

# Effective control of SARS-CoV-2 transmission between healthcare workers during a period of diminished community prevalence of COVID-19

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**Abstract** Previously, we showed that 3% (31/1032)of asymptomatic healthcare workers (HCWs) from a large teaching hospital in Cambridge, UK, tested positive for SARS-CoV-2 in April 2020. About 15% (26/169) HCWs with symptoms of coronavirus disease 2019 (COVID-19) also tested positive for SARS-CoV-2 (Rivett et al., 2020). Here, we show that the proportion of both asymptomatic and symptomatic HCWs testing positive for SARS-CoV-2 rapidly declined to near-zero between 25th April and 24th May 2020, corresponding to a decline in patient admissions with COVID-19 during the ongoing UK 'lockdown'. These data demonstrate how infection prevention and control measures including staff testing may help prevent hospitals from becoming independent 'hubs' of SARS-CoV-2 transmission, and illustrate how, with appropriate precautions, organizations in other sectors may be able to resume on-site work safely.

# Introduction

The role of nosocomial transmission of SARS-CoV-2 has been highlighted by recent evidence suggesting that 20% of SARS-CoV-2 infections among patients in UK hospitals and up to 89% of infections among HCWs may have originated in hospitals (*Evans et al., 2020; Iacobucci, 2020*). Since the introduction of 'lockdown' in the UK, community transmission rates of SARS-CoV-2 have generally declined (*Public Health England (PHE), 2020*). Conversely, concerns have been raised that hospitals could become independent 'hubs' for ongoing SARS-CoV-2 transmission between patients and HCWs, which would effectively prolong the epidemic (*Iacobucci, 2020*). In this context, the evolution of the epidemic curves of a hospital's symptomatic and asymptomatic workforce has not been well described.

We recently initiated a comprehensive HCW screening programme for SARS-CoV-2 in a large teaching hospital in Cambridge, UK. Over a 3-week period from 6th to 24th April 2020, 3% (31/ 1032) HCWs in the asymptomatic screening arm, 15.4% (26/169) HCWs in the symptomatic screening arm, and 7.7% (4/52) contacts in the symptomatic household contact screening arm tested positive for SARS-CoV-2 (*Rivett et al., 2020*). Our data from the asymptomatic screening arm were consistent with the results of Shields et al. (*Shields et al., 2020*). Over the next 4 weeks from 25th April to 24th May 2020, we performed a further 3388 additional tests. Here, we present these longitudinal data, in the context of the hospital patient population and wider local community.

### **Results**

Testing for SARS-CoV-2 RNA was performed with real-time RT-PCR using throat and nose swab samples of HCWs from Cambridge University Hospitals NHS Foundation Trust (CUHNFT) and their symptomatic household contacts. Over the new study period (25th April to 24th May 2020), 2611 additional tests were performed in the HCW asymptomatic screening arm, 555 additional tests in the HCW symptomatic screening arm, and 216 additional tests in the HCW household contact screening arm. A further six tests did not have a clearly recorded arm of origin. Over the entire study period, the median age of HCWs and their household contacts was 36.5 and 35.5 years, respectively. About 68.4% were female and 31.6% were male. Of the individuals testing positive over the entire study period, the median age of HCWs and their household contacts was 32 and 47 years, respectively. About 77.9% of all positive tests were from females and 22.1% from males. Table 1 summarizes the total number of HCWs testing positive through either arm of the screening programme, according to the job role. A comparison of the proportions of hospital employees from each job role that tested positive through the HCW symptomatic screening arm revealed no statistically significant difference (Pearson's chi-square test p=0.419). Reasonable comparison of the proportions testing positive through the HCW asymptomatic screening arm was not possible due to non-random sampling of different areas of the hospital, meaning some job roles had been more frequently targeted for asymptomatic screening than others.

Between 25th April and 24th May 2020, a total of 34 new positive tests were reported. In the *HCW symptomatic* and *HCW symptomatic household contact screening arms* combined (reflecting all individuals with self-reported symptoms at the time of testing), 13/771 (1.7%) tests were positive,

 Table 1. Combined data for SARS-CoV-2 RNA positive HCWs by role and screening arm, from the present study and our previous study (*Rivett et al., 2020*).

Difference in proportions of HCWs testing positive through the symptomatic screening arm was analysed using Pearson's chi-square test.

