INVESTIGATION OF SARS-CoV-2 OUTBREAKS IN SIX CARE HOMES IN LONDON, APRIL 2020

The London Care Home Investigation

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Running Head: COVID-19 outbreaks in care homes

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Abstract

Background

Care homes are experiencing large outbreaks of coronavirus disease 2019 (COVID-19) associated with high case-fatality. We conducted detailed investigations in six London care homes reporting suspected COVID-19 outbreaks during April 2020.

Methods

Residents and staff had nasal swabs taken for SARS CoV-2 testing using RT-PCR and were followed-up for 14 days. They were categorized as symptomatic, post-symptomatic or pre-symptomatic if they had symptoms at the time of testing, in the two weeks before or two weeks after testing, respectively, or asymptomatic throughout. Virus isolation and whole genome sequencing (WGS) was also performed.

Results

Across the six care homes, 107/268 (39.9%) residents were SARS CoV-2 positive, including 29 (27.1%) symptomatic, 9 (8.4%) post-symptomatic, 21 (19.6%) pre-symptomatic and 48 (44.9%) who remained asymptomatic. Case-fatality was highest among symptomatic SARS-CoV-2 positive residents (10/29, 34.5%) compared to 2/48 (4.2%) asymptomatic, 2/9 (11.8%) post-symptomatic, or 3/21 (14.3%) pre-symptomatic residents. Among staff, 51/250 (20.4%) were SARS CoV-2 positive and 29/51 (56.9%) remained asymptomatic. RT-PCR cycle thresholds and live virus recovery were similar between symptomatic/asymptomatic residents/staff. WGS identified multiple introductions of different SARS-CoV-2 strains into individual care homes. SARS-CoV-2 strains from residents and staff had identical sequences, as did strains from fatal and non-fatal cases.

Conclusions

In care homes reporting a COVID-19 outbreak, a high rate of SARS-CoV-2 positivity was found among residents and staff, half of whom were asymptomatic and are potential reservoirs for on-going

transmission. Symptomatic SARS-CoV-2 residents had high case-fatality, while asymptomatic infection was rarely fatal. Symptom-based screening alone is not sufficient for outbreak control.

Introduction

Amid the COVID-19 pandemic, community care facilities including nursing and residential homes have been termed "hubs" and "besieged castles" in North America and Europe, having experienced large outbreaks due to rapid transmission of SARS-CoV-2.[1,23] Care homes have a unique, mixed population of multi-disciplinary staff and frail residents with multiple underlying comorbidities.[4,5] Such residents are at high risk of severe complications and death due to respiratory viruses, such as influenza,[6] and now COVID-19.[7-10]

In the UK, the first imported COVID-19 cases were confirmed in late January 2020 and autochronous transmission confirmed in late February 2020. Case numbers increased rapidly from early March, with lockdown being announced on 23 March. London experienced faster transmission and higher rates of COVID-19 cases than any other region in the UK,[11] with many care homes reporting large and sustained outbreaks, associated with high case-fatality rates (CFR).[8] In England and Wales, there were 45,899 deaths among care home residents between March 02 and May 02, 2020, and 12,526 (27.3%) involved COVID-19.[12]

Beginning April 10, Public Health England (PHE) undertook an enhanced outbreak investigation in six London care homes experiencing COVID-19 outbreaks to increase understanding of disease transmission and inform urgent public health interventions. We assessed SARS-CoV-2 positivity in residents and staff at the care homes and followed them daily for two weeks. We investigated differences in outcomes according to SARS-CoV-2 positivity, viral load and recovery of infectious virus according to timing and presence or absence of symptoms. We also conducted detailed whole genomic sequence (WGS) analyses of recovered SARS-CoV-2 strains.

Methods

We identified six care homes reporting a suspected outbreak (≥2 suspected cases) of COVID-19 to PHE during 10-13 April 2020. These were mainly nursing or mixed nursing/residential homes of different sizes, providing care for 43-100 residents with 14-130 staff. The care homes were in different stages of a COVID-19 outbreak. The earliest care home outbreak began on March 11 and they had experienced 29 fatalities already at the time of swabbing while the last home's outbreak began on April 07 with two fatalities among residents (**Supplement S1**). Initial contact with the care home involved conducting a risk assessment undertaken, and providing immediate infection prevention and control advice was provided as standard (**Supplement S2**).

We assessed SARS-CoV-2 positivity in the residents and staff (carers and those without caring duties) recorded their symptoms in the two weeks prior to sampling and followed them daily for new symptoms and outcomes for two weeks through daily phone-call and datasheet completion. Care home data were collected systematically covering resident demographics, facilities, staffing and infection control measures in place at the time of swabbing (**Supplement S3**). Care workers took nasal swabs for the residents and submitted their own samples by self-swabbing with appropriate instructions.

Laboratory methods

Swabs from all six homes were couriered to the PHE reference laboratory on the day they were collected. Nucleic acid was extracted and analysed by a real-time reverse transcription (RT) PCR assay on an Applied Biosystems 7500 FAST system targeting a conserved region of the open reading frame (ORF1ab) gene of SARS-CoV-2, together with an internal control.[13] SARS-CoV-2 positive samples with a cycle threshold (Ct) value of <35 were incubated on Vero E6 mammalian cells and virus detection was confirmed by cytopathic effect (CPE) up to 14 days post-inoculation. Whole genome sequencing (WGS) was performed on all positive samples.[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-CoV-2 reference genome (NC_045512.2). A consensus sequence representing each genome base was derived from the reference alignment. Consensus sequences were assessed for quality, aligned using MAFFT (Multiple Alignment using Fast Fourier Transform, version 7.310), manually curated and maximum likelihood phylogenetic trees derived using IQtree (version 2.04). Care home derived genomes were compared within a comprehensive background of SARS-CoV2 genomes across the UK.

Case definitions

A symptomatic individual was defined as typical COVID-19 symptoms (fever, cough, sore throat, breathlessness, anosmia) in a staff member or resident and additionally atypical (new confusion, reduced alertness, fatigue, lethargy, reduced mobility, diarrhoea) COVID-19 symptoms in a resident at the time of swabbing. Post-symptomatic individuals had symptoms during the 14 days prior but were asymptomatic at the time of swabbing. Pre-symptomatic individuals developed symptoms in the 14 days after swabbing. Asymptomatic individuals did not exhibit any symptoms during the two weeks before or after swabbing.

Statistical analysis

Data are mainly descriptive. Data that did not follow a normal distribution were described as medians with interquartile ranges and compared using the Mann-Whitney U test. Categorical variables were described as proportions and compared using the chi-squared or Fisher's Exact test as appropriate. Logistic regression was used to assess independent risk factors for death among residents and included age in years, gender, symptom group (asymptomatic, post-symptomatic, pre-symptomatic and symptomatic) at the time of swabbing and RT-PCR result.

Results

Residents

A total of 268 residents were tested and 107 (39.9%) were SARS-COV-2 positive. Four residents were hospitalised and 21 (7.8%) died, including two of the hospitalised cases, within two weeks of testing. Their characteristics, symptomatology and clinical outcomes are summarised in **Table 1**. Of the 107 positive residents, only 29 (27.1%) were symptomatic at the time of testing. The positive predictive value for SARS-CoV-2 in a symptomatic resident was 54.7% (29/53). Additional follow-up identified 19/107 (8.4%) residents as post-symptomatic, 21 (19.6%) pre-symptomatic and 48 (44.9%) who remained asymptomatic throughout the surveillance period (**Figure 1**). The negative predictive value of being SARS-CoV-2 negative if asymptomatic at the time of testing was 63.7% (137/215).
Of the 69 (72.9%) SARS-COV-2 positive residents who were asymptomatic before or at the time of testing, 21 (30.4%) developed symptoms in the following two weeks. Among the 161 residents who tested negative, 24 (14.9%) were symptomatic at testing, 6 (3.7%) reported symptoms consistent with COVID-19 in the previous two weeks and 4 (2.5%) developed symptoms after the test but were not re-tested for SARS-CoV2 (**Table 2**). There was no difference in age or sex between symptomatic and asymptomatic residents overall or by SARS-CoV-2 positivity status.

