

**Unravelling the modes of transmission of SARS-CoV-2 during a nursing home outbreak: looking beyond the church super-spread event**

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Summary

Whole genome sequencing revealed that a COVID-19 outbreak in a nursing home in the Netherlands could not be attributed to an on-site church service, but to widespread regional virus circulation and multiple introductions into the facility before the visitor ban.

## Abstract

### Background

An outbreak of COVID-19 in a nursing home in the Netherlands, following an on-site church service held on March 8<sup>th</sup>, 2020, triggered an investigation to unravel sources and chain(s) of transmission.

### Methods

Epidemiological data were collected from registries and through a questionnaire among church attendees. Symptomatic residents and healthcare workers (HCWs) were tested for SARS-CoV-2 by RT-PCR and subjected to whole genome sequencing (WGS). Sequences from a selection of people from the same area were included as community reference.

### Results

After the church service, 30 of 39 attendees (77%) developed symptoms; 14 were tested and were positive for COVID-19 (11 residents and 3 non-residents). In the following five weeks, 62 of 300 residents (21%) and 30 of 640 HCWs (5%) tested positive for COVID-19; 21 of 62 residents (34%) died. The outbreak was controlled through a cascade of measures. WGS of samples from residents and HCWs identified a diversity of sequence types, grouped into eight clusters. Seven resident church attendees all were infected with distinct viruses, four of which belonged to two larger clusters in the nursing home.

## Conclusions

Although initial investigation suggested the church service as source of the outbreak, detailed analysis showed a more complex picture, most consistent with widespread regional circulation of the virus in the weeks before the outbreak, and multiple introductions into the nursing home before the visitor ban. The findings underscore the importance of careful outbreak investigations to understand SARS-CoV-2 transmission to develop evidence-based mitigation measures.

Key words: SARS-CoV-2, COVID-19, nursing homes, whole genome sequencing, outbreak

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## Introduction

In January 2020, the health authorities of China notified the World Health Organisation (WHO) of an outbreak of a severe acute respiratory syndrome caused by a SARS-like coronavirus (SARS-CoV-2). Although initial control efforts were directed at containment, following the model of the first SARS outbreak in 2003, the virus continued to spread and the WHO declared the disease COVID-19 to be a pandemic on March 11<sup>th</sup>, 2020. In the Netherlands, the first case of COVID-19 was diagnosed on February 27<sup>th</sup>, in a Dutch national who had returned from the Lombardy region of Italy [1]. On March 16<sup>th</sup>, the prime minister announced physical distancing measures, but a first pandemic wave occurred with 50.661 cases and 6118 deaths, particularly in elderly, by July 1<sup>st</sup>.

Two COVID-19 outbreaks in long-term care skilled nursing facilities in Washington US showed the potential for rapid spread among residents of these types of facilities [2, 3]. Nursing home residents are susceptible to severe COVID-19 outcomes as a consequence of their age and, in some cases, underlying health conditions. They accounted for 25% to 50% of the documented deaths due to COVID-19 in some countries [4]. The impact of COVID-19 in nursing homes is aggravated by delayed recognition due to atypical clinical presentation in elderly persons, and difficulties of implementing stringent control measures [5]. In addition, it was augmented by shortages of personal protection equipment (PPE) [6]. In view of the severe consequences, understanding how SARS-CoV-2 transmits in this population is crucial.

On March 15<sup>th</sup>, the day when country-wide measures were announced following confirmation of widespread community-circulation of SARS-COV-2 in a neighbouring province [7, 8], the local public health service was notified of a positive COVID-19 test result in a resident from a large nursing home

(300 beds), located on an island in the province South-Holland. The following week, more cases were confirmed among residents and health care workers (HCWs), triggering a cascade of infection control measures at the facility. Nursing home management was informed by church leaders on March 18<sup>th</sup> that many church attendees from the local community had fallen ill, supposedly after a church service that had been held on March 8<sup>th</sup> in the chapel of the nursing home facility. This raised the suspicion that the nursing home outbreak had been triggered by the church service. In this study, we aim to reconstruct the introduction and spread of SARS-CoV-2 in the nursing home, including the possible role of the church service, combining extensive diagnostic screening, epidemiological information and whole genome sequencing (WGS).

