccinated for both (adjusted IRR 1.47 (95% CI 1.38, 1.56)).

DISCUSSION

Results from the 2022/23 SIREN Winter Pressures pilot study demonstrate the impact of respiratory illness on the NHS workforce. Rates of SARS-CoV-2, influenza and RSV, and symptoms, all peaked in early December, resulting in increased levels of sickness absence over this time period.

The PCR positivity trends over winter 2022/23 in our cohort of HCW is consistent with national surveillance data (17) demonstrating the potential utility of conducting surveillance in this population to determine the prevalence and impact of respiratory viral infections in the working age population (20). Our detection of RSV infections in this population, which is rarely tested for this virus, suggests that RSV also contributes to winter pressures. The finding that symptom profiles were similar across the three viruses is consistent with existing published literature (21). Across all three viruses, a substantial proportion of infections were asymptomatic but could potentially contribute to transmission, in particular, influenza with over two-thirds of infections asymptomatic (22). This highlights the potential risk associated with nosocomial infections in healthcare workers, though we do not have strong evidence how transmissible asymptomatic infections is. The impact of respiratory illness on time off work in our cohort of HCW over winter 2022/23 was considerable, with 23% of participants reporting time off work due to being symptomatic, and all three viruses contributing to this. Sick leave

rates varied by demographics and vaccination status, with lower estimated rates among those who received the second COVID-19 booster and seasonal influenza vaccine. Given the impact that HCW time off work could have on healthcare resilience over winter, further research into associated factors, including behaviours and attitudes, is important.

A key limitation of this pilot study was the coverage and timing of multiplex PCR roll-out. There were fewer participants with PCR results for influenza and RSV than those with a SARS-CoV-2 test result. In this pilot, multiplex testing was introduced late in the winter season, with testing data only available from late November 2022, due to delays switching PCR platforms across NHS laboratories (using a decentralised study testing model), and the timing of establishing a new centralised postal PCR pathway. This delay was compounded by an unusually early influenza season in 2022/23 (17). Consequently, our surveillance of these viruses over winter 2022/23 may have missed some infections within our cohort, particularly influenza and RSV.

This pilot sub-study conducted during winter 2022/23 has demonstrated the adaptability and applicability of findings from the SIREN HCW cohort. Results from the study show the benefit of regular multiplex testing across NHS Trusts to understand the interplay and impact of seasonal viruses on workforce planning, patient care and healthcare resilience in the NHS during the Winter. We have demonstrated that all three viruses contribute to staff illness and time off work over winter, and that seasonal flu and COVID-19 vaccines were associated with lower sick leave rates. Future studies should consider using a centralised multiplex testing pathway to improve surveillance of respiratory infections and ensure the timing of testing is optimised.

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REFERENCES

1. Elliot AJ, Cross KW, Fleming DM. Acute respiratory infections and winter pressures on hospital admissions in England and Wales 1990-2005. J Public Health (Oxf). 2008;30(1):91-8.
2. Mahase E. NHS England announces "data driven war rooms" to tackle winter pressures. BMJ. 2022;379:o2515.
3. NHS Sickness Absence Interactive Dashboard [Internet]. 2024 [cited 06/02/2024]. Available from: <https://app.powerbi.com/view?r=eyJrljoiYTY3MjE0NmEtYzY2Yi00MmY4LTg4NDQtZTM2ZTI5YjZiOGMyliwidCI6IjUwZjYwNzFmLWJiZmUtNDExYS04ODAzLTY3Mzc0OGU2MjllMmIsImMiOiQjh9.>
4. UKHSA. Influenza: the green book, chapter 19. In: UKHSA, editor. The Green Book. gov.uk2023. p. 18.
5. UKHSA. Immunisation of healthcare and laboratory staff: the green book, chapter 12. In: UKHSA, editor. The Green Book. gov.uk: UKHSA; 2013. p. 1-8.
6. Atti A, Insalata F, Carr EJ, Otter AD, Foulkes S, Wu MY, et al. Antibody correlates of protection against Delta infection after vaccination: A nested case-control within the UK-based SIREN study. J Infect. 2023;87(5):420-7.
7. Regev-Yochay G, Lustig Y, Joseph G, Gilboa M, Barda N, Gens I, et al. Correlates of protection against COVID-19 infection and intensity of symptomatic disease in vaccinated