Symptomatic and asymptomatic residents

CFR within 14 days of testing was significantly higher in symptomatic residents than in asymptomatic residents, regardless of SARS-CoV-2 result (11/53 [20.8%] vs. 10/215 (4.7%); P=0.001). Ten (34.5%) of the 29 symptomatic SARS-CoV-2 positive residents died compared to 1/24 (4.2%) of symptomatic residents who tested negative (P=0.007). Of the 215 asymptomatic residents, 78 (36.3%) tested positive for SARS-CoV-2 and CFR was 9.0% (7/78) compared to 2.2% (3/137) in those who tested SARS-CoV-2 negative (P=0.023).

Of the SARS-CoV-2 positive residents, 10/29(34.5%) died compared to only 2/48 (4.2%) asymptomatic residents, 2/9 (22.2%) post-symptomatic and 3/21 (14.3%) pre-symptomatic residents (P=0.005). Among SARS-CoV-2 negative residents, 4/127 (3.2%) (3 asymptomatic, 1 symptomatic)

died. Using a logistic regression model, SARS-CoV-2 positivity (aOR 5.27; 95%CI, 1.62-17.1; P=0.006) and being symptomatic compared to being asymptomatic at the time of swabbing (aOR 4.5; 95%CI, 1.46-13.9; P=0.009) were independently associated death among residents after adjusting for age in years (adjusted odds ratio [aOR] 1.01; 95%CI, 0.96-1.06; P=0.38) and being female (aOR 1.67; 95%CI, 0.43-6.51; P=0.46).

Care Home Staff

Of the 250 staff tested, 51 (20.4%) were SARS-CoV-2 positive but only 11/51 (21.6%) were symptomatic. The positive predictive value of a symptomatic staff individual being positive for SARS-CoV-2 was 1436.7% (11/30) and the negative predictive value was 81.8% (180/220). Follow-up of 51 SARS-CoV-2 positive staff members found 29 (56.9%) did not develop any symptoms in the two weeks before or after testing, whereas four (7.8%) were pre-symptomatic and 7 (13.7%) were post-symptomatic. Thus, of the 33 staff who were asymptomatic at the time of swabbing, only 4 (7.8%) went on to develop symptoms in the subsequent two weeks. There was no difference in age or sex between symptomatic and asymptomatic staff overall or by SARS-CoV-2 positivity status.

Cycle Threshold and Viral Culture

There was no difference in Ct values for SARS-CoV-2 positive residents or staff who were post-symptomatic, symptomatic or pre-symptomatic at the time of swabbing compared to asymptomatic residents (**Figure 2a**). In total, 87 samples with Ct values <35 were cultured and infectious virus was recovered from all of categories of symptomatic, post-symptomatic, pre-symptomatic and asymptomatic residents and staff. Based on symptom reporting alone (without repeat SARS-CoV-2 testing), live virus was isolated up to 13 days after and 12 days before symptom onset among residents and up to 6 days before and 7 days after symptom onset among staff (**Supplement S4**). Higher Ct values (lower virus load) samples are associated with decreasing ability to recover infectious virus from 100% (2/2) with Ct <20.00 to 17.0% (9/53) with Ct 30.00-34.99 (χ^2 for trend,

P<0.001) (**Figure 2b**), but showed no correlation with presence or absence of symptoms in staff or residents (**Supplement S5**). Virus recovery rates were similar in symptomatic and asymptomatic residents (5/17 [29.4%] vs. 14/33 [42.4%]; P=0.37) and staff (2/6 [33.3% vs. 5/21 23%]; P=0.96) at the time of testing, and were not different between fatal and non-fatal cases among residents (5/10 [50.0%] vs. 14/40 [35.0%]; P=0.38).

WGS Analysis

All 158 PCR positive samples underwent WGS analysis and 99 (68 residents, 31 staff) distributed across all the care homes yielded sequence sufficient for WGS analysis (**Supplement S6**). Phylogenetic analysis identified informal clusters, with evidence for multiple introductions of the virus into care home settings. All care home clusters of SARS-CoV-2 genomes included at least one staff member, apart from care home B with no PCR positive staff and high rates of staff self-isolation. Care home A exhibited three distinct sequence clusters and six singletons, potentially representing up to nine separate introductions. Genomic analysis did not identify any differences between asymptomatic/symptomatic residents/staff. The ten sequences from residents who died were distributed across the lineages identified and were closely matched to sequences derived from non-fatal cases in the same care homes (**Figure 3**).

Discussion

Investigation of six London care homes experiencing SARS Cov-2 outbreaks identified a high proportion of residents and staff who tested positive for SARS-CoV-2, of whom 72.3% and 80.4%, respectively, were asymptomatic at the time of testing and 44.9% and 56.9% remained asymptomatic throughout the surveillance period, highlighting the silent nature of infection in this setting, despite the large age difference between the resident and staff groups. The homes were at different stages of a SARS-CoV-2 outbreak with some already having experienced a high number of deaths. Among residents, SARS-CoV-2 positivity and being symptomatic were strong predictors of

death. RT-PCR Ct values and recovery of live viruses were similar in among asymptomatic and symptomatic residents and staff. We identified multiple introductions of the virus into individual care homes and individual care home clusters included at least one staff member. Genomic analysis did not identify any differences between asymptomatic/symptomatic residents/staff or between fatal and non-fatal cases.

Our findings provide further evidence for pre-symptomatic infection among residents in care homes experiencing a COVID-19 outbreak,[10,15,16] but also identified a large cohort of residents and staff who remained asymptomatic throughout the surveillance period. A recent detailed longitudinal investigation of a COVID-19 outbreak in a single nursing facility in Seattle, Washington state, highlighted important common features and some key differences compared to our cohort.[10] The high rate of asymptomatic residents at the time of first (23/76, 30%) and second (24/49, 49%) swabbing a week later in the Seattle investigation is consistent with our findings of a high but variable prevalence of asymptomatic SARS-CoV-2 positive residents in care homes at different stages of a COVID-19 outbreak. The high case-fatality rate of 35.7% among symptomatic SARS-CoV-2 positive residents in our cohort was also consistent with the 26% reported in the Seattle care home.

However, while >85% of asymptomatic residents in the Seattle investigation went on to develop symptoms over the next seven days,[10] in our cohort, more than half the residents remained asymptomatic during the surveillance period, possibly because of the maturity of the outbreaks in the London care homes at the time of testing, as evidenced by the number of deaths that had already occurred, although mild/non-specific symptoms might not have been identified by the care staff.[17]

We did not observe any correlation in the RT-PCR CT values between symptomatic and asymptomatic residents or staff, nor any association with age, indicating that symptomatic and

asymptomatic residents and staff of all ages had similar viral loads when infected with SARS-CoV-2. Like the Seattle investigation,[10] and others,[16,18] we also found high rates of live virus isolation among symptomatic and asymptomatic residents and staff, highlighting the enormous potential for silent transmission of infection and the futility of symptom-based only surveillance in care homes and other similar settings.[6] We found that 19.0% of asymptomatic residents went on to develop symptoms at a median of four days after testing but, in our longer follow-up, some residents developed symptoms consistent with COVID-19 up to 13 days later, although repeat testing was not performed to confirm the diagnosis. Together with the Seattle investigation where live virus was isolated from specimens taken up to 6 days before and 9 days after the first symptoms,[10] these findings provide the evidence for current recommendations to isolate test-positive residents for at least 14 days and test-positive staff for 7 days.

