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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Research Article

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Abstract

Background

An outbreak of COVID-19 in a nursing home in the Netherlands, following an on-site church service held on March 8, 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 visitors. 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 visitors (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 visitors 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.

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 11th, 2020. In the Netherlands, the first case of COVID-19 was diagnosed on February 27th, in a Dutch national who had returned from the Lombardy region of Italy. On March 16, 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 1st.
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. 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. 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. In addition, it was augmented by shortages of personal protection equipment (PPE). In view of the severe consequences, understanding how SARS-CoV-2 transmits in this population is crucial.

On March 15th, the day when country-wide measures were announced following confirmation of widespread community-circulation of SARS-COV-2 in a neighbouring province, 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 18th that many church visitors from the local community had fallen ill, supposedly after a church service that had been held on March 8 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 (the day of the first suspected case) were tested for presence of SARS-CoV-2 RNA in throat and nose swabs by RT-PCR. All residents and HCWs testing positive before April 15 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.
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, 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.

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\(^\text{10}\). The consensus genome was generated only including positions with a coverage >30 as described previously\(^\text{11}\). 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\(^\text{12}\). Cluster A was assigned as a regional cluster where it was not possible to apply the cutoff and make a distinction between in-house and regional SARS-CoV-2 transmission.

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, 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 responded to the online questionnaire, between March 27 and April 7. On the day of the church service, four non-resident visitors 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 visitors 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 visitors 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 visitors shows onset date of symptoms between March 1\textsuperscript{st} and April 14\textsuperscript{th} for 21 non-resident church visitors, 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\textsuperscript{th} in non-resident church visitors, and from 2 – 16 (median 10) days after March 8\textsuperscript{th} 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. The outbreak started to decline after March 25\textsuperscript{th}, 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\textsuperscript{th} (study period), 62 of 300 residents (21%) and 30 of 640 HCWs (5%) tested positive for COVID-19 (3 more residents and 12 more HCWs tested positive after the study period; 1 more resident died).

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), indicating at least 17 separate introductions of SARS-CoV-2 into the nursing home. The seven resident church visitors were all infected with distinct viruses (≥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 visitors. Four church service visitors (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.

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 local 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 38/92 (41%) SARS-CoV-2 infections in the nursing home. All clusters started before March 28, which is 14 days after the start of testing and isolation of residents (on July 14), and 9 days after starting the total isolation of all units (on July 19). This shows the effectiveness of the measures in preventing new introductions into the nursing home, taking into account an incubation time of 14 days. However, these measures could not prevent all transmission within the nursing home.

**Discussion**

After the church service on 8 March, 30 of 39 visitors (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. 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, only 2 days before the first resident was tested positive. The use of PPE as from March 14 could have contributed to the limited number of cases per cluster, as well as other preventive measures such testing of symptomatic residents and HCWs, isolation of all units and all residents, and cohorting. This is supported by the whole genome sequencing data: all but two sequence clusters remained limited to four or less residents/HCWs, and 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 can make an essential contribution in this, by revealing transmission patterns that would otherwise remain concealed. Without whole genome sequencing, epidemiological data can easily be misinterpreted, resulting in jumping to conclusions. Other COVID-19 studies have also shown the added value of whole genome sequencing in epidemiological investigations\textsuperscript{8,12}. Furthermore, our findings show the efficacy of stringent measures to control 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.

