COVID-19 Outbreaks in Nursing Homes Despite Full Vaccination with BNT162b2 of a Majority of Residents

Carmelo Lafuente, Antonio Rainone, Olivier Guérin, Olivier Drunat, Claude Jeandel, Olivier Hanon, Joël Belmin

Research Article

COVID-19 outbreaks in nursing homes despite full vaccination with BNT162b2 of a majority of residents.

Authors

Carmelo Lafuente-Lafuente, MD, PhD (1, 2, 3)

Antonio Rainone, MD (1,2)

Olivier Guérin, MD, PhD (4,5)

Olivier Drunat, MD (6,7)

Claude Jeandel, MD, PhD (8,9)

Olivier Hanon, MD, PhD (10,11)

Joël Belmin, MD, PhD (1,2)

For the C-VENH (COVID-19 Vaccine Effectiveness in Older Patients) Investigators *

* See the complete list at the end of the manuscript

1. Service de gériatrie à orientation cardiologique et neurologique, APHP, Sorbonne Université, Hôpitaux universitaires Pitie-Salpêtrière-Charles Foix, F-94205 Ivry-sur-Seine, France

2. Faculté de médecine, Sorbonne Université, F-75013 Paris, France

3. Université Paris Est Créteil, INSERM, IMRB, F-94010 Creteil, France

4. Université Côte d'Azur, Centre Hospitalier Universitaire de Nice, Service de Médecine Gériatrique et Thérapeutique, F-06000 Nice, France.

5. Université Côte d'Azur, CNRS UMR 7284/INSERM U108, Institute for Research on Cancer and Aging Nice (IRCAN), Faculté de médecine, Nice, France

6. APHP, Université de Paris, Hôpital Bretonneau, Paris, France

7. Collégiale de Gériatrie de l'APHP, Paris, France

8. CHU de Montpellier, Université de Montpellier, Montpellier, France

9. Conseil National Professionnel de Gériatrie, Baillargés, France

10. APHP, Université Paris-Descartes, EA 4468, Hôpital Broca, Paris, France

11. Gérond'If, Gérontopôle d'Ile-de-France, Paris, France

Short title: COVID-19 outbreaks in nursing homes despite vaccination

Corresponding author:

Dr Carmelo Lafuente-Lafuente,

Service de Gériatrie à orientation Cardiologique et Neurologique.

Hôpital Charles Foix, 7 avenue de la République, 94200 Ivry-sur-Seine, France.

Tel: + 33 149 594 554 / 356

Email: carmelo.lafuente@aphp.fr

Metrics

Tables: 2, Figure: 1, References: 39

Word count: Abstract: 349, Text: 2 694.

Keywords:

COVID-19, SARS-CoV-2, vaccination, outbreak, older adults, nursing home

Abstract:

Background: It is not known if widespread vaccination can prevent the spread of SARS-CoV-2 in subpopulations at high risk, like older adults in nursing homes (NH).

Objective: To know if COVID-19 outbreaks can occur in NH with high vaccination coverage among its residents.

Methods: In this case series, we identified, using national professional networks, NH that suffered COVID-19 outbreaks despite having completed a vaccination campaign, and asked them to send data, using predefined collecting forms, on the number of residents exposed, their vaccination status and the number, characteristics and evolution of patients infected. The main outcome was to identify outbreaks occurring in NH with high vaccine coverage. Secondary outcomes were residents' risk of being infected, developing severe disease or dying from COVID-19 during the outbreak. SARS-CoV-2 infection was defined by a positive RT-PCR. All residents were serially tested whenever cases appeared in a facility. Unadjusted secondary attack rates, relative risks and vaccine effectiveness during the outbreak were estimated.

Results: We identified 31 NH suffering an outbreak during March - April 2021, of which 27 sent data, cumulating 1768 residents (mean age 88.4, 73.4% women, 78.2% fully vaccinated). BNT162b2 was the vaccine employed in all NH.

There were 365 cases of SARS-CoV-2 infection. Median secondary attack rates were 20.0% (IQR 4.4 – 50.0%) among unvaccinated residents and 16.7% (IQR 9.5 – 29.2%) among fully vaccinated ones. Severe cases developed in 42 of 80 (52.5%) unvaccinated patients, compared with 56 of 248 (22.6%) fully vaccinated ones (RR 4.17, 95%CI 2.43–7.17). Twenty of the unvaccinated patients (25.0%) and 16 of fully vaccinated ones (6.5%) died from COVID-19 (RR 5.11, 95%CI 2.49–10.5). Estimated vaccine effectiveness during the outbreak was 34.5% (95%CI 18.5–47.3) for preventing SARS-CoV-2 infection, 71.8% (58.8–80.7) for preventing severe disease and 83.1% (67.8–91.1) for preventing death.

Conclusions: Outbreaks of COVID-19 including severe cases and deaths can still occur in NH despite full vaccination of a majority of residents. Vaccine remains highly effective, however, for preventing severe disease and death. Prevention and control measures for SARS-CoV-2 should be maintained in NH at periods of high incidence in the community.

Introduction

Vaccines are a key component of any strategy for achieving long-term control of the current SARS-CoV-2 pandemic. In addition to preventing COVID-19 morbidity and mortality, they are also expected to limit further spread of the disease [**1, 2**]. There is great hope that extensive vaccination against SARS-CoV-2 will allow a progressive return to normal life.

Several vaccines have proven in large randomized trials to be highly effective for preventing COVID-19 symptomatic or severe disease and death [**3-7**]. However, most people enrolled in those trials were middle-aged adults and few data is available for some subpopulations at high risk. Frail older patients, in particular, like those living in nursing homes, are one of the groups most at risk of acquiring SARS-CoV-2 infection, suffering severe disease and dying [**8-10**]. However, they have been poorly represented in clinical trials. A few studies have analyzed antibody and/or cellular immune response following vaccination in limited numbers of older people (40 to 200 older people included), reaching inconsistent results [**11-14**]. A recent observational study using national surveillance data after a nationwide vaccination campaign in Israel found that BNT162b2 vaccine maintained high effectiveness in the general population of older adults, including adults aged 85 or older [**15**].