Some SARS-COV-2 negative residents and staff in our cohort became symptomatic in the second week after testing which may indicate on-going transmission, but we did not undertake additional testing to confirm this. More regular screening with systematic testing of all residents and staff, irrespective of symptoms, and longer follow-up may have provided additional information on SARS-CoV-2 transmission and outcomes.

Genomic analysis of SARS-COV-2 strains identified separate introductions with distinct clusters that included at least one member of staff within each cluster, raising the question as to whether staff members might be the source of the infection, although it was not possible to confirm the direction of infection with a single snapshot survey.

The strengths of this investigation lie in the large number of residents and staff tested through a single national reference centre across six different care homes each at different stages of a COVID-19 outbreak. Extensive and complete daily follow-up provided detailed understanding of symptom

progression and identified a high prevalence of asymptomatic SARS-CoV-2 residents and staff who may serve as potential reservoirs of infection. We collected minimal data on a large number of residents and staff to ensure complete ascertainment and did not use standard questionnaires to collect symptoms, allowing instead the staff to assess the residents who they knew well and report symptoms in free text. A limitation of the investigation was that we only tested the care homes once. Additional testing would have allowed more objective tracking of transmission and diagnosis in pre-symptomatic residents and staff, while testing for other viruses may have explained the development of new symptoms in SARS/CoV-2 positive and negative residents and staffs.

Implications

Our results highlight the difficulties in controlling SARS-CoV-2 outbreaks in care homes despite extensive infection control guidance and training.[19,20] Infectious virus recovery in asymptomatic staff and residents emphasises their likely importance as silent reservoirs and transmitters of infection and explains the failure of infection control measures which have been largely based on identification of symptomatic individuals. When transmission is occurring in the community, enhanced infection prevention and control measures should be quickly implemented in care homes, along with rigorous and systematic testing for SARS-Cov-2 among staff and residents, with particular attention to infection control measures for visitors, new residents and movement of residents and staff from other facilities. Early and wide testing of residents and staff, along with immediate isolation of suspected cases, may help control the introduction and spread of SARsCoV-2 into care homes (**Supplement 7**). Point-of-care testing for SARS-CoV2 antigens/antibodies, if sufficiently sensitive and accurate, could potentially have a role in the near future.

Conclusions

Care home residents are very vulnerable to COVID-19 and have a high case-fatality rate, particularly if symptomatic at the time of swabbing. With sustained community transmission, testing of all

residents and staff irrespective of symptoms combined with measures to prevent virus introduction into care homes and robust infection prevention and control measures will be needed to control SARS-CoV-2 outbreaks in care homes. Further investigations to better understand transmission dynamics in care home, especially in relation to asymptomatic infection among residents and staff, are needed to develop a more tailored approach to SARS-CoV-2 outbreak control

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Conflicts of interest

None

Ethical Approval

PHE has legal permission, provided by Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002, to process patient confidential information for national surveillance of communicable diseases and as such, individual patient consent is not required.

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Table 1. Investigation of symptomatic and asymptomatic residents and staff in six care homes experiencing different stages of a COVID-19 outbreak										
Care Home	Onset of first case	Died already at the time of swabbing	Date of nasal swab	Residents positive for SARS-CoV-2	SARS-COV-2 Positive Residents who were Symptomatic	SARS-CoV-2 Negative Residents who were Symptomatic	Self-isolating staff	Staff Positive for SARS-CoV-2	SARS-CoV-2 Positive Staff who were Symptomatic	SARS-CoV-2 Negative Staff who were Symptomatic
A (n=94)	11 March	29 (5 in hospital)	14 April	18/33 (54.5%)	2/18 (11.1%)	1/15 (6.7%)	4/130	17/61 (27.9%)	4/17 (23.5%)	6/44 (13.6%)
B (n=72)	20 March	9 (3 in hospital)	13 April	14/52 (26.9%)	4/14 (28.6%)	4/38 (10.5%)	7/85	0/20	-	0/20
F (n=97)	23 March	4	15 April	12/58 (20.7%)	3/12 (25.0%)	0/46 -	15/70	6/39 (15.4%)	0/6	0/33 -
E (n=83)	28 March	11	14-17 April	11/27 (40.7%)	2/11 (18.2%)	0/16 -	7/65	10/56 (17.9%)	2/10 (20.0%)	5/46 (10.9%)
C (n=98)	2 April	19	14 April	22/60 (36.7%)	10/22 (45.5%)	17/38 (44.7%)	19/110	1/38 (2.6%)	1/1 (100%)	3/37 (8.1%)
D (n=74)	7 April	2	13 April	30/38 (78.9%)	8/30 (26.7%)	2/8 (25.0%)	5/14	17/36 (47.2%)	4/17 (23.5%)	5/19 (26.3%)
Total N=518				**107/268 (39.9%)**	**29/107 (27.1%)**	**24/161 (14.9%)**		**51/250 (20.4%)**	**11/51 (21.6%)**	**19/199 (9.6%)**

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Table 2. Characteristics of residents and staff in all six care homes					
	Symptom status				
	Asymptomatic	Post-symptomatic	Pre-symptomatic	Symptomatic	All
RESIDENTS					
SARS-CoV-2 Positive	N=48	N=9	N=21	N=29	N=107
Female (%)	30 (62.5%)	9 (100%)	17 (81.0%)	25(86.2%)	81 (75.7%)
Median age in years (IQR)	84 (78-90)	88 (85-91)	84 (80-91)	87 (80-91)	85 (78-90)
Median days symptom onset (IQR)	x	-5 (-6 to -3)	4 (2 to 11)	-7 (-10 to -4)	
Hospitalised	x	x	1/16 (6.3%)	2/28 (7.1%)	
Died	2/48 (4.2%)	2/9 (22.2%)	3/21 (14.3%)	10/29 (34.5%)	17/107 (15.9%)
SARS-COV-2 Negative	n=128	n=6	n=4	n=23	n=161
Female (%)	85 (66.4%)	5 (83.3%)	1 (25.0%)	18 (75.0%	109 (67.7%)
Median age in years (IQR)	85 (78-90)	81 (74-87)	84 (80-88)	86 (80-89)	85 (80-91)
Median days symptom onset (IQR)	x	-7 (-8 to -5)	13 (12-13)	-8 (-13 to -6)	
Hospitalised	x	x	1/4 (25.0%)	x	
Died	3 (2.4%)	x	x	1/24 (4.2%)	4/161 (2.5%)
STAFF					
SARS-CoV-2 Positive	N=29	N=7	N=4	N=11	N=51
Female (%)	20 (69.0%)	4 (57.1%)	3 (75.0%)	7 (63.6%)	34 (66.7%)
Median age in years (IQR)	50 (40-56)	54 (41-59)	38 (34-49)	40 (26-55)	47 (38-57)
Median symptom onset (IQR)	x	-7 (-9 to -4)	3 (2-5)	-5 (-9 to -3)	
SARS-CoV-2 Negative	N=176	N=2	N=2	N=19	N=199
Female (%)	143 (81.3%)	1 (50.0%)	2 (100%)	16 (84.2%)	162 (81.4%)
Median age in years (IQR)	47 (39-56)	52 (26-77)	50 (35-65)	43 (29-57)	47 (35-56)
Median symptom onset (IQR)	x	N/A	9 days *	(-6 (-16 to -5)	