**Declarations**

**Ethics approval:** 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.

**Participant consent:** 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 participant consent.

**Competing interests:** The authors declare no competing interests.

**References**
1. Alderweireld CEA, Buiting AGM, Murk JAN, Verweij JJ, Berrevoets MAH, van Kasteren MEE. [COVID-19: patient zero in the Netherlands]. Ned Tijdschr Geneeskd 2020;164.
2. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N Engl J Med 2020;382:2081-90.
3. McMichael TM, Currie DW, Clark S, et al. Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington. N Engl J Med 2020;382:2005-11.
4. Grabowski DC, Mor V. Nursing Home Care in Crisis in the Wake of COVID-19. JAMA 2020.
5. Graham NSN, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. J Infect 2020.
6. Gordon AL, Goodman C, Achterberg W, et al. Commentary: COVID in Care Homes-Challenges and Dilemmas in Healthcare Delivery. Age Ageing 2020.
7. Kluytmans-van den Bergh MFQ, Buiting AGM, Pas SD, et al. Prevalence and Clinical Presentation of Health Care Workers With Symptoms of Coronavirus Disease 2019 in 2 Dutch Hospitals During an Early Phase of the Pandemic. JAMA Netw Open 2020;3:e209673.
8. Sikkema RS, Pas SD, Nieuwenhuijse DF, et al. COVID-19 in health-care workers in three hospitals in the south of the Netherlands: a cross-sectional study. Lancet Infect Dis 2020.
9. Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill 2020;25.
10. Oude Munnink BB, Nieuwenhuijse DF, Stein M, et al. Rapid SARS-CoV-2 whole-genome sequencing and analysis for informed public health decision-making in the Netherlands. Nat Med 2020.
11. Oude Munnink BB, Nieuwenhuijse DF, Sikkema RS, Koopmans M. Validating Whole Genome Nanopore Sequencing, using Usutu Virus as an Example. J Vis Exp 2020.
12. Meredith LW, Hamilton WL, Warne B, et al. Rapid implementation of SARS-CoV-2 sequencing to investigate cases of health-care associated COVID-19: a prospective genomic surveillance study. Lancet Infect Dis 2020.
13. James A, Eagle L, Phillips C, et al. High COVID-19 Attack Rate Among Attendees at Events at a Church - Arkansas, March 2020. MMWR Morb Mortal Wkly Rep 2020;69:632-5.
14. Kim S, Jeong YD, Byun JH, et al. Evaluation of COVID-19 epidemic outbreak caused by temporal contact-increase in South Korea. Int J Infect Dis 2020;96:454-7.
15. Yong SEF, Anderson DE, Wei WE, et al. Connecting clusters of COVID-19: an epidemiological and serological investigation. Lancet Infect Dis 2020;20:809-15

Tables

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

Age range (median) 56-98 (68 years)
Gender: male 14 54

Possible source of the outbreak

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

Affected by the outbreak

Developed symptoms after March 8 19 73
   Fever 16 84
   Cough 14 74
   Fatigue 13 68
   Runny/blocked nose 9 47
   Headache 9 47
   Muscle pain 9 47
   Sore throat 9 47
   Shortness of breath 6 32
   Diarrhea 4 21
   Difficulty breathing 1 11
   Nausea/vomiting 3 16
   Pneumonia 2 11
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 7 27
Household member who was admitted to hospital, ICU 1 4

ICU Intensive care unit

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

**Figures**
Figure 1

Epidemic curve of onset date of symptoms of 21 church visitors, 62 residents and 30 health care workers. HCW = health care worker Two church visitors with ongoing symptoms on March 8 are not included, because they could not remember the onset date.
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. HCW = health care worker The resident in C1 coloured red actually had an onset date of March 2

| Cluster A | Cluster B | Cluster C | Cluster D | Cluster E | Cluster F | Cluster G | Cluster H |
|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| March     | March     | March     | March     | March     | March     | March     | March     |
| 1 2 3 4 5 | 1 2 3 4 5 | 1 2 3 4 5 | 1 2 3 4 5 | 1 2 3 4 5 | 1 2 3 4 5 | 1 2 3 4 5 | 1 2 3 4 5 |
| resident  | resident  | resident  | resident  | resident  | resident  | resident  | resident  |
| x         | x         | x         | x         | x         | x         | x         | x         |
| resident  | resident  | resident  | resident  | resident  | resident  | resident  | resident  |
| x         | x         | x         | x         | x         | x         | x         | x         |
| resident  | resident  | resident  | resident  | resident  | resident  | resident  | resident  |
| x         | x         | x         | x         | x         | x         | x         | x         |

x = onset date of complaints  
† = date of death  
= incubation period since day of church service on 8 March
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

Supplementary Files

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- NieuwRijssenburg.fasta3.treefileannotated2.pdf