

Original Article

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A major outbreak of COVID-19 at a residential care home

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ABSTRACT

INTRODUCTION SARS-CoV-2 outbreaks at care homes are associated with a high morbidity and mortality. We aimed to study the molecular epidemiology of a major care home outbreak in Denmark.

METHODS After a staff member had been tested positive on 16 November 2020, a bundle approach programme was initiated including frequent surveillance screenings of residents and staff, isolation and cohorting procedures. This approach also involved limiting the number of visitors and enhancing the use of personal protective equipment, hand hygiene, and environmental cleaning. Naso/oropharyngeal swabs were tested for SARS-CoV-2 by polymerase chain reaction. Available positive samples were sequenced and phylogenetic relationships between the outbreak and local circulating strains were reconstructed.

RESULTS In all, 50% (56/114) of residents and 26% (49/190) of staff members became infected during the 46-day outbreak period. Altogether 16% of the infected residents died within 30 days after becoming infected. A total of 44% (46/105) of the samples with SARS-CoV-2 were sequenced, and phylogenetic analysis demonstrated a dominant outbreak lineage belonging to Global Lineage B.1.1.29 containing the mutation I233V in the S gene. The outbreak lineage was detected in the community 28 days before its introduction into the care home.

CONCLUSIONS Introduction of SARS-CoV-2 to care homes is associated with severe outbreaks. Initiation of a bundle approach infection control programme in addition to measures ensuring enhanced herd immunity were successful in controlling the outbreak. Genome sequencing proved to be a powerful tool to describe the relatedness of the various clones and may help focusing outbreak interventions.

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TRIAL REGISTRATION not relevant.

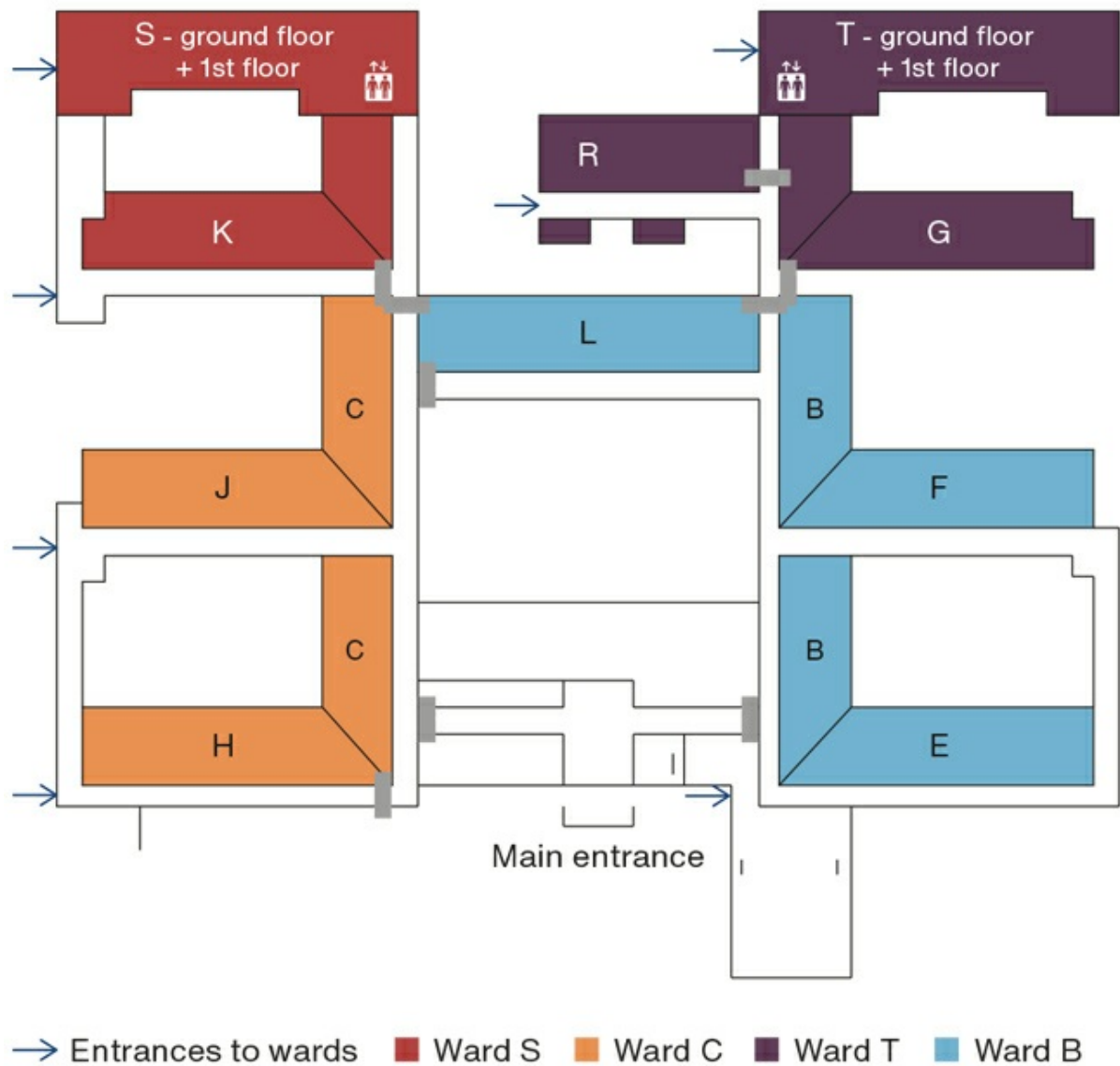
Residents in care homes/long-term care facilities are highly vulnerable to coronavirus disease, COVID-19, and multiple outbreaks with a high morbidity and mortality have been reported in such facilities worldwide [1-3]. A high prevalence of COVID-19 in the community is associated with an increased risk of transmission of the disease to care homes and with the number of COVID-19-related deaths among residents. It has been consistently demonstrated in several countries and throughout the COVID-19 pandemic that death at residential care homes accounts for up to two thirds of all COVID-19-related deaths [4]. In Denmark, a high mortality rate

