Gerontology

Clinical Section: Research Article

Gerontology
DOI: 10.1159/000524553

Received: July 15, 2021
Accepted: April 10, 2022
Published online: June 2, 2022

Cross-Sectional Analysis of Risk Factors for Outbreak of COVID-19 in Nursing Homes for Older Adults in the Community of Madrid

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Keywords
COVID-19 · SARS-CoV-2 · Seroprevalence · Outbreaks · Nursing homes

Abstract

Introduction: Nursing homes for older adults have been hot spots for SARS-CoV-2 infections and mortality. Factors that facilitate COVID-19 outbreaks in these settings need to be assessed. ***Methods:*** A retrospective cross-sectional study of a cohort of residents and workers in nursing homes taking occasion of a point seroprevalence survey was done in the Community of Madrid. Factors related to outbreaks in these facilities were analyzed. ***Results:*** A total of 369 nursing homes for older adults, making a population of 23,756 residents and 20,795 staff members, were followed from July to December 2020. There were 54.2% SARS-CoV-2 IgG+ results in residents and in 32.2% of workers. Sixty-two nursing homes (16.8%) had an outbreak during the follow-up. Nursing homes with outbreaks had more residents than those without (median number of 81 [IQR, 74] vs. 50 [IQR, 56], $p < 0.001$). Seropositivity for SARS-CoV-2 was lower in facilities with versus without outbreaks, for residents (42.2% [IQR, 55.7] vs. 58.7% [IQR, 43.4], $p = 0.002$) and for workers (23.9% [IQR, 26.4] vs. 32.8% [IQR, 26.3], $p = 0.01$). For both residents and staff, the number of infections in outbreaks was larger in centers with lower, as compared with intermediate or high seroprevalence. The size of the facility did not correlate with the number of cases in the outbreak. Taking the incidence of cases in the community as a time-dependent variable ($p = 0.03$), a Cox analysis (HR [95% CI], p) showed that intermediate or high seroprevalence among residents in the facility was related to a reduction of 55% (0.45 [0.25–0.80], $p = 0.007$) and 78% (0.22 [0.10–0.48], $p < 0.001$) in the

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risk of outbreaks, respectively, as compared with low seroprevalence. Also, as compared with smaller, medium (1.91 [1.00–3.65], $p = 0.05$) or large centers (4.57 [2.38–8.75], $p < 0.001$) had more respective risk of outbreaks. ***Conclusions:*** The size of the facility and the seroprevalence among residents in nursing homes, and the incidence of infections in the community, are associated with the risk of outbreaks of COVID-19. Facilities with greater proportion of seropositives had smaller number of cases. Monitoring of immunity in nursing homes may help detect those at a greater risk of future cases.

Introduction

The coronavirus infectious disease starting in 2019 (COVID-19) is most severe in the elderly, among men, and in patients with underlying chronic diseases or immunosuppression [1]. Nursing homes for older adults (NHOA) saw more severe cases and deaths from SARS-CoV-2 infection during the first wave than in any other setting [2–6]. The World Health Organization has estimated that up to half of all COVID-19 deaths in Europe occurred in nursing homes [7]. In Spain, in mid-July 2020, the number of deaths with confirmed or suspected COVID-19 in NHOA was almost 20,000, which constitutes more than half of all the deaths registered in the country at that time in the pandemic [4].

The proportion of SARS-CoV-2 IgG-positive individuals is very high among surviving residents and in staff members working in NHOA. According to a recent study, more than half of the residents and almost a third of the workers in long-term care centers in the Community of Madrid were seropositive for SARS-CoV-2 [8]. Immunity after infection [9–12], and rapid vaccination of residents and staff in these facilities, has reduced the incidence of new outbreaks in NHOA [13–15] – understanding outbreaks a one or more diagnosis of COVID-19 among residents or staff. Here, we analyzed the frequency of new cases of COVID-19 in the context of outbreaks among older adults and workers after a large point serosurvey and before vaccination campaigns began in NHOA of the Region. The objective was to determine the risks factors that contributed to the declaration of COVID-19 outbreaks in NHOA, including cases affecting both residents and employees working in these facilities, assuming in the context of the pandemic that the impact of these factors should also be analyzed in the function of time of exposure.