** onset date not available for one resident; N/A, not available for two staff members*

SARS-CoV-2 Positive	N=29	N=7	N=4	N=11	N=51
Female (%)	20 (69.0%)	4 (57.1%)	3 (75.0%)	7 (63.6%)	34 (66.7%)
Median age in years (IQR)	50 (40-56)	54 (41-59)	38 (34-49)	40 (26-55)	47 (38-57)
Median symptom onset (IQR)	x	-7 (-9 to -4)	3 (2-5)	-5 (-9 to -3)	
SARS-CoV-2 Negative	N=176	N=2	N=2	N=19	N=199
Female (%)	143 (81.3%)	1 (50.0%)	2 (100%)	16 (84.2%)	162 (81.4%)
Median age in years (IQR)	47 (39-56)	52 (26-77)	50 (35-65)	43 (29-57)	47 (35-56)
Median symptom onset (IQR)	x	N/A	9 days *	(-6 (-16 to -5)	

* onset date not available for one resident; N/A, not available for two staff members

Figure 1. SARS-CoV-2 positivity, symptoms, live virus isolation and deaths in residents and staff across six London care homes experiencing a COVID-19 outbreak during April 2020. In SARS-CoV-2 positive residents, live virus was isolated from 5/17 (29.4%) of symptomatic and 14/33 (42.4%) of asymptomatic residents at the time of testing (P=0.37) and 14/40 (35.0%) survivors compared with 5/10 (50.0%) of fatal cases (P=0.38).

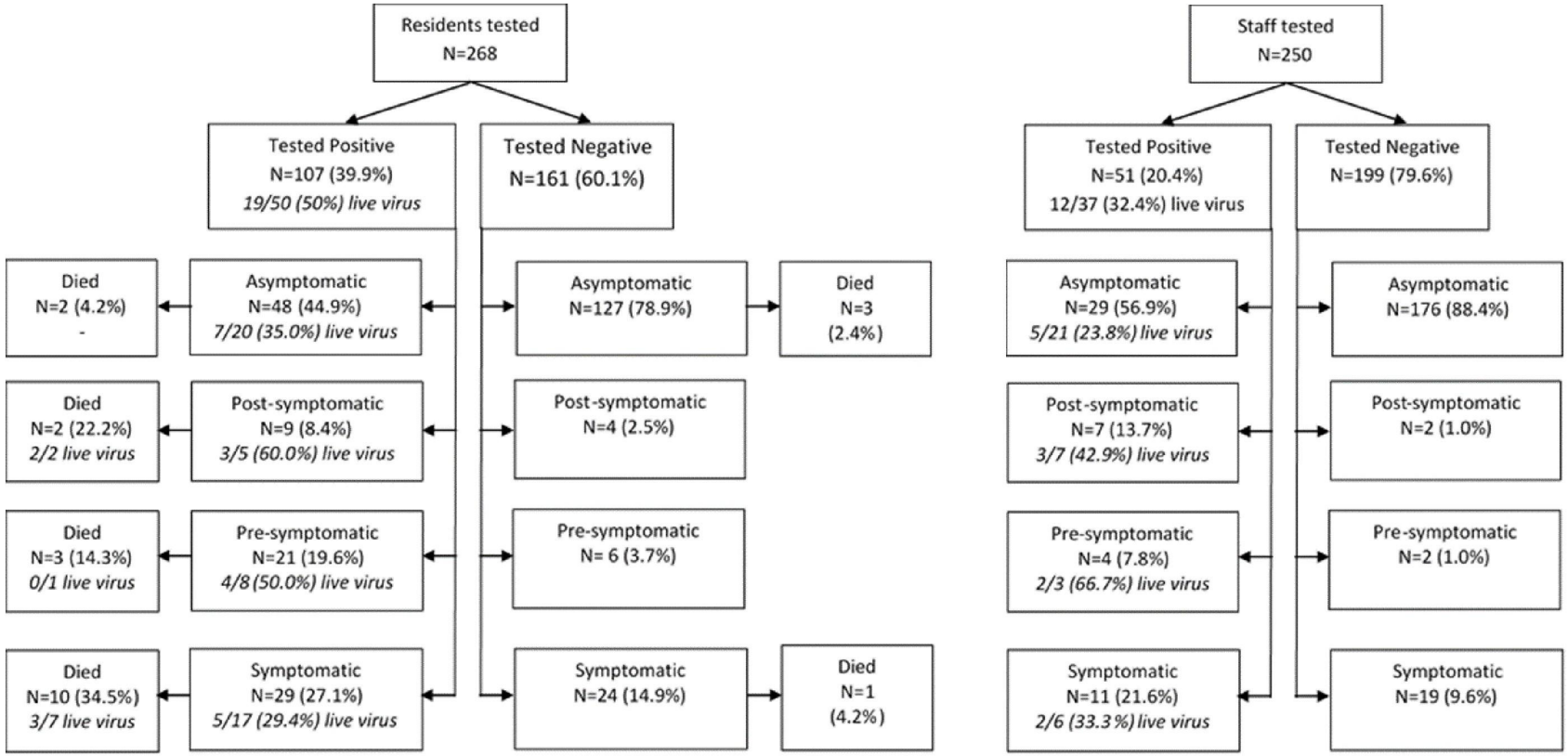


Figure 2. Maximum Likelihood phylogeny of 99 SARS-CoV-2 genomes from individuals within six care homes. Coloured branches are used to indicate the care home, staff are annotated on the tree with (S), genomes from patients who died after testing positive for covid-19 are shown with (X). Unannotated tips in the phylogeny represent genomes from care home residents.