has also been observed among care home residents (39% of all COVID-19-associated deaths) [5]. Thus, implementation of national guideline recommendations is important for preventing and controlling outbreaks in residential care homes [6, 7].

The aim of the present study was to describe a major COVID-19 outbreak at a care home facility in Denmark involving 56 infected residents and 49 infected staff members and to investigate the molecular epidemiology of the outbreak by whole genome sequencing (WGS).

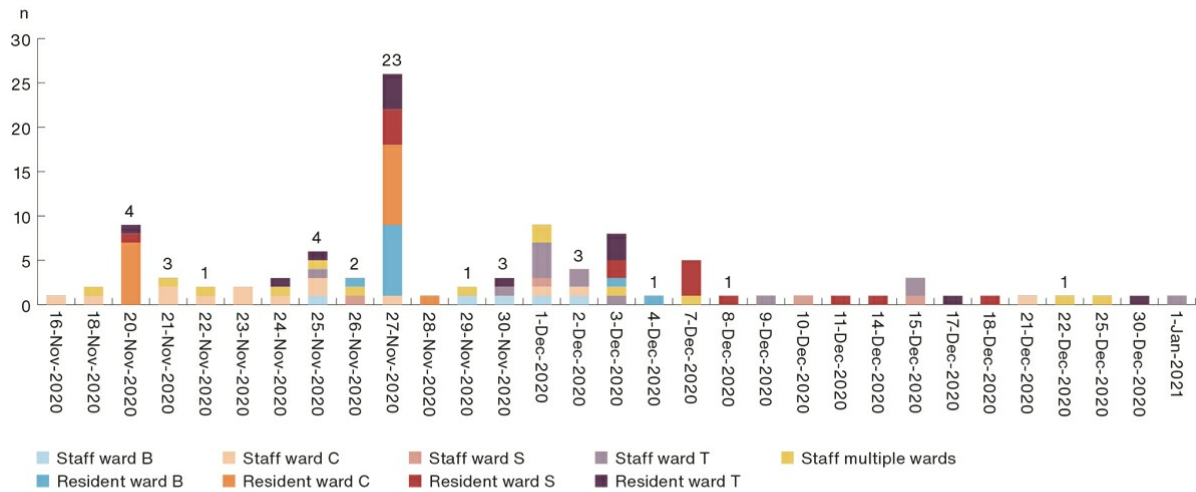
The outbreak occurred at a 114-bed residential care home situated in the Capital Region of Denmark. All resident homes were single bedrooms with separate washing and toilet facilities. The care home had four units counting a total of 76 long-term care beds primarily located at wards B, C and S, and two beds at Ward T. Furthermore, the care home had 38 short-term care beds located at ward T and eight at ward B (**Figure 1**). The care home had 193 staff in total, including 52 temporary staff members. Healthcare personnel worked in one unit only, whereas technicians, kitchen and cleaning staff and physical therapists visited and worked temporarily at all four units.

