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Research paper

Cross sectional investigation of a COVID-19 outbreak at a London Army barracks: Neutralising antibodies and virus isolation

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ABSTRACT

Background: Military personnel in enclosed societies are at increased risk of respiratory infections. We investigated an outbreak of Coronavirus Disease 2019 in a London Army barracks early in the pandemic.
Methods: Army personnel, their families and civilians had nasal and throat swabs for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by reverse transcriptase -polymerase chain reaction (RT-PCR), virus isolation and whole genome sequencing, along with blood samples for SARS-CoV-2 antibodies. All tests were repeated 36 days later.
Findings: During the first visit, 304 (254 Army personnel, 10 family members, 36 civilians, 4 not stated) participated and 24/304 (8%) were SARS-CoV-2 RT-PCR positive. Infectious virus was isolated from 7/24 (29%). Of the 285 who provided a blood sample, 7% (19/285) were antibody positive and 63% (12/19) had neutralising antibodies. Twenty-two (22/34, 64%) individuals with laboratory-confirmed infection were asymptomatic. Nine SARS-CoV-2 RT-PCR positive participants were also antibody positive but those who had neutralising antibodies did not have infectious virus. At the second visit, no new infections were detected, and 13% (25/193) were seropositive, including 52% (13/25) with neutralising antibodies. Risk factors for SARS-CoV-2 antibody positivity included contact with a confirmed case (RR 25.2; 95% CI 14–45), being female (RR 2.5; 95% CI 1.0–6.0) and two-person shared bathroom (RR 2.6; 95% CI 1.1–6.4).
Interpretation: We identified high rates of asymptomatic SARS-CoV-2 infection. Public Health control measures can mitigate spread but virus re-introduction from asymptomatic individuals remains a risk. Most seropositive individuals had neutralising antibodies and infectious virus was not recovered from anyone with neutralising antibodies.
Funding: PHE

1. Introduction

In the United Kingdom (UK), the first imported cases of Coronavirus Disease 2019 (COVID-19) were identified in late January 2020 and the number of cases increased rapidly from mid-March 2020, peaking in mid-April before declining gradually thereafter [1]. London was one of the earliest and most affected regions in the UK [2]. A characteristic of the COVID-19 pandemic has been its propensity to cause large outbreaks in enclosed settings, including the military [3–5]. In one London Army barracks, the Regimental Medical Officer (RMO) identified 36 Army personnel who had developed symptoms consistent with the contemporaneous COVID-19 case definition during the 30 days prior to 16 March 2020. Given the well-described risks of rapid spread of respiratory infections in military personnel in enclosed societies [6]. the RMO and Public Health England (PHE) declared a potential outbreak and implemented stringent social distancing and infection control measures within the barracks, including isolation of all symptomatic personnel and their close contacts. PHE, in collaboration with the RMO, Army Public Health team and

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Research in context

Evidence before this study

We searched PubMed with the terms "COVID-19 outbreak" or "SARS-CoV-2 outbreak" and "Army" or "military" to identify publications relating to COVID-19 outbreaks in military settings in the English Language between 01 January and 30 September 2020, focusing particularly on those where enhanced outbreak investigations were undertaken. Large outbreaks of COVID-19 have been reported in closed institutional settings such as care homes, prisons, detention centres and even cruise ships, but there are limited data on COVID-19 outbreaks in military settings, mainly reporting outbreak mitigation strategies through strict social distancing measures.

Added value of this study

We initiated one of the first outbreak investigations in Army barracks early in the course of the COVID-19 pandemic in London, England, and monitored the course of the outbreak until its resolution 5 weeks later. We identified high rates of asymptomatic infection, more so among females than males, and specific risk factors for infection in Army personnel. We have explored the relationship of neutralising antibodies to the recovery of infectious virus, as a proxy for infectiousness.

Implications of all the available evidence

Within the Army barracks where most personnel were healthy young white adults, asymptomatic individuals are likely to play an important role in spreading the virus. Those with neutralising antibodies did not have infectious virus even if RT-PCR positive. Neutralising antibodies are likely to be a relevant correlate of protective immunity.

Commanders initiated an urgent enhanced outbreak investigation, the first of its kind during the COVID-19 pandemic in England. All adult Army personnel, their families and civilians working in the Army barracks on 30 March 2020 were invited to have nasal and throat swabs and blood samples taken with repeat testing 5 weeks later.

The aim of the investigation was to assess the spread and progression of SARS-CoV-2 infection and to monitor the development and progress of SARS-CoV-2 antibodies in symptomatic and asymptomatic personnel in a single barracks experiencing a COVID-19 outbreak. Potential risk factors for SARS-CoV-2 infection and antibody positivity as well as functional activity of SARS-CoV-2 antibodies were also assessed as part of the investigation.

2. Methods

2.1. Setting

The Army barracks is a compact living and working environment, home to approximately 440 regular establishment users. It comprises of 300 soldiers, 70 musicians, some family dependents and civilians and contractors. Around 200 personnel live on site, either with families, or colleagues in single or shared flats, often with shared bathrooms. There are communal dining facilities and social areas, and only two points of regular entry and exit to the site. Working routines involve a mix of different indoor and outdoor activities within the barracks and around London. All civilians and around 70 Army personnel live off-site in London.

2.2. Outbreak investigation

All Army personnel, adult family members and civilians linked to the Army barracks were invited to participate in the enhanced surveillance on 30 March 2020. The same participants were invited for repeat investigations 36 days later. All mitigation measures recommended by Army Public Health and PHE on the 16 March 2020 have continued , along with additional enhanced cleaning regimes and, where possible, working from home, thereby reducing population density at the site. Nine personnel who were self-isolating with COVID-19 symptoms at the first visit were excluded. Because of limited availability of SARS-CoV-2 testing during the early phase of the pandemic, the diagnosis was not confirmed in these individuals and, since they did not take part in the initial investigations, they were also not invited for the second visit.

By the second visit, 45 Army personnel had self-isolated because they were symptomatic or close contacts of a symptomatic case, with one individual requiring hospital admission. The timelines for symptomatic cases and clusters are described in an epidemiological curve. Additional data on accommodation block and occupational group were collected as part of the outbreak investigation and used to support the implementation of targeted infection control measures in the barracks. Close contact of a confirmed case was defined as according to national guidance [7]. All participants from the first visit were invited for the second visit.