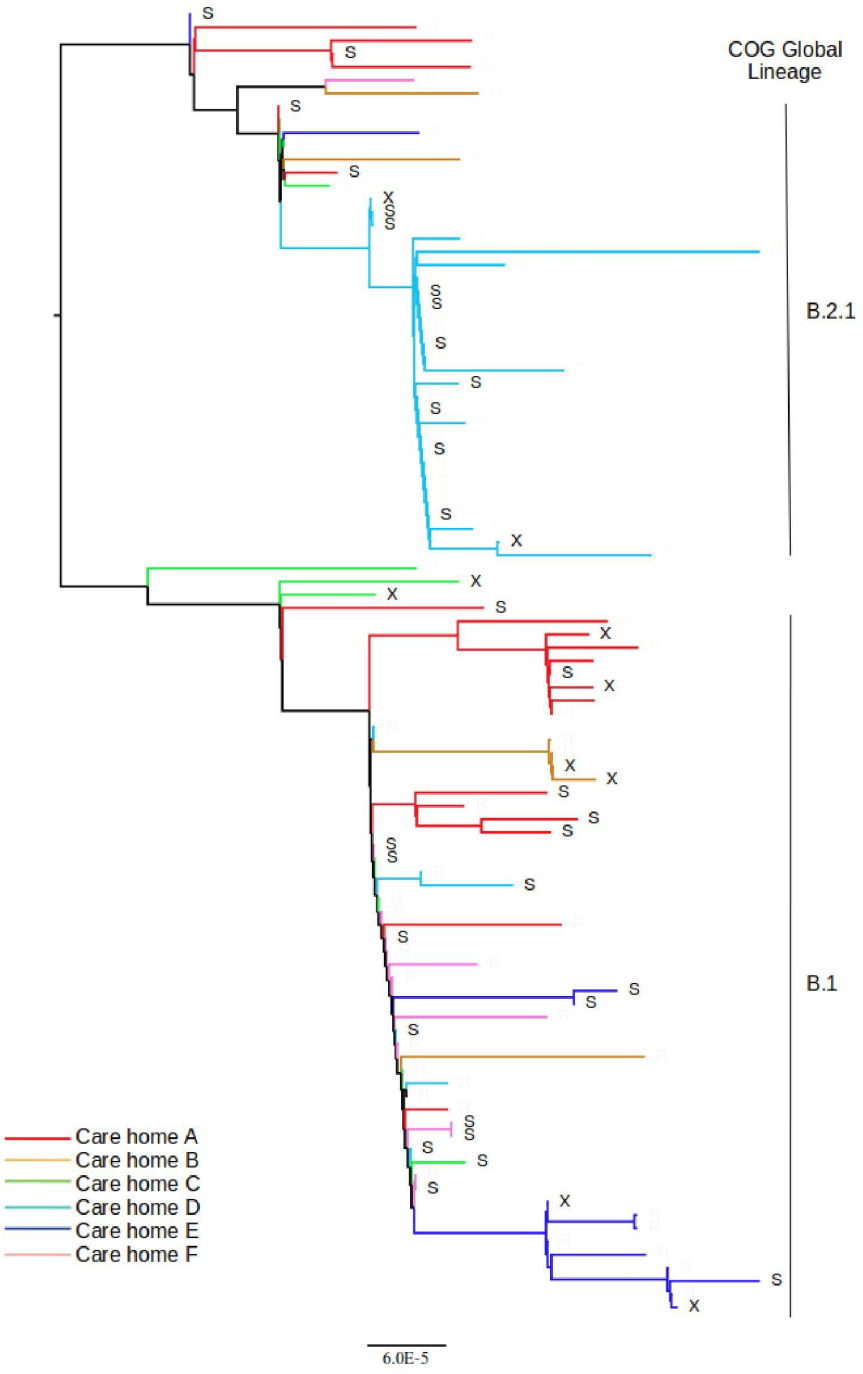


Figure 3a. Boxplot showing **median** Cycle Threshold (Ct) values with interquartile ranges (Boxes) along with minimum (Q1-1.5*IQR) and maximum (Q3+1.5*IQR) values (whiskers) and outlier values (blue circles) for asymptomatic, post-symptomatic, pre-symptomatic and symptomatic residents and staff.

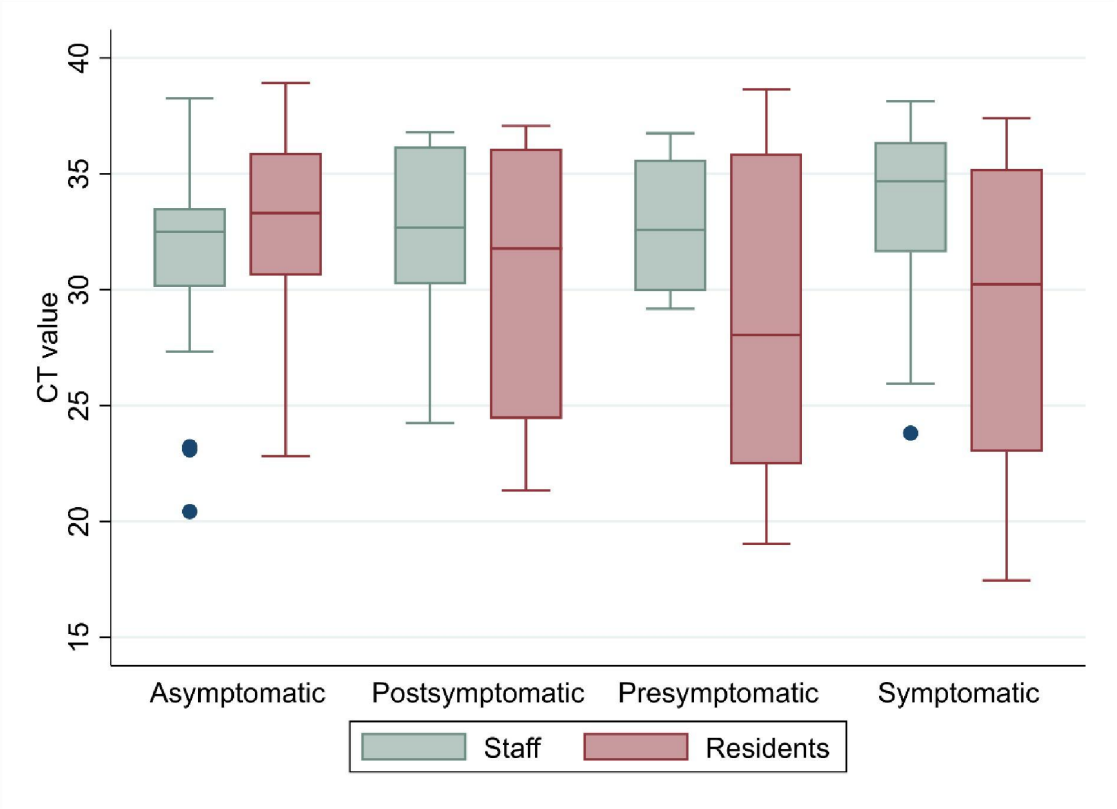
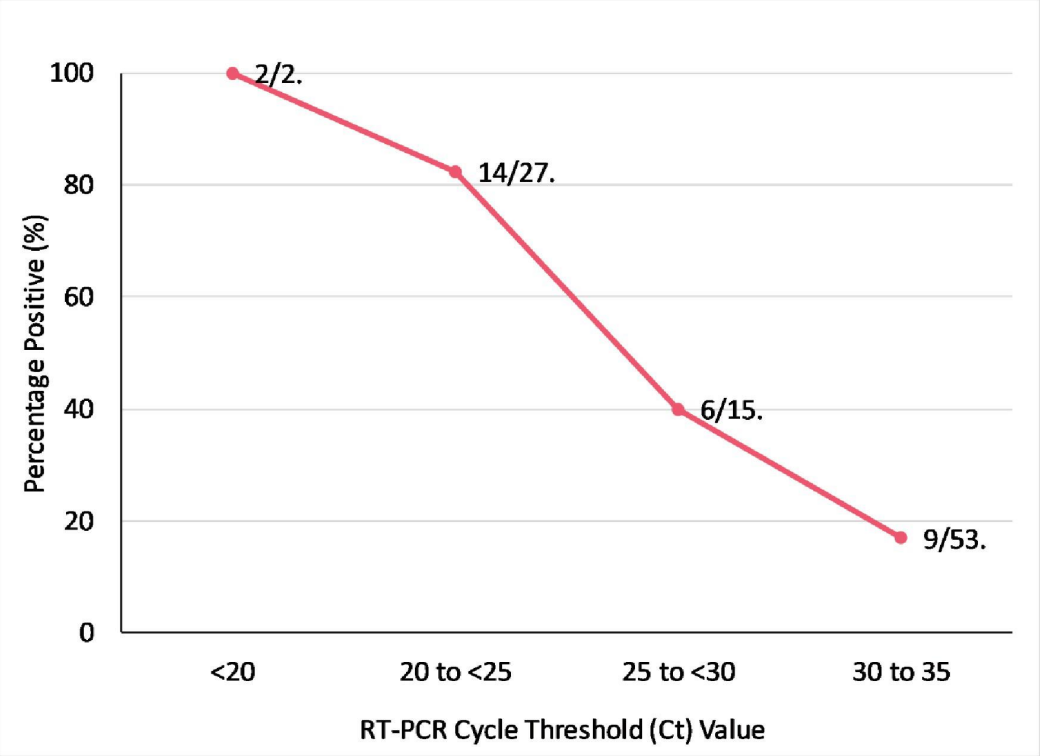