Methods

Design and Participants

The present study is a descriptive cross-sectional analysis of a number of NHOA with or without one outbreak of SARS-CoV-2 infections in the previous months.

Data

The period of study extended from July to October 2020. The unit of analyses was NHOA, and the main variables evaluated were the number of residents and staff members and the seroprevalence of SARS-CoV-2 infection in each center, and the cumulative incidence of COVID-19 in the basic health zone (BHZ) where the facility was located. The outcomes taken into consideration were the declaration of an outbreak in the center or remaining free of this event during the follow-up, and the number of residents and staff infected in the case of an outbreak.

Sample

At the beginning of the COVID-19 pandemic, more than 45,000 older adults [16] lived in 1 of the 476 long-term care facilities registered in the Community of Madrid [17]. As described elsewhere [8], a point seroprevalence survey was designed in June 2020, after the first wave of COVID-19 hit the NHOA hard, as part of a strategy to prevent future outbreaks at these facilities [18]. In accordance with the study protocol, all NHOAs were contacted by the liaison geriatrician of the corresponding hospital of reference; with consent to participate by the administration of the facility, an appointment was made for the blood draw of residents and staff. Samples were taken from each NHOA on one visit or on two consecutive days, and only one blood sample was obtained for each participant for the purpose of the study. Therefore, a retrospective subanalysis of the seroSOS study [8] was conducted analyzing the existence of an outbreak from the moment of the seroprevalence point survey was realized at the NHOA till the end of December 2020, when the vaccination campaign in NHOA began in the Community of Madrid. Centers with outbreaks that did not participate in the seroSOS study were excluded from this substudy. Information about centers with or without outbreaks was provided by liaison geriatricians and a centralized record. In case of NHOA with several outbreaks, only the first one was included in this analysis. According to European standards [19], any NHOA with one or more cases of COVID-19 among residents or workers was registered as having an outbreak at the General Directorate of Public Health. In this event, the liaison geriatrician in coordination with the primary care physician and the health-zone epidemiologist assigned to the NHOA oversaw the clinical evaluation of the cases, the study of contacts, and the indication of isolation measures for residents and leave of workers. Only outbreaks reported after 1 week of the seroprevalence survey (SeroSOS study) were recorded for the purpose of this study.

Measures

To better understand the intramural risks of COVID-19 among residents and workers, NHOA were classified by a number of residents into *large* (more than 100 residents), *medium* (between 50 and 100 residents), and *small* (less than 50 residents); and by seropositivity among residents according to the point survey as *low* seroprevalence (less than 50% seropositive individuals), *intermediate* seroprevalence (between 50% and 70% seropositive individuals), and *high* seroprevalence (more than 70% seropositive individuals).

Exposure of people in NHOA to SARS-CoV-2 circulating in the community was estimated as the average number of COVID-19 cases per 1,000 people in the basic health zone (BHZ) where each facility was located, during the 2 weeks prior to the outbreak. The follow-up period was extended until December 27, 2020, when the vaccination campaign in NHOA started in the Community of Madrid.

Ethics

This study was approved as a subanalysis of the SeroSOS study [8] by the Regional Clinical Research Ethics Committee of the Community of Madrid, and all participants gave informed consent before enrollment.

SARS-CoV-2 Serological and Molecular Tests

To assess the seropositivity for SARS-CoV-2 infection, the determination of the qualitative IgG response against the SARS-CoV-2 nucleoprotein was performed by the chemiluminescent microparticle immunoassay (ARCHITECT; Abbott Laboratories, Abbott Park, IL, USA; Reference 06R8620) [20, 21] in the context of the cross-sectional seroprevalence study [8].