Investigations were performed in a large on-site gymnasium with small groups and socially distanced arrivals to optimise flow. Following written informed consent, participants completed a short questionnaire on demographics, living arrangements, contacts and symptoms in the past month. The participants took their own nasal swabs (both nostrils) under guided and witnessed supervision and the throat swab and blood sample (~10 mls) were taken by the investigating team. Nasal self-swabs are less invasive and quicker to obtain, with less potential for coughing, sneezing or gagging and have similar sensitivities for detecting SARS-CoV-2 RNA as nasopharyngeal swabs [8]. The samples were transported to PHE where they were processed and stored until testing.

2.3. Laboratory testing

Nucleic acid was extracted from nasal and throat swab samples and analysed by a real-time reverse transcription (RT) PCR assay targeting a conserved region of the open reading frame of the **ORF 1ab** gene of SARS CoV-2 as previously described [9], together with detection of an assay internal control to monitor the extraction and RT-PCR processes. SARS-CoV-2 positive samples with a cycle threshold (Ct) value of <35 were subjected to virus isolation on Vero E6 cells swabs and virus detection was confirmed by cytopathic effect (CPE) up to 14 days after inoculation [10].

Serum samples were analysed for SARS-CoV-2 antibodies by indirect ELISA using England 2/2020 CoV as the viral antigen. The assay format compares the reactivity to native viral proteins expressed within a SARS-Cov-2 infected mammalian cell lysate with that of uninfected control cells. Assay cut-offs were previously determined by validation studies against panels of known seronegative human populations and blood taken prior to 2020 [11,12]. Antibodies titres >0.5 were considered to be positive and $0.35-0.5$ as equivocal. SARS-CoV-2 (isolate England/02/2020) specific neutralising antibody levels were measured using a modification of the WHO influenza micro-neutralisation methodology [13].

Whole genome sequencing (WGS) was performed on samples using reverse transcription and PCR amplification of extracted viral RNA with a PCR CT value <33 [14]. Viral amplicons were sequenced using Illumina library preparation kits (Nextera) and sequenced on Illumina short-read sequencing machines. Raw sequence data was trimmed and aligned against a SARS-CoV2 reference genome

(NC_045512.2). A consensus sequence representing each genome base derived from the reference alignment. Consensus sequences were collated from each sample, assessed for quality and then aligned (mafft). Maximum likelihood phylogenetic trees were derived from sequence alignments using IQtree.

2.4. Statistical analysis

As this was an outbreak investigation, sample size was determined by the population size in the barracks on the day of each visit. Completed paper questionnaires at each visit were entered into a bespoke Microsoft Access database (Microsoft Corporation®, WA) and electronically linked with SARS-CoV-2 RT-PCR and antibody results within PHE. Any missing information was followed-up with the RMO in the barracks and/or completed at the second investigation visit. At the end of the investigation, the complete dataset was transferred to Stata v15.0 (StataCorp, Texas) for analysis. Risk factors and symptoms were assessed as categorical variables with proportions positive for SARS-CoV-2 RNA and antibodies and compared by calculating relative risks and proportional risk differences, along with 95% confidence intervals (because of relatively rare outcome events). Data were not adjusted for multiple comparisons in the univariate analyses. Multivariable logistic regression was performed to assess the interaction of gender and symptoms following the univariable analysis. The risk was then calculated for the stratification of asymptomatic cases by gender. A full list of variables considered can be found in the Questionnaire (**Supplement S1**).

Ethics approval

The investigation protocol was approved by the PHE Research Ethics and Governance Group (REGG Ref: NR191, 27 March 2020).

Funding

This study was internally funded by PHE – which is a public body and an executive agency of the Department of Health – as part of the COVID-19 response. The authors had sole responsibility for the study design, data collection, data analysis, data interpretation, and writing of the report. The authors are employed by PHE or the Ministry of Defence within the Army Medical Services. SNL and MZ had full access to all the data in the study and final responsibility for the decision to submit for publication.

3. Results

The first round of the Army barracks investigation involved 304 participants, who all completed a questionnaire, 302 provided a nasal swab, 301 a throat swab and 285 a blood sample (Fig. 1). Participants included Army personnel (n = 254, 85%), their family members (n = 10, 3%) and civilians (n = 36, 12%), and the majority were male (n = 247, 81%); four participants did not declare status. Their demographics are summarised in Table 3 **& Supplement S2**. During the first visit, 24 (8%) participants had a positive throat swab for SARS-CoV-2, of whom 11 also were positive on nose swab (**Supplement S3**). Infectious virus was recovered from 7/24 (29%) participants, mainly from nose swabs (n = 6/7). Serological investigations identified 28 participants with detectable SARS-CoV-2 IgG antibodies, including 19 (7%) seropositive and 9 in the equivocal range. Among these 28 individuals, 12/19 (63%) and 4/9 (44%), respectively, had neutralising antibodies.

At the second visit 36 days later, 193 (64%) participants returned. Loss to follow-up was primarily due to essential military taskings as well as instructions to work from home where possible. All 193 completed a second questionnaire and provided a nose swab and blood sample and 192 had a throat swab taken. Of these, 28 participants (15%) had detectable SARS-CoV-2 antibodies, including 25 (13%) positive and 3 in the equivocal range, with 13/25 (52%) and 0/3, respectively, having neutralising antibodies. No one tested on the second visit remained RT-PCR positive for SARS-CoV-2 and none were newly positive for the virus.