- individuals exposed to SARS-CoV-2 in households in Israel (ICoFS): a prospective cohort study. *Lancet Microbe*. 2023;4(5):e309-e18.
8. Ma Q, Liu J, Liu Q, Kang L, Liu R, Jing W, et al. Global Percentage of Asymptomatic SARS-CoV-2 Infections Among the Tested Population and Individuals With Confirmed COVID-19 Diagnosis: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2021;4(12):e2137257.
9. Hall V, Foulkes S, Insalata F, Saei A, Kirwan P, Atti A, et al. Effectiveness and durability of protection against future SARS-CoV-2 infection conferred by COVID-19 vaccination and previous infection; findings from the UK SIREN prospective cohort study of healthcare workers March 2020 to September 2021. *medRxiv*. 2021:2021.11.29.21267006.
10. Kirwan PD, Hall VJ, Foulkes S, Otter AD, Munro K, Sparkes D, et al. Effect of second booster vaccinations and prior infection against SARS-CoV-2 in the UK SIREN healthcare worker cohort. *Lancet Reg Health Eur*. 2024;36:100809.
11. Huiberts AJ, de Gier B, Hoeve CE, de Melker HE, Hahne SJ, den Hartog G, et al. Effectiveness of bivalent mRNA booster vaccination against SARS-CoV-2 Omicron infection, the Netherlands, September to December 2022. *Euro Surveill*. 2023;28(7).
12. Riccio MD, Spreeuwenberg P, Osei-Yeboah R, Johannesen CK, Fernandez LV, Teirlinck AC, et al. Defining the Burden of Disease of RSV in Europe: estimates of RSV-associated hospitalisations in children under 5 years of age. A systematic review and modelling study. *medRxiv*. 2023:2023.02.10.23285756.
13. Coultas JA, Smyth R, Openshaw PJ. Respiratory syncytial virus (RSV): a scourge from infancy to old age. *Thorax*. 2019;74(10):986-93.
14. Vargese SS, Dev SS, Soman AS, Kurian N, Varghese VA, Mathew E. Exposure risk and COVID-19 infection among frontline health-care workers: A single tertiary care centre experience. *Clin Epidemiol Glob Health*. 2022;13:100933.
15. Macintyre CR, Seale H, Yang P, Zhang Y, Shi W, Almatroudi A, et al. Quantifying the risk of respiratory infection in healthcare workers performing high-risk procedures. *Epidemiol Infect*. 2014;142(9):1802-8.

16. Wallace S, Hall V, Charlett A, Kirwan PD, Cole M, Gillson N, et al. Impact of prior SARS-CoV-2 infection and COVID-19 vaccination on the subsequent incidence of COVID-19: a multicentre prospective cohort study among UK healthcare workers - the SIREN (Sarscov2 Immunity & REinfection EvaluationN) study protocol. *BMJ Open*. 2022;12(6):e054336.
17. UKHSA. National Influenza and COVID-19 surveillance report. .gov.uk; 2023.
18. Broad J, Sparkes D, Platt N, Howells A, Foulkes S, Khawam J, et al. Adapting COVID-19 research infrastructure to capture influenza and respiratory syncytial virus alongside SARS-CoV-2 in UK healthcare workers winter 2022/23 and beyond: protocol for a pragmatic sub-study [version 1; peer review: awaiting peer review]. *NIHR Open Research*. 2024;4(1).
19. UKHSA. SIREN Follow-up Questionnaire v6.1. 2022.
20. Foulkes S, Monk EJM, Sparkes D, Hettiarachchi N, Milligan ID, Munro K, et al. Early Warning Surveillance for SARS-CoV-2 Omicron Variants, United Kingdom, November 2021-September 2022. *Emerg Infect Dis*. 2023;29(1):184-8.
21. Ma X, Conrad T, Alchikh M, Reiche J, Schweiger B, Rath B. Can we distinguish respiratory viral infections based on clinical features? A prospective pediatric cohort compared to systematic literature review. *Rev Med Virol*. 2018;28(5):e1997.
22. Cohen C, Kleynhans J, Moyes J, McMorro ML, Treurnicht FK, Helfferscee O, et al. Asymptomatic transmission and high community burden of seasonal influenza in an urban and a rural community in South Africa, 2017-18 (PHIRST): a population cohort study. *Lancet Glob Health*. 2021;9(6):e863-e74.

