Assessing COVID-19 Vaccine Effectiveness in Frail Long-Term Care Facilities Residents in a Middle-Income Country

Joice Coutinho de Alvarenga
joice-alvarenga@hotmail.com
Universidade Federal de Minas Gerais
Flávia Lanna de Moraes
Universidade Federal de Minas Gerais
Jáder Freitas Maciel Garcia de Carvalho
Universidade Federal de Minas Gerais
Rodrigo Ribeiro dos Santos
Universidade Federal de Minas Gerais
Unaí Tupinambás
Universidade Federal de Minas Gerais
Edgar Nunes de Moraes
Universidade Federal de Minas Gerais

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Abstract

Background: During the COVID-19 pandemic, individuals residing in long-term care facilities (LTCF) are particularly vulnerable to adverse outcomes due to their higher rates of frailty, disabilities, cognitive impairment, dementia, and chronic illnesses. In low and middle-income nations, research on immunizing frail populations is lacking, while most studies on COVID-19 in LTCF come from wealthier nations and may not fully capture the situation in emerging countries.

Methods: We aimed to evaluate the effectiveness of first, second and third COVID-19 vaccine doses, against infections, hospitalizations, and deaths, and their association with frailty, age, sex and chronic disease, among older adults, in a social vulnerability context. This retrospective cohort study, comprises a total of 712 older adults, in a social vulnerability context, of 29 LTCF, in Brazil. Continuous variables were described by medians and interquartile ranges and categorical variables were represented by absolute and relative frequencies. The Mann-Whitney test was used. For evaluating the relation between categorical variables, Pearson's chi-square test was used. When comparing proportions, the Z test of proportion was applied. A significance level of 5% was considered.

Results: Median age was 81.37 years, 72.8% were female, 94.61% were frail, 79.97% had a cognitive impairment, 69.54% had a mobility impairment, 78.37% have, at least, one chronic disease and 72.73% use five or more medications per day. Before the vaccine, mobility impairment was associated with great contamination rates (p=.03); frailty (p=.02) and previous pulmonary disease (p=.03) with symptoms of gravity; frailty (p=.02), pulmonary disease (p=.04) and male sex (p=.02) with emergency care or hospital admission. After the third vaccine dose, only frailty remains associated with admissions (p=.03). The number of positive cases (p=.001), symptomatic patients (p<.001), admissions (p=.001) and deaths (p<.001) were substantially reduced after the three vaccine doses.

Conclusions and Implications: Even in a frail population, the vaccine was effective, in the reduction of positive cases, the number of symptomatic patients, admission to emergency or hospital care and deaths. Before the vaccine, frailty, previous pulmonary disease and male sex were associated with worse outcomes. After the vaccine, frailty remains associated with a major number of admissions.

Background

In the COVID-19 pandemic, long-term care facilities (LTCF) residents represent those at greatest risk of poor outcomes, including high mortality rates and prolongate hospitalization.[1,2]

Older adults who live in LTCF have an elevated prevalence of frailty, disabilities, cognitive impairment, dementia and a heightened burden of chronic infirmities, in comparison to their community-residing counterparts.[3,4]

In the general population, discernible risk factors for mortality and hospital admission encompass the male gender, advancing age, chronic diseases (diabetes, hypertension, kidney disease, cardiovascular disease, obesity, pulmonary disorders, malignancies) and frailty.[5-7] In the LTCF residents, increased age, frailty, male gender, impaired cognitive function and impaired physical function have all evinced association with mortality.[8-10]

In the context of low and middle-income nations, studies evaluating immunization in frail populations remain scarce, since they are routinely excluded from trials. The majority of the studies evaluating COVID-19 in LTCF have been conducted in developed countries, which may not reflect the realities of emerging countries. Inequality was shown as a determinant agent of disparate outcomes in the COVID-19 pandemic.[11-13] The suboptimal healthcare provisioning,

prevalent in low and middle-income countries, invariably contribute to a heightened prevalence of frail older adults, with a high number and gravity of chronic ailments.[14,15]

In this study, we aimed to evaluate the effectiveness of COVID-19 vaccines among frail and socially vulnerable LTCF residents, in a middle-income country. After a meticulous survey of existing literature, we could not identify prior studies that have evaluated the vaccine efficacy within a comparable demographic profile. Therefore, we sought to evaluate the response of first, second and third COVID-19 vaccine doses, against infections, hospitalizations, and deaths, and the association of frailty, age, sex, cognitive impairment, mobility impairment, chronic diseases and polypharmacy with those outcomes. This study encompasses the periods of alpha, gamma, delta, and omicron variants, which provides a better understanding of vaccine effectiveness, against different lineages.

Methods

Study Design

This is a retrospective cohort study, conducted across 29 LTCF located in a prominent city in southeastern Brazil. The study took place during the period from January 2021 to September 2022.

Study participants

The enrolled LTCF were characterized as philanthropic institutions, being financially supported by religious organizations as well as the local public social assistance department.

All residents within these institutions were invited to participate in the study. Exclusion criteria were limited to patients who declined research participation.

Data collection

Within the designated LTCF, a universal SARS-CoV-2 testing approach was adopted: when any resident or staff member exhibited symptoms, the entire population of residents and workers underwent testing, using PCR-based assays of nasopharyngeal swab.

The research team conducted a daily monitoring of newly confirmed positive cases and the clinical progression of participants who tested positive. Information concerning emergency care or hospital admissions and deaths was updated routinely. Reported mortality cases were subsequently cross-referenced with the national death registry.