## Methods

### Sample collection and SARS-CoV-2 diagnostic testing

All residents and HCWs in the nursing home who developed respiratory symptoms since March 14<sup>th</sup> (the day of the first suspected case) were tested for presence of SARS-CoV-2 RNA in throat and nose swabs by RT-PCR [9]. All residents and HCWs testing positive before April 15<sup>th</sup> were included in the study. In addition, to be able to compare the sequences from nursing home patients with those circulating in the local community, a random selection of unrelated SARS-CoV-2 positive COVID-patients living on the same island was included for sequence analysis. This selection was made based on postal codes, ensuring inclusion of patients from different parts of the island.

### Data collection

The public health service contacted all SARS-CoV-2 positive residents and HCWs to perform contact tracing and to collect disease specific information. These data were supplemented with data from the nursing home organisation and included information such as date of onset of symptoms, testing date, unit (for residents and HCWs), hospitalisation, death, and attendance to the church service of

March 8<sup>th</sup>. The nursing home organisation also provided a detailed timeline of the measures taken in order to mitigate the outbreak, and maps of the facility.

An online questionnaire was developed and forwarded to the non-residents who attended the church service by the reverend. The reverend also provided details on the church service. The questionnaire covered: age, gender, symptoms at day of the church service, recent travel abroad, contact with a COVID-19 patient, symptoms since church service, onset date of symptoms, perceived severity, hospitalisation, ICU admission, and testing for Sars-CoV-2. In addition, respondents were asked if they had any household member who had symptoms on the day of the church service, or developed symptoms or was hospitalised thereafter. Nursing home residents who attended the church service could not be included in the questionnaire, due to the severe impact of the outbreak in the nursing home, and because by the end of March many of them were too ill or passed away. Their data were retrieved from the nursing home registry, similar to other SARS-CoV-2 positive nursing home residents.

#### SARS-CoV-2 sequencing and analysis

RT-PCR-positive samples of residents, HCWs and inhabitants of the same island, with a viral load below a Ct value of 32, were selected for sequencing using a SARS-CoV-2 specific amplicon-based Nanopore sequencing protocol as previously described [10]. The consensus genome was generated only including positions with a coverage >30 as described previously [11]. Sequences were compared to a reference database developed for the national COVID-19 response effort. Sequences were assigned to a transmission cluster when they had a maximum of 2 nucleotides difference [12]. For cluster A, it was not possible to apply the 2 nucleotides cutoff. The cluster contained both sequences from the nursing home and unrelated SARS-CoV-2 sequences from the same island, with up to 6

nucleotides difference between sequences. Cluster A was therefore assigned as a regional cluster (as opposed to a possible transmission cluster).

#### Medical ethical clearance

Outbreak investigations of notifiable diseases such as COVID-19 are the legal tasks of the Public Health Service as described under the Public Health Act, and do not require separate medical ethical clearance.

#### Results

The nursing home is located in the South-West of the Netherlands in a small town on the rural island of Goeree-Overflakkee (260 square km with 50,000 inhabitants). It is a skilled nursing home facility with 300 beds, giving long and short term residential care, divided over five buildings with two to four stories. There are 146 long-term residential care/assisted living apartments, 24 short-term residential care apartments (medical rehabilitation), and 17 residential groups of 7 – 8 residents each (15 psychogeriatric care groups and 2 somatic care groups). Most of the HCWs live on the same island.

On March 8<sup>th</sup>, 39 persons attended a church service in the chapel of the nursing home: 26 were elderly non-resident community members including the reverend, and 13 residents of the nursing home. The service took approximately 50 minutes, in which people sang and shared supper by passing a serving bowl with pieces of bread. No hands were shaken. After the service, coffee was shared for about 20 minutes. The chapel had an air conditioning system, without recirculation. The



few church members who did not develop any symptoms in the weeks after the service (5 of 39, of whom 2 residents) were seated at random in the chapel.