All participants who were SARS-CoV-2 RT-PCR positive for infection in visit 1 were SARS-CoV-2 antibody positive at visit 2, and most of those with SARS-CoV-2 antibodies at the first visit had an increase in IgG and neutralising antibody levels (Fig. 2). Those who were RT-PCR positive in visit 1 were more likely to be seropositive than those

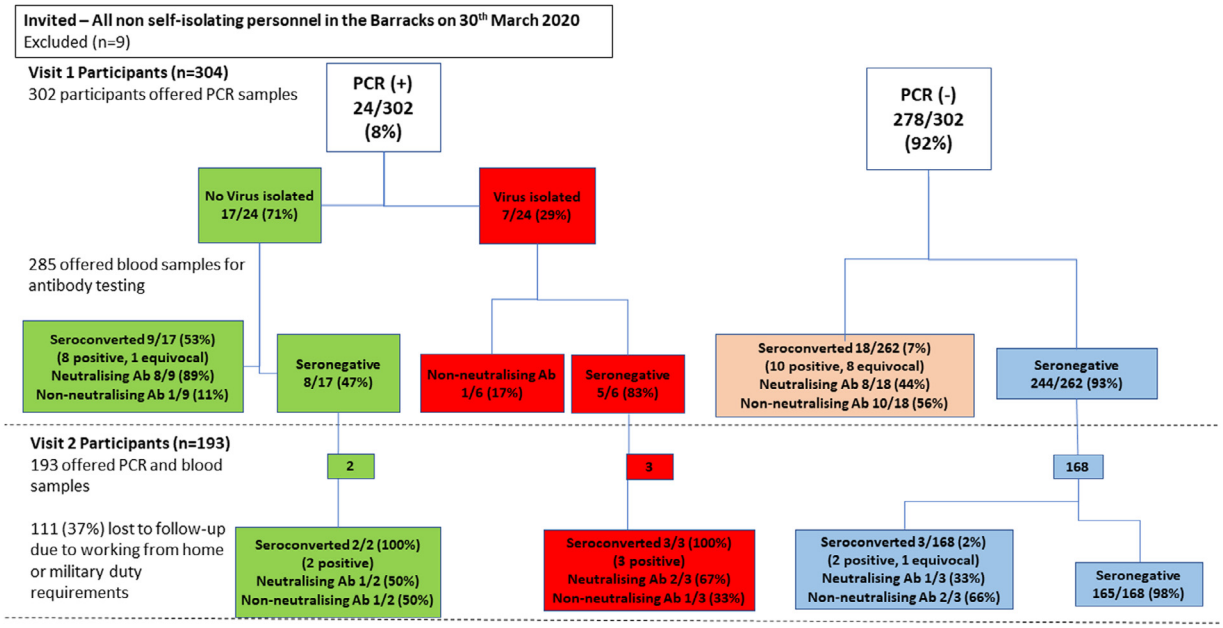

Fig. 1. SARS-CoV-2 antibody positivity by RT-PCR status at visit 1 in participants COVID-19 outbreak investigation in a London Army barracks.

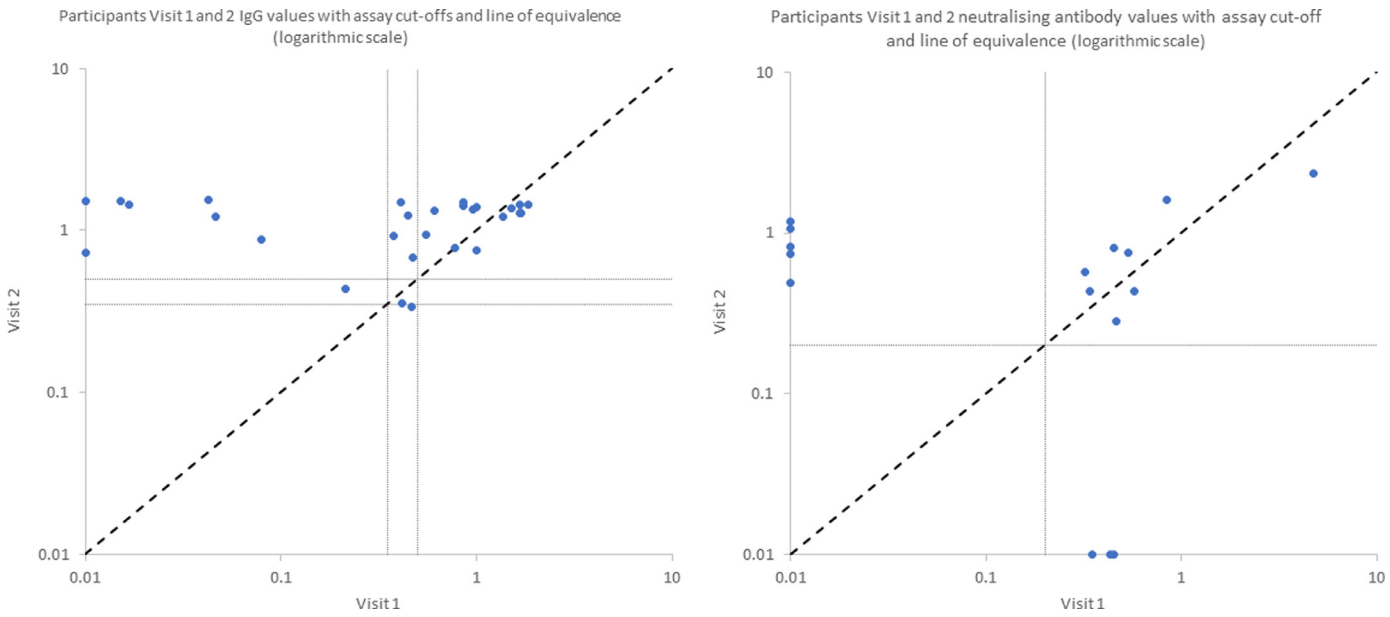

Fig. 2. Changes in IgG and Neutralising antibody levels on a log scale with lines of equivalence.

who were RT-PCR negative. Not all participants who seroconverted, however, had neutralising antibodies (Fig. 2). Nine participants at visit 1 were both RT-PCR and SARS-CoV-2 antibody positive. No participant from whom infectious virus was recovered had neutralising antibodies at the same time (Fig. 3).

Around two-thirds of participants (22/34, 64%) with positive RT-PCR or SARS-CoV-2 antibodies were asymptomatic. New onset symptoms were only seen in RT-PCR positive participants, while SARS-CoV-2 antibodies – and more specifically neutralising antibodies – were identified mainly in those who had been symptomatic prior to testing (**Supplement S4**).