Vaccination details encompassing dates, vaccine types, and the dosing regimen, were extracted from the national vaccination registry card, of each participant. The vaccination of LTCF residents was initiated in January 2021, with the administration of the CoronaVac vaccine (Sinovac Biotech). In February 2021, the ChAdOx1-S vaccine (Oxford–AstraZeneca) became additionally available for administration. For recipients of the CoronaVac vaccine, the second dose was administered within three to four weeks following the initial dose. Meanwhile, for the ChAdOx1-S vaccine, an interval of eight to twelve weeks was stipulated for the second dose administration. The third dose was deployed in LTCF in November 2021. During this period, the Comirnaty vaccine (Pfizer–BioNTech) and the Janssen Ad26.COV2.S vaccine (Johnson & Johnson) was also incorporated into the LTCF vaccination regimen.

Participant' characteristics, including sex, age, birth date, presence of chronic medical conditions and number of current medications in use were obtained from long-term facilities records. All participants underwent a comprehensive clinical and functional evaluation conducted by a team of geriatric medical specialists. Frailty was assessed using two different scales. The first one was the Clinical-Functional Vulnerability Index-20 (IVCF-20), a screening tool, validated in

Brazil to be used even for non-medical professionals.[16] In the IVCF-20, frailty is stratified from 1 to 40, with scores 1-6 denoting low clinical functional vulnerability; 7-14 indicating moderate vulnerability and 15-40 signifying high vulnerability. This score is detailed in Supplementary Figure 1.

The second scale employed was the Clinical-Functional Classification (CCF) of older adults[17] a standard scale in Brazil, based on Instrumental Activities of Daily Living (IADL), Basics Activities of Daily Living (BADL) and the presence of chronic health conditions. The CCF is an ordinal hierarchical scale ranging from 1 to 10: stratum 1-3 means a robust (fit) older adult, independent for all activities of daily living; stratum 4-5 denotes an older adult at risk of frail (vulnerable older adult); and 6 to 10 indicates frail older adult (stratum 6 are independent for BADL but dependent for some IADL; stratum 7 are independent for BADL but dependent for all IADL; stratum 8 are dependent for some BADL; stratum 9 are dependent for almost all BADL, but can eat independently; and 10, dependent for all BADL). Details of this scale are contemplated in Supplementary Figure 2.

As the defining criteria for typical symptoms of COVID-19, we relied upon the Centers for Disease Control and Prevention (CDC) study,[18] which outlines the most prevalent manifestations of the disease: cough, fever, myalgia, headaches, dyspnea, odynophagia, rhinorrhea, anosmia, and ageusia.

Study Variables

The selected categorical variables encompassed: sex, race, frailty accessed by CCF, RT-PCR for SARS-CoV-2 (classified into three categories: positive, negative, indeterminate) and vaccine type.

The dichotomous variables were: the presence of hypertension, diabetes, prior pulmonary disease, presence of cognitive impairment, mobility impairment, presence of typical symptoms associated with COVID-19, admission to emergency care, hospitalization and death.

Age, number of medications in use and the IVCF-20 score were evaluated both as quantitative and categorical variables. Age was stratified into four distinct categories: participants below 70 years, those between 70 and 79, individuals aged 80 to 89, and those aged 90 or above. For the number of medications in use, were created two categories: with polypharmacy (use of five or more medications per day), or without polypharmacy. For the IVCF-20 score, the instrument's reference values were used to create three categories: scores 1-6 denoting low clinical functional vulnerability; 7-14 indicating moderate vulnerability and 15-40 signifying high vulnerability.

Statistical analysis

In the descriptive analysis, categorical variables were described using absolute frequency and proportion, while continuous variables were summarized with measures of central tendency (mean and standard deviation, median and quartiles). To compare continuous variables, the Mann-Whitney test was used due to non-normal data distribution, assessed using the Shapiro-Wilk test. In the evaluation of categorical variables, Pearson's chi-square test was employed, and for proportion comparisons, the Z test of proportion was utilized. All analyses were performed using Stata software version 16 (StataCorp LLC, College Station, TX), with a significance level of 5%.

The primary outcome was overall vaccine effectiveness, irrespective of vaccine type, against infections, admissions to emergency care, hospitalizations, and deaths. Additionally, we evaluated the factors associated with a great risk of contamination, symptoms, admissions to emergency service, or hospital admissions.

Ethics approval

Brazilian Commission for Research Ethics (COEP-UFMG) approved the study protocol (CAAE: 40666720.0.0000.5149).

Results

A total of 712 LTCF residents were included. The characteristics of the participants are summarized in Table 1. The median age was 81.3 years (IQR 74-89), with 518 individuals (72.8%) being female. The prevalence of frailty was 94.6% (27.7% CCF 6-7, 24.8% CCF 8 and 42.05% CCF 9-10). Cognitive impairment was observed in 79.9% of participants, while 69.5% exhibited mobility impairment, 78.3% presented with at least one chronic disease, and 72.7% reported the use of five or more medications per day, ranging from a minimum of 1 to a maximum of 17 drugs daily.

Table 1: Descriptive Statistics of Overall Study Population

Characteristic	n	%
Age		
<70	86	12,1
70-79	222	31,22
80-89	244	34,32
90+	159	22,36
Sex		
Female	518	72,86
Male	193	27,14
Race		
White	238	37,01
Black	149	23,17
Pardo	256	39,81
CCF		
Robust (1-3)	7	0,99
Risk of frail (4-5)	31	4,4
Frail 6-7	195	27,7
Frail 8	175	24,86
Frail 9-10	296	42,05
IVCF-20		
Low Vulnerability (0-6)	58	8,43
Moderate Vulnerability (7-14)	112	16,28
High Vulnerability (15-40)	518	75,29
Polypharmacy		
< 4 different drugs/day	153	27,27
≥ 5 different drugs/day	408	72,73
Comorbidities		
Diabetes	148	24,07
Hypertension	415	67,48
Pulmonary disease	89	14,45
Cognitive impairment	491	79,97
Mobility impairment	443	69,54

The vaccination adherence was 99.5% of the cohort, all of whom received the complete three-dose regimen. In the first and second doses, 91.7% of the cohort received the ChAdOx1-S vaccine. In the third dose, 98.6% of the participants received the Comirnaty vaccine. Details regarding vaccine types are elaborated upon Supplementary Table 1.