FIGURE 1 The residential care home.



A staff member working at ward C tested positive for SARS-CoV-2 on 16 November 2020 (Figure 2). Therefore, a SARS-CoV-2 surveillance screening of all residents and the entire care home staff was initiated. During the following week, an additional six staff members and six residents at Ward C tested positive for SARS-CoV-2. However, infection was also detected in two other units (one resident tested positive for SARS-CoV-2 at ward S and T, respectively). Moreover, three staff members working at all four units were diagnosed with COVID-19. After consulting with the Danish Patient Safety Authority and the Infection Control Unit at Hvidovre Hospital, the following *bundle approach* was adopted to infection prevention. The following control measures were initiated at the care home:

FIGURE 2 Number of new COVID-19 cases each day among care home residents and staff members during the outbreak. The numbers above the columns indicate samples sequenced.



18 Nov: weekly surveillance screenings of staff and residents started.

22 Nov: infection control measures initiated including a visitor ban.

3 Dec: surveillance screenings × 2 weekly, no new admittance of short-term residents, cohorting infected residents at ward T.

5 Jan: COVID-19 vaccination was initiated on the care home.

1) Surveillance screenings. In addition to testing of symptomatic cases, weekly surveillance screenings for SARS-CoV-2 were conducted comprising all residents and staff. The screenings were increased to twice weekly two weeks after the outbreak started. Also, all residents had their body temperature measured daily.

2) Isolation. Residents with COVID-19 (symptomatic and/or laboratory confirmed) were separated and not allowed to leave their rooms. In pursuance of national health authority guidelines, staff who had become infected or had been exposed to COVID-19 were sent home for self-isolation or quarantine, respectively. External visits were restricted to include one person per resident. Cohort isolation with transfer of all residents with COVID-19 to one isolation unit (ward T) was initiated after two weeks from the start of the outbreak. Staff members were not allowed to work at more than one unit.

3) Personal protective equipment and hand hygiene. Wearing a face mask was mandatory for all staff members during working hours, whereas eye protection, isolation gowns and gloves were used at all contacts with residents. The focus on hand hygiene was intensified and access to hand disinfectants was enhanced. An educational programme on infection prevention and control measures was completed by care home staff.

4) Environmental cleaning. Environmental cleaning was intensified (daily cleaning of residential and communal areas), and contact sites with a high risk of COVID-19 transmission, e.g. door handles, were disinfected several times daily. Frequent open window ventilation of rooms and offices was effected when they were used by staff and residents.

5) Number of staff personnel. Supplementary staff were allocated to the care home to replace staff members who were in self-isolation or quarantine and to meet demands for additional work tasks related to the above infection control measures.

Altogether 81% of the COVID-19 infections occurred within the first three weeks of the outbreak. The last diagnosed case among residents occurred on 30 December 2020; among staff, on 1 January 2021. Thus, the duration of the outbreak was 46 days. Vaccination of residents and staff against COVID-19 was initiated on 5 January 2021.

METHODS

Laboratory testing for COVID-19. Screening for COVID-19 was based on naso/oropharyngeal swabs with subsequent PCR testing at the Departments of Clinical Microbiology at Rigshospitalet (RH), Hvidovre Hospital (HH) and Statens Serum Institut (SSI). To investigate any transmission of COVID-19 at the care home, SARS-CoV-2 genome diversity was studied by WGS of all positive samples for which residual material remained, provided that an adequate amount of RNA could be extracted to provide genomes of sufficient quality.