Figure 3b. Live virus isolation by RT-PCR Cycle threshold (t) range in residents and staff of care homes. The data points include live virus isolation by number of strains tested



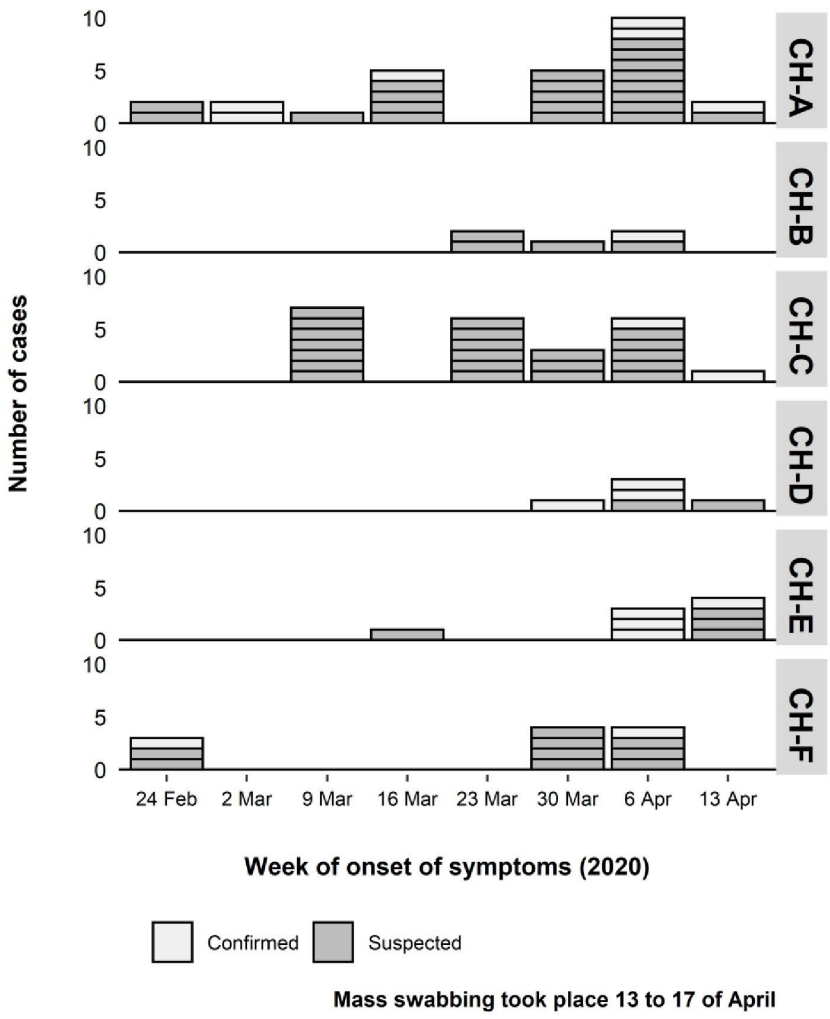
INVESTIGATION OF SARS-CoV-2 OUTBREAKS IN SIX CARE HOMES IN LONDON, APRIL 2020

The London Care Home Investigation

Ladhani S et al.

SUPPLEMENT

INFORMATION



Supplement Figure S1: Epidemic curves for the 6 London care homes with a COVID-19 outbreak that were investigated by Public Health England. Testing across the six care homes took place during the weekend ending 12 April 2020. The vertical column denotes the number of COVID-19 confirmed (orange), suspected (blue) and fatal (grey) cases among residents

Supplement Table S2: Summary of infection prevention and control advice

General infection prevention and control advice	
Hand hygiene	Reinforce education of staff and visitors about hand and respiratory hygiene and display PHE posters widely. Ensure PHE infection control policies are up to date, read and followed by all staff. Ensure liquid soap and disposable paper towels are available at each sink, and alcohol-based hand rub (at least 70%) is in every room/communal area, and stocks are adequately maintained. If it is not possible to have alcohol hand rub in rooms/communal areas, consider providing staff with individual containers.
Personal protective equipment (PPE)	Ensure that PPE is available, i.e. disposable gloves, aprons, and splash proof surgical masks, plus eye protection for procedures that may generate splashback. Ensure PPE is changed between residents (masks and eyewear can be sessional). PPE should be worn for all care activities regardless of whether residents have a suspected/confirmed case.
Linen and waste	Ensure linen management and clinical waste disposal systems are in place, including foot operated bins. Guidance on linen and waste handling is provided by PHE.
Environmental cleaning	Enhanced cleaning in home during outbreak e.g. 2 hourly cleaning in communal areas that are not closed. Clean surfaces, and high touch areas frequently (e.g. door handles). Clean common equipment between residents, e.g. hoists, aids, baths, showers. Maintain adequate levels of equipment in anticipation of increased cleaning (e.g. disposable cloths, mop heads, detergent, etc).
Staffing	Allocate a separate staff cohort to support residents with symptoms. Avoid, where possible allocating agency staff to this task. Any staff who have recovered from confirmed COVID-19 should be allocated to this. Staff should be advised not to rotate within groups of care homes.
Visitors	Any visitors should be limited to only essential persons, i.e. main carer. Discourage visits by children. Family and friends should be advised not to visit care homes, except next of kin in exceptional situations such as end of life. Healthcare visits should be restricted to those that are essential. Advise any visiting health professionals of an outbreak and rearrange non-urgent visits to the home.
Transfers	Transfer of residents to hospital or other institutions should be avoided unless clinically necessary/medical emergency and, if possible, advised by the GP. If transfer is required, transport services (including emergency ambulances) and the receiving hospital/setting should be made aware of any suspected outbreak in the home, and/or if the resident is a suspected case BEFORE transfer.
Closure	Discuss any potential closure to new admissions to the affected area/care home during an outbreak. However, with heightened bed pressures across the health and care sector, decisions around closure are not straight-forward. Where providers consider there to be imminent risks to the continuity of care, e.g. potential closure of a service, they should raise this with the Local Authority (Social Care commissioner) without delay.
For symptomatic or confirmed cases	
Residents	Isolate residents for 14 days from the onset of symptoms, or date of test if asymptomatic. • Cases should be isolated in their bedroom • Discourage use of communal areas • If communal areas remain open, advise that chairs should be 2 metres apart- magazines, books and games to be removed

	• Avoid the use of fans that re-circulate the air
Staff	Self-isolate for 7 days after onset of symptoms or date of test if asymptomatic. Household members should self-isolate for 14 days. If they develop symptoms, they should isolate for 7 days from the date of symptom onset. Staff members who have completed 7 days isolation and no longer have symptoms do not require a negative test before returning to work

Source:

Adapted from:
Public Health England. Winter-readiness information for London care homes. 2018.