The vaccination had a significant impact on the reduction in positive cases (p=.001), in admissions to emergency care (p<.001), hospitalization (p=.002) and deaths (p<.001). Prior to the vaccination, a total of 191 positive cases were documented, corresponding to 26.8% of the entire cohort. Among these contaminated individuals, 43.5% exhibited typical respiratory symptoms, 29.3% required emergency care or hospitalization, and 27 COVID-19 related deaths occurred, corresponding to a case fatality rate of 14.1%. After the first dose, 25 positive cases had occurred and after the second dose, 28 positive cases. Only six participants (24% of positive participants) were admitted to emergency care or hospital, after the first dose and six participants after the second dose. Two deaths were observed after both the first and second doses.

The period subsequent to the administration of the third dose coincided with the prevalence of the Omicron variant. During this period, the number of positive cases had arisen, with 136 positive cases, representing 19.2% of the cohort. Although, 85.3% were asymptomatic. Among the contaminated participants, 15 (11.1%) necessitated admission to emergency care or hospitalization. Five deaths have occurred, culminating in a post-vaccination case fatality rate of 3.8%, during the dominance of the Omicron variant. Details about vaccine effects are shown in Figure 1.

Figure 1. The number of positive cases, symptomatic participants, admission to emergency service, hospitalization and deaths, among LTCF residents, before the vaccine, and after the first, second and third vaccine doses. The red line corresponds to the proportion of positive cases in the general population.

When risk factors were analyzed (Figure 2), frailty, advanced age, presence of chronic diseases, cognitive impairment and polypharmacy were not associated with a higher rate of contamination by SARS-CoV-2. Mobility impairment, however, exhibited a significant correlation with a higher number of positive cases (p=.03) but not with typical symptoms and admission to emergency or hospital care.

Before the vaccination, individuals with a history of pulmonary disease (p=.03) and those dependent for BADL (p=.02) exhibited a higher prevalence of typical symptoms compared to other study participants. Furthermore, a significant association between dependence for BADL (p=.005), male sex (p=.02) and pulmonary disease (p=.008) was observed with a heightened number of admissions to emergency services and hospitalization (Figure 2).

In the non-vaccinated frail subgroup (CCF 8-10), 63 participants, which represents 48.4% of the positive cases exhibited typical symptoms and 45 participants (34.6%) necessitated emergency care or hospital admission. After the administration of three vaccine doses, the number of symptomatic patients in this group decreased to 16 (16.8%) and 12 participants (12.6%) needed admission, as depicted in Figure 2.

Prior to the vaccination, within the pulmonary disease group, 61.5% of the positive participants displayed typical respiratory symptoms and 50% required emergency care or hospital medical support. After the three doses, the number of symptomatic patients dwindled to 14.2%, with the same percentage necessitating medical intervention in this subgroup.

Male participants exhibited a higher frequency of hospitalization than females (p=.02). Pre-vaccination, 42% of male participants had been admitted to emergency care or hospital (Figure 2), compared to 24.8% of females. Following vaccination, admissions among males became comparable to those observed among females, with a comparable proportion of 13.5% of the positive cases in males and 15.1% in females, and no statistically significant difference between the two groups.

Age, hypertension, diabetes, cognitive impairment and polypharmacy did not exhibit significant associations with increased contamination rates, symptoms, admissions to emergency care and hospitalization.

Figure 2: The risk factors associated with a higher proportion of positive cases, symptomatic patients, and hospitalizations.

Table 2 compares the number of positive cases, symptomatic participants and participants requiring emergency or hospital care, before and after the three vaccine doses, across different risk factor subgroups. After the three vaccine doses, there was a significant reduction in the proportion of symptomatic patients and admissions, in almost all risk factor subgroups, with the exception of participants with diabetes, in which a reduction in the number of admissions occurred, although, was not statistically significant.

Table 2: Comparison between the number of positive cases, symptomatic participants and participants who need emergency or hospital care, before and after the three vaccine doses, in different subgroups of risk factors.

Characteristics	Positive cases					Symptoms					Admission				
	Before		After			Before		After			Before		After		
	N	%	N	%	p	N	%	N	%	p	N	%	N	%	p
Age ≥ 80	119	31	74	27	0.3	51	43	14	18	**<0.001**	34	28	10	13	**0.01**
CCF 8-10	130	31	94	29	0.6	63	48	16	16	**<0.001**	45	34	12	12	**<0.001**
IVCF-20 ≥ 15	139	30	99	28	0.6	61	44	15	15	**<0.001**	41	29	13	13	**0.002**
Male	49	30	37	25	0.3	25	50	5	13	**<0.001**	21	42	4	10	**0.001**
Cognitive impairment	142	30	93	27	0.2	64	45	12	12	**<0.001**	43	30	9	9	**<0.001**
Mobility impairment	116	27	89	30	0.4	53	45	13	14	**<0.001**	38	32	11	12	**<0.001**
Diabetes	42	31	26	26	0.4	17	40	3	11	**0.008**	12	28	3	11	0.8
Hypertension	112	28	73	25	0.4	47	42	13	17	**<0.001**	32	28	9	12	**0.007**
Pulmonary disease	25	29	14	24	0.5	16	61	2	14	**0.004**	13	50	2	14	**0.02**
Polypharmacy	125	32	63	23	**0.01**	55	44	11	17	**<0.001**	40	32	9	14	**0.007**

When the number of positive cases was evaluated in association with LTC characteristics (Figure 3), we observed a trend indicating higher proportions of positive cases in LTCFs with larger resident populations. The number of cases was significantly lower in LTC with a smaller number of residents, in contrast to LTCF with more than 20 residents (p=.002).