Despite limited effectiveness data, older patients in nursing homes have understandably been a priority target for vaccination in most countries. In France, residents of nursing homes were the first target of the national vaccination campaign [**16**]. In January and February 2021, BNT162b2 vaccine was offered to all residents and to their healthcare professionals aged 50 years or older, or with risk factors for severe COVID-19 disease. Most residents and many health care professionals accepted.

In March and April 2021, France suffered a third wave of the COVID-19 pandemic, in which the B.1.1.7 (Alpha) variant, more contagious, was dominant (82.6% of all strains analyzed) [**17**]. We were then concerned to learn that COVID-19 outbreaks had developed in some nursing homes despite previous vaccination of a large proportion of their residents, and that they included severe cases and even deaths. We described one of those outbreaks in a separate report [**18**]. We also wanted to

know if such outbreaks were just a rare, isolated event, or there were more. Therefore, we looked for other cases of COVID-19 outbreaks in nursing homes with high vaccination rates among its residents.

Methods

The objective of the study was to know if COVID-19 outbreaks could occur in nursing homes during a pandemic wave once a majority of its residents were fully vaccinated and to have a rough estimation of the frequency of such events – this is, if they were very rare or something more frequent. If such outbreaks did not appear to be rare, we secondarily aimed to estimate secondary attack rates and vaccine effectiveness in those particular circumstances (older patients in nursing homes, during an outbreak, in a period of high exposition to the virus), i.e. a worst-case scenario.

We contacted colleagues working in geriatric facilities in France, from April 15th to May 10th 2021, by e-mail and phone, using personal contacts and several regional and national professional networks (*Société Française de Gériatrie et Gérontologie*, *Gérontopôle d'Île-de-France*, *Collégiale de gériatrie de l'APHP, Conseil National des Professionnels de Gériatrie*). We asked them to report to us any recent COVID-19 outbreak (three or more grouped cases over a ten-day period) arising in nursing homes that included patients previously vaccinated.

One investigator (A.R., J.B.) called the medical coordinator of any nursing homes that answered the survey, or that we had identified as possibly having had an outbreak, to confirm the outbreak and proportion of vaccinated residents, and request him or her to participate in the study. Centers that accepted to participate were asked to send data, using predefined collecting forms, on the number of persons exposed, their vaccination status, the vaccine administered, time elapsed from vaccination to the onset of the outbreak and the number, basic demographic data and evolution of patients infected, including deaths and the cause of death, as well as any data available on SARS-CoV-2 variants or sequencing, if those have been performed.

COVID-19 infection was defined on the basis of a positive reverse transcriptase polymerase chain reaction (RT-PCR) test. French national procedures mandate that, when a case is detected in a nursing home, a systematic screening by RT-PCR on nasopharyngeal swabs of all residents and healthcare professionals were conducted [**19**]. The screening is repeated seven days later on those residents initially negative. For the purposes of this study, we defined severe COVID-19 disease as any patient requiring oxygen or intravenous fluids for more than 48 hours, requiring hospitalization, or dying from COVID-19 (defined as any patient who died from COVID-19 disease or from a decompensation of previous pathologies precipitated by the COVID-19 infection).

Persons who had received their second vaccine dose ≥7 days before the outbreak were considered fully vaccinated, consistent with the effect observed in the BNT162b2 mRNA vaccine clinical trials [**3**]. Persons who had received only one dose or a second dose less than 7 days before the onset of the outbreak were considered partially vaccinated.

We estimated secondary attack rates following the index case for each outbreak, in fully vaccinated, partially vaccinated and unvaccinated patients. Relative risks (RRs) were calculated comparing unvaccinated residents versus fully vaccinated residents (i.e. fully vaccinated residents were set as the reference group). Vaccine effectiveness in fully vaccinated residents during the outbreak ([risk among unvaccinated group − risk among vaccinated group] / risk among unvaccinated group) was calculated for the following outcomes: SARS-CoV-2 infection (including asymptomatic cases), severe COVID-19 disease, and death from COVID-19. Correlation between vaccination rates among residents and secondary attack rates was explored using univariate regression. While we initially planned for, the data we finally retrieved did not allow us to conduct a multivariate analysis in order to adjust for important covariates like vaccine coverage in staff, staff numbers, clustering of observations, and individual characteristics of vaccinated and unvaccinated residents. Thus, only crude estimates were calculated.

We followed the STROBE statement for improving the reporting of observational studies [**20**]. A completed STROBE checklist is available as Supplementary Material.

Results

We identified 31 nursing homes which experienced a COVID-19 outbreak occurring from February 1st to April 30th, 2021. Four declined to participate or did not send data. We report the analysis of 27 nursing homes, distributed all along the national territory (**Figure 1**).

Data summarized by nursing homes is shown in **Table 1**. Of the 1768 residents present in the 27 facilities, 78.2% were fully vaccinated (95% CI, 71.9 – 83.9), 5.7% partially vaccinated (95% CI, 3.38 – 8.02) and 16.5% were not vaccinated (95% CI, 11.9 – 21.1). BNT162b2, an mRNA vaccine, was the vaccine administered in all nursing homes. Vaccine has been administrated in most cases in January and February, 2021, during a national vaccination campaign targeting nursing homes residents.

There were a total of 365 cases of SARS-CoV-2 infection in the facilities. Attack rates varied largely between facilities. Among fully vaccinated residents, the secondary attack rate ranged from 5.0% to 60.7% (median 16.7%, IQR 9.5 – 29.2%). Secondary attack rate among partially vaccinated and unvaccinated residents ranged from 0 to 100% in both groups. Median values were 17.4% (IQR 0.0 – 66.7%) for partly vaccinated residents and 20.0% (IQR 4.4 – 50.0%) for unvaccinated residents. There was no correlation between the proportion of residents fully vaccinated in each NH and its global secondary attack rate ($r = -0.12$, $p = 0.72$).

