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Evaluation of the Effectiveness of the Policy of Holding the Second Dose of Vaccination: Lessons from the Outbreak in Ho Chi Minh City

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Citation: Trang, V.T.T.; Van Truong, L.; Van Dat, T.; Elsheikh, R.; Anh, N.T.; Thang, D.X.; Thang, V.V.; Makram, A.M.; Huy, N.T.; Nagasaki University Collaborative. Evaluation of the Effectiveness of the Policy of Holding the Second Dose of Vaccination: Lessons from the Outbreak in Ho Chi Minh City. *Vaccines* **2023**, *11*, 293. https://doi.org/10.3390/vaccines11020293

Academic Editors: Shumaila Hanif and Ravinder Kumar

Received: 13 December 2022
Revised: 11 January 2023
Accepted: 21 January 2023
Published: 29 January 2023

Highlights:

- Many low-and-middle-income countries (LMICs) are facing massive delays in the administration of the second and even the first doses of the COVID-19 vaccines
- However, the delays in the administration of the second dose could help governments of LMICs administer the first dose of the vaccine on a larger scale.
- A more than 21-day delay in the administration of the second dose may further improve the efficacy of the first dose.
- A longer interval between vaccination and COVID-19 is associated with improved saturation of peripheral oxygen (SPO_2) rates, indicating that a second dose delay can help lower ICU admissions and mortality rates.

Abstract: The coronavirus disease 2019 (COVID-19) pandemic has caused a lot of ethical controversy in the equal provision of healthcare, including vaccination. Therefore, our study was designed to assess the impact of Ho Chi Minh City's policy to hold the second dose of the COVID-19 vaccine. Using a cross-sectional study design to assess low saturation of peripheral oxygen (SPO2) risk based on vaccination status, we included patients who were confirmed to have SARS-CoV-2 and were treated at home. The stepwise method was used to determine participants' low SPO2 risk-related factors. The average age of the 2836 respondents was 46.43 ± 17.33 (years). Research results have shown that seven factors are related to the low SPO2 status of participants, including age, sneezing, shortness of breath, coughing, and fainting as COVID-19 symptoms, the number of people living with COVID-19, and a history of lung disease. A statistically significant ($p = 0.032$) finding in this study was that fully vaccinated patients had a 6% lower risk of low SPO2 compared to the first dose less than 21 days group. This result was similar in the vaccine holder group ($p < 0.001$). Holding the second dose of the COVID-19 vaccine is associated with a lower SPO2 risk than that of fully

vaccinated patients. Therefore, this approach should be considered by governments as it could bring a greater benefit to the community.

Keywords: COVID-19; low- and middle-income countries; Vietnam; vaccination; health policy; holding the second vaccine dose

1. Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease was first identified in December 2019 in Wuhan, China [1]. It then spread rapidly on a global scale and, as of June 2022, there were nearly 600 million confirmed cases and over 6 million deaths [2]. To overcome the global burden of this devastating pandemic, rapid transmission control actions were widely implemented [3] and vaccines were developed with international collaborations [4]. Most studies suggest that vaccines are still effective against circulating variants, and possibly against severe disease and death [5]. However, how long vaccine-induced immunity lasts and how transmissibility has been affected by the vaccine are still unanswered questions [5,6].

The situation in low- and middle-income countries (LMICs) may be somewhat different from their counterparts (middle- and higher-income countries) due to various reasons. These include different incremental cost-effectiveness ratios of various vaccine types in different situations [7], vaccine hesitancy or low acceptance rates [8], the usage of vaccines with lower efficacy [9], and the lower overall purchasing capacity for the vaccines [10]. In Vietnam, an LMIC, the fourth wave of the pandemic lasted for more than eight months with a total of over two million confirmed COVID-19 cases and 35,480 deaths nationwide, of which the largest contribution came from Ho Chi Minh City, with over 20,000 deaths. According to the report of the Vietnam National Steering Committee on COVID-19 prevention and control, in the fourth wave, almost 100% of COVID-19 patients were infected with the Delta variant [11]. Infection control policies such as social distancing and mandatory mask-wearing did not seem to be effective at this stage [12].