3.1. *Outbreak evolution and progression*

Concerns of an outbreak at the Army barracks were first raised on 16 March, by which time 36 Army personnel had reported symptoms consistent with COVID-19, including 11 had self-isolated in line with national guidance since 12 March. These 11 Army personnel attended the first investigation visit and 10/11 also attended the second visit. Seven of these 11 symptomatic personnel had evidence of COVID-19 exposure, either through RT-PCR, antibody detection or both. One individual who was PCR and antibody negative on both occasions had confirmed picornavirus infection.

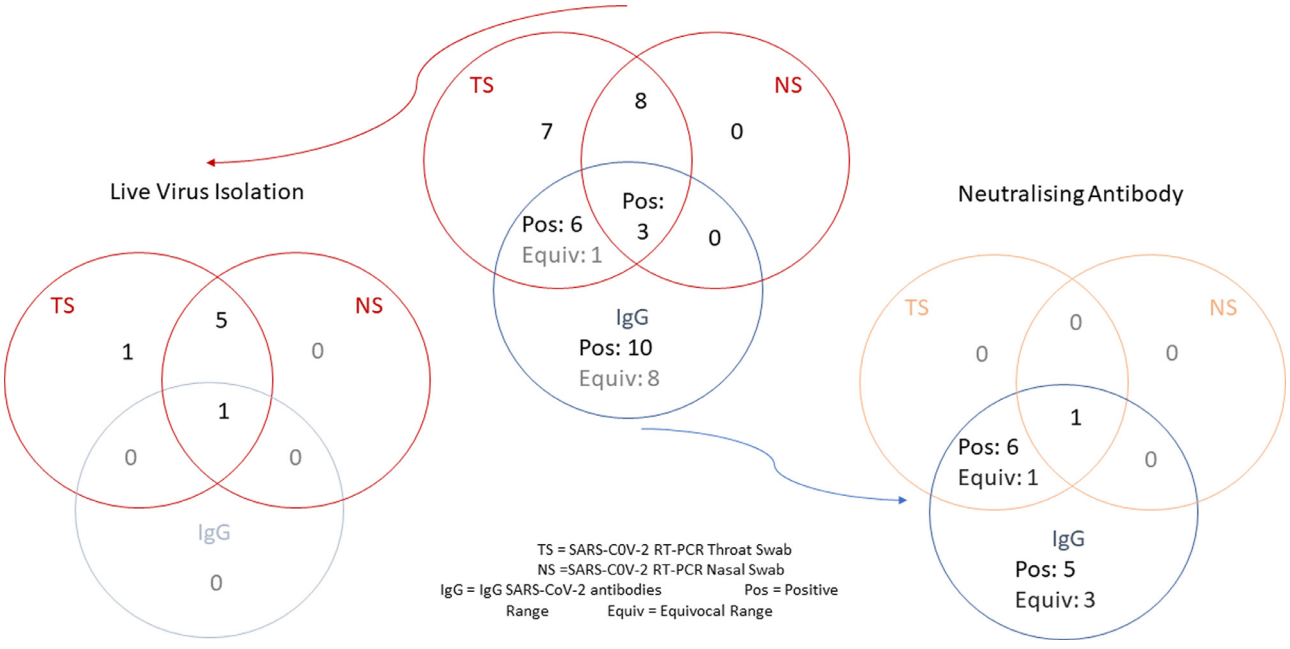

Fig. 3. Venn diagrams showing interaction of RT-PCR results and serology outcomes of participants during a COVID-19 outbreak investigation in a London Army barracks.

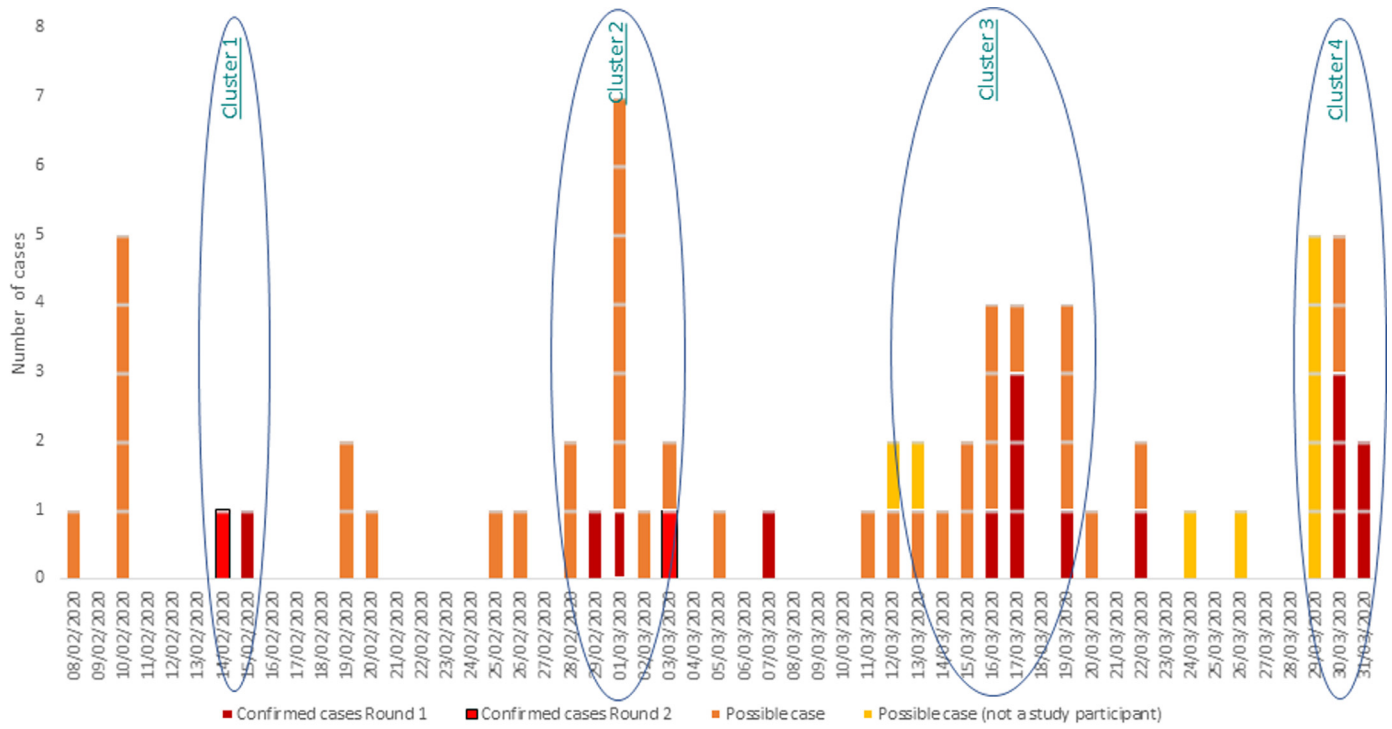

Fig. 4. Epidemiological curve of possible and confirmed cases during a COVID-19 outbreak investigation in a London Army barracks.