All 26 non-residents who visited the church service on March 8<sup>th</sup> responded to the online questionnaire, between March 27<sup>th</sup> and April 7<sup>th</sup>. On the day of the church service, four non-resident attendees had symptoms fitting the case definition of COVID-19 and three reported a household member with symptoms (Table 1). Nobody reported contact with a confirmed COVID-19 case. In the 16 days following the church service, 19 of 26 (73%) non-resident church attendees developed symptoms indicative of COVID-19 (Table 1); 3 persons did not develop any symptoms, and 4 persons continued having symptoms. Seven persons reported a household member who also developed symptoms. Three church attendees with severe symptoms tested positive for SARS-CoV-2; two after admission to hospital/ICU and the third after admission of his spouse.

The epidemic curve of the outbreak in the nursing home and church attendees shows onset date of symptoms between March 1<sup>st</sup> and April 14<sup>th</sup> for 21 non-resident church attendees, 11 residents who did and 51 who did not attend the church service, as well as 30 HCWs (Figure 1). All residents and HCWs in the curve were RT-PCR-positive, and 21 residents died (of whom five had attended the church service). At the peak of the outbreak, 200 out of 300 residents were cared for in isolation or quarantine. The onset of symptoms ranged from 1 – 10 (median 4) days after March 8<sup>th</sup> in non-resident church attendees, and from 2 – 16 (median 10) days after March 8<sup>th</sup> in residents attending the church service (Figure 1). The reported symptom onset of other residents and HCWs who did not attend the church service ranged from 4 to 37 (median 16,5) days following the service, except for one resident who already had symptoms since March 2<sup>nd</sup> and could have been the source of other cluster A resident and HCW infections. The outbreak started to decline after March 25<sup>th</sup>, about 8 –

12 days after first control measures were taken (see Table 2 for detailed timeline of infection prevention and control measures). Until April 14<sup>th</sup> (study period), 62 of 300 residents (21%) and 30 of 640 HCWs (5%) tested positive for SARS-CoV-2, while 51 residents and 69 HCWs developed respiratory symptoms but tested negative (3 more residents and 12 more HCWs tested positive after the study period; 1 more resident died). The attack rate for residents who attended the church service was 85% (11/13) while for residents who did not attend it was 18% (51/287). Attendees did not differ from non-attendees with regard to age, mobility, or number of contacts with visitors.

The outbreak started in the first and second floor of the nursing home, with most affected units housing at least one resident who attended the church service (Figure 2a). Residents on the ground floor (residential groups) were mostly infected later. Some residential groups were more affected than others (ranging from 0 – 7 of 8 residents affected). The air conditioning system did not recirculate used air.

We obtained complete genome sequences of 7 of 11 SARS-CoV-2 positive residents who attended the church service, 35 of 51 residents who did not attend, 20 of 30 HCWs, and 21 inhabitants of the island (of whom one attended the church service). Sequences of viruses from residents and HCWs grouped in eight different clusters, and an additional eight residents and one HCW had unique sequences (Figure 3 and Supplementary Figure 1), indicating at least 17 separate introductions of SARS-CoV-2 into the nursing home. The seven resident church attendees were all infected with distinct viruses ( $\geq 3$  nucleotides difference), making one common source of infection unlikely. However, it is possible that several people infected with different viruses visited the church service, which may have caused further transmission amongst attendees. Four church service attendees (three residents and one non-resident) were part of the large regional cluster A. Cluster A likely

reflects widespread circulation in the region rather than direct transmission, in contrast to the other seven defined clusters which are likely transmission clusters. Of the eight clusters with residents and HCWs of the nursing home, 6 clusters (A-F) also contained sequences of the inhabitants of the island, confirming regional circulation before and during the closure of the nursing home.

Overall, the genetic clusters were scattered across the nursing home (figure 2b), with no clear pattern. Viruses belonging to several clusters were found on each floor. In some units there may have been spread of one cluster type, such as cluster H in unit A0, cluster G in unit A1, and cluster B among residents of unit B2 and HCWs of unit B1 (both short term care units with some exchange of HCWs). The majority of the introductions seemed to have been controlled quickly, staying limited to 1 – 4 residents and/or HCWs (cluster C to H plus 9 unique sequences). Two clusters (A+B) grew bigger over time, resulting in 38 SARS-CoV-2 infections in the nursing home. However, not all SARS-CoV-2 positive cases were sequenced, so making definite conclusions on cluster sizes was not possible. All clusters started before March 28<sup>th</sup>, which is 14 days after the start of testing and isolation of residents (on July 14<sup>th</sup>), and 9 days after starting the total isolation of all units (on July 19<sup>th</sup>). This shows the effectiveness of the measures in preventing new introductions into the nursing home, taking into account a maximum incubation time of 14 days. However, these measures could not prevent all transmission within the nursing home.

