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Ewijk, C.E. van

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Chapter 3

COVID-19 outbreak in an elderly care home: very low vaccine effectiveness and late impact of booster vaccination campaign.

Catharine E. van Ewijk and Elizabeth I. Hazelhorst

Susan J.M. Hahné

Mirjam J. Knol

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ABSTRACT

Background

Elderly in long-term care facilities (LTCF) are at higher risk for (severe) COVID-19, yet evidence of vaccine effectiveness (VE) in this population is scarce. In November 2021 (Delta period), a COVID-19 outbreak occurred at a LTCF in the Netherlands, continuing despite measures and booster vaccination campaign. We investigated the outbreak to assess VE of primary COVID-19 vaccination against SARS-CoV-2 infection and mortality, and to describe the impact of the booster vaccination.

Methods:

We calculated attack rate (AR) and case fatality (CF) per vaccination status (unvaccinated, primarily vaccinated and boosted). We calculated VE – at on average 6 months after vaccination – as $1 - \text{risk ratio (RR)}$ using the crude risk ratio (RR) with 95% confidence intervals (CI) for the association between vaccination status (primary vaccination versus unvaccinated) and outcomes (SARS-CoV-2 infection and mortality <30 days after testing positive for SARS-CoV-2).

Results:

The overall AR was 67% (70/105). CF was 33% (2/6) among unvaccinated cases, 12% among primarily vaccinated (7/58) and 0% (0/5) among boosted. The VE of primary vaccination was 17% (95% CI -28%; 46%) against SARS-CoV-2 infection and 70% (95% CI -44%; 96%) against mortality. Among boosted residents (N=55), there were 25 cases in the first week after receiving the booster dose, declining to 5 in the second and none in the third week.

Conclusion:

VE of primary vaccination in residents of LTCF was low against SARS-CoV-2 infection and moderate against mortality. There were few cases at 2 weeks after the booster dose and no deaths, despite the presence of susceptible residents. These data are consistent with the positive impact of the booster vaccination in curbing transmission. Timely booster vaccination in residents of LTCF is therefore important.

BACKGROUND

Elderly people in long-term care facilities (LTCF) are at risk for (severe) COVID-19 due to living in a congregated setting, immunosenescence, and pre-existing medical conditions such as dementia, heart- and lung diseases. [1]

Evidence on COVID-19 vaccine effectiveness in residents of LTCF in the Netherlands is scarce. Residents of LTCF are not often admitted to hospitals, not tested for SARS-CoV-2 at community testing centres, and accurate data on vaccination coverage in this population is lacking. Previous research shows substantial waning of vaccine effectiveness against both infection and mortality in resident of LTCF 12+ weeks after primary vaccination, highlighting the frailty of elderly people and the need for continuous vaccine effectiveness monitoring in order to assess the requirement of booster doses in this population. [2, 3]

In November 2021, a SARS-CoV-2 outbreak occurred at a LTCF in the Netherlands, affecting both staff and residents, and continuing despite measures and the initiation of the booster COVID-19 vaccination campaign. We conducted a retrospective cohort study to describe the outbreak and to assess vaccine effectiveness of the primary COVID-19 vaccination series among residents living at the LTCF during the outbreak against SARS-CoV-2 infection and mortality due to COVID-19. In addition, we describe the impact of the booster vaccination campaign that took place at the end of the outbreak.

THE AFFECTED LONG-TERM CARE FACILITY

The affected LTCF contained four separate wards – two psycho-geriatric and two somatic wards – each with 16 beds with a total of 63 residents. In addition there were three semi-attached housing estates, that offered assisted living to 42, 30 and 16 residents respectively. Residents from the estates lived independently from the wards, but could choose to share the same day-care activities and restaurant facilities as the residents from the wards of the LTCF. Predominantly the residents from the biggest assisted living estate (42 residents) tended to share facilities with residents from the wards. Staff of wards and the individual living estates were different, whereas residents of the other two estates did not socially mix with residents of the wards. At the time of the outbreak, the LTCF including the three estates consisted of 151 residents and approximately 160 staff (such as nurses, facilitators, paramedics, cleaners, kitchen staff).