Data on SARS-CoV-2 infection severity and related deaths is displayed on **Table 2**. In the pooled population of patients who suffered SARS-CoV-2 infection despite previous full vaccination, 143 (57.7%) were asymptomatic at all times, 49 (19.7%) had mild symptoms and 56 (22.6%) developed severe disease. Among unvaccinated patients, 19 (23.7%) were asymptomatic, 19 (23.7%) had mild symptoms and 42 (52.5%) developed severe disease. Death rate was 6.5% among fully vaccinated patients and 25.0% among unvaccinated ones. The relative risks of unvaccinated persons, compared to vaccinated, were 1.52 (95%CI 1.23 – 1.90) for being infected with SARS-CoV-2, 2.75 (95%CI 1.90 – 3.03) for developing symptomatic disease, 4.17 (95%CI 2.43 – 7.17) for developing severe disease and 5.11 (95%CI 2.49 – 10.5) for dying from COVID-19.

BNT162b2 vaccine estimated effectiveness during the outbreak was 34.5% (95%CI 18.5 – 47.3) for preventing SARS-CoV-2 infection, 63.6% (95%CI 51.4 – 72.8) for preventing symptomatic disease, 71.8% (95%CI 58.8 – 80.7) for preventing severe disease and 83.1% (95%CI 67.8 – 91.1) for preventing death from COVID-19.

Finally, we were able to retrieve only very limited data regarding SARS-CoV-2 variants and staff vaccination coverage. A search for variants was negative in two of the facilities, variant B.1.1.7 was found in one facility and variant B.1.351 was found to be the responsible of the outbreak in another facility. Staff vaccination coverage was obtained from three nursing homes only. Health caregivers fully vaccinated at the beginning of the outbreak were 1 of 32 (3.1%), 33 of 100 (33.0%) and 35 of 50 (70.0%).

Discussion

Our study shows that outbreaks of COVID-19 can definitely occur in fully-vaccinated older patients residing in nursing homes, leading to severe cases, hospitalizations and even deaths. We observed a high secondary attack rate in many facilities, despite high vaccine coverage among residents, suggesting that vaccination did not block SARS-CoV-2 transmission in this population. On the other hand, the risk of severe disease and death was considerably lower in vaccinated residents than in non-vaccinated.

A limitation of our work is that we did not systematically surveyed all 7 200 nursing homes existing in France. Probably there were other nursing homes that suffered outbreaks but that our survey did not reach, or they did not answered, so it is not possible to obtain a reliable estimate of the incidence of this type of outbreaks. In any case, we can say that they are not rare, isolated events.

It is also important to note that attack rates in our study are secondary attack rates during an outbreak, and are not an estimation of the general incidence of cases among vaccinated individuals in nursing homes. Similarly, it is important to understand that the vaccine effectiveness we estimate here is a measure during the outbreak; this is, in a situation of high exposure to the virus and in a subgroup of older people, residents of nursing homes, who typically are very frail. This is a worst-case scenario and not an estimation of the actual effectiveness of BNT162b2 vaccine in the general population of older persons residing in nursing homes.

Few COVID-19 outbreaks had been reported to date in groups of persons well vaccinated against SARS-CoV-2. In separate reports, we documented COVID-19 in vaccinated older persons during an outbreak in a hospital rehabilitation unit and in a nursing home, both in France [**18, 21**]. Cavanaugh et al. recently described a COVID-19 outbreak in a nursing home in Kentucky, USA, involving 26 residents, of whom 18 have been fully vaccinated [**22**]. By contrast, Teran et al. followed COVID-19 cases for several months in 75 skilled nursing facilities in Chicago after a vaccination campaign. They

found only 22 residents developing SARS-CoV-2 infection after full vaccination, and no case of secondary transmission inside facilities [**23**].

A lower effectiveness of COVID-19 vaccines among older and frail patients, as compared to the efficacy documented in randomized clinical trials, is not completely unexpected. Impaired immunogenicity of vaccines, attributed to immunosenescence, a broad term for declining immunity with age, involving both humoral and cellular immune responses, has been well described in older patients with frailty or living in nursing homes [**24,25**]. Several studies have documented a reduced antibody response to influenza vaccine [**26,27**] and other virus vaccines [**28,29**] in nursing homes residents. Two published studies [**14,30**] and one still unpublished [**31**] (at the moment of writing this report) have found a reduced antibody response to BNT162b2 vaccine in older long-term care residents. Nonetheless, even if a decreased effectiveness of SARS-CoV-2 vaccines could be expected in this population, the occurrence of outbreaks in geriatric settings among vaccinated residents is highly concerning. It is also very different from data obtained in the general population of older persons, as in a recent national observational study in Israel that found a preserved high effectiveness (94.1 to 97.4%) of BNT162b2 vaccine in persons 85 years or older [**15**].

It is important to note that SARS-CoV-2 vaccine was not completely ineffective in our study. The risk of developing severe disease or dying from COVID-19 was greatly reduced in vaccinated residents. Mortality, in particular, was largely reduced among vaccinated persons, compared with non-vaccinated residents in the same facilities. Overall, those finding suggests that the main effect of vaccination in these patients might be reducing the severity of the infection rather than avoiding the infection itself or blocking its transmission.

There are other reasons which might explain our observations. One is a lower effectiveness of the BNT162b2 vaccine against some SARS-CoV-2 variants. Data on variants in ours study was very limited, but identified two variants involved in outbreaks. Variant B.1.1.7 (Alpha), which was confirmed in one facility, was highly prevalent (82.6% of all strains) in France during the period studied [**17**]. It has

been reported that BNT162b2 vaccine induces a reduced neutralizing antibody response against this variant [**32**]. Variant B.1.351 (Beta) was found to be the responsible of the outbreak in another center. B.1.351 variant has been found to escape neutralization by several monoclonal antibodies and by plasma from convalescent patients [**33,34**]. Other factor that may facilitate outbreaks in NH is low vaccination coverage among staff members. We retrieved staff vaccination rates from few facilities, but it was clearly lower than in residents. Finally, all the outbreaks described in this work happened during a pandemic wave, and it is known that the incidence of COVID-19 among NH residents and staff members usually follows closely the incidence of COVID-19 in surrounding communities [**35**].