An expected solution to the problem is vaccination; however, the Vietnamese government is facing a shortage of vaccine supplies and medical staff. The solution applied by the government was to prioritize vaccines based on people's risk factors and to administer the vaccines through a center-based policy, where people receive vaccines at larger, more crowded healthcare facilities [12]. The centralized vaccination process, however, has resulted in the exposure of uninfected individuals. Ho Chi Minh City government has applied the measure of vaccination with the first dose widely throughout the city, starting with the elderly, people who have comorbidities, and medical staff [11]. The solution has proved effective when counting the number of people having access to the COVID-19 vaccine; specifically, by the end of September 2021 in District 5, Ho Chi Minh City, 98% of people over 18 years old have received COVID-19 vaccines, of which 31% have received two doses [13]. However, this approach has generated controversy throughout implementation regarding doubts about the evidence for the benefit of a single dose of vaccine [12,14]. Therefore, our study was designed to evaluate the effectiveness of administering only one dose on the saturation of peripheral oxygen (SPO_2) index of future COVID-19 patients treated at home.

2. Methods

2.1. Study Design, Population, and Conduction

The cross-sectional descriptive study which follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (checklist available as Supplementary Table S1) [14] was conducted from 15 August to 15 November 2021, according to decision No. 980/UBND-VP issued on 14 August 2021 by the People's Committee

of District 5, Ho Chi Minh City, Vietnam. The main purpose of the study was to detect the severe condition of COVID-19 patients treated at home through a low SPO_2 index ($SPO_2 \leq 93\%$) [15], thus making a timely admission decision. All patients with confirmed COVID-19 being treated at home were provided a link by the medical staff to take part in a Zalo® group, a WhatsApp®-comparable software program, after which they were provided with a questionnaire study to assess their initial status.

2.2. Questionnaire Design and Survey Conduction

The questionnaire consisted of two parts. The first part had ten questions about basic demographics. The second part contained 40 questions about the clinical status and the 23 symptoms of COVID-19 based on the WHO report, SPO_2 index, highest and lowest body temperature in the last 24 h, and sneezing, which is a common finding in COVID-19 patients but not reported in the WHO list [15]. Our study divided the characteristics of COVID-19 vaccination into three groups, including the first dose less than 21 days group, which included patients who were infected with COVID-19 within 21 days following the administration of the first dose; the full vaccination group, which included patients with COVID-19 who have received the second dose at or after 21 days; and the delayed second dose group, which included COVID-19 patients who had had their first dose for more than 21 days but had not yet received their second dose. The time of 21 days after vaccination was established based on the evidence of stable immunity formation following the first and second doses of vaccine [16–18].

2.3. Data Analysis

We underwent a descriptive statistical analysis using T-test student, Chi-square, and ANOVA tests to compare demographic characteristics and clinical characteristics according to vaccination status and classification of SPO_2 index (normal SPO_2 and low SPO_2). Multivariable linear regression analysis was used to evaluate factors related to the low SPO2 of patients vaccinated against COVID-19, using the stepwise AIC method on the MASS package to determine the optimal model. All analyses were performed on R language version 4.1.0.

2.4. Ethical Considerations

Before the conduction of this study, data were collected from the home care program for COVID-19 patients at the People's Committee of District 5, Ho Chi Minh City (Decision No. 980/UBND-VP dated 14 August 2021). The benefits (e.g., increased knowledge about the policy impact) and probable burdens (e.g., time burden and some feelings of discomfort) were explained to all patients before the distribution of the survey. It was emphasized that there are no direct benefits to the patients, including financial incentives. It was also emphasized that patients can withdraw at any time by quitting the survey page; however, once the questionnaire has been submitted, there was no way of deleting the collected data as personal data were not collected. To ensure further confidentiality, the IP address tracking was disabled to disallow any attempt at identifying the enrolled participants. All data will be stored for five years after the publication of this manuscript.

Before moving on to the questionnaire page, electronic informed consent was obtained from all patients after reading all the details about the project. If the participant ticked "I consent to fill in the questionnaire", they were redirected to the questionnaire page. Otherwise, a skip-logic function ended the survey.

3. Results

Our program had a response rate of 38.5% (2548/6616 patients), of which 56.3% were female. The average age of participants was 46.43 ± 17.33 (years), and 7.3% (186/2548) of the patients were in the full vaccination group.