RNA was extracted from SARS-CoV-2 PCR-positive samples using a viral DNA and RNA extraction kit (Tianlong) at the RH and using the Agencourt RNAdvance Blood kit (Beckman Coulter) at the HH. Complementary DNA was synthesised with SuperScript IV Vilo and Maxima Reverse Transcriptase (Thermo Fischer Scientific) at the RH and HH, respectively. Viral amplicons were produced according to the ARTIC Network SARS-CoV-2 sequencing protocols. DNA libraries were prepared using the Nextera XT DNA Library Prep kit (Illumina) and were sequenced on a NextSeq or Miseq instrument (Illumina) generating 150 and 75 base paired-end sequencing reads, respectively. Reads were aligned against the National Center for Biotechnology Information's SARS-CoV-2 reference genome (NC_045512.2) using BWA-MEM (v.0.7.10). ARTIC nCoV-2019-V3 primers were trimmed with iVar [8] (v.1.2.3). Consensus sequences were made with samtools mpileup (-d 0 -A -Q 0) (v.1.9) [9] and iVar consensus (-q 20 -t 0.8 -m 10) and were aligned using MAFFT. A phylogenetic tree was constructed using IQ-TREE [10] as part of the Nextstrain default pipeline [11]. SARS-CoV-2 lineages were assigned with pangolin/pangoLEARN (v.2.3.2, 2021-02-21) [12, 13].

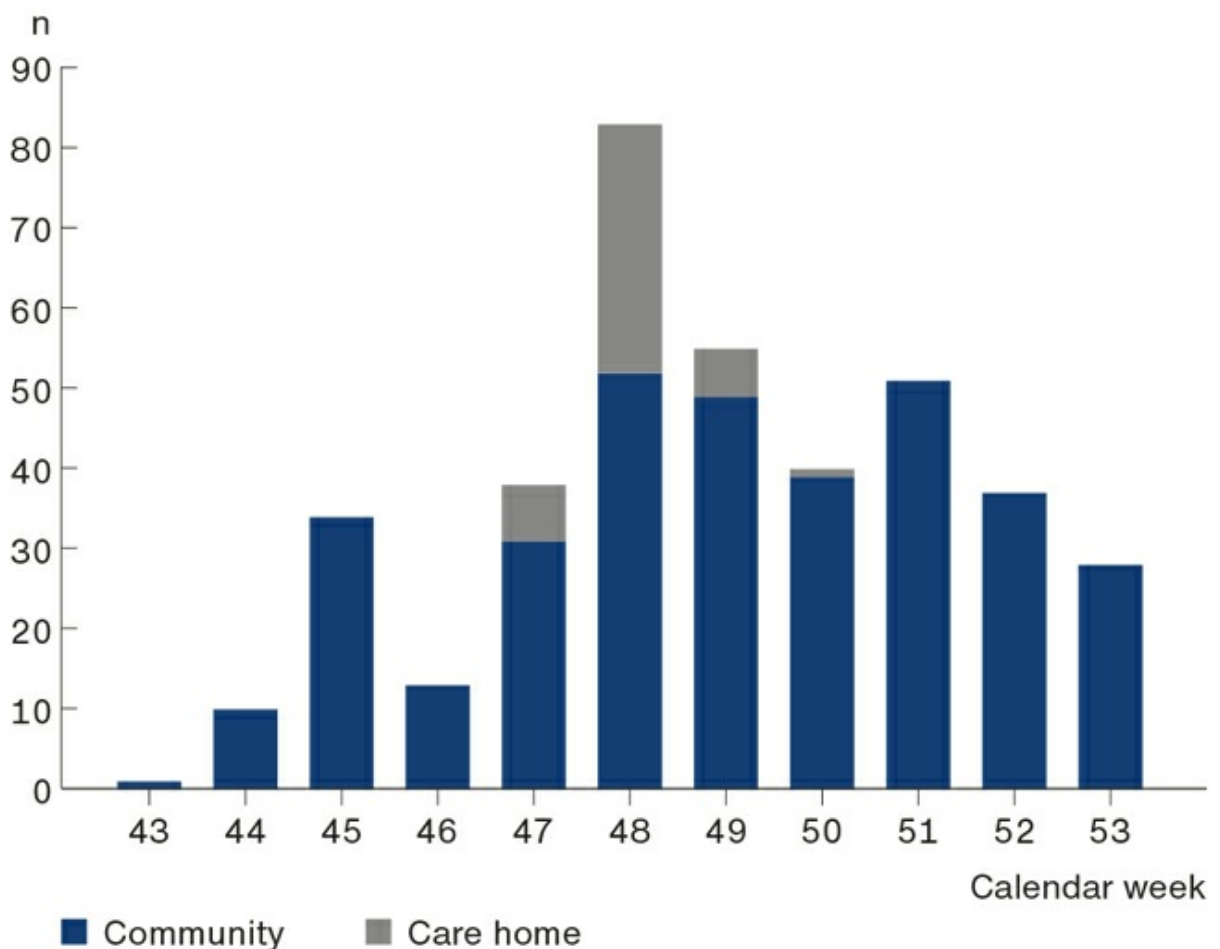
Trial registration: not relevant.