## **Discussion**

After the church service on March 8<sup>th</sup>, 30 of 39 attendees (77%) developed symptoms or tested positive for COVID-19. Although the church service initially was thought to be the source of the outbreak in the nursing home, the genomic analysis showed a more complex picture. Residents who had attended the church service were infected with distinct viruses, and subsequent transmission

within the nursing home was limited. Analysis of sequence data from viruses from residents and HCWs suggested that there were at least 17 separate introductions, with limited within-home transmission. The data are most consistent with widespread regional circulation of the virus in the weeks before the outbreak, and multiple introductions through contacts between residents and visitors or HCWs before the visitor ban on March 17<sup>th</sup>. The combination of extensive epidemiological data collection and whole genome sequencing, and comparison of sequences to a national reference database, allowed us to interpret transmission patterns in a unique way.

Based on this investigation it is not possible to assess exactly how many persons were infected at the church service, as only a minority of non-residents who attended the church service were tested for SARS-CoV-2. This was in line with the national guidance at the time, that recommended testing for persons with recent travel history or persons with severe respiratory disease. Religious gatherings have been linked to outbreaks of COVID-19 in South Korea, Singapore and the US [13-15]. Here, the high prevalence of respiratory symptoms in the community members who attended the church service does suggest that this was an amplifying event. However, finding considerable diversity of viruses in the affected nursing home residents who attended the church service showed that this was not a single superspreading event, and that multiple viruses were already present.

The nursing home where the epidemic took place is a large facility of 300 beds, with many volunteers and family caregivers, and many social activities and facilities. Being located on an island, with a homogenous religious background, the close social bonds facilitate frequent contacts between residents and non-residents. This may all have contributed to the multiple introductions and spread of SARS-CoV-2 within the nursing home (and within the island) in the week(s) before the visitor ban. Initial spread could stay unnoticed, probably due to people having mild complaints and not knowing that the virus was already present on the island. The first COVID-19 patient on the island was diagnosed on March 12<sup>th</sup>, only 2 days before the first resident was tested positive. Before then, the nursing home was

still open to visitors, and residents and HCWs frequently interacted in the restaurant and joint activities, both inside and outside of the nursing home. This likely facilitated both the high number of virus introductions and subsequent spread within the nursing home. The use of PPE as from March 14<sup>th</sup> could have contributed to limiting the number of cases per cluster, as well as other preventive measures such as testing of symptomatic residents (March 14<sup>th</sup>) and HCWs (March 17<sup>th</sup>), isolation of all units (March 19<sup>th</sup>) and all residents (March 24<sup>th</sup>), and finally cohorting (April 5<sup>th</sup>). This is supported by the whole genome sequencing data: no new clusters started later than 14 days after the start of testing and isolating of residents. Unfortunately, complete genome sequences could not be obtained for about one third of samples, because viral load was too low and/or the storage conditions of the swabs sub-optimal.

Our findings underscore the importance of careful outbreak investigations to understand how SARS-CoV-2 transmits, to develop evidence-based mitigation measures. Whole genome sequencing (WGS) can make an essential contribution in this, by revealing transmission patterns that would otherwise remain concealed. In this case, epidemiological data would have pointed towards large scale within nursing home transmission following the church service, while WGS showed that the situation was more complex. Other COVID-19 studies have also shown the added value of whole genome sequencing in epidemiological investigations [8, 12]. Furthermore, our findings show the possible implications if there are no measures in place to prevent introductions of the virus when there is extensive community transmission, but also the efficacy of stringent measures to control subsequent SARS-CoV-2 outbreaks in nursing homes, especially when implemented at an early stage. As the measures have a huge social and mental impact and can last for many weeks, an ethical discussion, including opinions of residents, family, and HCWs, is needed to strengthen compliance and acceptance, for example during the second wave of SARS-CoV-2.