(n=55), received a COVID-19 vaccine booster dose. Despite these measures, the SARS-CoV-2 outbreak affecting now all wards of the LTCF, also spreading to the biggest living estate (42 residents) but not to the other two smaller estates since residents had not mixed socially with residents from the wards. As a result, all residents of the LTCF and the one affected estate were tested and put into individual isolation, and common areas were shut down for all residents. The outbreak stopped and the last cases left isolation on 22 December 2021.

METHODS

Definitions

The cohort of the outbreak investigation was defined as residents living on one of the four wards of the LTCF or the biggest assisted living estate (42 residents) between 20 November 2021 (two days before onset symptom of first case) and 3 January 2022 (14 days after last case).

Case finding was done actively and generally followed national protocol by testing all residents of the separate wards of the LTCF every 5 days once the outbreak was established until no further cases were found and isolation/quarantine could be lifted. We defined a case as a person living at the LTCF who tested positive for SARS-CoV-2 with a Polymerase-Chain-Reaction test (PCR-test) after 22 November 2021 until 3 January 2022.

Asymptomatic cases were defined as cases who did not develop any COVID-19 related symptoms. A mild COVID-19 case was defined as a person with any non-fatal signs or symptoms of COVID-19 who did not need hospitalisation and who did not die within 30 days of testing positive. A severe COVID-19 case was defined as a person with any signs and symptoms of COVID-19 requiring hospitalisation and/or leading to death within 30 days of the positive test.

An unvaccinated person did not receive any COVID-19 vaccination at least 14 days before onset symptoms (or test in case of asymptomatic), or had received only one dose <14 days before. A partially vaccinated person had received only one dose of COVID-19 vaccination at least 14 days before onset symptoms (or test in case of asymptomatic). A fully vaccinated person had received two COVID-19 vaccines at least 14 days before onset symptoms (or test in case of asymptomatic) as part of a primary series, or had received only one dose after a confirmed SARS-CoV-2 infection prior to this outbreak (n=2). We assume that fully vaccinated residents of whom vaccination dates were unknown (N=31) were vaccinated at least 14 days before the start of the outbreak. A boosted person had received a

booster dose of COVID-19 vaccine at least 7 days before onset symptoms (or test in case of asymptomatic).

Data collection

Data were collected as part of the routine (public health) surveillance for COVID-19. In the Netherlands, confirmed SARS-CoV-2 infections are notifiable to the regional Public Health Service (PHS). For each case data were obtained on demographics, date of symptoms onset and test, type of ward, hospital admission due to COVID-19, or death within 30 days of testing positive, previous COVID-19 episodes, and vaccination status (vaccine type, number of doses, dates of administration). LTCF staff filled in a protected online form per case which was subsequently submitted to the regional PHS, according to standard PHS protocol. Missing data regarding cases and data on non-cases were retrospectively collected where possible and collected by the LTCF managers in collaboration with one of the researchers (E.I.H.) from the regional PHS. For each non-case, data were collected on year of birth, sex, ward, date of last negative test, vaccination status, and any previous confirmed COVID-19 episode.

Sequencing

Whole genome sequencing was performed for 12 PCR-positive swabs; these samples were from all four wards and throughout the whole outbreak period.

Analyses

We conducted descriptive statistics and calculated attack rates overall and by ward. In addition, we calculated case fatality per vaccination status (unvaccinated, fully vaccinated and boosted). We calculated the crude risk ratio (RR) and 95% confidence intervals (CI) for the association between vaccination status (complete primary vaccination series versus unvaccinated) and outcomes (SARS-CoV-2 infection and mortality within 30 days after testing positive for SARS-CoV-2) using `epi.2by2` function from the `EpiR` package [4]. For calculating the RR, residents who became cases (date of onset symptoms or test if asymptomatic) <7 days after they received a booster dose were still considered as fully vaccinated. Vaccine effectiveness was calculated as $1 - RR$. Residents with unknown vaccination status were excluded from analyses. Sensitivity analyses were performed restricting these analyses to residents without a confirmed SARS-CoV-2 infection prior to this outbreak. Analyses were conducted using R version 4.0.2.