Table 1 shows that the rate of asymptomatic patients in the "first dose less than 21 days", "holding the second dose", and "full vaccination" groups tends to increase

statistically as the time from injection and number of vaccinations increases, with rates of 25.1%, 28.8%, and 39.3%, respectively. The number of symptoms with which the patients typically presented revealed a similar trend, with the average number of symptoms being 3.27 ± 3.47 (points), 3.12 ± 3.42 (points), and 1.92 ± 2.58 (points), respectively. The study results also showed that the lowest and highest temperature and the lowest SPO_2 recorded in the last 24 h of patients who were not previously vaccinated showed statistically significantly higher values than those of the vaccinated group. Furthermore, the number of presenting symptoms in the unvaccinated group was significantly higher than in the rest of the groups, with a positive rate of 17/23 symptoms.

Table 1. Baseline patients' characteristics according to their vaccination status.

Characteristics	Total N = 2548	First Dose Less Than 21 Days N = 905	Holding the Second Dose N = 1457	Full Vaccination N = 186	*p*-Value
Type of vaccination					<0.001 *
AstraZeneca	2202 (86.42%)	695 (76.80%)	1329 (91.21%)	178 (95.70%)	
Moderna	286 (11.22%)	177 (19.56%)	108 (7.41%)	1 (0.54%)	
Pfizer	33 (1.30%)	22 (2.43%)	9 (0.62%)	2 (1.08%)	
Not specified	27 (1.06%)	11 (1.22%)	11 (0.75%)	5 (2.69%)	
Total symptom scores (points)	3.09 (3.40)	3.27 (3.47)	3.12 (3.42)	1.92 (2.58)	<0.001 *
Day of infection (days)	8.11 (5.35)	9.21 (5.70)	7.45 (5.02)	7.86 (5.27)	<0.001 *
Asymptomatic					<0.001 *
No	719 (28.22%)	227 (25.08%)	419 (28.76%)	73 (39.25%)	
Yes	1829 (71.78%)	678 (74.92%)	1038 (71.24%)	113 (60.75%)	
Highest temperature	36.79 (0.66)	36.86 (0.77)	36.77 (0.60)	36.63 (0.55)	0.001 *
Lowest temperature	36.34 (0.48)	36.36 (0.50)	36.33 (0.47)	36.30 (0.50)	0.186
Lowest SPO_2	96.48 (3.36)	95.39 (4.27)	96.77 (3.03)	97.38 (1.63)	<0.001 *
Cough (Yes)	1064 (41.76%)	400 (44.20%)	596 (40.91%)	68 (36.56%)	0.094
Not eating well (Yes)	745 (29.24%)	303 (33.48%)	402 (27.59%)	40 (21.51%)	0.001 *
Stuffy nose (Yes)	703 (27.59%)	219 (24.20%)	450 (30.89%)	34 (18.28%)	<0.001 *
Decrease/loss of smell (Yes)	614 (24.10%)	209 (23.09%)	373 (25.60%)	32 (17.20%)	0.028 *
Fatigue (Yes)	517 (20.29%)	207 (22.87%)	295 (20.25%)	15 (8.06%)	<0.001 *
Insomnia (Yes)	466 (18.29%)	174 (19.23%)	276 (18.94%)	16 (8.60%)	0.002 *
Decrease/loss of taste (Yes)	435 (17.07%)	158 (17.46%)	249 (17.09%)	28 (15.05%)	0.729
Sore throat (Yes)	424 (16.64%)	136 (15.03%)	270 (18.53%)	18 (9.68%)	0.003 *
Muscle pain (Yes)	392 (15.38%)	163 (18.01%)	219 (15.03%)	10 (5.38%)	<0.001 *
Runny nose (Yes)	390 (15.31%)	150 (16.57%)	216 (14.82%)	24 (12.90%)	0.331
Headache (Yes)	369 (14.48%)	145 (16.02%)	213 (14.62%)	11 (5.91%)	0.002 *
Diarrhea (Yes)	322 (12.64%)	155 (17.13%)	161 (11.05%)	6 (3.23%)	<0.001 *
Chills (Yes)	308 (12.09%)	137 (15.14%)	159 (10.91%)	12 (6.45%)	<0.001 *
Dizziness (Yes)	224 (8.79%)	100 (11.05%)	118 (8.10%)	6 (3.23%)	0.001 *
Joint pain (Yes)	220 (8.63%)	119 (13.15%)	97 (6.66%)	4 (2.15%)	<0.001 *
Fever (Yes)	212 (8.32%)	100 (11.05%)	102 (7.00%)	10 (5.38%)	0.001 *
Shortness of breath (Yes)	163 (6.40%)	61 (6.74%)	98 (6.73%)	4 (2.15%)	0.049 *