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**Conflict of interests:**

MK reports a patent pending for Crossactive Antibody COVID-19 (A scientist in their department holds IP on a monoclonal antibody that is explored for clinical use). The authors have no conflicts interests.

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Table 1. Survey among non-residents who visited the church service on March 8<sup>th</sup>, regarding being the possible source of the SARS-CoV-2 outbreak, and being affected by the outbreak (n=26)

<b>Background characteristics</b>	<b>n</b>	<b>%</b>
Age range (median)	56-98 (68 years)	
Gender: male	14	54
<b>Possible source of the outbreak</b>		
Symptoms at day of church service	4	15
Household member with symptoms at day of church service	3	12
Recent visit abroad (Lebanon)	1	4
Contact with a confirmed COVID-19 case	0	0
<b>Affected by the outbreak</b>		
Developed symptoms after March 8 <sup>th</sup>	19	73
Fever	16	84 <sup>1</sup>
Cough	14	74 <sup>1</sup>
Fatigue	13	68 <sup>1</sup>
Runny/blocked nose	9	47 <sup>1</sup>
Headache	9	47 <sup>1</sup>
Muscle pain	9	47 <sup>1</sup>
Sore throat	9	47 <sup>1</sup>
Shortness of breath	6	32 <sup>1</sup>
Diarrhea	4	21 <sup>1</sup>
Difficulty breathing	1	11 <sup>1</sup>
Nausea/vomiting	3	16 <sup>1</sup>
Pneumonia	2	11 <sup>1</sup>
Perceived symptoms as severe (score 6-10 on scale 1-10)	10	52
Tested for SARS-CoV-2, with positive test results	3	12
Admitted to hospital, ICU	2	8
Household member who developed symptoms after March 8 <sup>th</sup>	7	27
Household member who was admitted to hospital, ICU	1	4

<sup>1</sup> n=19, i.e. the 19 persons who developed symptoms after March 8<sup>th</sup>

Table 2. Timeline showing implementation of infection prevention and control measures at the nursing home

Date	Infection prevention / control measure ( <i>transmission event</i> )
February 27 <sup>th</sup>	Start extra cleaning of communal toilets and frequently touched surfaces (twice daily)
March 8 <sup>th</sup>	( <i>day of church service</i> )
March 9 <sup>th</sup>	Prohibiting symptomatic staff coming from risk areas to work
March 13 <sup>th</sup>	Closing of restaurant; Stop communal activities and church services
March 14 <sup>th</sup>	Start testing and isolation of symptomatic residents; Use of personal protective equipment (PPE) around suspected and confirmed residents ( <i>1<sup>st</sup> suspected resident</i> )
March 15 <sup>th</sup>	Stop resident coffee groups ( <i>1<sup>st</sup> confirmed resident</i> )
March 16 <sup>th</sup>	( <i>2<sup>nd</sup> confirmed resident</i> )
March 17 <sup>th</sup>	Start visitor ban; Start testing of symptomatic staff
March 18 <sup>th</sup>	Stop daycare ( <i>2 confirmed staff members, 6 suspected residents; management informed by the church leaders of many ill church attendees</i> )
March 19 <sup>th</sup>	Isolation of all buildings and all units ( <i>first COVID-19 death</i> )
March 20 <sup>th</sup>	Stop exchanging staff between units and groups
March 23 <sup>th</sup>	Stop new admissions; stop all contact between residents
March 24 <sup>th</sup>	Total isolation of all residents, also non-symptomatic; PPE is also used with non-symptomatic residents ( <i>13 positive residents, 13 suspected residents, 3 deaths</i> )
April 5 <sup>th</sup>	Cohorting of positive/negative/exposed/suspected residents; Relocation of 12 positive residents to a different facility

Figure Legends:

Figure 1. Epidemic curve of onset date of symptoms of 21 church attendees, 62 residents and 30 health care workers.

Two church attendees with ongoing symptoms on March 8<sup>th</sup> are not included, because they could not remember the onset date.