Role	HCW asymptomatic screening arm	HCW symptomatic screening arm	Total number of hospital employees
Nurse	25	19	3621
Healthcare assistant	14	8	1734
Doctor	8	6	1871
Cleaners	2	3	560
Radiographer	2	1	217
Radiology support worker	0	1	35
Physiotherapist	1	0	116

Overall, 360 individuals underwent repeat testing, either as part of the asymptomatic screening programme, or for other reasons as previously described (**Rivett et al., 2020**). The median turnaround time from sample arrival in the laboratory to final verification was 18 hr 45 min. Positive results were called out on the same day, with negative results emailed within 24 hr.

which was significantly lower than 30/221 (13%) in the original study period (Fisher's exact test p<0.0001). In the HCW asymptomatic screening arm, 21/2611 (0.8%) tests were positive, which again was significantly lower than 31/1032 (3%) in the original study period (Fisher's exact test p<0.0001). As we previously observed (*Rivett et al., 2020*), individuals captured in the HCW asymptomatic screening arm were generally asymptomatic at the time of screening; however, these individuals could be divided into subgroups. In the first subgroup, 8/21 (38%) HCWs had no symptoms at all. Of these, 5/8 (63%) remained entirely asymptomatic 5-7 weeks after their positive test, whereas 2/8 (25%) developed symptoms 24-48 hr after testing. One HCW could not be contacted to obtain further history. In the second subgroup, 6/21 (29%) had retrospectively experienced some symptoms prior to screening. Of these, 5/6 (83%) had symptoms with a high pre-test probability of COVID-19 (Rivett et al., 2020) commencing >7 days prior to screening, of whom 3/5 had appropriately self-isolated then returned to work, and 1/5 was tested shortly after developing symptoms. 1/6 (17%) had symptoms with a low pre-test probability of COVID-19 (Rivett et al., 2020) commencing <7 days prior to screening and had not self-isolated. In the third subgroup, 7/21 (33%) were detected through repeat sampling of HCW who previously tested positive. Of these, 4/7 (57%) were tested to determine their suitability to return to work with severely immunocompromised/immunosuppressed patients, as dictated by UK national guidance (National Institute for Health and Care Excellence (NICE), 2020). The remaining 3/7 (43%) were from HCWs tested incidentally for the second time in the asymptomatic HCW screening programme. The median interval between serial positive tests was 16.5 days (IQR 9.5–19.5). All cases were attributable to prolonged SARS-CoV-2 RNA detection from a single infection, rather than re-infection. Our approach to patients with repeatedly positive SARS-CoV-2 PCR tests is described in the Methods.

The fraction of positive tests among the *HCW asymptomatic, and HCW symptomatic* and *house-hold contact screening groups* combined varied over time (*Figure 1A, Table 2*). In particular, during the last 2 weeks of the study period (11th to 24th May 2020), we identified only four positive SARS-CoV-2 samples from 2016 tests performed, two from the *HCW asymptomatic* and two from the *HCW symptomatic/symptomatic household contact arms*. This fall in positive HCW tests mirrored the decline in both patients testing positive at CUHNFT and those tested throughout the wider region (*Figure 1B*). Similar trends were observed in a smaller cohort study of HCWs in London (*Treibel et al., 2020*).

In our original study between 6th and 24th April 2020, we described in detail two clusters of HCW infections (*Rivett et al., 2020*). From 25th April to 24th May 2020, we detected one additional cluster on a general medical ward with a separate area for patients with proven COVID-19 and another area for those without. This was identified through targeted screening of the ward over a 24 hr period from 4th to 5th May 2020, in response to four staff testing positive through the *HCW symptomatic arm* of the screening programme from 27th to 30th April 2020. Reactive screening of a

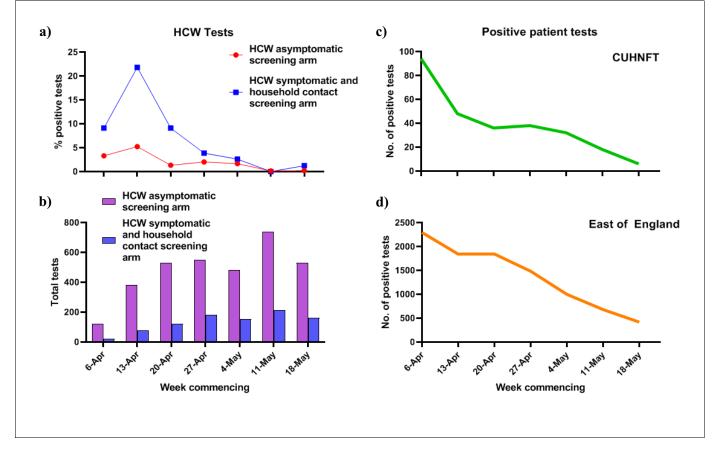


Figure 1. Trends in positive SARS-CoV-2 PCR tests among HCWs, hospital patients and the wider community over time. (a) Positive SARS-CoV-2 tests for asymptomatic and symptomatic screening arms by week. (b) Total HCW SARS-CoV-2 tests in CUHNFT performed by week. (c) Total positive SARS-CoV-2 patient tests in Cambridge University Hospital NHS Foundation Trust (CUHNFT) by week. (d) Total positive SARS-CoV-2 tests in the East of England (EOE) by week.