Table 1. *Cont.*

Characteristics	Total N = 2548	First Dose Less Than 21 Days N = 905	Holding the Second Dose N = 1457	Full Vaccination N = 186	*p*-Value
Chest pain (Yes)	145 (5.69%)	46 (5.08%)	94 (6.45%)	5 (2.69%)	0.070
Red eyes (Yes)	115 (4.51%)	39 (4.31%)	69 (4.74%)	7 (3.76%)	0.780
Faint (Yes)	109 (4.30%)	48 (5.33%)	60 (4.15%)	1 (0.54%)	0.012 *
Nausea/vomiting (Yes)	75 (2.94%)	35 (3.87%)	35 (2.40%)	5 (2.69%)	0.120
Rash on skin (Yes)	59 (2.32%)	21 (2.32%)	36 (2.47%)	2 (1.08%)	0.582
Loss of speech (Yes)	27 (1.06%)	7 (0.77%)	19 (1.30%)	1 (0.54%)	0.478
Sneeze (Yes) †	540 (21.19%)	179 (19.78%)	324 (22.24%)	37 (19.89%)	0.329

Abbreviations: NA (not applicable). † Sneezing is a common clinical symptom but has not been reported as a symptom of COVID-19 according to WHO. * Indicates a statistically significant *p*-value of less than 0.05. The statistical tests used include ANOVA, chi-square, and Phi and Cramer's V.

Table 2 shows that the group of normal SPO_2 patients has a statistically significantly lower mean age than the low SPO_2 group. The average time from vaccination to confirmed COVID-19 in the low SPO_2 group was 24.33 ± 12.05 (days), which was statistically significantly lower than that of the normal SPO_2 group, with 27.52 ± 13.65 (days). According to the medical record, the low SPO_2 group had a statistically significantly higher rate of underlying disease (63.0%) than the normal SPO_2 group, including hypertension, cardiovascular disease, diabetes, other lung diseases, dementia, and kidney disease.

Table 2. Baseline characteristics of the included patients according to the SPO_2 status.

Characteristics	Total N = 1173	SPO_2 > 93% N = 1081	$SPO_2 \leq$ 93% N = 92	*p*-Value
Age (years)	45.21 (16.04)	44.40 (15.73)	54.77 (16.70)	<0.001 *
Gender				0.110
Male	463 (39.47%)	419 (38.76%)	44 (47.83%)	
Female	710 (60.53%)	662 (61.24%)	48 (52.17%)	
BMI (kg/m^2)	23.14 (3.73)	23.17 (3.78)	22.81 (3.16)	0.307
Time from vaccination to confirmed COVID-19 (days)	27.28 (13.56)	27.52 (13.65)	24.33 (12.05)	0.021 *
Time from confirmed COVID-19 to survey (days)	9.09 (5.18)	9.08 (5.14)	9.15 (5.59)	0.911
Healthcare staff				0.100
No	1167 (99.49%)	1075 (99.44%)	92 (100.00%)	
Yes	6 (0.51%)	6 (0.56%)	0 (0.00%)	
Number of people living with COVID-19 patients	2.60 (1.62)	2.57 (1.64)	2.88 (1.27)	0.033 *
Total symptom scores (points)	2.82 (3.26)	2.58 (3.11)	5.63 (3.72)	<0.001 *
Asymptomatic				<0.001 *
No	365 (31.12%)	357 (33.02%)	8 (8.70%)	
Yes	808 (68.88%)	724 (66.98%)	84 (91.30%)	
Type of vaccination				<0.001 *
AstraZeneca	994 (84.74%)	930 (86.03%)	64 (69.57%)	
Moderna	147 (12.53%)	127 (11.75%)	20 (21.74%)	
Pfizer	24 (2.05%)	19 (1.76%)	5 (5.43%)	
Not specified	8 (0.68%)	5 (0.46%)	3 (3.26%)	