Ethical considerations

The PHS has legal permission, provided by the Dutch Public Health Act, to process personal information on notifiable diseases for local and national surveillance. [5] Pseudo-anonymised data on non-cases were provided by the LTCF to the regional PHS as part of

the legal duties of a PHS in case of an outbreak investigation. This study received medical ethical clearance (EPI-543) by the Centre for Clinical Expertise (KEC) at the RIVM.

RESULTS

The total cohort consisted of 105 residents, which included residents of the wards and the biggest living estate but excluded the two small living estates (Table 1). The residents had a median age of 85 (min 57; max 106) years and 66% was female. Thirteen residents (14%) had confirmed COVID-19 prior to this outbreak. At the start of the outbreak 8/101 (8%) residents were considered unvaccinated, and 93/101 (92%) were considered fully vaccinated. The vaccination status was unknown for 4 residents. All fully vaccinated residents of whom vaccination dates were known (n=74), received their last dose between 2 March 2021 and 6 July 2021.

On 6 December 2021, 55 (52%) residents – who had not tested positive for SARS-CoV-2 so far during the outbreak – received their booster vaccination with Comirnaty or Spikevax.

Determined at the end of outbreak (for non-cases) or at time of infection (for cases) taking into account time since booster vaccination, 63/101 residents (62%) were considered fully vaccinated and 30/101 (30%) boosted.

Table 1: Characteristics of residents of the LTCF, Netherlands, 20 November 2021 to 3 January 2022 (N=105)

Characteristic	n / N (%)
Age in years median (min – max)	85.0 (57 - 106)
Sex	
Female	69 / 105 (66%)
Type of ward	
Assisted living	42 / 105 (40%)
Psycho-geriatric ward 1	16 / 105 (15%)
Psycho-geriatric ward 2	16 / 105 (15%)
Somatic ward 1	16 / 105 (15%)
Somatic ward 2	15 / 105 (14%)
Vaccinated^a	
Yes	94 / 101 (93%)

Table 1 *Continued*

Characteristic	n / N (%)
Vaccination status^b	
Unvaccinated	8 / 101 (8%)
Fully vaccinated	63 / 101 (62%)
Boostered	30 / 101 (30%)
Previously confirmed COVID-19 episode^c	
Yes	13 / 94 (14%)
SARS-CoV-2 positive^d	
Yes	70 / 105 (67%)
Severity of COVID-19^e	
Asymptomatic	5 / 70 (7%)
Mild COVID-19	53 / 70 (76%)
Severe COVID-19	12 / 70 (17%)
Hospital admission^f	
Yes	4 / 69 (6%)
Deceased^g	
Yes	9 / 70 (13%)

LTCF = long-term care facility ^a missing vaccination status in 4/105 residents; ^b determined at end of the outbreak (non-cases) or at time of infection through date of onset symptoms or positive test if asymptomatic (cases) and taking time since booster vaccination into account; ^c prior to the outbreak, missing data on 11 residents; ^d with Polymerase-chain reaction test; ^e asymptomatic = cases who did not develop COVID-19 related symptoms, mild-COVID = any non-fatal signs or symptoms of COVID-19 without need of hospitalization or death, severe COVID-19 = any signs and symptoms of COVID-19 requiring hospitalization and/or leading to death within 30 days of testing positive; ^f due to COVID-19, missing data on 1 resident; ^g within 30 days of testing positive.