The case diagnosis and study of contacts in the event of an outbreak in a NHOA were always carried out using molecular techniques (polymerase chain reaction or transcription-mediated amplification), either at the referral hospital or at the Regional Public Health Laboratory. Information about outbreaks was obtained from the official records of the General Directorate of Social Health Affairs (namely, NHOA affected, number of cases, number of contacts, number of hospitalizations and date) [22]. Information about the characteristics of each NHOA, residents, and workers was available in the initial seroprevalence point survey [8].

Statistical Analysis

Dependent variables with normal distribution are expressed as means and standard deviations (SD); otherwise, data are given as medians and interquartile ranges (IQR). Parametric or not parametric tests were applied as needed. The Kolmogorov-Smirnov test was used to analyze the distribution of variables. In addition to the descriptive statistics for all variables, bivariate analyses between NHOA with and without outbreaks were carried out. The Student's *t* test or ANOVA was used to compare normally distributed continuous variables. In the case of nonnormally distributed variables, Mann-Whitney's U or Kruskal-Wallis tests were applied. The comparison of proportions for categorical variables was done either by χ^2 or by Fisher's exact tests. To analyze the factors associated with the occurrence of outbreaks in NHOA, a Cox regression analysis (HR [95% CI], *p*) was performed using the biweekly average number of COVID-19 cases per 1,000 people in the BHZ, where each facility was located as a time-dependent variable. An extended model was used in which the variable referred to the cumulative incidence of cases in the BHZ of each NHOA was considered as a time-dependent variable by weeks interval in a counting process style, or start-stop form, as described previously [23, 24]. Proportional hazards tests and diagnostics based on weighted residuals using R (cox.zph function by coefficients) were performed with no significant differences ($p > 0.05$) [25]. Linear regression analysis was also used to find relationships between the independent variables and the number of cases within the outbreak. Statistical analyses were performed using SPSS® Version 20 (IBM®, Chicago, IL, USA) and R software (RStudio®, Boston, MA, USA).

Results

Characteristics of the Facilities

A total of 369 NHOA were evaluated during the period of study; only 6 (1.6%) centers were for fully autonomous individuals, while in the other there was a mixture of dependent and autonomous individuals. With respect to type of administration, 55 (14.9%) NHOA were public, 61 (16.5%) were nonprofit institutions, and 253 (68.6%) were private centers. According to the size of NHOA, 76 centers (20.6%) had more than 100 residents (large size), 123 (33.3%) between 50 and 100 (medium size), and 170 (46.1%) less than 50 (small size).

Blood samples were analyzed from a total of 44,551 individuals, 23,756 were residents and 20,795 were members of the staff. The median number of blood samples tested per NHAO was 97.0 (IQR, 116.0), 55.0 (IQR, 65.0) of older adults and 40.0 (IQR, 55.0) of staff. The workers and residents of the NHOA studied belong to a cohort whose characteristics have been described previously [8].

A total of 12,880 (54.2%) residents and 6,688 (32.2%) workers resulted SARS-CoV-2 IgG positive. The mean rate of seropositivity by NHOA was 47.7% (SD, 29.0) for older adults and 30.4% (SD, 18.6) for staff. According to the results of the seroprevalence point survey, 150 NHOA (40.7%) had a low rate of seropositivity among residents (less than 50%), 120 (32.5%) intermediate (between 50 and 70%), and 99 (26.8%) high (more than 70%) (Table 1).

Mean seroprevalence in residents was directly related to the size of the NHOA, 59.1% (SD, 19.0) in large, 55.0% (SD, 23.6) in medium, and 37.4% (SD, 32.6) in small centers ($p < 0.001$). A similar association was observed for seropositivity in staff, but only when comparing NHOA with less versus more than 50 residents (Table 1).

Outbreaks in the Facilities

The mean follow-up of NHOA was 18.5 (SD, 5.7) weeks, either due to the appearance of the outbreak (9.8 [SD, 5.6] weeks) or at the end of follow-up (20.3 [SD, 3.9] weeks) ($p < 0.001$). A total of 62 NHOA (16.8%) presented with an outbreak during the follow-up. The calculated incidence density rate was 0.91% outbreaks in NHOA per week of follow-up.