Table 2. *Cont.*

Characteristics	Total N = 1173	SPO_2 > 93% N = 1081	$SPO_2 \leq 93\%$ N = 92	*p*-Value
Medical record				<0.001 *
No	645 (54.99%)	611 (56.52%)	34 (36.96%)	
Yes	528 (45.01%)	470 (43.48%)	58 (63.04%)	
Hypertension (Yes)	225 (19.18%)	198 (18.32%)	27 (29.35%)	0.015 *
Cardiovascular disease (Yes)	126 (10.74%)	108 (9.99%)	18 (19.57%)	0.008 *
Diabetes (Yes)	106 (9.04%)	91 (8.42%)	15 (16.30%)	0.019 *
Dementia (Yes)	19 (1.62%)	12 (1.11%)	7 (7.61%)	<0.001 *
Kidney disease (Yes)	14 (1.19%)	10 (0.93%)	4 (4.35%)	0.019 *
Other lung disease (Yes)	14 (1.19%)	4 (0.37%)	10 (10.87%)	<0.001 *
Obesity (Yes) †	258 (21.99%)	245 (22.66%)	13 (14.13%)	0.077
Systemic disease (Yes)	69 (5.88%)	62 (5.74%)	7 (7.61%)	0.615
Cancer (Yes)	33 (2.81%)	28 (2.59%)	5 (5.43%)	0.175
Liver disease (Yes)	24 (2.05%)	24 (2.22%)	0 (0.00%)	0.250
Asthma (Yes)	11 (0.94%)	10 (0.93%)	1 (1.09%)	0.594
COPD (Yes)	8 (0.68%)	8 (0.74%)	0 (0.00%)	1.000
Organ transplants (Yes)	3 (0.26%)	3 (0.28%)	0 (0.00%)	1.000
Down syndrome (Yes)	3 (0.26%)	3 (0.28%)	0 (0.00%)	1.000
HIV/AIDS (Yes)	3 (0.26%)	3 (0.28%)	0 (0.00%)	1.000
Sickle cell anemia (Yes)	3 (0.26%)	3 (0.28%)	0 (0.00%)	1.000
Addiction (Yes)	3 (0.26%)	3 (0.28%)	0 (0.00%)	1.000

Abbreviations: BMI (body mass index); COPD (chronic obstructive lung disease); HIV/AIDS (human immunodeficiency virus/acute immunodeficiency syndrome). † Obesity is defined according to the Western Pacific region standards, with a body mass index (BMI) of $\geq$25 kg/m^2 [19]. * Indicates a statistically significant *p*-value of less than 0.05. The statistical tests used include T-test, chi-square, and Phi and Cramer's V.

Figure 1 shows that the total number of symptoms corresponding to patients taking the first dose less than 21 days, holding the second dose, and fully vaccinated reached the highest value on the first day after a confirmed infection with SARS-CoV-2 and tended to decrease and maintain a steady rate over the next ten days.

Figure 2 shows that patients in the first dose less than 21 days group had an average SPO_2 value of 95.4 $\pm$ 4.3%, the index of holding the second dose group was 96.8 $\pm$ 3.0%, and the full vaccination group had an index of 97.4 $\pm$ 1.6%. The group of patients with a first dose from 21 days to 50 days and a full vaccine from 21 days to 65 days showed a stable SPO_2 index above 97%.

Table 3 shows that a ten-year increase in patient age was associated with a 2% (95% CI: 1–3%, $p < 0.001$) increased risk of low SPO_2. Each increase in cohabitation was associated with a 1% (95% CI: 0–2%, $p = 0.025$) increase in the risk of low SPO_2. Patients with a history of lung diseases were associated with a 35% (95% CI: 21–51%, $p < 0.001$) increased risk of low SPO_2. The female gender was associated with a 5% (95% CI: 2–7%, $p = 0.002$) reduction in the risk of low SPO_2. Positive symptoms including shortness of breath, sneezing, fainting, and cough were significantly associated with an increased risk of low SPO_2 of 30%, 10%, 8%, and 5%, respectively. Patients infected with SARS-CoV-2, including both the first dose of less than 21 days and full vaccination groups, were statistically significantly associated with a 6% reduction in the risk of low SPO_2. The above model recorded a good forecast of the low SPO_2 situation, expressed through the area under the curve (AUC) reaching 86.4%. Supplementary Table S2 presents the same models along with a comparison between males and females with respect to the other covariates.