Our study has thus several important limitations. We did not cover all nursing homes in our country and probably there were other outbreaks our survey did not found, so we cannot make an estimation of its actual incidence. Data retrieved on SARS-CoV-2 variants, staff vaccination coverage and resident's individual characteristics (especially co-morbidities, immune suppression and data on previous SARS-CoV-2 infection or antibody levels) were limited, hence their influence on the risk of developing an outbreak could not be analyzed. It is also important to note, as already discussed, that the estimations of vaccine effectiveness here made are circumscribed to a particular situation – high virus exposure during an outbreak. Moreover, older people living in nursing homes are usually frailer and cumulate more co-morbidities than other groups of older persons, so the estimations made for this population should not be extrapolated to the general population of older persons.

In spite of these limitations, our findings have practical implications. First, they underscore that vaccination alone, even when extensive, cannot guarantee an absence of outbreaks in NH. Prevention and control measures against SARS-CoV-2 in NH and other geriatric facilities should be maintained for the moment, at least at times of high COVID-19 incidence in the surrounding community. Such measures would need to be adapted, though, as prolonged isolation or reduced human contact can have important psychological consequences in older people [**36-38**]. Secondly,

our findings stress that more research is needed to improve vaccines effectiveness in this population – and probably in other populations also at risk, like immunosuppressed patients. Possible strategies might be the administration of additional doses, strategy supported by recent studies [**39**] and chosen by many countries, but also the administration of a higher dose of antigen, or the sequential combination of different vaccines.

In conclusion, in this study we found that COVID-19 outbreaks can still occur in older residents in nursing homes despite full vaccination with BNT162b2 of a majority of them. In this setting and under similar circumstances – high COVID-19 incidence during a pandemic wave – high vaccination coverage among residents does not guarantee to prevent SARS-CoV-2 from spreading in the facility. Nonetheless, BNT162b2 vaccine appears to remain highly effective for preventing severe disease, hospitalization and death.

Prevention and control measures for SARS-CoV-2 should be still maintained in nursing homes at periods of high incidence in the community. More research is needed to improve the effectiveness of SARS-CoV-2 vaccines in frail older persons.

Acknowledgments

To the *Société Française de Gériatrie et Gérontologie*, *Gérontopôle d'Île-de-France*, *Collégiale de gériatrie de l'APHP* and the *Conseil National des Professionnels de Gériatrie* for their support contacting nursing homes and collecting data, and to Dr Jacques Gaillat for his useful comments on the mansucript.

C-VENH (COVID-19 Vaccine Effectiveness in Nursing Homes) Investigators

Dr Catherine Burugorri-Pierre, EHPAD Léon Dubédat, Biscarosse

Dr Henri Castagnede, EHPAD Logis de l'Impernal, Luzech

Dr Amina Lahlou, Dr Souhila Larabi, Mr. Stéphane Bordé, Hôpital Charles Foix, Ivry-sur-Seine

Dr Jerome Guibert, Ms Cindy Bourdenet, EHPAD Lecornu, Flers

Dr Karine Guignery-Kadri, EHPAD-USLD Boucicaut, Rouen

Dr François Bertin-Hugaul, EHPAD Quai des Brumes, Parmain ; EHPAD Les cèdres de Paron, Paron ; EHPAD Villa Garlande, Bagneux ; EHPAD La Tour Pujols, Villeneuve-sur-Lot

Dr Maurice Tartulier, EHPAD Balcons du Lot, Prayssac

Dr Emmanuelle Sadin, EHPAD Résidence Guy Maros, Plouagat

Dr Aliou Simaga, EHPAD Résidence du Launay, Pleubian

Dr Virginie Morin Chouarbi, USLD La Tauvrais CHU Rennes, Rennes

Ms Linda Lodé, EHPAD Résidence Jeanne d'Arc, Saint Quay

Dr Michel Idrac, EHPAD Marie Lehmann, Balma

Dr Mariem Mahjoub, Dr Benoit De Wazieres, Centre de Gérontologie de Serre-Cavalier, CHU de Nîmes, Nîmes

Dr Bruno Pocard, Centre Hospitalier Emile Durkheim, Golbey

Dr Pierre da Col, Hôpital St Jacques, Josselin ; EHPAD Saint Antoine, Ploermel

Dr Patrick Sagot, Mr Vincent Mauras, EHPAD Les Mimosas, Albi

Dr Christine Sophoclis, EHPAD Résidence du Mont Bayard, Saint-Claude

Dr Gresset Persico, Centre Hospitalier Jura Sud, Champagnole

Dr Malassigne Martine, Me Cathy Chartrain, EHPAD Delante, Nogent le Bernard

Dr Sebastien Convent, Mr Cyril Lora Runco, EHPAD La Petite Camargue, Beauvoisin

Me Armelle Devarenne, EHPAD Nouvelle Orléans, Toulouse

Dr Françoise Bercet, EHPAD L'impérial, Colombes

Ms Stéphanie Ernesta, EHPAD Les Sources, Clermont-Ferrant

Pr Benoit de Wazière, CHU de Nîmes, Nîmes

Dr Hélène Villars, CHU de Toulouse, Toulouse

Pr Dominique Somme, CHU de Rennes, Rennes

Statement of Ethics

The study was conducted in accordance with the Declaration of Helsinki. This type of study is exempt from ethic committee review or oral or written participants consent according to French law (Décret n° 2016-1537, November 17, 2016). All data collected was anonymous and was managed according to the requirements of the French national *Commission Informatique et Libertés* (CNIL) for the use of data in non-interventional health studies (declaration number 2216052v0).

Conflict of Interest Statement

Dr. Hanon reports personal fees from Bayer Healthcare, Servier, Astra-Zeneca, Boston Scientific, Vifor, BMS, Pfizer and Boehringer Ingelheim, outside the submitted work.

Dr. Jeandel reports personal fees from Bayer, Boerhinger Ingelheim, BMS, Pfizer, Novartis, Servier and Vifor, outside the submitted work.