NHOA with outbreaks were larger than those without outbreaks (median number of residents 81 [IQR, 74] vs. 50 [IQR, 56], $p < 0.001$). Seropositivity was lower in NHOA with outbreaks compared to that without outbreaks, both in residents (42.2% [IQR, 55.7] vs. 58.7% [IQR, 43.4], $p = 0.002$) and in workers (23.9% [IQR, 26.4] vs. 32.8% [IQR, 26.3], $p = 0.01$).

Table 1. Main characteristics of NHOA studied

	Total NHOA	With outbreak	Without outbreak	*p* value
NHOA, *n* (%)	369	62	307	
By number of residents, *n* (%)				
Large (>100)	76 (20.6)	23 (37.1)	53 (17.2)	0.001
Medium (50–100)	123 (33.3)	20 (32.3)	103 (33.6)	
Small (<50)	170 (46.1)	19 (30.6)	151 (49.2)	
By seroprevalence in residents, *n* (%)				
Low (<50)	150 (40.7)	34 (54.8)	116 (37.8)	0.011
Intermediate (50–70)	120 (32.5)	20 (32.3)	100 (32.6)	
High (>70)	99 (26.8)	8 (12.9)	91 (29.6)	
Mean (SD) percentage of seropositivity				
Residents	47.7 (29.0)	37.6 (28.0)	49.8 (28.8)	0.002
By number of residents, *n* (%)				
Large (>100)	59.1 (19.0)	48.2 (22.9)	63.8 (14.8)	0.003
Medium (50–100)	55.0 (23.6)	42.9 (25.6)	57.3 (22.7)	0.015
Small (<50)	37.4 (32.6)	19.1 (27.9)	39.7 (32.5)	0.008
Workers	30.3 (18.6)	25.0 (16.8)	31.5 (18.8)	0.009
By the number of residents, *n* (%)				
Large (>100)	33.0 (12.0)	29.1 (12.5)	34.7 (11.5)	0.06
Medium (50–100)	33.8 (15.1)	25.2 (15.9)	35.5 (14.5)	0.009
Small (<50)	26.5 (22.4)	19.8 (21.1)	27.4 (22.5)	0.13
Median (IQR) cases among residents per NHOA	–	12.0 (15.3)	–	
By seroprevalence in residents, *n* (%)				
Low (<50)	–	18.0 (26.0)	–	0.06
Intermediate (50–70)	–	10.5 (9.8)	–	
High (>70)	–	4.0 (2.8)	–	
Median (IQR) cases among workers per NHOA	–	2.0 (6.0)	–	
By seroprevalence in residents, *n* (%)				
Low (<50)	–	4.5 (8.5)	–	0.03
Intermediate (50–70)	–	2.0 (3.8)	–	
High (>70)	–	1.0 (2.8)	–	

An association was observed between the rate of outbreaks and seroprevalence of COVID-19 in residents: in NHOAs with seroprevalence <50%, 34 (22.7%) had outbreaks; with seroprevalence 50–70%, 20 (16.7%) had outbreaks; and with seroprevalence >70%, 8 (8.1%) had outbreaks ($p = 0.01$). The size of the NHOA also affected the rate of outbreaks: 23 (30.3%) happened in large centers (>100 residents), 20 (16.3%) in medium (50–100 residents), and 19 (11.2%) in small (<50 residents) ($p = 0.001$).

Size of Outbreaks

The number of individuals infected in outbreaks was 1,387, among whom 1,110 were residents and 277 staff. Overall, the median number of cases per outbreak was 14.0 (IQR, 22.3); more specifically, it was 12.0 (IQR, 15.3) in residents and 2.0 (IQR, 6.0) in staff ($p < 0.001$). The smallest outbreak affected 3 individuals and the largest 130 individuals. The number of infected residents that needed hospitalization was 203 (18.3% of cases) (median per NHOA of 2.0 [IQR, 3.0]).