Based on confirmed cases, 4 symptomatic clusters were identified at 2 week intervals from 6 weeks prior to the first day of testing **(Fig. 4)**. The first two clusters occurred prior to the implementation of self-isolation for symptomatic cases. The third cluster was spread across eight days, predominately affecting those living on-site, and moving from a group of musicians (who accounted for two-thirds of cases in the third cluster) to other personnel who also lived on-site. This third symptomatic cluster started at the same time as infection control measures were introduced on 12th March 2020 which was associated with a rapid reduction in the interval between symptom onset and time to self-isolation **(Supplement S5)**. Following the final case in the third cluster, there were no further cases in the barracks for 14 days until the fourth cluster started on the day of testing, likely introduced by individuals living off-site.

3.2. Whole genome sequencing (WGS)

All 24 RT-PCR positive samples with Ct <33 were subjected to WGS and 17 sequences were obtained (**Supplement S6**). WGS indicated multiple different introductions, likely between 6 and 9, of the virus into the barracks, two of which were associated with clusters of 4 cases with genetically indistinguishable SARS-CoV-2 strains. These two clusters each included symptomatic individuals who were part of the final symptomatic cluster which started on the day of the first sampling visit (**Fig. 4**). The four individuals in one of these clusters all worked in the same department within the barracks. The remaining cases, included eight other individuals infected with strains that had less than 3 base differences, were all asymptomatic and with only a workplace connection between them, indicating silent transmission within the barracks.

3.3. Gender

Females were 2.5 (95% CI, 1.0–6.0) times more likely to be antibody positive than males, and, in the multivariable logistic regression analysis, there was an interaction with risk of a positive test being even higher in females who were asymptomatic ($P = 0.032$). On stratification of asymptomatic participants by gender, asymptomatic female were 6.5 (95% CI, 1.9–22.1) times more likely to be positive than asymptomatic males (**Tables 1 & 2a**).

3.4. Smoking

Information on smoking was limited by low response rates. Where recorded, however, smokers were less likely to have a positive RT-PCR for SARS-CoV-2 (1/9 [11%] vs 23/34 [68%]; $P = 0.005$) compared to non-smokers, and none of the smokers were positive on nose swab or had live virus isolated from a throat swab, or had neutralising antibodies at the first or second visit.

3.5. Symptoms

Fever and cough were associated with SARS-CoV-2 antibody positivity at visit 1, as well as ageusia and anosmia, but since the latter symptoms were not part of the initial case definition for COVID-19 and because of limited testing at the time, these cases did not self-isolate (**Tables 2a & b**).

3.6. Close contact with a confirmed case

Close contacts of a confirmed case of COVID-19 were 7.3 (95% CI, 3.3–16.5), 25.2 (95% CI, 14.0–45.0) and 3.2 (95% CI, 1.7–6.0) times more likely to be RT-PCR positive, SARS-CoV-2 IgG antibody positive and neutralising antibody positive, respectively, compared to those

Table 1
Factors associated with SARS-CoV-2 RT-PCR positivity in Visit 1 during a COVID-19 outbreak investigation in a London Army barracks.

Demographic variable	PCR-positivity (Visit 1)		
	Risk	RR (95% CI)	Risk Difference (95% CI)
Gender			
Female	7/57 (12%)	1.8 (0.8 to 4.1)	0.05 (-0.04 to 0.2)
Male	17/245 (7%)	Baseline	
Shared bedroom			
Yes	9/128 (7%)	0.8 (0.4 to 1.9)	- 0.01 (-0.08 to 0.05)
No	14/166 (8%)	Baseline	
Shared bathroom			
Yes	22/271 (8%)	1.2 (0.3 to 4.9)	0.01 (-0.08 to 0.1)
No	2/30 (7%)	Baseline	
Bathroom shared with one other Army Colleague			
Yes	14/115 (12%)	2.4 (1.1 to 5.4)	0.07 (0.003 to 0.1)
No	9/179 (5%)	Baseline	
Close contact with a confirmed case			
Yes	4/8 (50%)	7.3 (3.3 to 16.5)	0.4 (0.08 to 0.8)
No	20/293 (7%)	Baseline	
Smoke or Vape (limited data available)			
Yes	1/9 (11%)	0.2 (0.03 to 1.1)	-0.5 (-0.8 to -0.3)
No	22/34 (65%)	Baseline	
Asymptomatic cases by gender			
Asymptomatic Female	5/42 (12%)	1.8 (0.7 to 4.8)	0.05 (-0.05 to 0.2)
Asymptomatic Male	12/180 (7%)	Baseline	
Symptomatic cases by gender			
Symptomatic Female	2/15 (13%	1.7 (0.4 to 8.1)	0.06 (-0.1 to 0.2)
Symptomatic Male	5/65 (8%)	Baseline	

Symptom Variable	PCR-positivity		
	Risk	RR (95% CI)	Risk Difference (95% CI)
Any Symptoms			
Yes	7/80 (9%)	1.1 (0.5 to 2.7)	0.01 (-0.06 to 0.08)
No	17/222 (8%)	Baseline	
Fever			
Yes	3/27 (11%)	1.5 (0.5 to 4.6)	0.03 (-0.09 to 0.2)
No	21/275 (8%)	Baseline	
Cough			
Yes	4/46 (9%)	1.1 (0.4 to 3.1)	0.008 (-0.08 to 0.09)
No	20/256 (8%)	Baseline	
Anosmia (Loss of Smell)			
Yes	2/7 (29%)	3.8 (1.1 to 13.2)	0.2 (-0.1 to 0.6)
No	22/295 (7%)	Baseline	
Ageusia (Loss of Taste)			
Yes	2/6 (33%)	4.5 (1.5 to 15)	0.3 (-0.1 to 0.6)
No	22/296 (7%)	Baseline	

Army/civilian/family status is not included as the results are confounded by the transmission dynamics of the virus through the barracks with civilians most likely to have recent infection and Army personnel previous infection.

individuals who did not have close contact with a confirmed case (**Tables 1 & 2a**). In total, 24 participants were close contacts of a confirmed case; 8 were household contacts, including two who had a personal/social contact, and 16 had close contact (<2 metres) with a confirmed case for >15 minutes, including 13 who had only contact through the workplace.