Dr. Belmin reports personal fees from Novartis and Pfizer, outside the submitted work.

Dr. Lafuente-Lafuente, Dr. Rainone, Dr. Guérin and Dr. Drunat have nothing to disclose.

Funding Sources

This work was supported by the Assistance Publique - Hôpitaux de Paris (APHP) and Sorbonne Université. The funding sources had no role in data collection, analysis or interpretation; nor in the design of the study or its conduct. We were not paid to write this article by a pharmaceutical company or other agency.

Author Contributions

Carmelo Lafuente-Lafuente: conceptualisation, methodology, formal analysis, software, supervision, validation, writing – original draft

Antonio Rainone: investigation, data curation, formal analysis, visualisation, validation, writing – original draft

Olivier Guérin: investigation, data curation, project administration

Olivier Drunat: investigation, resources, supervision

Claude Jeandel: investigation, resources, supervision

Olivier Hanon: project administration, resources, validation, writing – review & editing

Joël Belmin: conceptualisation, formal analysis, funding acquisition, project administration, supervision, validation, visualisation, writing – review & editing

Data Availability Statement

The data that supports the findings of this study is openly available in the Open Science Framework (DOI: 10.17605/OSF.IO/7R349).

References

1. Rubin EJ, Longo DL. SARS-CoV-2 Vaccination - An ounce (actually, much less) of prevention. *N Engl J Med*. 2020;383(27):2677-2678. doi: 10.1056/NEJMe2034717.
2. He Q, Mao Q, Zhang J, Bian L, Gao F, Wang J, Xu M, Liang Z. COVID-19 Vaccines: Current Understanding on Immunogenicity, Safety, and Further Considerations. *Front Immunol*. 2021;12:669339. doi: 10.3389/fimmu.2021.669339.
3. Polack FP, Thomas SJ, Kitchin N, et al; C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *N Engl J Med.* 2020;383(27):2603-2615. doi: 10.1056/NEJMoa2034577.
4. Voysey M, Clemens SAC, Madhi SA, et al; Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet*. 2021; 397(10269):99-111. doi: 10.1016/S0140-6736(20)32661-1.
5. Baden LR, El Sahly HM, Essink B, et al; COVE Study Group. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med.* 2021; 384(5):403-416. doi: 10.1056/NEJMoa2035389.
6. Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, Kovyrshina AV, et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. *Lancet*. 2021;397(10275):671-681. doi: 10.1016/S0140-6736(21)00234-8
7. Sadoff J, Gray G, Vandebosch A, Cárdenas V, Shukarev G, Grinsztejn B, Goepfert PA et al. Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19. *N Engl J Med*. 2021;384(23):2187-2201. doi: 10.1056/NEJMoa2101544.

8. Bonanad C, Garcia-Blas S, Tarazona-Santabalbina F, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. *J Am Med Dir Assoc.* 2020;21:915–918. doi: 10.1016/j.jamda.2020.05.045.

9. Ho FK, Petermann-Rocha F, Gray SR, et al. Is older age associated with COVID-19 mortality in the absence of other risk factors? General population cohort study of 470,034 participants. *PLoS One.* 2020;15:e0241824. doi: 10.1371/journal.pone.0241824.

10. Panagiotou OA, Kosar CM, White EM, Bantis LE, Yang X, Santostefano CM, Feifer RA, et al. Risk factors associated with all-cause 30-day mortality in nursing home residents with COVID-19. *JAMA Intern Med.* 2021;181(4):439-448. doi: 10.1001/jamainternmed.2020.7968.

11. Anderson EJ, Rouphael NG, Widge AT, Jackson LA, Roberts PC, Makhene M, Chappell JD, et al. Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults. *N Engl J Med*. 2020;383(25):2427-2438. doi: 10.1056/NEJMoa2028436.

12. Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, Voysey M, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet*. 2021;396(10267):1979-1993. doi: 10.1016/S0140-6736(20)32466-1.

13. Salmerón Ríos S, Mas Romero M, Cortés Zamora EB, Tabernero Sahuquillo MT, Romero Rizos L, Sánchez-Jurado PM, Sánchez-Nievas G, et al. Immunogenicity of the BNT162b2 vaccine in frail or disabled nursing home residents: COVID-A study. *J Am Geriatr Soc.* 2021;69(6):1441-1447. doi: 10.1111/jgs.17153.

14. Van Praet JT, Vandecasteele S, De Roo A, De Vriese AS, Reynders M. Humoral and cellular immunogenicity of the BNT162b2 mRNA Covid-19 Vaccine in nursing home residents. *Clin Infect Dis*. 2021:ciab300. doi: 10.1093/cid/ciab300.

15. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. *Lancet*. 2021;397(10287):1819-1829. doi: 10.1016/S0140-6736(21)00947-8.

16. Ministère des solidarités et de la santé. Campagne de vaccination contre la COVID-19. Guide Phase 1. Organisation de la vaccination en EHPAD et USLD. Décembre 2020. URL: https://solidarites-sante.gouv.fr/IMG/pdf/guide_vaccination_contre_la_covid_ehpad_-_usld.pdf. Accessed April 18, 2021.

17. Santé Publique France. Analyse de risque liée aux variants émergents de SARS-CoV-2 réalisée conjointement par le CNR des virus des infections respiratoires et Santé publique France. Mise à jour du 08/04/2021. URL: https://www.santepubliquefrance.fr/media/files/01-maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/analyse-de-risque-des-variants-emergents-de-sars-cov-2-08-04-21. Accessed June 10, 2021.

18. Burugorri-Pierre C, Lafuente-Lafuente C, Oasi C, Lecorche E, Pariel S, Donadio C, Belmin J. Investigation of an Outbreak of COVID-19 in a French Nursing Home With the Majority of Residents Vaccinated. JAMA Network Open. 2021 (In press).