Attack rates

From 20 November 2021 to 3 January 2022, 70 cases among residents of the LTCF were identified with dates of onset symptoms or test in case of asymptomatic between 22 November 2021 and 16 December 2021, and a peak on 10 December 2021 (Figure 1). The overall attack rate (AR) among residents of the LTCF was 67% (70/105). The ARs were highest for the two wards where the outbreak started first: psycho-geriatric ward 1 with an AR of 94% (15/16) and somatic ward 1 with an AR of 81% (13/16). The AR for psycho-geriatric ward 2 was 56% (9/16) and 47% (7/15) for somatic ward 2. The AR for the assisted living estate was 62% (26/42).

Genome sequencing

Sequencing was successful for 8/12 samples, showing pangolineage B.1.617.2, subclade AY.43 in all samples, consistent with Delta variant circulating at that time.

Characteristics of residents by vaccination status

Table 2 shows the characteristics of the residents by vaccination status determined at the end of the outbreak (non-cases) or at time of infection determined by date of onset symptom (or test in case of asymptomatic) (cases).

Of all boosted residents, 8/23 (38%) had a COVID-19 episode prior to this outbreak compared to 1/7 (14%) unvaccinated and 4/62 (6.5%) fully vaccinated ($p=0.002$). These reported prior infections had been between March 2020 and February 2021, and one in September 2021.

Table 2: Characteristics of residents of the LTCF by vaccination status determined at the end of the outbreak or by date of infection, The Netherlands, 20 November to 3 January 2022 (N=101^a).

Variable	Vaccination status			p-value ¹
	Unvaccinated, N = 8 n / N (%)	Fully vaccinated, N = 63 n / N (%)	Boostered, N = 30 n / N (%)	
Age in years median (min – max)	91 (67 - 95)	83 (57 - 99)	86 (66 - 106)	0.34
Sex				0.22
Female	7 / 8 (88%)	37 / 63 (59%)	21 / 30 (70%)	
Type of ward				
Assisted living	1 / 8 (12%)	26 / 63 (41%)	12 / 30 (40%)	
Psycho-geriatric ward 1	1 / 8 (12%)	14 / 63 (22%)	1 / 30 (3%)	
Psycho-geriatric ward 2	3 / 8 (38%)	7 / 63 (11%)	6 / 30 (20%)	
Somatic ward 1	1 / 8 (12%)	12 / 63 (19%)	2 / 30 (7%)	
Somatic ward 2	2 / 8 (25%)	4 / 63 (6%)	9 / 30 (30%)	
Previously confirmed COVID-19 episode^b				0.002
Yes	1 / 7 (14%)	4 / 62 (6.5%)	8 / 21 (38%)	
SARS-CoV-2 positive^c				<0.001
Yes	6 / 8 (75%)	58 / 63 (92%)	5 / 30 (17%)	
Severity of COVID-19^d				0.74
Asymptomatic	0 / 6 (0%)	5 / 58 (9%)	0 / 5 (0%)	

Table 2 Continued

Variable	Vaccination status			p-value ¹
	Unvaccinated, N = 8 n / N (%)	Fully vaccinated, N = 63 n / N (%)	Boostered, N = 30 n / N (%)	
Mild COVID-19	4 / 6 (67%)	43 / 58 (74%)	4 / 5 (80%)	
Severe COVID-19	2 / 6 (33%)	10 / 58 (17%)	0 / 5 (0%)	
Hospital admission^e				0.59
Yes	1 / 6 (17%)	3 / 58 (5.2%)	0 / 5 (0%)	
Deceased^f				0.28
Yes	2 / 6 (33%)	7 / 58 (12%)	0 / 5 (0%)	

LTCF = long-term care facility ¹Kruskal-Wallis rank sum test; Fisher's exact test

^a missing data on vaccination status in 4/105 residents ^b prior to the outbreak, missing data on 1 unvaccinated, 1 fully vaccinated, 9 boosted residents; ^c with Polymerase-chain reaction test; ^d asymptomatic = cases who did not develop COVID-19 related symptoms, mild-COVID = any non-fatal signs or symptoms of COVID-19 without need of hospitalization or death, severe COVID-19 = any signs and symptoms of COVID-19 requiring hospitalization and/or leading to death within three weeks of testing positive; ^e due to COVID-19; ^f within 30 days of testing positive.