Figure 3. Correlation between the number of residents in each LTCF and the proportion of positive cases.

Discussion

Our cohort comprised over 700 profoundly frail residents within a LTCF setting, in a context marked by social vulnerability. Among these individuals, over 50% were aged above 80 years, with more than 90% displaying signs of

frailty and over 60% exhibiting a state of extreme frailty, with BADL dependence. Nearly 80% of the participants had cognitive impairment, while close to 70% with mobility limitations. Additionally, over 70% had at least one chronic medical condition, and more than 70% necessitated the administration of five or more medications on a daily basis. Even within this cohort marked by a high degree of frailty, disabilities, and clinical severity conditions, we consistently observed the effectiveness of vaccines. To our knowledge, subsequent to an extensive literature review, this is the first Brazilian study that evaluated the vaccine effectiveness in this population profile. Another distinguishing aspect of this study is that all participants underwent a specialized geriatric assessment, enhancing the reliability of the disclosed information.

Our study is in concordance with several previous studies, which attest to the vaccine's effectiveness in preventing infections, hospitalizations and deaths.[19,20] A clear benefit was already observed after the first dose in our study population. Following the administration of first and second vaccine doses, the number of positive cases, symptomatic patients, admission to emergency service, admission to hospital and deaths diminish significantly, even during periods marked by heightened caseloads in the general populace.

In the period corresponding to Omicron variant predominance, the number of infected participants arises, even after three vaccine doses. Within our cohort, even with an increase in the number of positive cases, the proportion of symptomatic patients, patients who needed admission to emergency service or hospitalization and deaths, remains low, when compared to the period before the first dose. Regarding the Omicron variant, the vaccine effectiveness remained high for preventing death and serious cases but reduced for infection.

Before the vaccine, we found an association between contamination and mobility impairment. This finding is in concordance with previous studies, that evidence the role of staff contact in the contamination of LTCF residents.[22-25] Residents who have mobility impairment inherently necessitate increased support for ambulation, personal hygiene, and dressing, heightening the proximity to caregiving assistants. Furthermore, we found an association between the number of LTCF residents and heightened contamination rates. A LTCF characterized by a larger resident population necessitates a correspondingly increased staffing capacity. It is plausible that a substantial circulation of staff members might significantly contribute to the transmission of viral infections among the residents.[26]

Previous studies have shown male sex as a risk factor for worse outcomes.[27-29] In our cohort, before the vaccination, male sex was associated with a great proportion of emergency and hospital admissions. However, subsequent to vaccination, the risk profile among males became comparable to that observed among females.

Hypertension[10] and diabetes[10,27,30] were considered risk factors for hospital admission and death, due to COVID-19. In our cohort, these chronic diseases were not associated with contamination, symptoms or admissions. It is conceivable that within this highly frail population profile, the overarching influence of frailty supersedes the individual impact of these chronic conditions. Notably, frailty manifests as a condition of heightened severity compared to standalone chronic diseases.

Corroborating this idea, similarly to previous studies[31-36], frailty was associated with more typical symptoms and more admissions to emergency or hospital care. The vaccine was capable of mitigating this effect, by reducing the number of symptomatic patients and admissions.

Some previous studies have shown age as a risk factor for worse outcomes in COVID-19[8,37] and other studies refute this association.[9] In our cohort, age was not associated with greater contamination, symptoms or admissions.

In accordance with prior research findings, it has been found that pulmonary disease exhibits a correlation with the severity of symptoms and the need for emergency and hospital care.[38] After the three vaccine doses, a significant reduction in symptomatic patients and admissions was noticed in this subgroup, showing the potential of the vaccine to protect the most susceptible groups.

When we compare the period before and after the vaccination, we observe a reduction in symptomatic patients and those who need admission, in all subgroups of risk factors. Frail individuals are particularly susceptible to the deterioration of their health status due to acute illnesses.[40] Mitigating the severity of such acute insults holds paramount significance in the reduction of the propensity toward aggravated disabilities and frailty.

Moreover, admission to emergency care or hospitalization among frail older adults, is accompanied by deleterious complications including delirium, agitation, aggressiveness, disorientation;[41] falls;[42] iatrogenic treatments, sarcopenia and pressure injuries.[43] These complications are associated with major mortality rates.[44] Consequently, the implementation of preventive measures with the potential to reduce hospitalizations is crucial in this population.

Conclusion and implications

Our study provides important insights into vaccine effectiveness, even in an extremely frail and socially vulnerable population. The vaccine was effective in the reduction of severe cases and admissions, even in the Omicron variant wave and in all subgroups of risk factors. Aging is a risk factor for several infectious diseases, including COVID-19 and although immune senescence may compromise vaccine effectiveness, it was not observed in our study.

Limitations

Our study was unable to undertake a comprehensive evaluation of distinctions among various vaccine types, as the number of recipients for both CoronaVac and Ad26.COV2.S was reduced.

Given that a substantial proportion of participants exhibited cognitive impairment, hindering their ability to provide self-reported health statuses and medication regimens, we relied on indirect information sourced from LTCF medical records, which could have caused some information bias. However, the LTCF assumed responsibility for overseeing all aspects of participants' healthcare, thus potentially enhancing the reliability of our data.

Within our cohort, a small number of individuals with antecedent pulmonary conditions and diabetes was observed, potentially restricting our subgroup analyses.

List Of Abbreviations

BADL Basics Activities of Daily Living

CCF Clinical-Functional Classification

CDC Centers for Disease Control and Prevention

IADL Instrumental Activities of Daily Living

IVCF-20 Clinical-Functional Vulnerability Index-20

LTCF Long-term care facilities

RT-PCR Reverse transcription polymerase chain reaction

SARS-CoV-2 S*evere acute respiratory syndrome coronavirus 2*

Declarations

Ethics approval and consent to participate: Brazilian Commission for Research Ethics (COEP-UFMG) approved the study protocol (CAAE: 40666720.0.0000.5149). Informed consent was obtained from all enrolled institutions.