3.7. Accommodation factors

SARS-CoV-2 RT-PCR positivity or antibody detection was not associated with the number of individuals in shared collegial or family settings. Personnel who shared a bathroom with just one other colleague compared to any other number, were 2.4 (95% CI; 1.1–5.4) and 2.6 (95% CI; 1.1–6.4) times more likely to be PCR and antibody positive, respectively (**Tables 1 & 2a**). These results remained similar when adjusting for gender (data not shown).

4. Discussion

In one of the first COVID-19 outbreak investigations undertaken in England, we found evidence of asymptomatic infection and transmission among Army personnel and civilians in a London barracks. Through detailed epidemiological, laboratory and genomic investigations, we identified the potential source of infection into the barracks and monitored its progression before and after implementation of strict infection control measures on 16 March 2020. We found that nasal swabs were less likely to be RT-PCR positive for SARS-CoV-2 than throat swabs but more likely to have higher viral loads with lower RT-PCR cycle threshold values and more likely to have live virus isolated, suggesting a greater risk for transmission to others.. PCR-testing provided a point prevalence for SARS-CoV-2 infection but significantly underestimated the extent and spread of infection within the barracks when compared to serology, as has been noted in other

Table 2a
Factors associated with SARS-CoV-2 IgG and Neutralising antibody positivity in Visit 1.

Variable	IgG Antibody positivity (Visit 1)			Neutralising Antibody positivity (Visit 1)		
	Risk	RR (95% CI)	Risk Difference (95% CI)	Risk	RR (95% CI)	Risk Difference (95% CI)
Gender						
Female	7/54 (13%)	2.5 (1.0 to 6.0)	0.08 (-0.02 to 0.2)	9/15 (60%)	2.2 (1 to 4.7)	0.3 (0.03 to 0.6)
Male	12/231 (5%)	Baseline		7/26 (27%)	Baseline	
Shared Bedroom						
Yes	8/119 (7%)	1.0 (0.4 to 2.3)	-0.002 (-0.06 to 0.06)	7/14 (50%)	1.4 (0.7 to 2.9)	0.1 (-0.2 to 0.5)
No	11/159 (7%)	Baseline		9/25 (36%)	Baseline	
Shared Bathroom						
Yes	19/257 (8%)	_	0.08 (0.04 to 0.1)	15/36 (42%)	2 (0.3 to 12.5)	0.2 (-0.2 to 0.6)
No	0/28 (0%)	Baseline		1/5 (20%)	Baseline	
Bathroom shared with one other Army Colleague						
Yes	12/110 (11%)	2.6 (1.1 to 6.4)	0.07 (0.002 to 0.1)	11/22 (50%)	1.7 (0.7 to 4)	0.2 (-0.09 to 0.5)
No	7/168 (4%)	Baseline		5/17 (29%)	Baseline	
Close contact with a confirmed case						
Yes	8/8 (100%)	25.2 (14.0 to 45.0)	0.96 (0.9 to 0.98)	7/8 (88%)	3.2 (1.7 to 6.0)	0.6 (0.3 to 0.9)
No	11/277 (4%)	Baseline		9/33 (27%)	Baseline	
Smoke or Vape (limited data available)						
Yes	3/9 (33%)	0.7 (0.3 to 1.8)	-0.2 (-0.5 to 0.2)	0/4	NA	-0.5 (-0.6 to -0.3)
No	16/33 (48%)	Baseline		13/28 (46%)	Baseline	
Asymptomatic cases by gender						
Asymptomatic Female	6/39 (15%)	6.5 (1.9 to 22.1)	0.1 (0.01 to 0.2)	8/12 (67%)	3.8 (1.3 to 11.4)	0.5 (0.2 to 0.8)
Asymptomatic Male	4/170 (2%)	Baseline		3/17 (18%)	Baseline	
Symptomatic cases by gender						
Symptomatic Female	1/15 (7%)	0.5 (0.1 to 3.8)	-0.06 (-0.2 to 0.09)	1/3 (33%)	0.8 (0.1 to 4.4)	-0.1 (-0.7 to 0.5)
Symptomatic Male	8/61 (13%)	Baseline		4/9 (44%)	Baseline	

Symptom Variable	IgG Antibody positivity			Neutralising Antibody positivity		
	Risk	RR (95% CI)	Risk Difference (95% CI)	Risk	RR (95% CI)	Risk Difference (95% CI)
Any Symptoms						
Yes	9/76 (12%)	2.5 (1 to 5.9)	0.07 (-0.01 to 0.2)	5/12 (42%)	1.1 (0.5 to 2.5)	0.04 (-0.2 to 0.4)
No	10/209 (5%)	Baseline		11/29 (38%)	Baseline	
Fever						
Yes	6/26 (23%)	4.6 (1.9 to 11.1)	0.2 (0.02 to 0.3)	5/7 (71%)	2.2 (1.2 to 4.3)	0.39 (0.02 to 0.8)
No	13/259 (5%)	Baseline		11/34 (32%)	Baseline	
Cough						
Yes	6/44 (14%)	2.5 (1 to 6.3)	0.08 (-0.02 to 0.2)	3/8 (38%)	1 (0.4 to 2.6)	- 0.02 (-0.4 to 0.4)
No	13/241 (5%)	Baseline		13/33 (39%)	Baseline	
Anosmia (Loss of Smell)						
Yes	3/7 (43%)	7.4 (2.8 to 19.8)	0.4 (0.004 to 0.7)	2/4 (50%)	1.3 (0.5 to 3.8)	0.1 (-0.4 to 0.6)
No	16/278 (6%)	Baseline		14/37 (38%)	Baseline	
Ageusia (Loss of Taste)						
Yes	4/6 (67%)	12.4 (5.9 to 26.2)	0.6 (0.2 to 0.99)	3/5 (60%)	1.7 (0.7 to 3.8)	0.2 (-0.2 to 0.7)
No	15/279 (5%)	Baseline		13/36 (36%)	Baseline	

settings [15]. We identified individuals who were both SARS-CoV-2 RT-PCR and antibody positive but, importantly, we were unable to isolate infectious virus from anyone who had neutralising antibodies.

