Clinical Infectious Diseases
CORRESPONDENCE

Vaccination Did Not Prevent Severe Coronavirus Disease 2019 in an Outbreak Among Older Residents of a Nursing Home, B.1.617.2 Variant, July 2021

To the Editor—We read with interest the brief report by Bailly et al [1] who demonstrated partial vaccine effectiveness (VE) of the BNT162b2 messenger RNA (mRNA) vaccine against the 501Y.V2 (Beta) variant during a nursing home outbreak in France (VE of 50% among elderly residents). After vaccination, social distancing measures were removed despite low vaccination coverage among staff at the home (32%). We welcome the authors' call for vigilance in syndromic screening and viral testing and would like to highlight an outbreak that occurred in a similar setting in the Netherlands but where severe disease related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was not reduced despite very high levels of vaccination.

Between January 2021 and April 2021, 86% of residents of a nursing home (26 of 31) were vaccinated with 2 doses of the BNT162b2 mRNA vaccine ≥1 month apart. Infection control and social distancing measures were in place for residents and staff throughout. Despite these measures, 3 coronavirus disease 2019 cases were confirmed on 13 July (2 residents and 1 healthcare provider [HCP]). Immediate action was taken to limit onward transmission: all HCPs continuously wore filtering facepiece particles (FFP) 2 masks and gloves; HCPs caring for SARS-CoV-2–positive residents wore disposable, long-sleeved gowns and face shields; floors in the unit were segregated; and residents went into isolation. The outbreak rapidly evolved, however, and an

Table 1. Demographic Characteristics of Resident Cases and Noncases in a Severe Acute Respiratory Syndrome Coronavirus 2 Outbreak Caused by the Delta Variant in a Skilled Nursing Facility, Rotterdam Area, The Netherlands

Variable	Category	Total (%) n = 31	Cases (%) n = 15	Noncases (%) n = 16
Sex	Women	23 (74)	11 (73)	12 (75)
	Men	8 (26)	4 (27)	4 (25)
Age, median [range], years	…	86 [59–99]	87 [71–99]	84 [59–92]
Medical history	Neurodegenerative	18 (58)	13 (87)	5 (38)
	Cerebrovascular	12 (39)	3 (20)	9 (56)
	Oncological	6 (19)	0 (0)	6 (38)
	Diabetes	5 (16)	1 (7)	4 (25)
	Cardiovascular	4 (13)	0 (0)	4 (25)
	Peripheral vascular	3 (10)	0 (0)	3 (19)
	Other	16 (49)	2 (14)	14 (90)
Previous coronavirus disease 2019, no. (%)	Yes	4 (13)	2 (13)	2 (12)
	No	27 (87)	13 (87)	14 (88)
Vaccination status,[a] no. (%)	Yes	26 (84)	14 (93)	12 (75)
	No	5 (16)	1 (7)	4 (25)
Time since vaccination in weeks,[a] median [range]	…	…	21 [15–21]	…
Cycle threshold value, median [range]	…	…	21 [10–35]	…
Symptomatic,[b] no. (%)	Yes	17 (55)	15 (100)	2 (12)
	No	14 (45)	0 (0)	14 (88)
Symptoms, no. (%)	Cough	12 (39)	12 (80)	0 (0)
	Fever	12 (39)	10 (67)	2 (12)
	Malaise	8 (26)	8 (53)	0 (0)
	Decreased intake	6 (19)	6 (40)	0 (0)
	Fatigue	6 (19)	6 (40)	0 (0)
	Nasal cold	3 (10)	3 (20)	0 (0)
	Shortness of breath	2 (6)	2 (13)	0 (0)
	Smell and/or taste loss	1 (3)	1 (7)	0 (0)
Antibiotics	…	4 (13)	4 (27)	0 (0)
Oxygen	…	4 (13)	4 (27)	0 (0)
Death	…	2 (6)	2 (13)	0 (0)

[a]All but 1 of the vaccines administered were Pfizer-BioNTech (BNT162b2 messenger RNA). We could not retrieve type of vaccination and time since vaccination from 1 resident. This person moved to the facility in the beginning of June. One resident received only 1 vaccine and was severe acute respiratory syndrome coronavirus 2–negative. This person was considered unvaccinated for this table.

[b]Symptomatic means anyone who reported 1 or more of the above-listed symptoms. Symptoms were self-reported.

outbreak investigation was undertaken. This included testing of all residents on the affected floors for SARS-CoV-2 using reverse-transcriptase polymerase chain reaction, evaluation of residents' clinical and vaccination status, and evaluation of the infection control measures. As in France, vaccination is not compulsory among HCPs in the Netherlands. Staff were surveyed separately regarding their vaccination status.