Consent for publication: not applicable.

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References

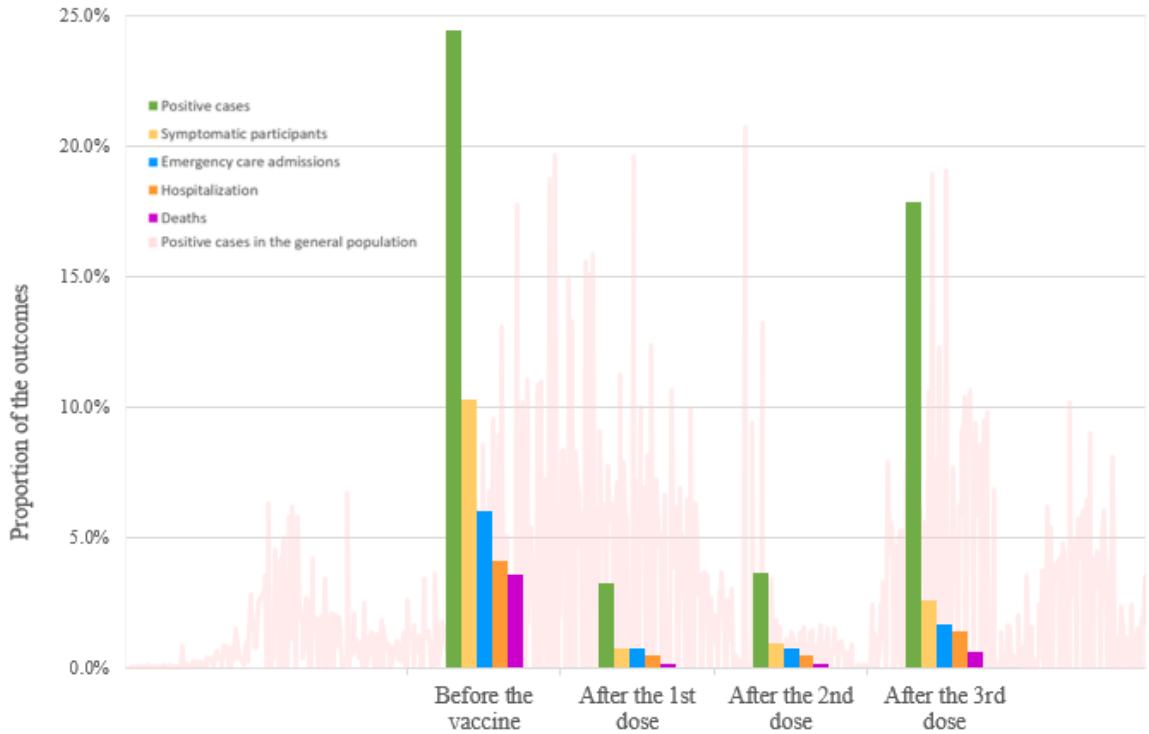
1. Comas-Herrera A MJ, Byrd W, Lorenz-Dant K, et al. Mortality associated with COVID-19 outbreaks in care homes: international evidence. 2020-04-12 2020;doi:https://doi.org/10.21953/lse.mlre15e0u6s6
2. Lee D CC, Tang A, Brister S, Ezike N. *Notes from the Field:* COVID-19–Associated Mortality Risk Among Long-Term Care Facility Residents and Community-Dwelling Adults Aged ≥65 Years. *MMWR Morb Mortal Wkly*. 2022-06-15T06:27:48Z 2022;(Rep 2022;71:803–805)doi:DOI: http://dx.doi.org/10.15585/mmwr.mm7124a4
3. Briggs R CT, Collins R, O'Neill D, Kennelly SP. Nursing home residents attending the emergency department: clinical characteristics and outcomes. *QJM: An International Journal of Medicine*. 2023;106(9):803-808. doi:10.1093/qjmed/hct136