The online version of this article includes the following source data for figure 1:

Source data 1. Source data for trends in SARS-CoV-2 PCR positive HCWs, hospital patients and individuals in the wider community.

further 40 staff from the same ward identified a further three positive asymptomatic HCWs. In addition, a further two HCWs tested positive in an asymptomatic screen of 30 individuals from a closely related clinical area (designated for non-COVID patients) on 6th May 2020.

### Discussion

Our data demonstrate a dramatic fall in the prevalence of symptomatic and asymptomatic SARS-CoV-2 infection among HCWs in our hospital during the study period. On average, the number of secondary infections among HCWs arising from each infected HCW (effectively, the reproduction number (R) for SARS-CoV-2 transmission between HCWs) must therefore be <1.

As well as an acquisition from other HCWs, infections among HCWs may also be acquired from patients, as well as other individuals outside the hospital. Our study period coincided with a decline in the rate of infection across our local community, and our data are consistent with a reduction in transmission within the hospital, a reduction in community-based acquisition of infection by HCWs, or (most likely) a combination of both. In the absence of detailed epidemiological data, it is not possible to formally differentiate between these possibilities or determine their relative effect sizes. Nonetheless, our identification of HCW infection clusters in specific areas of the hospital highlighted the potential for workplace acquisition of SARS-CoV-2, which may lead to self-sustaining outbreaks if left uninterrupted (*Rivett et al., 2020*; *Meredeth et al., 2020*). For each of these clusters, timely

**Table 2.** Positive tests and total number of SARS-CoV-2 tests performed in each screening arm categorised according to week since starting the healthcare worker testing programme (6th April-24th May 2020).

		Week commencing						
	6th April	13th April	20th April	27th April	4th May	11th May	18th May	Total
HCW asymptomatic screening arm	4/121	20/383	7/529	11/550	8/483	1/738	1/840	52/ 3644
								(1.4%)
HCW symptomatic screening arm	1/15	14/60	11/95	7/119	3/104	0/164	2/168	38/725
								(5.2%)
HCW symptomatic household contacts	1/7	3/18	0/26	0/62	1/50	0/51	0/53	5/267
								(1.8%)
Unknown	0/0	0/2	0/13	0/0	0/4	0/1	0/1	0/21
All	6/143 (4.1%)	37/463 (7.9%)	18/663 (2.7%)	18/731 (2.4%)	12/641 (1.8%)	1/954 (0.1%)	3/1062 (0.2%)	95/ 4657 (2%)

identification of HCW infection proved effective in terminating chains of hospital transmission between staff, preventing ongoing nosocomial infection.

With the incidence of infection having fallen significantly in hospitalised patients, HCWs and the wider community, many hospitals across the UK and further afield have been afforded precious time to build the infrastructure necessary to establish comprehensive screening programmes in anticipation of a possible second epidemic peak. For hospitals already operating newly established screening programmes, the challenge now is to up-scale to the point that screening can occur at a frequency that permits pre-symptomatic capture of as close to 100% of all new infections as possible. This approach will enable staff to be removed from the workplace at the time of peak infectivity (He et al., 2020). The minimum screening frequency required needs to be carefully modelled, with recent estimates suggesting the need for weekly testing to prevent 16-33% of onward transmission from HCWs, depending on the time taken for results to be reported, and another study estimating the need for daily screening to prevent 65% of HCW-to-HCW transmission events (Evans et al., 2020; Grassly et al., 2020). In practice, we have observed good results in our hospital with a current frequency of asymptomatic screening every 2-4 weeks. Those being screened are prioritised by anticipated ward-based exposure to COVID-19, with additional targeted screens triggered by excess staff sickness or the identification of symptomatic cases on specific wards (Rivett et al., 2020). In addition to asymptomatic screening, testing of symptomatic HCWs is essential for preventing excessive erosion of the hospital workforce by self-isolation on the basis of symptoms alone, and testing of symptomatic HCW household contacts negates the need for unnecessary self-guarantine periods for co-habiting HCWs. We found uptake to the HCW symptomatic household contact screening arm of our programme to be notably lower than the HCW symptomatic arm despite regular communications to advertise the service within CUHNFT. This lack of uptake may reflect a lack of awareness that symptomatic non-HCWs were eligible for testing, provided they shared a household with a hospital employee. Many non-hospital employees may also have been more inclined to attend national testing centres or be less aware of the spectrum of COVID-19 symptoms.