HCW = health care worker

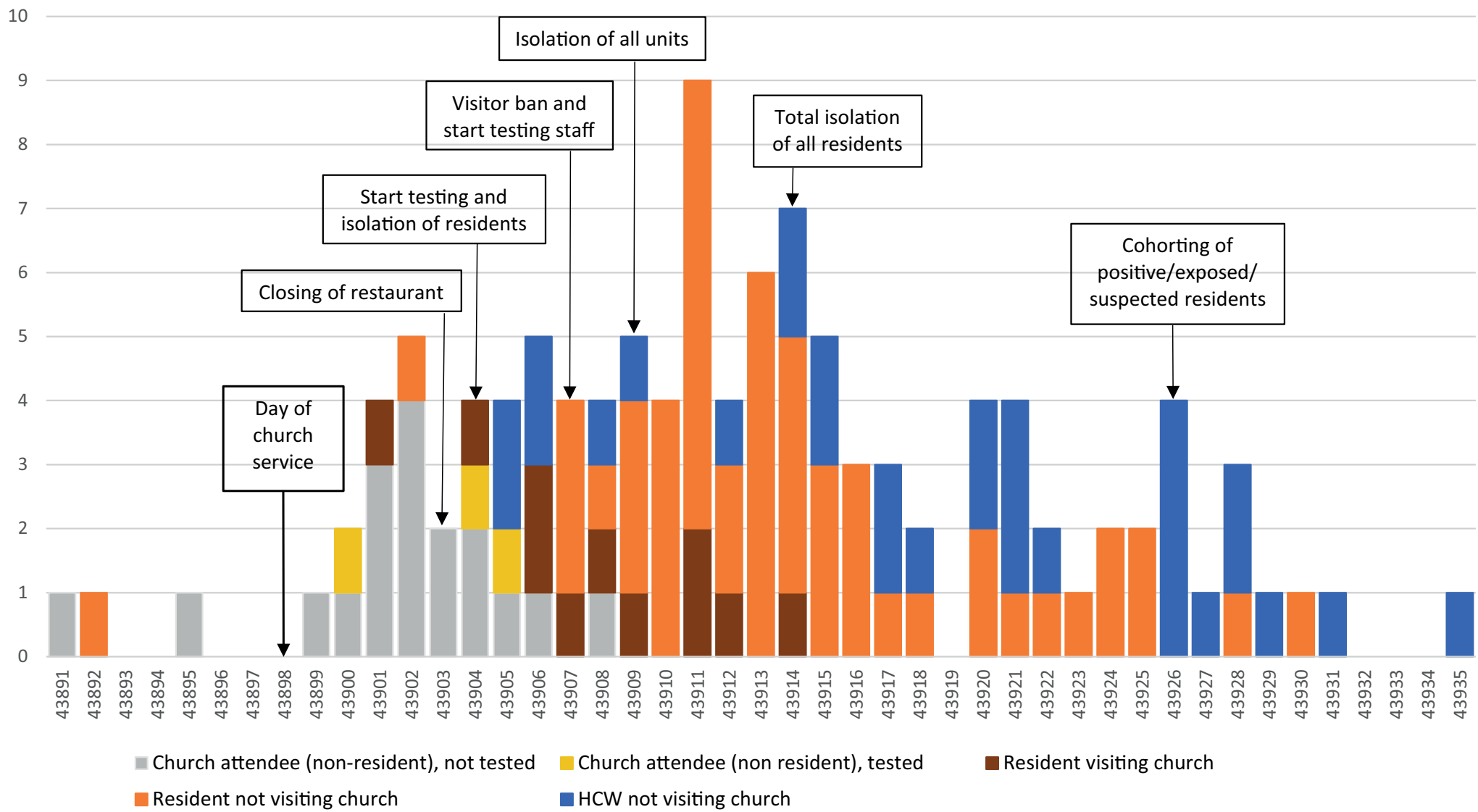
Figure 2. Map of the nursing home indicating rooms/units with COVID-19 positive patients and HCWs: a. by onset date of symptoms; b. by genetic cluster.