RESULTS

In total, 56 out of 114 residents (50%) and 49 out of 190 (26%) staff members became infected with SARS-CoV-2 during the outbreak, which involved all four wards (Figure 2 and **Supplementary Figure 1**, https://ugeskriftet.dk/files/a03210227_-_supplementary.pdf). Three additional cross-border working staff members reported that they had tested positive for SARS-CoV-2 in Sweden. However, since data detailing this were unavailable, these staff members were excluded from the study. The median age of infected residents was 84 years (63-97), and 42 out of 56 (75%) were females. The median age of infected staff members was 48 years (25-64), and 47 out of 49 (96%) were females. Ten residents and one staff member diagnosed with COVID-19 were hospitalised. The 30-day all-cause mortality among residents infected with COVID-19 was 16% (9/56); eight of these nine fatal cases were females. No staff member died from COVID-19.

WGS analysis. To determine genetic relatedness of the SARS-CoV-2 identified at the care home, samples from 31 out of 56 (55%) residents and 15 out of 49 (31%) staff members underwent WGS analysis. 53% (41/77) of the positive samples were sequenced at the RH/HH; 18% (5/28) at the SSI. Phylogenetic analysis revealed closely related genomes containing 36 identical genomes, eight genomes with 1-3 mutation differences and one genome with four mutation differences (Figure 3). The eight genomes with 1-3 mutation differences were interpreted as probably related based on the phylogeny and epidemiological data. In addition, three staff members had SARS-CoV-2 genomes distinctly different from the outbreak lineage and from each other. Residents from all four wards and staff were distributed across the lineage. The outbreak lineage belongs to Global Lineage B.1.1.29 and contains the mutation I233V in the S gene. The first case with the outbreak lineage in the Capital Region of Denmark was identified in the community on 19 October 2020; 28 days before the first identified case at the care home (Figure 4). According to the Danish Covid-19 Genome Consortium, approximately 9,000 genomes sequences were produced during the 46-days outbreak period of which 333 (4% of the genomes) belonged to the outbreak lineage [14].

FIGURE 4 Number of strains with the mutation I233 in the S-gene identified in the Capital Region of Denmark from October to December 2020 by calendar week (N = 390). During the 46-day outbreak period (calendar week 47-53), 333 strains had the I233 mutation.



DISCUSSION

In the present study, 26% of staff members and 50% of care home residents became infected with COVID-19 during a 46-day outbreak period, demonstrating a high risk of SARS-CoV-2 transmission when the virus becomes introduced into a care home. In addition, WGS-data showed that a single SARS-CoV-2 lineage was dominant and responsible for the outbreak. Acquisition of herd immunity after the infection most likely contributed to the conclusion of the outbreak. However, we are fairly sure that implementation of infection control measures played a significant role in controlling the outbreak, since no other lineages were spread during the outbreak despite three staff members becoming infected with lineages divergent from those of the outbreak lineage. Surveillance screenings were not performed regularly (i.e. weekly) before the outbreak was discovered. Thus, we cannot determine how the outbreak lineage was introduced into the care home. Therefore, further

epidemiological studies are warranted on these cases to clarify the transmission of the outbreak lineage in the community and to determine whether multiple introductions of this lineage into the care home may have occurred during the outbreak.