19. Ministère des Solidarités et de la Santé. Plan de lutte contre l'épidémie de COVID-19 dans les établissements médico-sociaux hébergeant des personnes à risque de forme grave de COVID-19. Avril 2021. URL: https://solidarites-sante.gouv.fr/IMG/pdf/plan_de_lutte_contre_le_covid_covid_esms.pdf. Accessed May 2, 2021.

20. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008; 61(4):344-9. doi: 10.1016/j.jclinepi.2007.11.008.

21. Donadio C, Rainone A, Gouronnec A, Belmin J, Lafuente-Lafuente C. Asymptomatic COVID-19 cases among older patients despite BNT162b2 vaccination: a case series in a geriatric rehabilitation ward during an outbreak. *J Infect*. 2021:S0163-4453(21)00167-5. doi: 10.1016/j.jinf.2021.04.004.

22. Cavanaugh AM, Fortier S, Lewis P, Arora V, Johnson M, George K, Tobias J, et al. COVID-19 Outbreak Associated with a SARS-CoV-2 R.1 Lineage Variant in a Skilled Nursing Facility After Vaccination Program - Kentucky, March 2021. *MMWR Morb Mortal Wkly Rep*. 2021; 70(17):639-643. doi: 10.15585/mmwr.mm7017e2.

23. Teran RA, Walblay KA, Shane EL, Xydis S, Gretsch S, Gagner A, Samala U, et al. Postvaccination SARS-CoV-2 Infections Among Skilled Nursing Facility Residents and Staff Members - Chicago, Illinois, December 2020-March 2021. MMWR Morb Mortal Wkly Rep. 2021;70(17):632-638. doi: 10.15585/mmwr.mm7017e1.

24. Fulop T, Pawelec G, Castle S, Loeb M. Immunosenescence and vaccination in nursing home residents. *Clin Infect Dis*. 2009;48(4):443-8. doi: 10.1086/596475.

25. Gustafson CE, Chulwoo K, Weyand C, Goronzy JJ. Influence of immune aging on vaccine responses. *J Allergy Clin Immunol* 2020;145:1309–21.

26. Hara M, Tanaka K, Hirota Y. Immune response to influenza vaccine in healthy adults and the elderly: association with nutritional status. *Vaccine*. 2005;23(12):1457-63. doi: 10.1016/j.vaccine.2004.09.022.

27. Sato M, Saito R, Tanabe N, et al. Antibody response to influenza vaccination in nursing home residents and healthcare workers during four successive seasons in Niigata, Japan. *Infect Control Hosp Epidemiol.* 2005;26(11):859-66. doi: 10.1086/502509.

28. Williams RE, Sena AC, Moorman AC, et al. Hepatitis B vaccination of susceptible elderly residents of long term care facilities during a hepatitis B outbreak. *Vaccine*. 2012;30(21):3147-50. doi: 10.1016/j.vaccine.2012.02.078.

29. Lelic A, Verschoor CP, Lau VW, et al. Immunogenicity of varicella vaccine and immunologic predictors of response in a cohort of elderly nursing home residents. *J Infect Dis.* 2016;214(12):1905-1910. doi: 10.1093/infdis/jiw462.

30. Canaday DH, Carias L, Oyebanji OA, Keresztesy D, Wilk D, Payne M, Aung H, et al. Reduced BNT162b2 mRNA vaccine response in SARS-CoV-2-naive nursing home residents. *Clin Infect Dis*. 2021 May 16:ciab447. doi: 10.1093/cid/ciab447.

31. Brockman MA, Mwimanzi F, Sang Y, Ng K, Agafitei O, Ennis S, Lapointe H, et al. Weak humoral immune reactivity among residents of long-term care facilities following one dose of the BNT162b2 mRNA COVID-19 vaccine. *medRxiv [Preprint].* 2021 Mar 24:2021.03.17.21253773. doi: 10.1101/2021.03.17.21253773.

32. Collier DA, De Marco A, Ferreira IATM, Meng B, Datir RP, Walls AC, Kemp SA, et al. Sensitivity of SARS-CoV-2 B.1.1.7 to mRNA vaccine-elicited antibodies. *Nature*. 2021;593(7857):136-141. doi: 10.1038/s41586-021-03412-7.

33. Wibmer CK, Ayres F, Hermanus T, Madzivhandila M, Kgagudi P, Oosthuysen B, Lambson BE, et al. SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma. *Nat Med*. 2021;27(4):622-625. doi: 10.1038/s41591-021-01285-x.

34. Chen RE, Zhang X, Case JB, et al. Resistance of SARS-CoV-2 variants to neutralization by monoclonal and serum-derived polyclonal antibodies. *Nat Med.* 2021;27(4):717-726. doi: 10.1038/s41591-021-01294-w.

35. Bagchi S, Mak J, Li Q, Sheriff E, Mungai E, Anttila A, Soe MM, et al. Rates of COVID-19 Among Residents and Staff Members in Nursing Homes - United States, May 25-November 22, 2020. *MMWR Morb Mortal Wkly Rep*. 2021;70(2):52-55. doi: 10.15585/mmwr.mm7002e2.