Importantly, our data demonstrate that CUHNFT was not acting as an independent 'hub' for ongoing COVID-19 transmission among HCWs. The absence of nosocomial transmission likely reflects the combined efficacy of HCW testing, stringent prospective, and reactive infection prevention and control measures, and appropriate social distancing among the workforce. These findings should give reassurance to both hospital staff and patients that healthcare facilities remain safe places to give and receive care. Furthermore, since CUHNFT, with approximately 11,000 staff members (many of whom are based in the hospital) is a major regional employer, we predict that comparable

organisations in other sectors may also be able to resume on-site work safely by instigating similar precautions.

# **Materials and methods**

# Staff screening protocols

We previously described protocols for staff screening, sample collection, laboratory processing, and results reporting in detail (*Rivett et al., 2020*). These methods remained unchanged throughout this study period. Two parallel streams of entry into the testing programme included (i) *HCW symptomatic, and HCW symptomatic household contact screening arms* and (ii) an *HCW asymptomatic screening arm*. In the former, any patient-facing or non-patient-facing HCW could voluntarily refer themselves or a household contact, should they develop symptoms suggestive of COVID-19. In the latter, HCWs could volunteer to take part in a rolling programme of testing for all patient-facing and non-patient-facing staff working in defined clinical areas thought to be at risk of SARS-CoV-2 transmission. Testing was performed (i) at temporary on-site 'Pods'; (ii) via self-swabbing kits delivered to HCWs in their area of work. All individuals in each arm of the programme performed a self-swab at the back of the throat then the nasal cavity, followed by RNA extraction and amplification using real-time RT-PCR (*Sridhar et al., 2020*). Cluster investigation was initiated when three or more HCWs working in the same clinical area tested positive for SARS-CoV-2 in 1 week .

# Management of HCW with repeat positive tests

Current National Institute for Health and Care Excellence (NICE) guidelines require a negative test before returning to work with immunocompromised patients (*National Institute for Health and Care Excellence (NICE), 2020*). In accordance with the UK national guidance, individuals with repeat positive screens following a minimum period of 7 days self-isolation were advised to continue working if they were not scheduled to come into close contact with heavily immunocompromised patients, provided they remained asymptomatic (*UK Government, 2020*). This approach to managing repeat positive screens is further supported by recent data from the Korea Centers for Disease Control and Prevention, which showed no clear evidence of onward transmission to the contacts of 285 repeat-positive individuals, 108 of whom had samples taken for attempted viral culture, which was universally unsuccessful (*Korea Centers for Disease Control & Prevention (KCDC), 2020*). Additional small studies have also demonstrated an inability to culture virus from clinical samples obtained later than 8 days after symptom onset, suggesting prolonged detection of viral RNA is unlikely to indicate an ongoing risk of transmission (*Wölfel et al., 2020*; *Bullard et al., 2020*).

# Data extraction and analysis

Swab result data for HCWs and patients were extracted directly from the hospital-laboratory interface software, Epic (Verona, WI) and from SARS-CoV-2 point of care testing. Data for SARS-CoV-2 infections from the local community were extracted from Public Health England's Data Dashboard (**Public Health England (PHE), 2020**). Data were collated using Microsoft Excel, and figures produced with GraphPad Prism (GraphPad Software, La Jolla, CA). Fisher's exact test was used to compare the proportion of HCWs testing positive in this study period to that of our previous study period (**Rivett et al., 2020**). Pearson's chi-square test was used for comparison of the proportions of HCWs testing positive in each job role.

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#### **Ethics**

Human subjects: As a study of healthcare-associated infections, this investigation is exempt from requiring ethical approval under Section 251 of the NHS Act 2006 (see also the NHS Health Research Authority algorithm, available at http://www.hra-decisiontools.org.uk/research/, which concludes that no formal ethical approval is required). Our study was performed as a service evaluation of the Cambridge Universith Hospitals NHS Foundation Trust screening programme. The service provided was not changed in any way in order to undertake this evaluation.