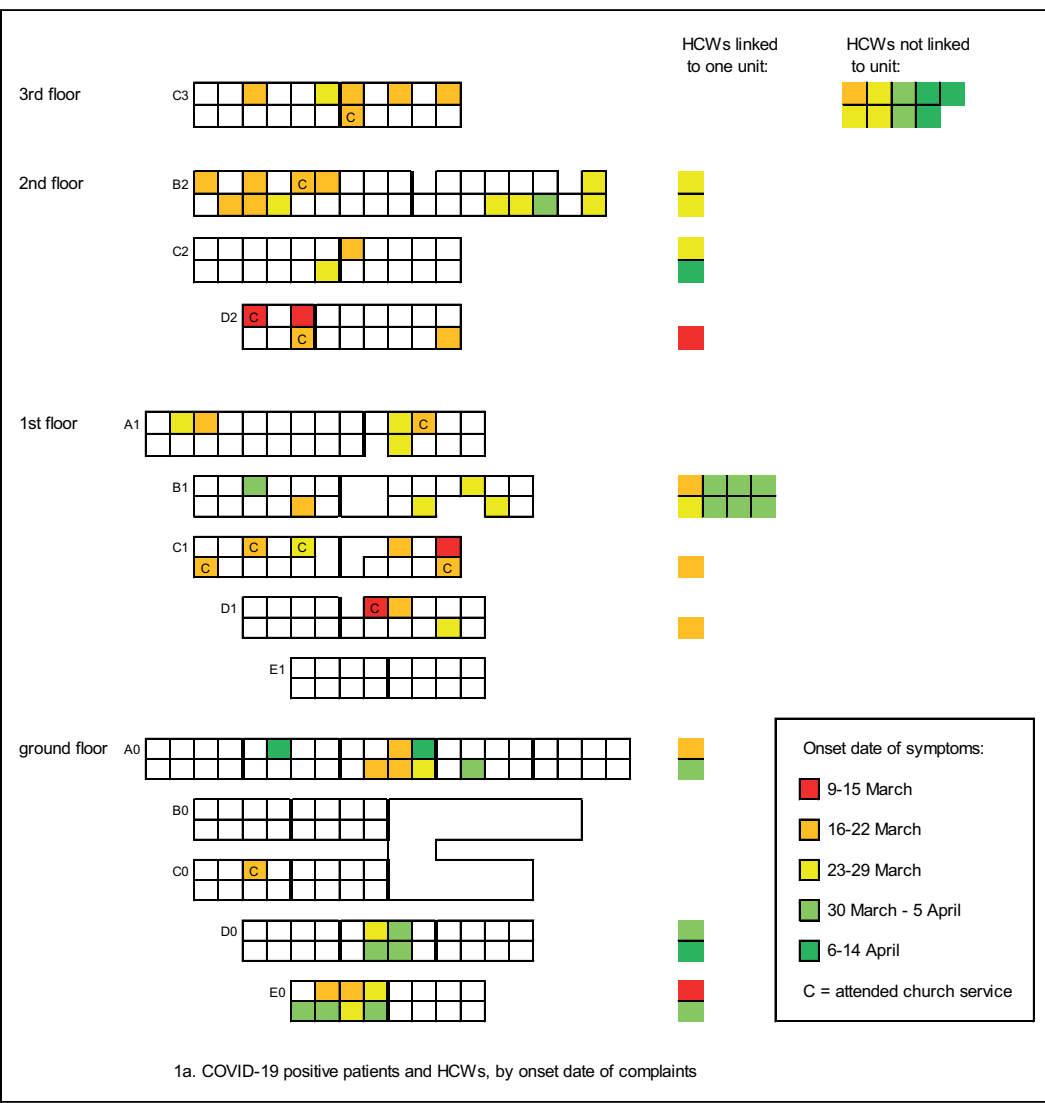
The ground floor and part of the first floor (D1/E1) consist of residential groups of 7/8 residents; half of B1 and B2 (right wings in the map) are short-term care apartments; the remaining units are long-term care apartments, with many residents mingling during meals in the restaurant or communal activities. The resident in C1 coloured red actually had an onset date of March 2<sup>nd</sup>