Thirty-one residents resided on the affected floors (median age, 86; range, 59–99). Within 2 weeks, the attack rate was 54% (14 of 26) among vaccinated residents and 20% (1 of 5) among unvaccinated residents (relative risk, 2.7; 95% confidence interval, .3–13.2). The median time since vaccination was 21 weeks (range, 15–21). All cases were symptomatic, of whom >50% reported cough, fever, or malaise; 3 required oxygen; and 2 died (Table 1). Nine staff were symptomatic and tested positive, of whom 6 were fully vaccinated. Of 11 specimens from residents and staff, 7 were successfully sequenced. A B.1.617.2. (Delta) variant cluster was evident and suggestive of 1 introduction (this included the first symptomatic HCP). The response to the staff questionnaire was suboptimal at 54% (88 of 162), of whom 68% were fully vaccinated. No breaches in infection control were identified. Approximately 30% of the staff has since received a booster dose (personal communication).

VE against infection varies by variant and wanes over time [2]; however, high vaccination rates were insufficient to prevent rapid spread and severe disease less than 5 months post-vaccination. We agree that syndromic surveillance and prompt testing are key to limit outbreaks in highly vaccinated, vulnerable populations. However, as SARS-CoV-2 becomes endemic, further action will be required to counter "pandemic fatigue" [3]. This includes targeted strategies to encourage vaccine and booster uptake among staff and close, ongoing engagement between all stakeholders to agree to risk reduction measures and maintain residents' and staff resilience if or when new variants emerge.

Note

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Maaike Buskermolen,[1,a] Irene Molthof,[1,a] Helene A. C. M. Voeten,[1,2] Joanna van Twillert,[1] Annette Schriek,[3] Carla Flach,[3] Marlies Dijkers,[3] Pieter W. Smit,[4] Tirsah Koster,[1] Ewout B. Fanoy,[1] Jane Whelan,[1] and Aimée Tjon-A-Tsien[1]

[1]Public Health Service Rotterdam-Rijnmond, Rotterdam, The Netherlands; [2]Department of Public Health, Erasmus MC, Rotterdam, The Netherlands; [3]Riederborgh, Ridderkerk, The Netherlands; and [4]Maasstad Laboratory, Medical Microbiology, Maasstad Hospital, Rotterdam, The Netherlands

References

1. Bailly B, Guilpain L, Bouiller K, et al. BNT162b2 messenger RNA vaccination did not prevent an outbreak of severe acute respiratory syndrome coronavirus 2 variant 501Y.V2 in an elderly nursing home but reduced transmission and disease severity. Clin Infect Dis **2022**; 74:517–20.
2. Feikin DR, Higdon MM, Abu-Raddad LJ, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. Lancet **2022**; 399:924–44.
3. World Health Organization, Regional Office for Europe. Pandemic fatigue: reinvigorating the public to prevent COVID-19: policy considerations for Member States in the WHO European Region. World Health Organization. Regional Office for Europe, **2020**.

Correspondence: A. Tjon-A-Tsien, Public Health Service, Rotterdam-Rijnmond, Schiedamsedijk 95, Rotterdam, The Netherlands (aml.tjonatsien@rotterdam.nl).

Clinical Infectious Diseases® 2022;75(6):1111–2

https://doi.org/10.1093/cid/ciac329

Is Inhaled Zanamivir Non-inferior to Oral Oseltamivir in the Treatment of Outpatients With Influenza?

To the Editor—We read with great interest the recent article by Su et al [1], which compared the clinical efficacy of inhaled zanamivir and oral oseltamivir in the prevention of influenza-related hospitalization or death. They found that the clinical outcome of outpatients receiving inhaled zanamivir was comparable to that in those using oral oseltamivir. However, we have several serious concerns about the study's methodology.

First, the signs and symptoms of influenza are nonspecific, which can mimic the common cold or lower respiratory tract infection, so it is difficult to confirm the diagnosis based on clinical manifestations [2]. Based on the flowchart of the study population selection, more than 3 million patients had a diagnosis of influenza during the study period, but only 1 048 685 of them received antiviral agents. Therefore, we had serious concerns about the diagnosis of influenza in this study. A further sensitivity test of patients with laboratory-confirmed influenza would provide more robust evidence to convince the readers. Furthermore, patients with influenza may have coinfection with bacteria and they may receive antibiotics at the same time. It is better to exclude the patients who had a diagnosis of bacterial infection or who are receiving antibiotics during enrollment.

Second, although the study used comprehensive propensity score matching methods to balance the baseline characteristics, including each chronic medical condition between the 2 study groups, patients at high risk of disease progression could have multiple comorbidities [3]. To minimize the confounding effect of multiple comorbidities, further matching to balance the Charlson comorbidity index between groups is needed.

Third, this study used the term "non-inferior to" many times. However, they did not mention what the non-inferiority margin is and how to choose the margin [4]. This issue should be clarified.

Fourth, oseltamivir was given via oral route and is easy to use. In contrast, zanamivir was given through inhalation and required the patients' cooperation [5]. Therefore, patients with consciousness disturbance or with low inspiratory effort are not appropriate candidates and there could be a selection bias.

Finally, this study identified patients from 3 influenza seasons from 2013 to 2016, but it is not uncommon for patients to repeatedly acquire influenza. However, it was not reported whether this study only included patients once to avoid duplicate counts of baseline characteristics.

In conclusion, this nationwide population-based study provides great insight into using anti-influenza agents for outpatients. However, several issues need to be clarified to confirm the role of inhaled zanamivir.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

[a]M. B. and I. M. are shared first authors.