The number of cases of COVID-19 was larger in NHOA with lower seroprevalence (22.0 [IQR, 29.8]) as compared with intermediate (11.5 [IQR, 10.8]) or high (5.0 [IQR, 2.0]) seroprevalence ($p = 0.003$). This number of cases was 18.0 (IQR, 26.0), 10.5 (IQR, 9.8), and 4.0 (IQR, 2.8) ($p = 0.006$) for residents; and 4.5 (IQR, 8.5), 2.0 (IQR, 3.8), and 1.0 (IQR, 2.8) ($p = 0.03$) for staff, respectively, for low and intermediate of high seroprevalence. Conversely, the size of the facility did not affect the number of infections in outbreaks (Fig. 1; Table 1).

The proportion of infected residents that needed hospitalization was 20.0% (IQR, 36), with no differences according to the level of immunity in the facility. However, the proportion of hospitalizations was 32.4% (IQR, 30.9) in large, 10.1% (IQR, 21.5) in intermediate, and 21.4%

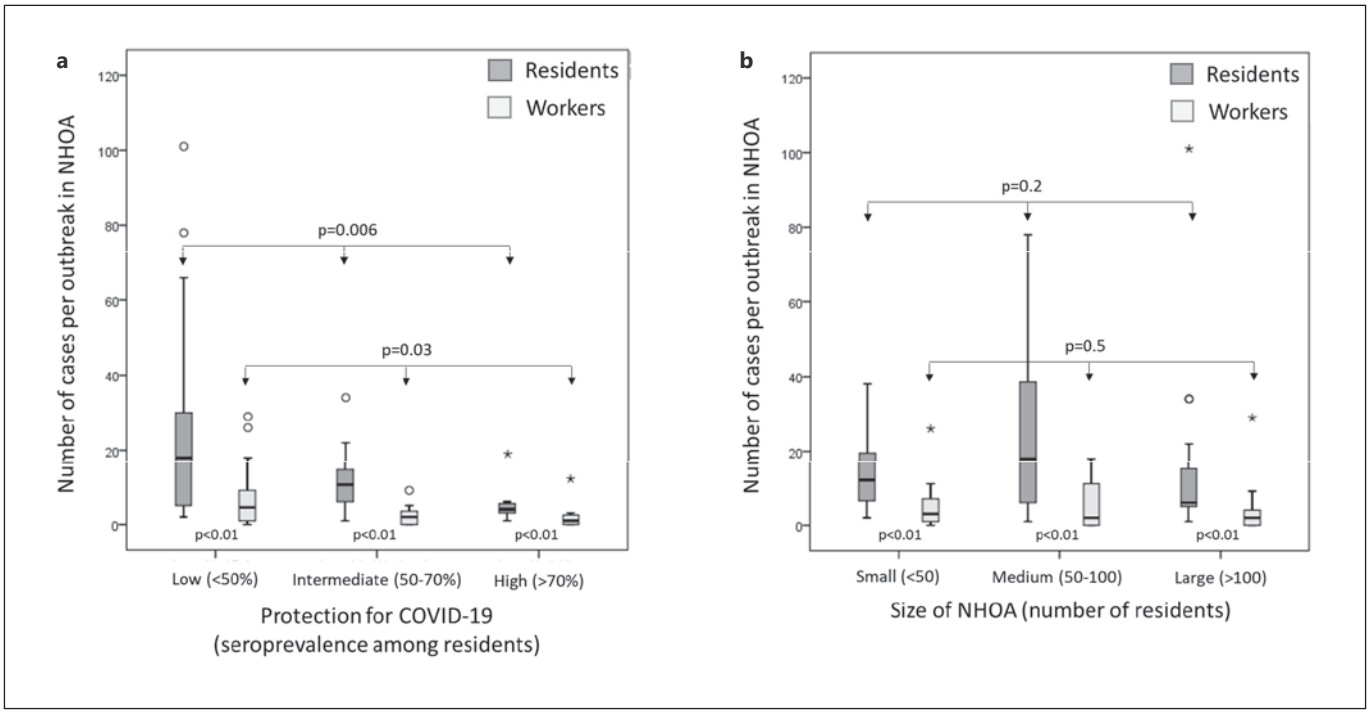

Fig. 1. a, **b** Number of COVID-19 cases in residents and workers in NHOA with outbreaks.