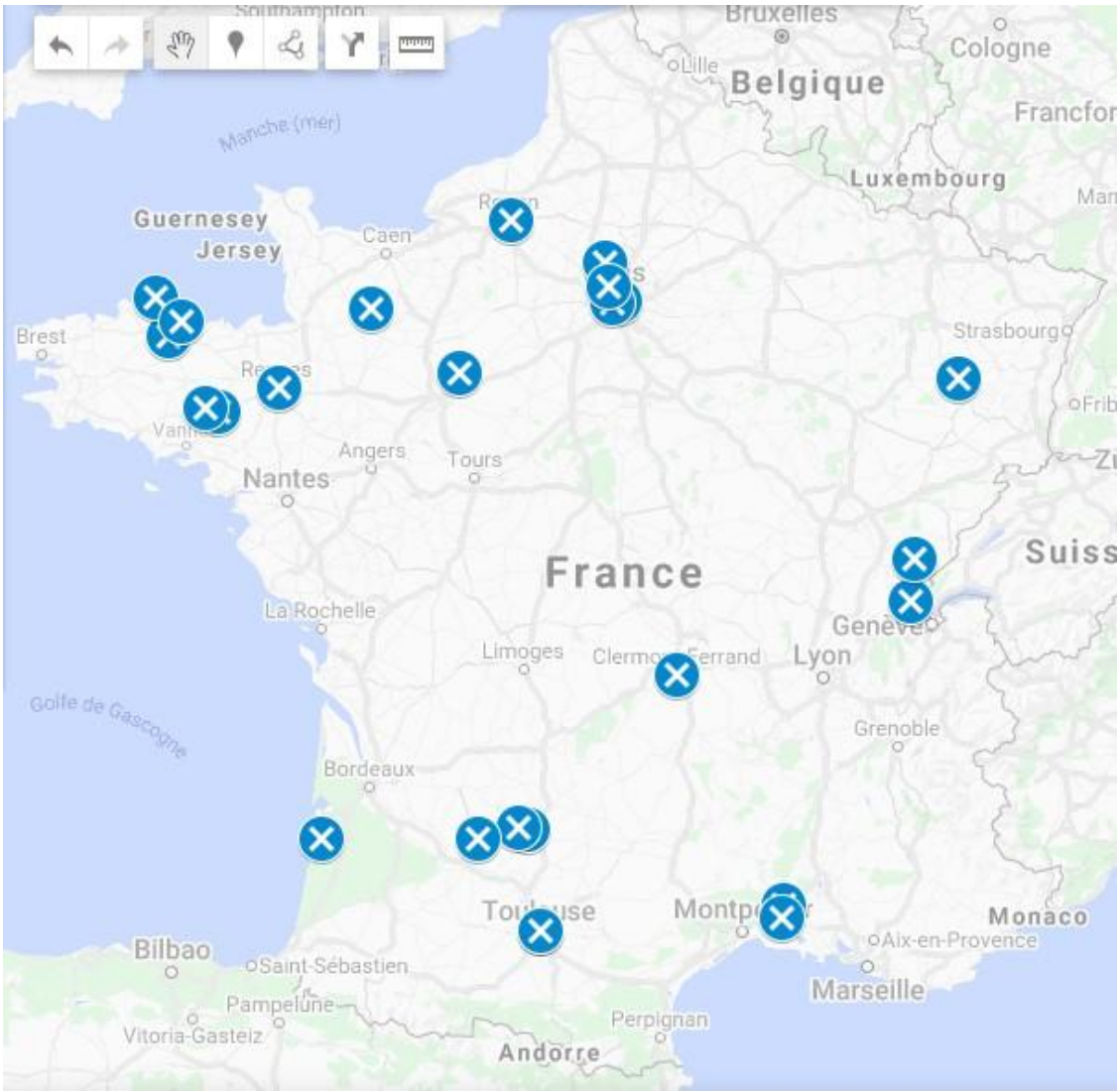
36. Sepúlveda-Loyola W, Rodríguez-Sánchez I, Pérez-Rodríguez P, Ganz F, Torralba R, Oliveira DV, Rodríguez-Mañas L. Impact of Social Isolation Due to COVID-19 on Health in Older People: Mental and Physical Effects and Recommendations. *J Nutr Health Aging*. 2020;24(9):938-947. doi: 10.1007/s12603-020-1469-2.

37. Wong SYS, Zhang D, Sit RWS, Yip BHK, Chung RY, Wong CKM, Chan DCC, et al. Impact of COVID-19 on loneliness, mental health, and health service utilisation: a prospective cohort study of older adults with multimorbidity in primary care. *Br J Gen Pract*. 2020;70(700):e817-e824. doi: 10.3399/bjgp20X713021.

38. Tsapanou A, Papatriantafyllou JD, Yiannopoulou K, Sali D, Kalligerou F, Ntanasi E, Zoi P, Margioti E, Kamtsadeli V, et al. The impact of COVID-19 pandemic on people with mild cognitive impairment/dementia and on their caregivers. *Int J Geriatr Psychiatry*. 2021;36(4):583-587. doi: 10.1002/gps.5457.

39. Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Freedman L, Alroy-Preis S, Ash N, Huppert A, Milo R. Protection against Covid-19 by BNT162b2 Booster across Age Groups. *N Engl J Med*. 2021;385(26):2421-2430. doi: 10.1056/NEJMoa2115926

Figure 1. Geographical localization of long-term care facilities affected by SARS-CoV-2 outbreaks



Footnote :

Generated using *Google My Maps*

Table 1. Number of residents, vaccination status and SARS-CoV-2 infection cases, by facility.