The Army barracks outbreak provided a unique opportunity to understand infection and transmission of SARS-CoV-2. Within this high-density and a relatively closed community, we found that 14% of individuals were positive on RT-PCR or serology at the first visit. SARS-CoV-2 seroprevalence (7%) was around 5-fold higher than estimated for London at the time (Week 13) [2]. SARS-CoV-2 infection rates, however, were substantially lower than reported for outbreaks in other institutional settings such as care homes [11], ships [16], homeless shelters [17,18], detention centres [19], and prisons [20]. Reassuringly, early implementation of social distancing measures successfully mitigated the outbreak, as reported in other military settings [3–5]. By the second visit, 36 days later (Week 19), SARS-CoV-2 seroprevalence in the barracks was 12.9% compared to 14.8% in London overall [2]. Serosurveillance and symptomatic cluster contact mapping suggest that internal transmission can be controlled, but WGS, highlights the difficulties of preventing new introductions from external community.

4.1. Neutralising antibodies and live virus isolation

At the time of testing, the Army personnel were at different stages of SARS-CoV-2 infection. Some had active infection, while others had recovered and were antibody positive. Nine individuals, however, tested positive for both the virus and serum SARS-CoV-2 antibodies. Notably, though, these personnel either had live virus isolated or neutralising antibodies, but not both. This is consistent with a recent report of a strong inverse association between serum neutralising antibodies and isolation of live virus from the respiratory tract of patients with confirmed COVID-19 [21], indicating that individuals with neutralising antibodies are unlikely to be infectious to others.

In our cohort, all RT-PCR positive individuals showed a serological response emphasising the clear relationship between virus detection and an adaptive host immune response, a point which had been uncertain early in the pandemic. Not all symptomatic individuals, however, had SARS-CoV-2 infection based on RT-PCR or serology testing, highlighting the lack of specificity of clinical case definitions. Additionally, some seropositive participants did not have neutralising antibodies. It is possible that they might be protected through cellular immune responses [22,23], but we did not investigate this in our cohort.

Table 2b
Factors associated with SARS-CoV-2 IgG and Neutralising antibody positivity in Visit 2.

Variable	IgG Antibody positivity (Visit 2)			Neutralising Antibody positivity (Visit 2)		
	Risk	RR (95% CI)	Risk Difference (95% CI)	Risk	RR (95% CI)	Risk Difference (95% CI)
Gender						
Female	5/37 (14%)	1.1 (0.4 to 2.6)	0.007 (-0.1 to 0.1)	2/6 (33%)	0.7 (0.2 to 2.2)	-0.2 (-0.6 to 0.3)
Male	20/156 (13%)	Baseline		11/22 (50%)	Baseline	
Shared Bedroom						
Yes	7/87 (8%)	0.5 (0.2 to 1.0)	-0.09 (-0.2 to -0.003)	5/8 (63%)	1.6 (0.7 to 3.3)	0.23 (-0.2 to 0.6)
No	18/102 (18%)	Baseline		8/20 (40%)	Baseline	
Shared Bathroom						
Yes	22/172 (13%)	0.9 (0.3 to 2.7)	-0.01 (-0.2 to 0.1)	11/24 (46%)	0.9 (0.3 to 2.7)	-0.04 (-0.6 to 0.5)
No	3/21 (14%)	Baseline		2/4 (50%)	Baseline	
Bathroom shared with one other Army Colleague						
Yes	16/72 (22%)	2.9 (1.3 to 6.2)	0.2 (0.04 to 0.3)	8/17 (47%)	1 (0.5 to 2.4)	0.02 (-0.4 to 0.4)
No	9/117 (8%)	Baseline		5/11 (45%)	Baseline	
Smoke or Vape (limited data available)						
Yes	3/8 (38%)	0.5 (0.2-1.2)	-0.4(-0.8 to -0.1)	0/3	NA	-0.7 (-0.9 to -0.5)
No	17/21 (81%)	Baseline		12/17 (71%)	Baseline	
Asymptomatic cases by gender						
Asymptomatic Female	5/29 (17%)	2.1 (0.8 to 5.7)	0.1 (-0.6 to 0.2)	2/6 (33%)	0.6 (0.2 to 2.1)	-0.2 (-0.7 to 0.3)
Asymptomatic Male	9/109 (8%)	Baseline		6/11 (55%)	Baseline	
Symptomatic cases by gender						
Symptomatic Female	0/8 (0%)	NA	-0.2 (-0.4 to -0.1)	0/0	NA	NA
Symptomatic Male	11/47 (23%)	Baseline		5/11 (45%)	Baseline	
Close contact with a confirmed case						
Yes	5/5 (100%)	9.4 (6.2 to 14.2)	0.9 (0.8 to 0.94)	3/5 (60%)	1.4 (0.6 to 3.2)	0.17 (-0.3 to 0.6)
No	20/188 (11%)	Baseline		10/23 (43%)	Baseline	