Vaccine effectiveness

The vaccine effectiveness of primary vaccination against SARS-CoV-2 infection (58/93 cases) was 17% (95% CI: - 28%; 46%). The vaccine effectiveness against mortality within 30 days after testing positive was 70% (95%CI - 44%; 96%) (Table 3). Excluding residents with confirmed previous SARS-CoV-2 infections prior to this outbreak did not change the vaccine effectiveness estimates against infection (16%; 95%CI -16; 40%) or mortality (70%; 95% CI -45%; 96%).

The case fatality among unvaccinated cases was 33% (2/6), 12% among fully vaccinated (7/58) and 0% (0/5) among boosted residents (Table 2).

In the first 6 days after introduction of the booster, and when residents were still considered fully vaccinated and included in the calculations of vaccine effectiveness estimates of primary vaccination, there were 25 cases out of the 55 residents that had received their booster dose on 6 December 2021. However, there were relatively few cases in the second week (5 of 30 remaining boosted residents) and zero in the third week after introduction of the booster vaccination (Figure 1).

Table 3: The vaccine effectiveness of complete primary vaccination series against SARS-CoV-2 infection and mortality, LTCF, The Netherlands, 20 November to 12 December 2021 (N=101)^a.

Vaccination status	Total no.of residents	No. SARS-coV-2 positives	Vaccine effectiveness against infection	95% CI	Total no. of death ^b	Vaccine effectiveness against mortality	95% CI
Unvaccinated	8	6	Ref.		2	Ref.	
Fully vaccinated	93	58	17%	(-28%; 46%)	7	70%	(-44%; 96%)
Excluding previous infections^c							
Unvaccinated	7	6	Ref.		2	Ref.	
Fully vaccinated	81	58	16%	(-16%; 40%)	7	70%	(-45%; 96%)

LTCF = long-term care facility; ^a missing data on vaccination status in 4/105 residents; ^b within 30 days after testing SARS-CoV-2 positive; ^claboratory confirmed SARS-CoV-2 infections prior to this outbreak.

DISCUSSION

Our outbreak investigation found a very high overall SARS-CoV-2 infection attack rate (67%) in a LTCF despite a high COVID-19 vaccination coverage among the residents (92%) and non-pharmaceutical interventions (NPI). Attack rates varied across wards from 47% to 94%.

Data on vaccine effectiveness in residents of LTCF is scarce. Through this outbreak investigation we were able to estimate vaccine effectiveness for primary vaccination in a LTCF population that on average completed their primary vaccination more than six months prior to this outbreak. Vaccine effectiveness against SARS-CoV-2 infection of complete primary vaccination was low (17%, 95% CI -28%; 46%), but higher against mortality (70%, 95%CI -44%; 96%).

High attack rates despite high vaccination coverage in a LTCF have been reported previously. [1] Possible explanations are a high force of infection (through highly infectious case(s) or persistent exposure through a large outbreak), suboptimal adherence to NPI, or an outbreak due to a new SARS-CoV-2 variant associated with decreased vaccine effectiveness. The omicron variant that was discovered in South-Africa end of November 2021 and that is associated with a decrease in vaccine effectiveness, was not yet widely spread in the Netherlands at the time of this outbreak. [6, 7] Whole genome sequencing from infections in cases from different time points in the outbreak and different wards confirmed SARS-CoV-2 Delta variant.