4. Falconer M. Profiling disability within nursing homes: a census-based approach. *Age and Ageing*. 2023;36(2):209-213. doi:10.1093/ageing/afl185
5. Guan W-j, Ni Z-y, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. research-article. *https://doiorg/101056/NEJMoa2002032*. 2020-02-28 2020;doi:NJ202004303821810
6. Izcovich A RM, Tortosa F, Lavena Marzio MA, et al. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review | PLOS ONE. 2023;doi:10.1371/journal.pone.0241955
7. Hewitt J CB, Vilches-Moraga A, Quinn TJ, et al. The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study. *The Lancet Public health*. 2020 Aug 2020;5(8)doi:10.1016/S2468-2667(20)30146-8
8. Panagiotou OA, White EM, et al. Risk Factors Associated With All-Cause 30-Day Mortality in Nursing Home Residents With COVID-19. *JAMA Internal Medicine*. 2023;181(4):439-448. doi:10.1001/jamainternmed.2020.7968
9. Bielza R SJ, Zambrana F, Arias E, et al. Clinical Characteristics, Frailty, and Mortality of Residents With COVID-19 in Nursing Homes of a Region of Madrid - Journal of the American Medical Directors Association. 2023;doi:doi:10.1016/j.jamda.2020.12.003
10. Richardson S HJ, Narasimhan M, Crawford JM, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA*. 2023;323(20):2052-2059. doi:10.1001/jama.2020.6775
11. Bach-Mortensen AM, Degli Esposti M. Is area deprivation associated with greater impacts of COVID-19 in care homes across England? A preliminary analysis of COVID-19 outbreaks and deaths. *J Epidemiol Community Health*. Feb 08 2021;doi:10.1136/jech-2020-215039
12. Souza-Silva MVR, Ziegelmann PK, Nobre V, et al. Hospital characteristics associated with COVID-19 mortality: data from the multicenter cohort Brazilian Registry. *Intern Emerg Med*. Nov 2022;17(8):2299-2313. doi:10.1007/s11739-022-03092-9
13. Santos MM, Lucena EES, Bonfada D, et al. Brazilian Older People Hospitalized by COVID-19: Characteristics and Prognostic Factors in a Retrospective Cohort Study. *J Appl Gerontol*. Jun 2021;40(6):571-581. doi:10.1177/0733464820983976
14. Organization WHO. Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care. Technical documents. 2019 2019; doi:https://apps.who.int/iris/handle/10665/326843
15. Hoogendijk EO, Afilalo J, Ensrud KE, et al. Frailty: implications for clinical practice and public health. *Lancet*. Oct 12 2019;394(10206):1365-1375. doi:10.1016/S0140-6736(19)31786-6
16. Moraes EN, Moraes FL de, Azevedo RS, et al. Clinical-Functional Vulnerability Index-20 (IVCF-20): rapid recognition of frail older adults. *Revista de Saúde Pública*. 2023;50:81. doi:https://doi.org/10.1590/S1518-8787.2016050006963
17. Nota Técnica para Organização da Rede de Atenção à Saúde com foco na Atenção Primária à Saúde e na Atenção Ambulatorial Especializada - Saúde da Pessoa Idosa (2019).
18. Stokes EK, Zambrano LD, Anderson KN, et al. Coronavirus Disease 2019 Case Surveillance - United States, January 22-May 30, 2020. *MMWR Morb Mortal Wkly Rep*. Jun 19 2020;69(24):759-765. doi:10.15585/mmwr.mm6924e2
19. Feikin DR HM, Abu-Raddad LJ, Andrews N, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. *The Lancet Healthy Longevity*. 2022;doi:doi:10.1016/S2666-7568(22)00147-7
20. Graña C GL, Evrenoglou T, Jarde A, et al. Efficacy and safety of COVID-19 vaccines - Graña, C - 2022 | Cochrane Library. 2023;doi:10.1002/14651858.CD015477

21. Rabilloud M RB, Etard JF, Elsensohn M-H, Voirin N, Bénet T, et al. COVID-19 outbreaks in nursing homes: A strong link with the coronavirus spread in the surrounding population, France, March to July 2020. PLoS ONE.
22. Burton JK, McMinn M, Vaughan JE, et al. Care-home outbreaks of COVID-19 in Scotland March to May 2020: National linked data cohort analysis. *Age Ageing*. Sep 11 2021;50(5):1482-1492. doi:10.1093/ageing/afab099
23. Costa AP, Manis DR, Jones A, et al. Risk factors for outbreaks of SARS-CoV-2 infection at retirement homes in Ontario, Canada: a population-level cohort study. *CMAJ*. May 10 2021;193(19):E672-E680. doi:10.1503/cmaj.202756
24. Lee DS, Wang CX, McAlister FA, et al. Factors associated with SARS-CoV-2 test positivity in long-term care homes: A population-based cohort analysis using machine learning. *Lancet Reg Health Am*. Feb 2022;6:100146. doi:10.1016/j.lana.2021.100146
25. Konetzka RT, White EM, Pralea A, et al. A systematic review of long-term care facility characteristics associated with COVID-19 outcomes. *J Am Geriatr Soc*. Oct 2021;69(10):2766-2777. doi:10.1111/jgs.17434
26. Dyer AH, Noonan C, Dolphin H, et al. Managing the Impact of COVID-19 in Nursing Homes and Long-Term Care Facilities: An Update. *Journal of the American Medical Directors Association*. 2022 Sep 2022;23(9)doi:10.1016/j.jamda.2022.06.028
27. Panagiotou OA, Kosar CM, White EM, et al. Risk Factors Associated With All-Cause 30-Day Mortality in Nursing Home Residents With COVID-19. *JAMA Intern Med*. Apr 01 2021;181(4):439-448. doi:10.1001/jamainternmed.2020.7968
28. Burgaña Agoües A, Serra Gallego M, Hernández Resa R, et al. Risk Factors for COVID-19 Morbidity and Mortality in Institutionalised Elderly People. *Int J Environ Res Public Health*. Sep 28 2021;18(19)doi:10.3390/ijerph181910221
29. De Vito A, Fiore V, Princic E, et al. Predictors of infection, symptoms development, and mortality in people with SARS-CoV-2 living in retirement nursing homes. *PLoS One*. 2021;16(3):e0248009. doi:10.1371/journal.pone.0248009
30. Ballin M, Bergman J, Kivipelto M, et al. Excess Mortality After COVID-19 in Swedish Long-Term Care Facilities. *J Am Med Dir Assoc*. Aug 2021;22(8):1574-1580.e8. doi:10.1016/j.jamda.2021.06.010
31. Pranata R, Henrina J, Lim MA, et al. Clinical frailty scale and mortality in COVID-19: A systematic review and dose-response meta-analysis. *Arch Gerontol Geriatr*. 2021;93:104324. doi:10.1016/j.archger.2020.104324
32. Maltese G, Corsonello A, Di Rosa M, et al. Frailty and COVID-19: A Systematic Scoping Review. *J Clin Med*. Jul 04 2020;9(7)doi:10.3390/jcm9072106
33. Cangiano B, Fatti LM, Danesi L, et al. Mortality in an Italian nursing home during COVID-19 pandemic: correlation with gender, age, ADL, vitamin D supplementation, and limitations of the diagnostic tests. *Aging (Albany NY)*. Dec 22 2020;12(24):24522-24534. doi:10.18632/aging.202307
34. A BA, M SG, R HR, et al. Risk Factors for COVID-19 Morbidity and Mortality in Institutionalised Elderly People. *International journal of environmental research and public health*. 09/28/2021 2021;18(19)doi:10.3390/ijerph181910221
35. Zou Y, Han M, Wang J, et al. Predictive value of frailty in the mortality of hospitalized patients with COVID-19: a systematic review and meta-analysis. *Ann Transl Med*. Feb 2022;10(4):166. doi:10.21037/atm-22-274
36. Zhang XM, Jiao J, Cao J, et al. Frailty as a predictor of mortality among patients with COVID-19: a systematic review and meta-analysis. *BMC Geriatr*. Mar 17 2021;21(1):186. doi:10.1186/s12877-021-02138-5
37. Hägg S, Jylhävä J, Wang Y, et al. Age, Frailty, and Comorbidity as Prognostic Factors for Short-Term Outcomes in Patients With Coronavirus Disease 2019 in Geriatric Care. *J Am Med Dir Assoc*. Nov 2020;21(11):1555-1559.e2. doi:10.1016/j.jamda.2020.08.014

38. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. OriginalPaper. *BMC Infectious Diseases*. 2021-08-21 2021;21(1):1-28. doi:doi:10.1186/s12879-021-06536-3
39. Araf Y, Akter F, Tang YD, et al. Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. *J Med Virol*. May 2022;94(5):1825-1832. doi:10.1002/jmv.27588
40. Hussien H, Nastasa A, Apetrii M, et al. Different aspects of frailty and COVID-19: points to consider in the current pandemic and future ones. *BMC Geriatr*. Jun 27 2021;21(1):389. doi:10.1186/s12877-021-02316-5
41. Zhang XM, Jiao J, Xie XH, Wu XJ. The Association Between Frailty and Delirium Among Hospitalized Patients: An Updated Meta-Analysis. *J Am Med Dir Assoc*. Mar 2021;22(3):527-534. doi:10.1016/j.jamda.2021.01.065
42. Brand CA, Sundararajan V. A 10-year cohort study of the burden and risk of in-hospital falls and fractures using routinely collected hospital data. *Qual Saf Health Care*. Dec 2010;19(6):e51. doi:10.1136/qshc.2009.038273
43. Mart MF, Pun BT, Pandharipande P, et al. ICU Survivorship-The Relationship of Delirium, Sedation, Dementia, and Acquired Weakness. *Crit Care Med*. Aug 01 2021;49(8):1227-1240. doi:10.1097/CCM.0000000000005125
44. Flaatten H, De Lange DW, Morandi A, et al. The impact of frailty on ICU and 30-day mortality and the level of care in very elderly patients (≥ 80 years). *Intensive Care Med*. Dec 2017;43(12):1820-1828. doi:10.1007/s00134-017-4940-8

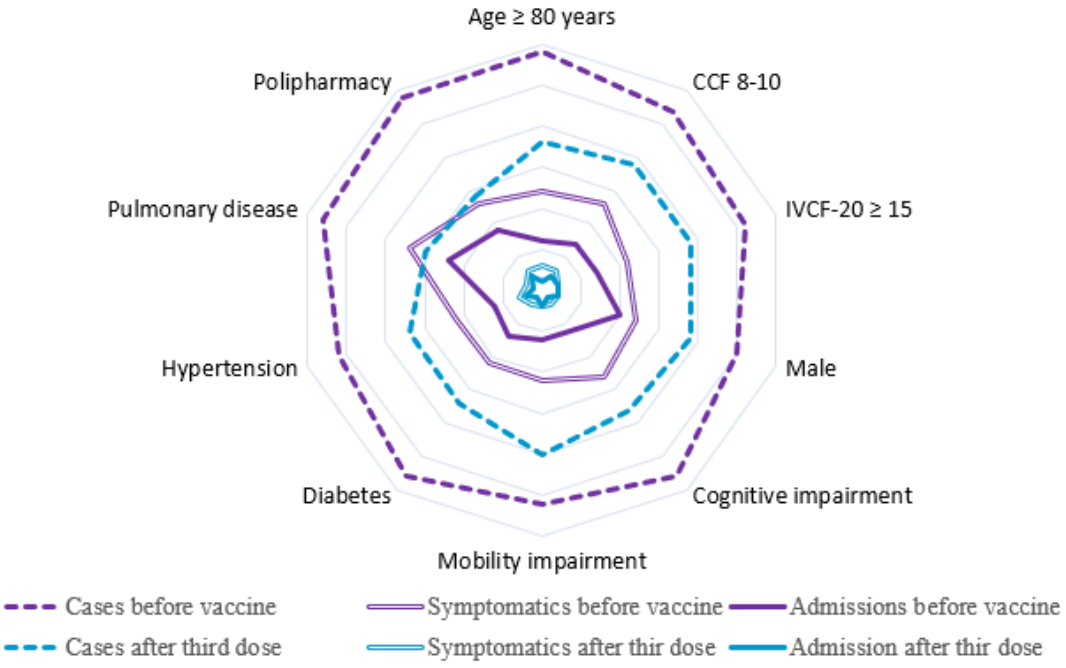
Figures



	Before the vaccine (%)	After the 1st dose (%)	After the 2nd dose (%)	After the 3rd dose (%)	Before the vaccine x 1 dose p-value	1st dose x 2nd doses p-value	2nd doses x 3rd doses p-value	Before the vaccine x 3rd dose p-value
Positive	191 (26.8)	25 (3.5)	28 (3.9)	136 (19.2)	**<0.001**	0.690	**<0.001**	**0.001**
Symptomatic	83 (11.7)	6 (0.8)	8 (1.1)	20 (2.8)	**<0.001**	0.560	**0.021**	**<0.001**
Emergency	46 (6.5)	6 (0.8)	6 (0.8)	13 (1.8)	**<0.001**	0.999	0.096	**<0.001**
Hospital	32 (4.5)	4 (0.6)	3 (0.4)	11 (1.6)	**<0.001**	0.593	**0.023**	**0.002**
Deaths	27 (3.8)	2 (0.3)	2 (0.3)	5 (0.7)	**<0.001**	0.999	0.285	**<0.001**

Figure 1

The number of positive cases, symptomatic participants, admission to emergency service, hospitalization and deaths, among LTCF residents, before the vaccine, and after the first, second and third vaccine doses. The red line corresponds to the proportion of positive cases in the general population.