	Residents, at outbreak onset				SARS-CoV-2 infection				
Facility ID number – Region	**Total** n	**Fully vaccinated** n (%)	**Partially vaccinated** n (%)	**Unvaccinated** n (%)	**Total** n	**Fully vaccinated** n (% attack rate*)	**Partially vaccinated** n (% attack rate*)	**Unvaccinated** n (% attack rate*)	**Unvaccinated versus vaccinated RR** RR (95% CI)
1 - Côtes-d'Armor	53	52 (98.1)	0	1 (1.9)	5	5 (9.6)	0	0	–
2 - Côtes-d'Armor	58	52 (89.7)	2 (3.4)	4 (6.9)	6	5 (9.6)	0	1 (25.0)	2.60 (0.39 – 17.2)
3 - Côtes-d'Armor	58	45 (77.6)	5 (8.6)	8 (13.8)	4	3 (6.7)	0	1 (12.5)	1.87 (0.22 – 15.8)
4 - Gard	23	14 (60.9)	3 (13.0)	6 (26.1)	3	3 (21.4)	0	0	–
5 - Gard	59	54 (91.5)	0	5 (8.5)	13	13 (22.0)	0	0	–
6 - Haute-Garonne	74	62 (83.8)	11 (14.9)	1 (1.3)	10	4 (6.4)	5 (45.4)	1 (100)	15.5 (6.01 – 40.0)
7 - Haute-Garonne	79	62 (78.5)	8 (10.1)	9 (11.4)	29	21 (33.9)	3 (37.5)	5 (55.6)	1.64 (0.83 – 3.24)
8 - Hauts-de-Seine	95	63 (66.3)	8 (8.4)	24 (25.3)	26	6 (9.5)	8 (100)	12 (50.0)	5.25 (2.22 – 12.4)
9 - Ille-et-Vilaine	107	56 (52.3)	23 (21.5)	28 (26.2)	15	7 (12.5)	4 (17.4)	4 (14.3)	1.14 (0.36 – 3.56)
10 - Jura	57	44 (77.2)	1 (1.7)	12 (21.1)	22	17 (38.6)	1 (100)	4 (33.3)	0.86 (0.36 – 2.08)
11 - Jura	26	23 (88.5)	1 (3.8)	2 (7.7)	13	12 (47.8)	1 (100)	0	–
12 - Landes	74	70 (94.6)	2 (2.7)	2 (2.7)	17	14 (20.0)	2 (100)	1 (50.0)	2.50 (0.58 - 10.8)
13 - Lot	41	28 (68.3)	3 (7.3)	10 (24.4)	29	17 (60.7)	2 (66.7)	10 (100)	1.64 (1.22 – 2.22)
14 - Lot	60	48 (80.0)	0	12 (20.0)	18	14 (29.2)	0	4 (33.3)	1.14 (0.46 – 2.85)
15 - Lot-et-Garonne	71	54 (76.1)	2 (2.8)	15 (21.1	18	16 (29.6)	2 (100)	0	–
16 - Morbihan	62	50 (80.6)	0	12 (19.3)	6	5 (10.0)	0	1 (8.3)	0.83 (0.11 – 6.49)
17 - Morbihan	28	22 (78.6)	1 (3.6)	5 (17.9)	12	8 (36.4)	0	4 (80.0)	2.20 (1.09 – 4.45)
18 - Orne	84	80 (95,2)	0	4 (4.8)	4	4 (5.0)	0	0	–
19 - Puy de Dôme	72	65 (90.3)	0	7 (9.7)	19	15 (23.1)	0	4 (57.1)	2.48 (1.13 – 5.40)
20 - Sarthe	75	71 (94.7)	0	4 (5.3)	11	10 (14.1)	0	1 (25.0)	1.77 (0.30 – 10.6)
21 - Seine-Maritime	68	56 (82,4)	2 (2.9)	10 (14.7)	15	11 (19.6)	2 (100)	2 (20.0)	1.02 (0.26 – 3.92)
22 - Val de Marne	80	21 (26.2)	14 (17.5)	45 (56.2)	17	2 (9.5)	3 (21.4)	12 (26.7)	2.80 (0.69 – 11.4)
23 - Val d'Oise	54	42 (77,7)	0	12 (22.2)	4	3 (7.1)	0	1 (8.3)	1.17 (0.13 – 10.2)
24 - Tarn	89	80 (89,9)	4 (4.5)	5 (5.6)	20	17 (21.2)	2 (50.0)	1 (20.0)	0.94 (0.15 – 5.71)
25 - Vosges	37	24 (64.9)	0	13 (35.1)	11	4 (16.7)	0	7 (53.8)	3.23 (1.16 – 9.02)
26 - Yonne	105	93 (88,6)	0	12 (11.4)	7	5 (5.4)	0	2 (16.7)	3.10 (0.67 – 14.2)
27 - Yonne	79	46 (58.2)	10 (12.7)	23 (29.1)	11	7 (15.2)	2 (20.0)	2 (8.7)	0.57 (0.13 – 2.53)
Totals	**1768**	**1377 (78.2)**	**100 (5.7)**	**291 (16.5)**	**365**	**248 (18.0)**	**37 (37.0)**	**80 (27.5)**	**1.52 (1.23 – 1.90)**

* Secondary attack rate, after the index case.

Table 2: SARS-CoV-2 total cases, severe disease, mortality, relative risks and estimated vaccine effectiveness in unvaccinated residents compared with vaccinated residents of long-term care facilities.

	Total (n=365)	Unvaccinated (n=80)	Partially vaccinated (n=37)	Fully vaccinated (n=248)	P	Unvaccinated versus fully vaccinated relative risk (95% CI)	Vaccine effectiveness (95% CI)
Age (years), mean (SD)	88.3 (8.1)	86.6 (8.8)	88.8 (6.1)	88.6 (8.1)	0.148	-	-
Women, no (%)	268 (73.4)	59 (77.6)	32 (72.7)	177 (72.2)	0.646	-	-
SARS-CoV-2 infection, any severity, no	365	80	37	248	<0.001	1.52 (1.23 - 1.90)	34.5 (18.5 - 47.3)
Asymptomatic, no (%)	189 (51.8)	19 (23.7)	23 (62.2)	143 (57.7)	<0.001	0.23 (0.14 - 0.42)	-
Symptomatic, no (%)	176 (48.2)	61 (76.3)	14 (37.8)	105 (42.3)	<0.001	2.75 (1.90 – 3.03)	63.6 (51.4 – 72.8)
Severe COVID-19*, no (%)	112 (30.7)	42 (52.5)	10 (27.0)	56 (22.6)	<0.001	4.17 (2.43 - 7.17)	71.8 (58.8 – 80.7)
Requiring O2, no (%)	76 (20.8)	35 (43.7)	9 (24.3)	32 (12.9)	<0.001	5.69 (3.17 - 10.2)	-
Requiring IV fluids, no (%)	58 (15.8)	22 (27.5)	6 (16.2)	30 (12.1)	0.002	2.92 (1.56 - 5.46)	-
Hospitalization, no (%)	46 (12.6)	24 (30.0)	5 (13.5)	17 (6.9)	<0.001	6.19 (3.10 - 12.3)	85.0 (72.5 – 91.9)
Death, no (%)	38 (10.4)	20 (25.0)	2 (5.4)	16 (6.5)	<0.001	5.11 (2.49 - 10.5)	83.1 (67.8 – 91.1)

*Severe disease was defined as COVID-19 requiring oxygen (O2) therapy, intravenous (IV) fluid infusion, hospitalization, or leading to death.