Previous results from household studies – associated with more intense exposure compared to community level – show lower COVID-19 vaccine effectiveness compared to community vaccine effectiveness estimates. [8, 9] Wards of LTCF could be considered a type of household with more intense exposure, possibly contributing to the observed lower vaccine effectiveness compared to the same age group in the community in the Netherlands: 73% (95%CI 71%; 74%) for age group 70+ years at 6 months after complete primary series with mRNA vaccines (Comirnaty and Vaxzevria). [10-12] Research shows vaccination protects against onward transmission of SARS-CoV-2. [8] Although the national COVID-19 vaccination turnout among personnel caring for elderly people, including LTCF, was high (80%), we do not have data on vaccination coverage among staff of the LTCF where the outbreak occurred. Unvaccinated and infected staff might have contributed to higher force of infection during the outbreak leading to lower vaccine effectiveness. [13]

Additionally, studies show COVID-19 vaccine effectiveness wanes over time, especially in elderly people. [2, 14] Adults living in LTCF were prioritised in the Netherlands for

vaccination during the Dutch COVID-19 vaccination campaign that started in January 2021. [15] In our study, the majority (86% of those with known vaccination dates) received their last dose of the primary vaccination series before end of April 2021.

The low vaccine effectiveness of primary vaccination series against infection at (on average) six months after vaccination with a case fatality of 12% (7/58) within 30 days of positive, highlight the vulnerability of adults living in LTCF and the need of timely booster vaccinations to increase protection. [16, 17]

The booster vaccination campaign was rolled-out during this outbreak on 6 December 2021. Research suggests that the effect of booster vaccination in adults 50+ years can be seen 7 days after the booster dose. [16, 17] In this outbreak there were still 25 cases among the 55 boosted residents in the first week after the booster dose, with a peak on day 4 with 14 cases. There were relatively few cases in the second week (5 of 30 remaining negatively tested boosted residents) and zero in the third week after introduction of the booster vaccination, despite the fact there were still susceptible residents. These data seem consistent with the positive impact of the booster dose in curbing transmission. [3] Yet optimal protection of a booster vaccination might take longer to develop in residents of LTCF compared to younger population.

Among the residents receiving a booster vaccination there were more individuals with a confirmed SARS-CoV-2 infection prior to this outbreak. These residents had already gained protection through vaccination as well infection, potentially giving them more protection during this outbreak compared to those without a prior infection. [18] This could lead to a biased selection of residents receiving a booster vaccination – since residents who tested positive during this outbreak were not given a booster dose – and thus overestimation of the role of the booster vaccination in curbing the transmission during this outbreak. Nonetheless, vaccinating residents of LTCF, when vaccination coverage is low and/or time since last vaccination is more than three months, as intervention in case of a SARS-CoV-2 outbreak to curb transmission and prevent morbidity, might be considered. More research is needed, however, to assess the true effect of such an intervention.

Limitations

There are several limitations to our study. Although the SARS-CoV-2 infection outbreak was large and greatly impacted staff and residents of the LTCF, the sample size for analyses remained small.

We were therefore unable to adjust for potential confounders when estimating vaccine effectiveness for primary vaccination series. Although the cohort can be considered

relatively homogenous regarding age, sex, and time since vaccination, there is likely to be residual confounding. For example, we were unable to adjust for or stratify by type of ward as proxy for differences in exposure and unmeasured confounding per ward.

We were unable to estimate vaccine effectiveness for the booster vaccination either against infection or mortality due to small sample size, and the booster being administered during the outbreak leading to survivor bias. Nonetheless, we observed few cases in the second and none in the third week after introduction of the booster despite the presence of susceptible residents, and a low case fatality (0%). We therefore believe that the booster vaccination may have contributed to stopping this SARS-CoV-2 outbreak in the LTCF.

CONCLUSION

During this outbreak in a LTCF, the COVID-19 vaccine effectiveness at more than 6 months after vaccination was very low against SARS-CoV-2 infection and moderate against mortality. These results highlight the vulnerability of adults in LTCF. There were few cases in the second and none in the third week after booster, despite the presence of susceptible residents. These data are consistent with the positive impact of the booster vaccination. Importantly, optimal protection of a booster vaccination might take longer to develop in residents of LTCF compared to younger population. Timely booster vaccination in residents of LTCF is therefore important.

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