	Before the vaccine									After the three vaccine doses								
	Positive cases			Symptoms			Admission			Positive cases			Symptoms			Admission		
	N	(%)	p	N	(%)	p	N	(%)	p	N	(%)	p	N	(%)	p	N	(%)	p
Age ≥ 80	119	31.4	0.3	51	43.2	0.9	34	28.8	0.08	74	27.7	0.8	14	18.6	0.1	10	13.3	0.3
CCF 8-10	130	31.1	0.5	63	48.4	**0.02**	45	34.6	**0.005**	94	29.6	0.2	16	16.8	0.3	12	12.6	0.3
IVCF-20 ≥ 15	139	30.1	0.2	61	44.2	0.4	41	29.7	0.5	99	28.6	0.4	15	15.0	0.4	13	13.0	0.1
Male	49	30.4	0.9	25	50.0	0.2	21	42.0	**0.02**	37	25.8	0.6	5	13.5	0.8	4	10.8	0.9
Cognitive impairment	142	30.6	0.2	64	45.3	0.1	43	30.4	0.2	93	27.2	0.5	12	12.7	0.1	9	9.5	0.3
Mobility impairment	116	27.9	**0.03**	53	45.2	0.4	38	32.4	0.1	89	30.3	0.06	13	14.4	0.6	11	12.2	0.6
Diabetes	42	31.1	0.6	17	40.4	0.7	12	28.5	0.9	26	26.2	0.6	3	11.1	0.5	2	7.4	0.6
Hypertension	112	28.6	0.4	47	42.3	0.9	32	28.8	0.9	73	25.7	0.1	13	17.5	0.3	9	12.2	0.5
Pulmonary disease	25	29.4	0.9	16	61.5	**0.03**	13	50.0	**0.008**	14	24.5	0.5	2	14.2	0.9	2	14.2	0.6
Polypharmacy	125	32.1	0.8	55	44.0	0.5	40	32.0	0.08	63	23.0	0.4	11	17.1	0.6	9	14.0	0.6

Figure 2

The risk factors associated with a higher proportion of positive cases, symptomatic patients, and hospitalizations.

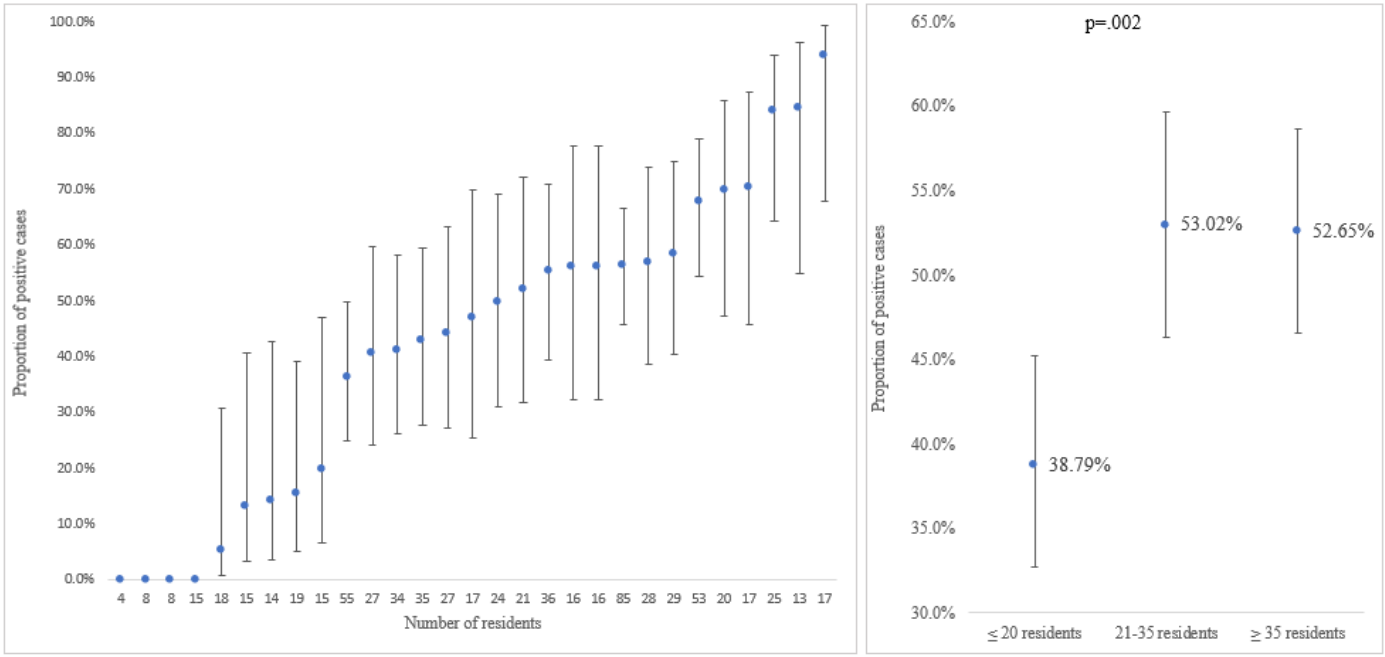


Figure 3

Correlation between the number of residents in each LTCF and the proportion of positive cases.

Supplementary Files

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- SupplementaryFiles.docx