(IQR, 23.3) in small facilities ($p = 0.02$). By linear regression analysis, the number of residents in outbreaks, converted into a logarithmic distribution (OR [95% CI], p), was positively associated with the number of seronegative residents (0.11 [0.04–0.18] per 10 residents, $p = 0.02$) and negatively associated with the number of seropositive staff (−0.19 [−0.31 to −0.06] per 10 workers, $p = 0.04$).

Multivariable Analysis

The mean biweekly cumulative incidence of cases in BHZ was of 377 (SD, 207) per 100,000 in NHOA with outbreaks, and of 254 per 100,000 (SD, 76) in NHOA without outbreaks ($p < 0.001$). An extended time-dependent-variable Cox regression analysis (HR [95% CI], p) following a counting process style [23, 24] was done. Centers with intermediate and high seroprevalence among residents had a respective 55% (0.45 [0.25–0.80], $p = 0.007$) and 78% (0.22 [0.10–0.48], $p < 0.001$) reduction in the risk of outbreaks compared to NHOAs with low seroprevalence. Furthermore, compared to smaller facilities, facilities with 50–100 residents (1.91 [1.00–3.65], $p = 0.05$) or with more than 100 residents (4.57 [2.38–8.75], $p < 0.001$) were at a higher risk of outbreaks (Fig. 2).

Discussion

The monitoring of a large number of residents in NHOA, following a seroprevalence survey after the first wave of COVID-19, has shown that the risk of outbreaks affecting residents is related to the total number of residents in the facility, the rate of seropositivity among residents, and the incidence of new cases in the community around the facility. These findings are consistent with other recent studies [26, 27]; there is information to support that workers and visitors are the main carriers of SARS-CoV-2 in NHOA [28–30]. Despite the screening protocols implemented after the first wave of COVID-19, it is likely that asymptomatic or minimally symptomatic individuals entering the NHOA have caused newer outbreaks [31–33]. Evidence that staff are frequently hired part time and work in different facilities favors this mechanism of viral spread [34].

As COVID-19 frequently presents with little or with atypical symptoms among residents, diagnosis of internal cases in NHOA may also be difficult [35, 36]. The association of the number of residents with the risk of an outbreak in the facility may result from the sum of both factors mentioned, that is, more intruders entering the facility and more candidates for infection within the