Reference:

Department of Health and Social Care. *Admission and Care of Residents during COVID-19 Incident in a Care Home.* Published 2 April 2020. https://www.gov.uk/government/publications/coronavirus-covid-19-admission-and-care-of-people-in-care-homes

Public Health England. *How to work safely in care homes.*
https://www.gov.uk/government/publications/covid-19-how-to-work-safely-in-care-homes

Public Health England. COVID-19: infection prevention and control guidance.
https://www.gov.uk/government/publications/wuhan-novel-coronavirus-infection-prevention-and-control
https://www.gov.uk/government/publications/wuhan-novel-coronavirus-infection-prevention-and-control/covid-19-personal-protective-equipment-ppe

Supplement Table S3: Summary of the 6 care homes investigated during the Easter Weekend

Care Home	Care home type	Layout of care home	Room types	Infection Control
A	Nursing & end of life care	5 floors	Single occupancy rooms with ensuite	Staff did not have full PPE. They had gloves & aprons but no face masks for 3 weeks
B	Nursing and Dementia care	2 floors, 21 general nursing, 26 dementia	Single occupancy rooms with ensuite	Staff were using PPE for care duties regardless of residents' symptoms. No issues with PPE stock
F	Nursing	Layout: 3 floors; ground floor 9 needed unit, middle floor 18 bedded unit, top floor 18 bedded unit	Single occupancy rooms with ensuite	Staff using PPE for all the residents; increased cleaning of touch surfaces, hoists etc. since first case confirmed
E	½ nursing, ½ residential for dementia	4 floors: units 2 nursing, 2 residential	Single occupancy rooms with ensuite	PPE regardless of symptoms of residents, keeping all residents in isolation as much as possible.
C	Residential & Nursing	Distributed over 3 floors	Single occupancy rooms with ensuite	Adequate PPE and linen and waste management systems in place; closed to admissions and transfers
D	Nursing Care Home	3 floors; currently most people staying in their rooms with social distancing in room	Single ensuite rooms for all but 3 residents who were sharing a room	Rigorous infection prevention and control measures already in place. All staff were using PPE throughout the care home

PPE (aprons, gloves, surgical masks and visors); IPC = infection control measures in place

Supplement Table S4: Live virus isolation among asymptomatic and symptomatic residents and staff, according to timing of symptom onset

RESIDENTS	STAFF
Post-symptomatic -7 days (1/1 positive) -6 days (1/1 positive) -4 days (1/1 positive) -3 days (0/1 positive) -1 days (0/1 positive)	**Post-symptomatic** -13 days (0/1 positive) -9 days (0/2 positive) -7 days (1/1 positive) -6 days (0/1 positive) -4 days (1/1 positive) -2 day (1/1 positive)
Pre-symptomatic +1 days (0/1 positive) +9 days (0/1 positive) +11 days (1/2 positive) +13 days (1/1 positive)	**Pre-symptomatic** +2 day (0/1 positive) +4 days (1/1 positive) +6 days (1/1 positive)
Symptomatic -15 days (0/1 positive) -12 days (1/2 positive) -11 days (1/2 positive) -10 days (0/1 positive) -9 days (0/1 positive) -8 days (0/1 positive) -7 days (1/2 positive) -6 days (0/3 positive) -4 days (0/1 positive) -2 days (1/1 positive) 0 days (1/1 positive)	**Symptomatic** -10 days (0/1 positive) -9 days (0/1 positive) -5 days (1/1 positive) -4 days (1/1 positive) -3 days (0/1 positive)
Asymptomatic 5/17 (29.4%) positive	**Asymptomatic** 2/6 (33.3%) positive

Supplement Table S5: Live virus isolation by RT-PCR cycle threshold (Ct) values among asymptomatic and symptomatic residents and staff, according to timing of symptom onset.
Numbers in parenthesis for residents and staff indicate timing of symptom onset from the day of testing (x denotes symptom onset date not available)

Ct Value	RESIDENTS	STAFF
<20 (2/2 positive, 100%)	**2 POSITIVE** Pre-symptomatic (11) Symptomatic (-12)	-
20 to <25 (14/17 positive, 82.4%)	**10 POSITIVE** 2 Asymptomatic 3 Symptomatic (-11, -7, -2) 3 Post-symptomatic (-4, -6, -7) 2 Pre-symptomatic (9, 13) **2 NEGATIVE** 1 Asymptomatic 1 Symptomatic (-7)	**4 POSITIVE** 2 Asymptomatic 1 symptomatic (-5) 1 post-symptomatic (-4) **1 NEGATIVE** Asymptomatic
25 to <30 (6/15 positive, 40.0%)	**2 POSITIVE** 1 Asymptomatic 1 Symptomatic (0) **8 NEGATIVE** 2 Asymptomatic 3 Symptomatic (-6, -10, -15) 3 Pre-symptomatic (1, 11, X)	**4 POSITIVE** 1 Asymptomatic 1 Symptomatic (-4) 1 Post-symptomatic (-7) 1 Pre-symptomatic (+6) **5 NEGATIVE** 5 Asymptomatic
30 to <35 (9/53 positive, 17.0%)	**5 POSITIVE** 4 Asymptomatic 1 Pre-symptomatic (x) **21 NEGATIVE** 10 Asymptomatic 8 Symptomatic (-4, -6, -6, -8, -9, -11, -12, X) 2 Post-symptomatic (-3, -1) 1 Pre-symptomatic (2)	**4 POSITIVE** 2 Asymptomatic 1 Post-symptomatic (-2) 1 Pre-symptomatic (+4) **23 NEGATIVE** 14 Asymptomatic 4 Symptomatic (-3, -6, -9, -10) 4 Post-symptomatic (-9, -9, -13)

Supplement Data S6. Whole genome sequence analysis of SARS-CoV-2 strains causing an outbreak in 6 London Care Homes

Care home	Number samples tried	Number sequences derived	Staff	Residents
Care home A	55	21	8	13
Care home B	14	7	0	7
Care home F	21	13	5	8
Care home E	19 (one duplicate)	13	4	9
Care home C	26	11	2	9
Care home D	47	34	12	22

Table S6a. SARS-CoV-2 strains selected for whole genome sequencing by care homes

All 158 PCR positive samples were used for WGS analysis. Of these, 99 yielded sequence sufficient for WGS analysis distributed amongst all the care homes; 31/99 from staff and 68/99 from residents. Sequences were aligned using maaft (version 7.310), manually curated and a phylogenetic tree was built using IQtree (version 2.04). This phylogenetic tree (**Figure 3 in the manuscript**) was coloured to indicate care home of origin and annotated to indicate sequences derived from staff members and sequences from residents who had died. In order to place care home derived sequences within a comprehensive background of SARS-CoV2 genomes from within the UK, care home sequences were identified within the COG consortium maximum likelihood phylogeny containing 27,768 sequences (tree included as **Supplement Figure S6b** below).