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7,774
participants consented
to the study

18 participants withdrawn
and requested data to be
removed from the study

917 participants did
not complete a follow-
up survey

1,789 participants did
not complete a PCR
test

6,839 participants
with survey data

5,967 participants
with testing data

5,863 participants
with survey and testing
data

Figure1

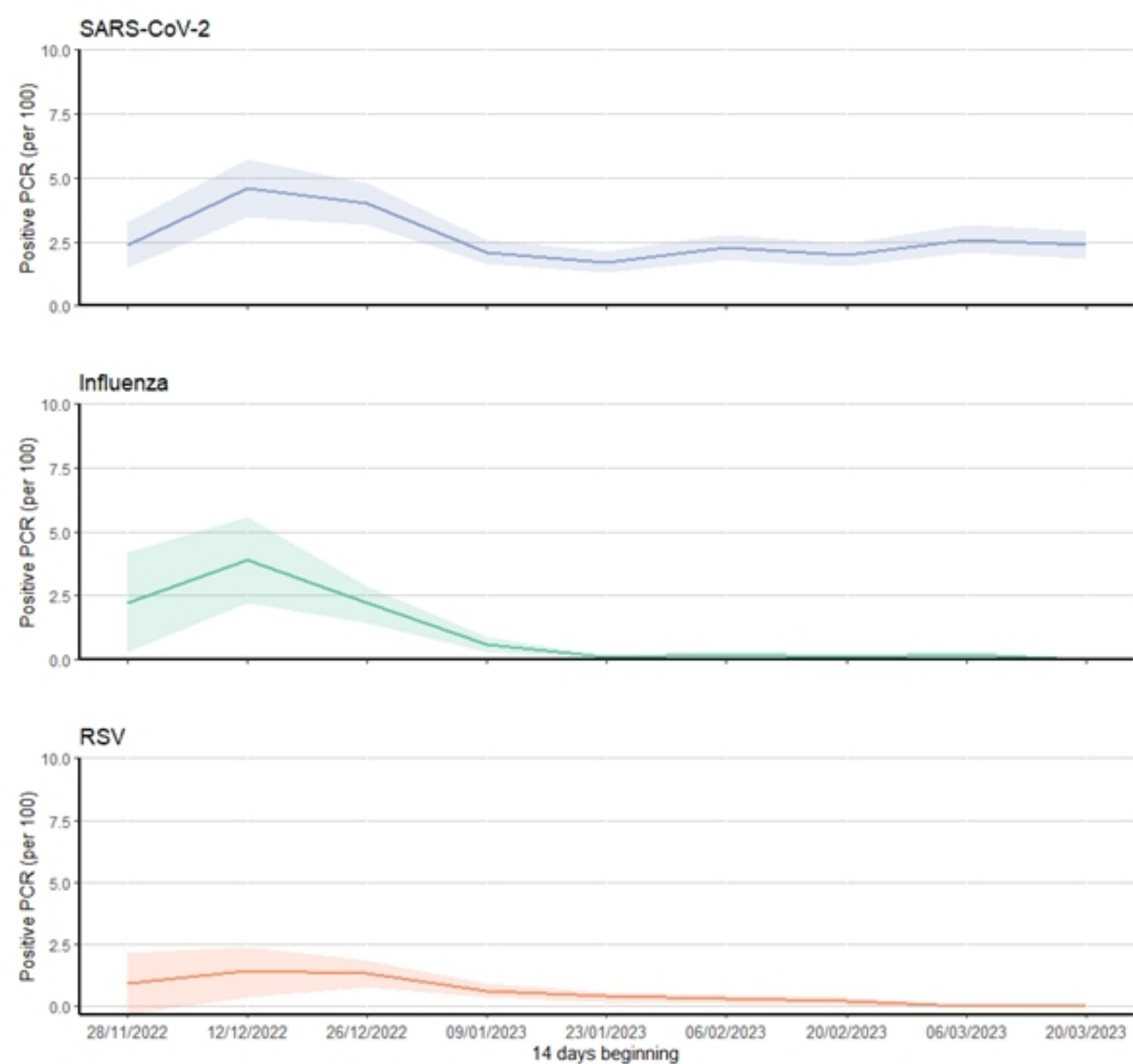


Figure2

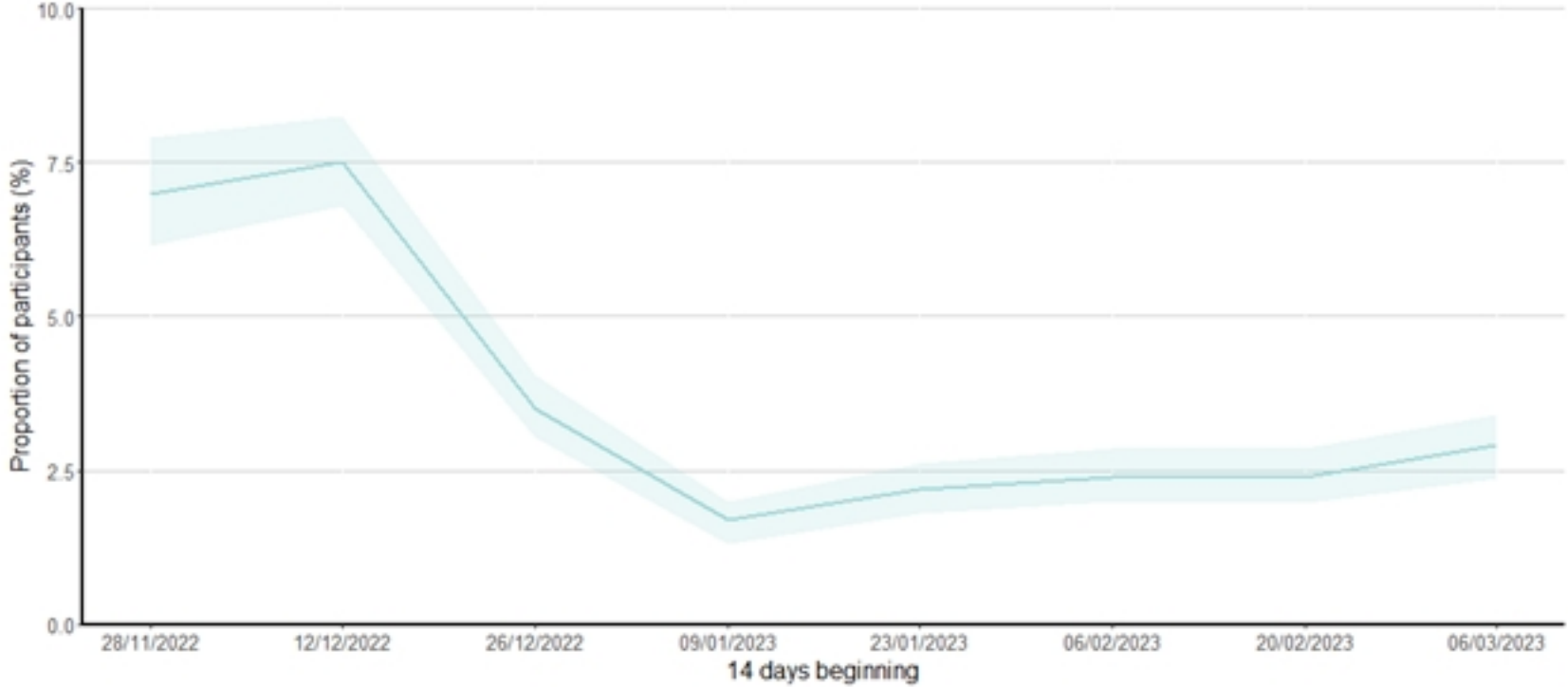


Figure3

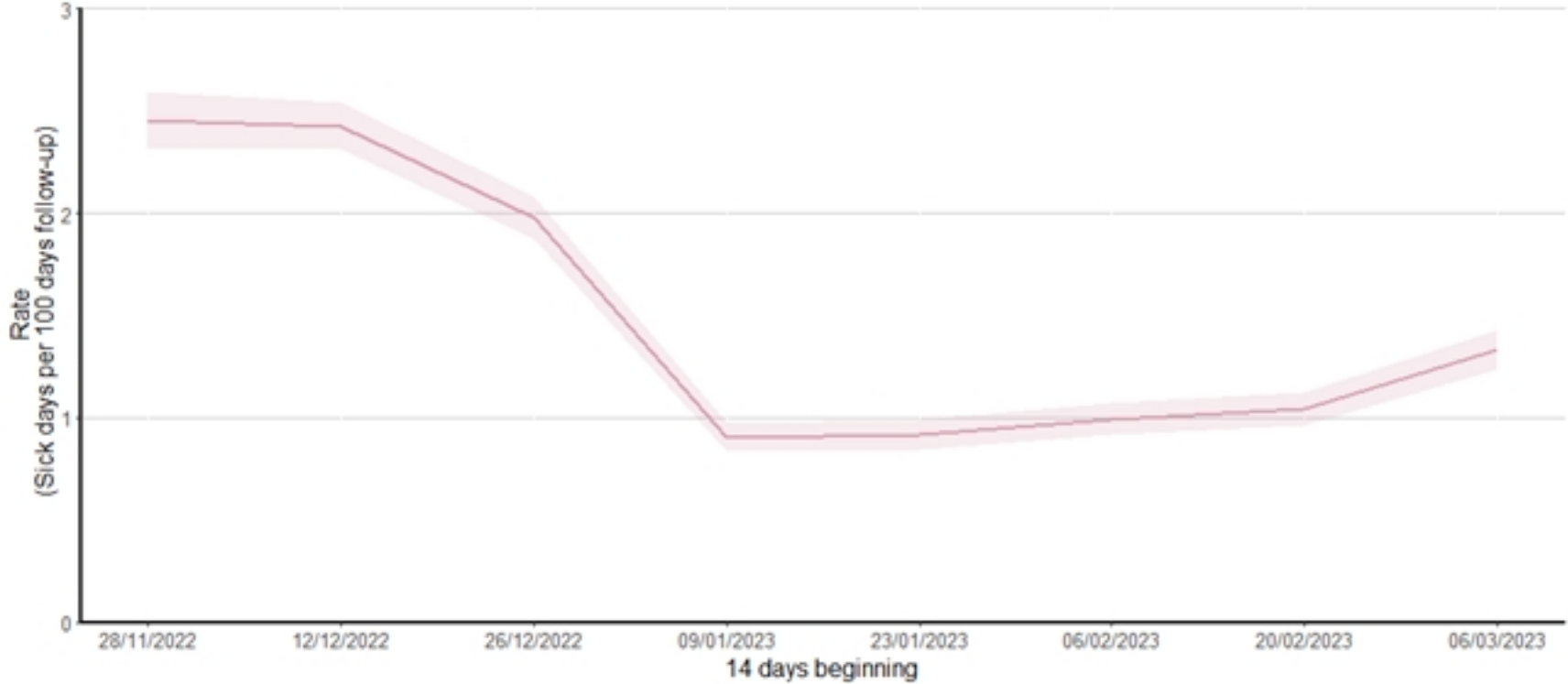


Figure4