HCW = health care worker

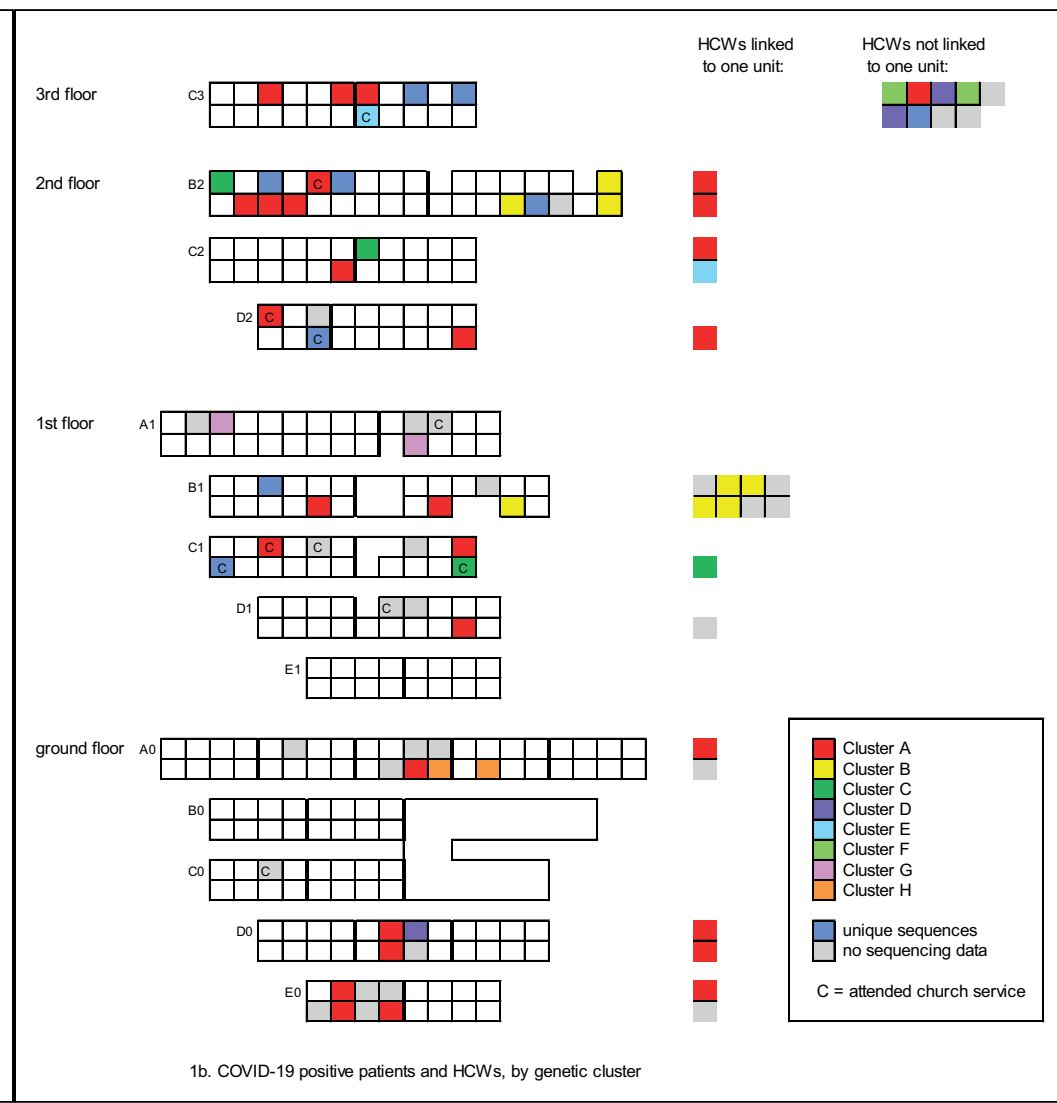
Figure 3. Clusters of SARS-CoV-2 positive residents, health care workers (HCWs), church visitors and other citizens of the region, by dates of onset of symptoms and death.

HCW = health care worker





1a. COVID-19 positive patients and HCWs, by onset date of complaints



1b. COVID-19 positive patients and HCWs, by genetic cluster