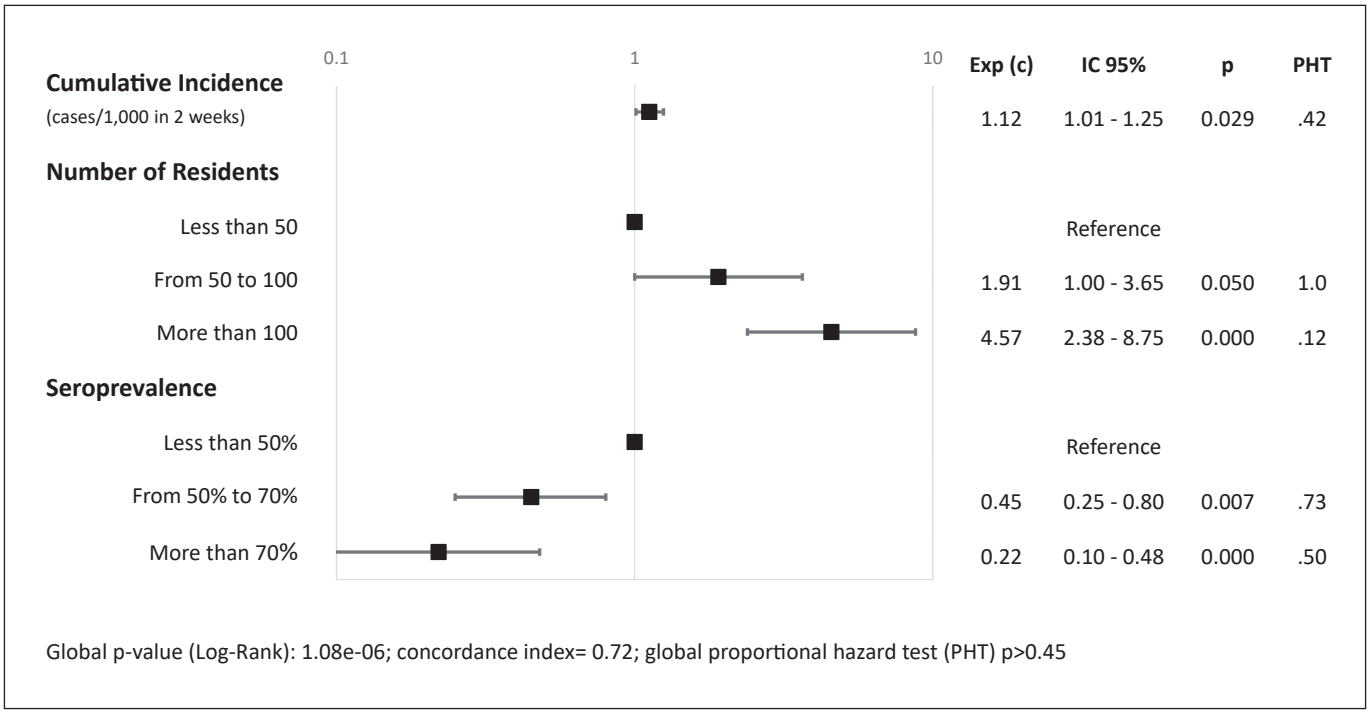

Fig. 2. Cox regression analysis for the risk of outbreak adjusted to cumulative incidence in the BHZ as a time-dependent variable.

residency [37]. In fact, we identified five facilities that had a second outbreak during the follow-up (these episodes are not included in the analysis); all of them were NHOA with more than 100 beds. As a possible conclusion, if it is ever necessary to prioritize certain NHOA for vaccination, these should be facilities with a larger number of residents, being 100 residents a good cut point.

For the risk of outbreaks, estimating the effect of COVID-19 in the community from the cumulative incidence in BHZ introduces a bias, as workers or visitors may not always come from the area around the NHOA. Other factors not explored in this study, which may have mostly contributed to the occurrence of cases in NHOA during the first pandemic wave, were the inadequate preparation against the pandemic, mainly dependent on the shortage of supplies and personnel [38–42].

After the first pandemic wave severely affected NHOA in the Community of Madrid, a mandatory protocol was implemented to prevent outbreaks. Briefly, NHOA were sectorized into three areas: red for residents with COVID-19, green for residents with discarded or past COVID-19, and yellow for residents under study for COVID-19 [43]. Each area had different levels of restrictions on visits and mobility. Before the vaccination strategy was completed in the NHOA in April 2021, the regulation of residents' and workers' permits, and visitor admission was established based on the composite of the level of seropositivity in residents and the weekly cumulative incidence in the Community of Madrid [44, 45]. This study proves that the seropositivity to SARS-CoV-2 is related to the risk of outbreaks in NHOA, but does not prove the efficacy of the restrictions implemented by the level of seropositivity among residents, as a direct evaluation of these protocols is outside the scope of this analysis. As a limitation of the study, we were unable to evaluate the level of adherence to these recommendations in each facility.

According to several studies, subjects with positive IgG against SARS-CoV-2 are considered protected from a serious infection, which can also lead to less viral transmission [12, 46]. As we have later learnt, the dramatic reduction in COVID-19 cases in NHOA following vaccination of residents supports that immunity is key to preventing outbreaks [13–15].