Symptom Variable	IgG Antibody positivity			Neutralising Antibody positivity		
	Risk	RR (95% CI)	Risk Difference (95% CI)	Risk	RR (95% CI)	Risk Difference (95% CI)
Any Symptoms						
Yes	11/55 (20%)	1.98 (0.96 to 4.1)	0.1 (-0.02 to 0.2)	5/11 (45%)	0.97 (0.4 to 2.2)	-0.02 (-0.4 to 0.4)
No	14/138 (10%)	Baseline		8/17 (47%)	Baseline	
Fever						
Yes	6/20 (30%)	2.7 (1.2 to 6.0)	0.2 (-0.02 to 0.4)	4/6 (67%)	1.6 (0.8 to 3.5)	0.3 (-0.2 to 0.7)
No	19/173 (11%)	Baseline		9/22 (40%)	Baseline	
Cough						
Yes	9/33 (27%)	2.7 (1.3 to 5.6)	0.2 (0.1 to 0.3)	4/9 (44%)	0.9 (0.4 to 2.2)	-0.03 (-0.4 to 0.4)
No	16/160 (10%)	Baseline		9/19 (47%)	Baseline	
Anosmia (Loss of Smell)						
Yes	2/5 (40%)	3.3 (1.0 to 10.2)	0.3 (-0.2 to 0.7)	0/2 (0%)	_	-0.5 (-0.7 to -0.3)
No	23/188 (12%)	Baseline		13/26 (50%)	Baseline	
Ageusia (Loss of Taste)						
Yes	3/4 (75%)	6.4 (3.2 to 12.8)	0.6 (0.2 to 1.1)	1/3 (33%)	0.7 (0.1 to 3.6)	-0.1 (-0.7 to 0.4)
No	22/189 (12%)	Baseline		12/25 (48%)	Baseline	

Army/civilian/family status is not included as the results are confounded by the transmission dynamics of the virus through the barracks with civilians most likely to have recent infection and Army personnel with previous infection.

4.2. Symptoms

Nearly two-thirds of personnel who were either RT-PCR or antibody positive or both were asymptomatic throughout their infection, which highlights the high degree of heterogeneity in the clinical spectrum of COVID-19 in different age-groups and populations [24]. We isolated infectious virus from asymptomatic individuals [11,25], demonstrating their potential to transmit the infection [26]. Additionally, although <10% of participants were females, they were significantly more likely to be asymptomatic and become antibody positive than males. A gender difference in asymptomatic SARS-CoV-2 has not been reported [24,27], but universal screening of pregnant women found that the vast majority of SARS-CoV-2 positive women were asymptomatic [28]. In symptomatic personnel, fever and respiratory tract symptoms were the most common symptoms, although anosmia and ageusia had only just been identified as possible manifestations of COVID-19 and were not included in the case definition at the time [29], which may partly have contributed to ongoing transmission within the barracks [30].

4.3. Risk factors

We identified other risk factors for COVID-19. Musicians accounted for two-thirds of personnel in the third symptomatic cluster, flagging concerns of potential aerosol transmission from brass and woodwind instruments [31]. In this group, however, there were other potential explanations including exposure to a community source at a local event and personal/household/social contact with a confirmed case, which was identified in 7 of the 8 musicians. We also identified sharing a bathroom with one person as another risk factor, highlighting the importance of ventilating and cleaning shared ablutions, particularly in complex accommodation settings. The increased risk among two persons sharing a bathroom could be due to aerosol generation in smaller bathroom spaces following oral hygiene and/or physical contact through sharing of sinks. Smokers had a low risk of SARS-CoV-2 infection and antibody positivity but the poor response for this question precludes any firm conclusions, although other large population-based studies have also reported significantly lower odds of SARS-CoV-2 positivity among active smokers compared to non-smokers [32].

Table 3
Key demographics of 304 participant at visit 1.

Demographics of 304 Participants		
Age	n=	302
Median	IQR	Range
28 years	23-36 years	18-57 years
Gender (n=304)		
Count (Rate)		
Male	247 (81%)	
Female	57 (19%)	
Status (n=300)		
Army	254 (85%)	
Civilian	36 (12%)	
Family	10 (3%)	
Share Bedroom (n=296)		
No	167 (56%)	
Yes	129 (44%)	
Share Bathroom (n=303)		
No	273 (90%)	
Yes	30 (10%)	
COVID-19 close contact (n=303)		
No	283 (93%)	
Yes	20 (7%)	
Smoke or Vape (n=43)		
No	34 (79%)	
Yes	9 (21%	
Symptoms (n=304)		
Count if Yes to Symptom (Rate)		
Fever	27 (9%)	
Cough	46 (37%)	
Anosmia	7 (2%)	
Ageusia	6 (2%)	

Further details are contained in Supplement Table S2.

4.4. Strengths and limitations

The strength of this investigation lies in the rapidity of initiating the outbreak investigation during a period of high community transmission in London and the high participation rate. The findings of this outbreak are likely to be applicable to other similar shared living situations such as university dormitories, prisons and care homes, although the investigation involved a single Army barracks where participants were mainly young white healthy men.

Other potential biases include higher participation rates among those were directly affected by COVID-19 and exclusion of symptomatic personnel who were self-isolating at visit 1; the former may overestimate an effect size, whilst the latter may underestimate it.

Other potential limitations include the limited sensitivity of RT-PCR tests for SARS-CoV-2 and the lack of correlates for antibody protection against infection and re-infection. We also did not measure cellular immune responses in our cohort. Additionally, we relied on participant recall for symptom onset and timing, most of whom were not tested for SARS-CoV-2 infection prior to the investigation. At least some reported illnesses were likely due to other viruses, as highlighted by the picornavirus infection in one participant and, therefore, the true rate of asymptomatic infection may be underestimated.

5. Conclusions

Army barracks are a high-risk, high-density complex setting at increased risk of SARS-CoV-2 transmission and outbreaks. Potential risk factors for transmission included contact with a confirmed case, fomite transmission in indoor settings and specifically two-person shared ablutions. We identified high rates of asymptomatic infection, especially in women, and asymptomatic spread within the barracks through identification of genetically indistinguishable strains among Army personnel. Importantly, we demonstrated that individuals could be SARS-CoV-2 RT-PCR and antibody positive, but those with neutralising antibodies did not have infectious virus isolates even if RT-PCR positive and were, therefore, potentially not infectious to others.

Contributors

JYC, WW, MZ, SNL and MER conceived the idea. SNL was the principal investigator. HT, WW, DR, RJ, LW, FA, JYC and SNL performed the investigations. JE, RG, MP, AL, and MZ led the laboratory investigations. RM led to genomic analysis. NA led the statistical analysis. HT wrote the protocol and the first draft of the manuscript. HT, SNL, MZ, RJ, LW and FA contributed to the literature search. All authors contributed to the analysis and discussion. All authors approved the final manuscript.

Data access

This was a public health investigation and, therefore, limited additional data for wider sharing – all available data are included in the manuscript.

Declaration of Competing Interests

The authors declare no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanepe.2020.100015.

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