#### Decision letter and Author response

Decision letter https://doi.org/10.7554/eLife.59391.sa1 Author response https://doi.org/10.7554/eLife.59391.sa2

### Additional files

#### **Supplementary files**

Transparent reporting form

#### **Data availability**

All data generated or analysed during this study are included in the manuscript and supporting files.

### References

- Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, Boodman C, Bello A, Hedley A, Schiffman Z, Doan K, Bastien N, Li Y, Van Caeseele PG, Poliquin G. 2020. Predicting infectious SARS-CoV-2 from diagnostic samples. *Clinical Infectious Diseases* **22**:ciaa638. DOI: https://doi.org/10.1093/cid/ciaa638
- **Evans S**, Agnew E, Vynnycky E. 2020. The impact of testing and infection prevention and control strategies on within-hospital transmission dynamics of COVID-19 in hospitals. *medRxiv*. DOI: https://doi.org/10.1101/2020. 05.12.20095562
- Grassly NC, Pons-Salort M, Parker EPK. 2020. Role of Testing in COIVD-19 Control London, United Kingdom:: Imperial College.
- He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, Lau YC, Wong JY, Guan Y, Tan X, Mo X, Chen Y, Liao B, Chen W, Hu F, Zhang Q, Zhong M, Wu Y, Zhao L, Zhang F, et al. 2020. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nature Medicine 26:672–675. DOI: https://doi.org/10.1038/s41591-020-0869-5, PMID: 32296168
- lacobucci G. 2020. Covid-19: doctors sound alarm over hospital transmissions. *BMJ* **369**:m2013. DOI: https://doi.org/10.1136/bmj.m2013
- Korea Centers for Disease Control & Prevention (KCDC). 2020. Findings from investigation and analysis of repositive cases. https://www.cdc.go.kr/board/board.es?mid=a3040200000&bid=0030 [Accessed May 23, 2020].
- **Meredeth LW**, Hamilton WL, Warne B. 2020. Rapid implementation of real-time SARS-CoV-2 sequencing to investigate healthcare associated COVID-19 infections. *medRxiv*. DOI: https://doi.org/10.1101/2020.05.08. 20095687
- National Institute for Health and Care Excellence (NICE). 2020. COVID-19 rapid guideline: haematopoietic stem cell transplantation. https://www.nice.org.uk/guidance/ng164/chapter/6-Supporting-staff-including-staff-who-are-self-isolating [Accessed May 23, 2020].
- Public Health England (PHE). 2020. Coronavirus (COVID-19) in the UK. https://coronavirus.data.gov.uk/ [Accessed May 23, 2020].
- Rivett L, Sridhar S, Sparkes D, Routledge M, Jones NK, Forrest S, Young J, Pereira-Dias J, Hamilton WL, Ferris M, Torok ME, Meredith L, Curran MD, Fuller S, Chaudhry A, Shaw A, Samworth RJ, Bradley JR, Dougan G, Smith KGC, et al. 2020. Screening of healthcare workers for SARS-CoV-2 highlights the role of asymptomatic carriage in COVID-19 transmission. *eLife* 9:e58728. DOI: https://doi.org/10.7554/eLife.58728, PMID: 32392129
- Shields AM, Faustini SE, Perez-Toledo M. 2020. SARS-CoV-2 seroconversion in health care workers. *medRxiv*. DOI: https://doi.org/10.1101/2020.05.18.20105197
- Sridhar S, Forrest S, Kean I. 2020. A blueprint for the implementation of a validated approach for the detection of SARS-Cov2 in clinical samples in academic facilities. *bioRxiv*. DOI: https://doi.org/10.1101/2020.04.14. 041319
- Treibel TA, Manisty C, Burton M, McKnight Áine, Lambourne J, Augusto JB, Couto-Parada X, Cutino-Moguel T, Noursadeghi M, Moon JC. 2020. COVID-19: pcr screening of asymptomatic health-care workers at London hospital. The Lancet 395:1608–1610. DOI: https://doi.org/10.1016/S0140-6736(20)31100-4
- UK Government. 2020. Stay at home advice. 2020. https://www.gov.uk/government/publications/covid-19-stayat-home-guidance/stay-at-home-guidance-for-households-with-possible-coronavirus-covid-19-infection [Accessed June 12, 2020].
- Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, Niemeyer D, Jones TC, Vollmar P, Rothe C, Hoelscher M, Bleicker T, Brünink S, Schneider J, Ehmann R, Zwirglmaier K, Drosten C, Wendtner C. 2020. Virological assessment of hospitalized patients with COVID-2019. *Nature* 581:465–469. DOI: https://doi.org/ 10.1038/s41586-020-2196-x, PMID: 32235945