The period of the study, June to December 2020, coincides with the beginning and decay of the second pandemic wave in Madrid, when the original SARS-CoV-2 strain was the most prevalent [47]. In the Summer of 2020, still 40.9% of residencies in Madrid had more than half of the residents without detectable immune protec-

tion for COVID-19; in fact, 21.9% of the facilities studied had a seropositivity rate of less than 10%. The selection of NHOA as the first line of vaccination campaigns has for sure saved a great number of lives in these hot spots.

Several limitations of this study need to be recognized. The level of seropositivity was studied an average of 18.4 ± 5.8 weeks before the time of evaluation, either due to the appearance of the outbreak (10.2 ± 5.7) or at the end of follow-up (20.2 ± 3.9 weeks). This lag may be long enough to have caused the loss of immune protection in those considered seropositive or allow an asymptomatic infection in those considered seronegative, which could be particularly more frequent in older adults in these facilities [48]. For the analysis of risks, we have not considered individual factors that could also affect the global risk of outbreak in any given facility – i.e., age, morbidities, frailty, history of COVID-19, etc. – other than seropositivity.

Other airborne (i.e., influenza) or intestinal (i.e., norovirus) viral infections are cause of outbreaks in nursing homes in NHOA; factors analyzed in this study as the number of susceptible subjects, seroprevalence, or the incidence of infections in the general population may also modulate the risk of those other infections [49].

Conclusions

The risk of outbreaks in NHOA depends not only on the size of the facility but also on the level of immunity among residents and the incidence of cases in the community surrounding the facility. The size of outbreaks is limited by a greater level of immunity among residents and workers.

Appendix

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Acknowledgments

To the Section of Epidemiology, Public Health Directorate, Council of Health; to Fundación UNIR for their logistical commitment to the project; to Colonel Herraiz, Commander Serrano, and the entire Criminalistics Department of the Guardia Civil for their invaluable help in the preanalytical phase; to Cecilia Pérez, Francisco Javier Álvarez-Timón, Carlos de Lucas, and the technicians of Madrid Digital for their collaboration in the recording of the data; to Mayra Matesanz, Lucía Candel, Rodrigo Candel, Ma Pilar Barreiro, Carmen de Lucas, and Jose Luís Marqués for the review of results; to the entire technical team of the Microbiology Department of the Regional Public Health Laboratory; and to all the residents of the NHOA in Madrid for their participation, our generation owes you a debt of gratitude.

Statement of Ethics

Subjects studied have given their written informed consent and that the study protocol was approved by the Regional Ethics Committee of the Community of Madrid (Ref. SeroSOS).

Conflict of Interest Statement

F.J.C., J.S.R., and P.B. work part time as advisors to the Council of Public Health in the Community of Madrid. J.C. is an assistant to the Vice Counselor of public health in the Community of Madrid. F.J.M.P. is the Director of Social and Health Coordination in the Community of Madrid. A.Z. is the Vice Counselor of Public Health in the Community of Madrid.

Funding Sources

This study was funded by the Health Council of the Community of Madrid.

Author Contributions

Conceptualization of ideas (CI): formulation or evolution of overarching research goals and aims. Investigation conducting research (ICR): specifically performing the experiments, or data/evidence collection. Methodology (M): development or design of methodology; creation of models. Writing original draft (WOD): creation and/or presentation of the published work, specifically writing the initial draft. Critical draft review (CDR): creation and/or presentation of the published work by those from the original research group, specifically a critical review. Francisco J. Candel, Pablo Barreiro, and Jesús San Román contributed to CI, ICR, M, and WOD; María del Mar Carretero contributed to ICM, M, and CDR; Juan C. Sanz, Marta Pérez-Abeledo, Belén Ramos, and José M. Vinuesa-Prieto contributed to ICR and M; Jesús Canora, Francisco J. Martínez-Peromingo, Raquel Barba, and Antonio Zapatero contributed to CDR. Both geriatricians and health-trained interviewers participated in ICR, M, and CDR.

Data Availability Statement

Datasets on which the conclusions of the paper rely may be made available to editors, reviewers, and readers upon request to the corresponding author.

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