National surveillance data show that approximately 11% of tested Danish care home residents have become infected with COVID-19, accounting for 1.7% of all COVID-19 cases in Denmark [5]. In accordance with our findings of a 16% mortality rate in the present outbreak, COVID-19-related death in Danish care homes is high with an all-cause mortality rate of 25% among infected residents. The high mortality rate emphasises the severity of such outbreaks and the continuous efforts needed to prevent and control COVID-19 infections in residential care homes.

In the UK, COVID-19 outbreaks occurred in 37% of care homes, and the size of the care home correlated strongly with an increased risk of nosocomial transmission [15], which was most likely due to a high number of residents, staff and visitors at large facilities [4]. SARS-CoV-2 was detected in 43% of all Danish care homes that have a median size of 38 beds. Thus, the outbreak presented here occurred in a high-risk facility (76 long-term and 38 short-term beds). Other SARS-CoV-2 transmission risk factors directly related to residential care homes are a low frequency of cleaning in communal areas, a poor staff-to-bed ratio, staff working across multiple units, including wards with infected and uninfected residents, use of temporary staff, number of new admissions and difficulties in isolating residents [16].

Recommendations to prevent and control COVID-19 outbreaks at care home facilities have been prepared by the European Centre for Disease Prevention and Control [4] and by the Danish authorities that have regularly updated national guidelines and legislation during the pandemic [6, 7, 17, 18]. Despite national guidelines being implemented at the care home, the outbreak was not prevented. Consequently, additional infection control measures were established, as described above. The last case with COVID-19 was a staff member who was infected 46 days after the start of the outbreak. Moreover, vaccination of residents and staff against COVID-19 has nearly been concluded. Thus, the risk of new outbreaks at care homes has diminished. We believe, however, that frequent SARS-CoV-2 testing of staff, residents and visitors should continue because of the high vulnerability of care homes to COVID-19. In particular, point-of-care-testing against SARS-CoV-2-antigens may be highly valuable in such settings, since a short turnaround time may be critical for prevention of COVID-19 [19].

WGS analysis is a powerful tool with which to describe the relatedness of SARS-CoV-2 clones in an outbreak but also to discover new emerging mutations with an impact on the transmission, pathogenicity, diagnostics and therapy against the virus [20]. Therefore, it is an important limitation of the present study that only 45% of all samples were sequenced. This was partly due to a low content of SARS-CoV-2 RNA in samples why we were unable to provide genomes of a sufficient quality for WGS analysis. Indeed, genome coverage was associated with the RNA concentration of the sample, and a low coverage was found for cycle threshold-values > 30 (data not shown). Furthermore, sequencing capacity is a limiting factor in many laboratories and countries. Moreover, in Denmark, only 16-34% of positive SARS-CoV-2 samples were sequenced during the 46-day outbreak period [14]. We believe that WGS should be performed on all positive samples to help outbreak decisions in public health.

CONCLUSIONS

We have demonstrated that introduction of SARS-CoV-2 to a large care homes resulted in a major outbreak involving residents and staff alike. Initiation of a *bundle approach* infection control programme in addition to enhanced herd immunity were successful in controlling the outbreak. WGS analysis of SARS-CoV-2 is a powerful tool to describe the relatedness of the various strains of an outbreak and may help infection control units to

diminish transmission of SARS-CoV-2 in vulnerable facilities like care homes. Any further introduction of SARS-CoV-2 to care homes should be prevented by vaccination programmes and frequent testing of staff and visitors before they enter the facilities.

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Conflicts of interest Potential conflicts of interest have been declared. Disclosure forms provided by the authors are available with the article at ugeskriftet.dk/dmj

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References can be found with the article at ugeskriftet.dk/dmj

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