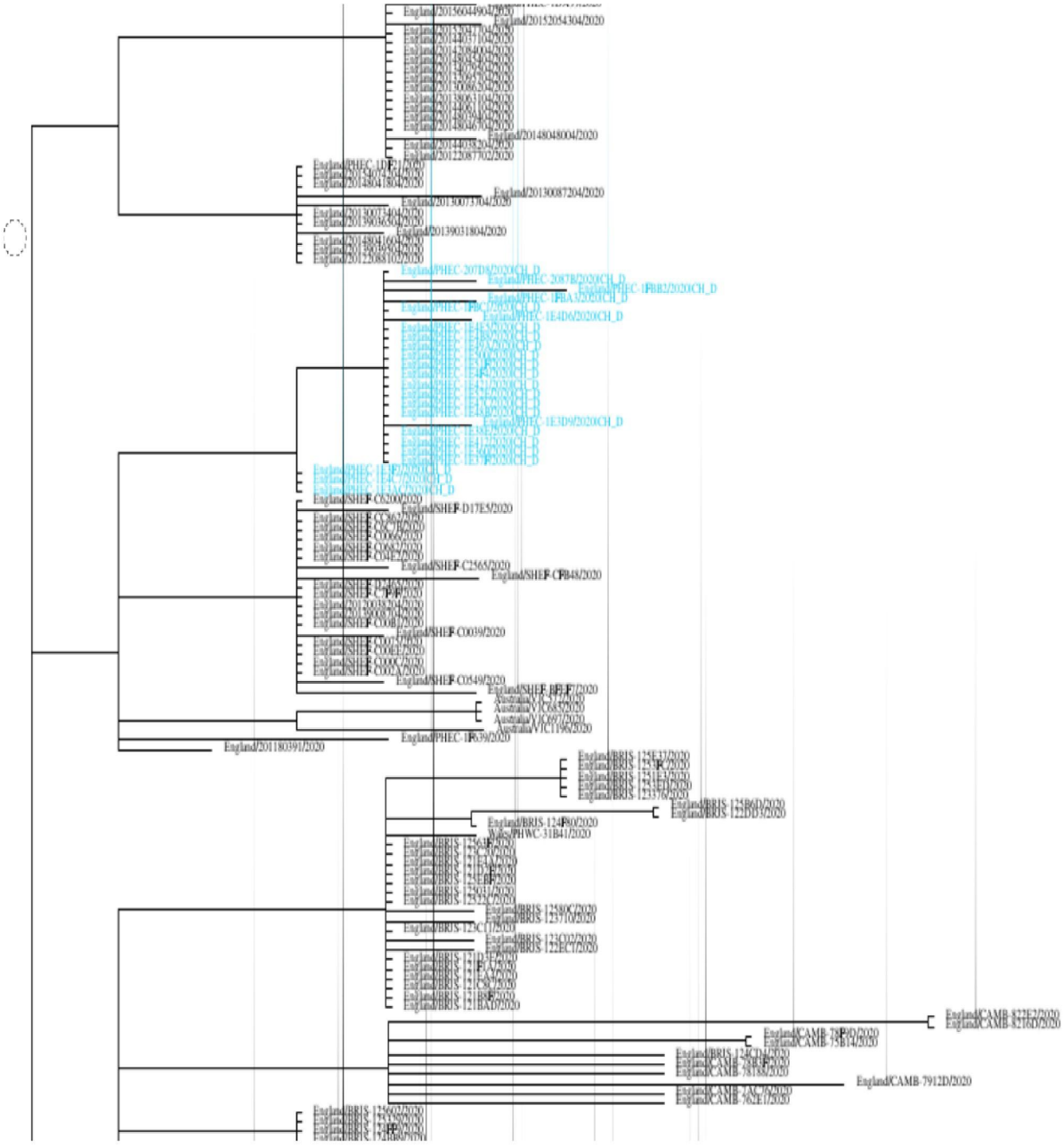
Phylogenetic analysis indicated the presence of informal clusters from Care homes A, B, D, E present in both the phylogeny from care home sequences ((**Figure 2 in the manuscript**) and within the large background dataset (**Supplement Figure S6c**). The largest cluster (care home D) contained 28 sequences of which 15 sequences exhibited zero SNPs difference and the maximum distance between sequences was three SNPs. The presence of clusters containing care home sequences, that did not contain background sequences and were distinct from that background, provided good evidence for introduction and subsequent spread of a SARS-CoV2 strain in a care home setting.

Each of the six care homes contained SARS-CoV-2 genomes from lineages B.1 and B.2 and the distance between sequences in the large cluster (n. 28) in care home D (lineage B.2.1) and the sequences in lineage B.1 was 13 - 18 SNPs. This provides good evidence for multiple introductions of the virus into care home settings. The placement of sequences in the phylogeny indicated that care home A exhibited three distinct sequence clusters along with six singletons, potentially representing up to nine separate introductions.

There were ten sequences that had a 0 SNP distance between them which were from three different care homes However, these sequences were part of a large clade of sequences within the B.1 lineage (n. > 5,500). Comparison of these sequences with the background data showed that the care home sequences did not form a discrete cluster (**Supplement Figure S6d**). Some lineage B.1 sequences that were not from care homes were also identical to the ten sequences from the three different care homes. It is therefore possible that identical viruses were introduced from other settings into all three homes separately, instead of being transferred from home to home. This observation means that genomics can neither exclude nor confirm that the cases in separate homes were linked.

All care home clusters of SARS-CoV-2 genomes included at least one staff member, apart from those from the care home with no PCR positive staff. Other than this observation, there was no genetic

signal within the SARS-CoV-2 genomes that differentiated staff and residents or symptomatic and asymptomatic individuals. The ten available sequences from fatalities, were distributed across the diversity of sequences derived from the care homes (**Figure 3 in the manuscript**) and were closely matched to sequences derived from non-fatal cases in the same locations, indicating the absence of a particular strain associated with fatality in this study.



Supplemental S6b. Maximum likelihood phylogenetic tree of 27768 SARS-CoV-2 genomes using data from the COG consortium and Gisaid. The phylogeny was generated on the 2020-05-15 by the COG Consortium. Carehome sequences are annotated within the tree with care home A (CH_A) to F (CH_F).

Supplemental S6c. Image take from COG Consortium phylogeny of 27768 SARS-CoV-2 genomes. The taxa labelled in light blue are a cluster of sequences from Care home D, The cluster of taxa in dark blue are sequences from Care home E. In both examples the informal cluster of sequences derived from care home settings is retained in the presence of a large background

Supplemental Figure S6d. Image take from COG Consortium phylogeny of 27768 SARS-CoV-2 genomes. Coloured taxa are used to illustrate the location of sequences derived from care home settings. Seven of the eight coloured taxa are identical (two additional sequences are not shown in this portion of the phylogeny). These sequences are part of a large lineage of SARS-Cov-2 genomes (>5,500) with little sequence diversity. Sequences shown within this portion of the image cannot be considered as part of a cluster of care home cases.

Supplement Table S7. Potential strategies for prevention of COVID-19 in care home

• **Prevention is fundamental** to controlling outbreaks in care homes by reducing introduction of SARS-CoV2, increasing infection prevention control (IPC) and early detection of COVID-19 cases in Care homes. • **Ensure early testing of unwell residents** including those with atypical COVID-19 symptoms (drowsiness, reduced appetite, lethargy and fatigue) • **Limit close contact between residents** along with immediate isolation of residents as soon as a single case is suspected • **Ensure residents are isolated for 14 days after a known high-risk exposure** (e.g. admission to hospital), consider intermediate care and other local support to minimise risk of introduction into the home. • **Test Staff** (any staff, not just carers) who are unwell with any symptoms, typical or atypical and ensure that they are negative for SARS-CoV-2 and asymptomatic (other viruses can cause similar illnesses) before they enter care home • **Exclude SARS-CoV-2 positive staff for 7 days** from work, irrespective of whether symptomatic or asymptomatic at the time of testing • Avoid where possible, **agency staff** and ensure they get appropriate IPC training before they enter the care home • **Wider testing in the care home during the early detection of an outbreak**: test all (including staff) those in contact with unwell resident including staff – this may be one part or one floor or the whole care home (residents and staff). The same principle applies for testing staff and residents who have been in contact with symptomatic staff • **Enhanced cleaning of high touch surfaces** and hand hygiene before and after every resident contact • Rigorous and systematic testing policy for staff and residents, with particular attention to **infection control measures for visitors, new residents** and **movement of residents and staff from other facilities**.