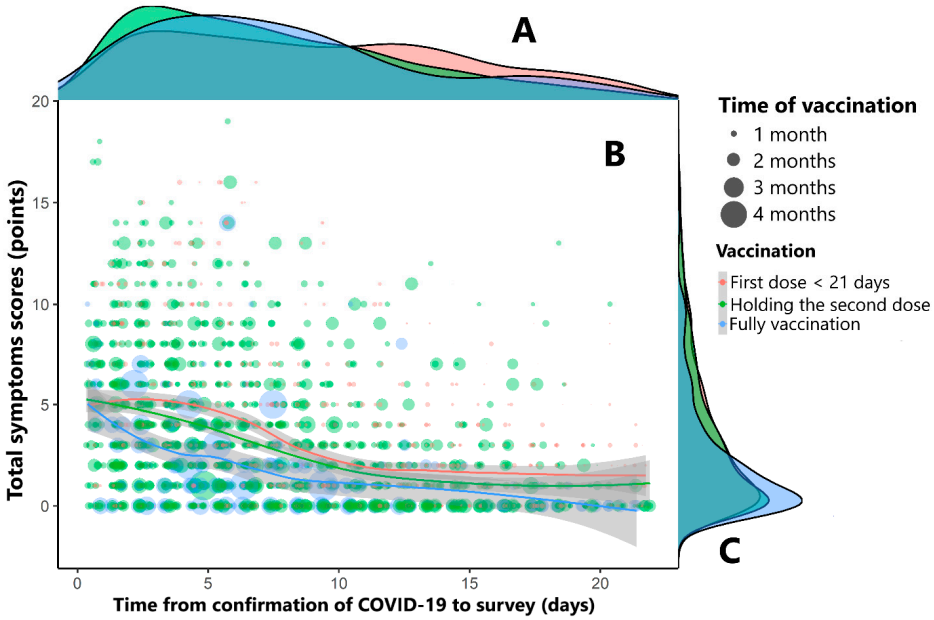

Figure 1. The relationship between the duration of COVID-19, the number of clinical symptoms, and vaccination type. Three colors have been used to represent the characteristics of COVID-19 patients, as follows: red represents patients with "first dose < 21 days", green for "holding the second doses", and blue for "fully vaccinated". (**A**,**C**) use density histograms to show the distribution of the study subjects from the time of illness to the time of the survey, and the number of symptoms of COVID-19 patients. (**B**) uses a scatterplot to show the relationship between the duration of illness and the number of symptoms, and the size of the circle corresponds to the time between the last vaccination and the survey. Loess regression was used to draw smoothing lines according to the vaccination status of COVID-19 patients. Time of vaccination refers to the time from the last dose of the vaccine to the time of study participation.

Table 3. Univariable and multivariable logistic regression model to predict low SPO_2.

	Univariable			Multivariable		
Predictors	**Estimates**	**95% CI**	***p*-Value**	**Estimates**	**95% CI**	***p*-Value**
(Intercept)	–	–	–	0.96	0.91–1.02	0.237
Age (each 10 years)	1.03	1.02–1.04	<0.001 *	1.02	1.01–1.03	<0.001 *
Number of people living with COVID-19 patients in the same household	1.01	1.00–1.02	0.02 *	1.01	1.00–1.02	0.025 *
Lung diseases [#]						
No		Reference			Reference	
Yes	1.54	1.38–1.73	<0.001 *	1.35	1.21–1.51	<0.001 *
Gender						
Male		Reference			Reference	
Female	0.97	0.94–1.00	0.028 *	0.95	0.93–0.98	0.002 *
Shortness of breath						
No		Reference			Reference	
Yes	1.37	1.28–1.46	<0.001 *	1.30	1.22–1.38	<0.001 *
Sneeze						
No		Reference			Reference	

Table 3. *Cont.*

	Univariable			Multivariable		
Predictors	**Estimates**	**95% CI**	***p*-Value**	**Estimates**	**95% CI**	***p*-Value**
Yes	1.16	1.11–1.20	<0.001 *	1.10	1.06–1.15	<0.001 *
Fainting						
No		Reference			Reference	
Yes	1.12	1.05–1.20	0.001 *	1.08	1.02–1.15	0.014 *
Cough						
No		Reference			Reference	
Yes	1.12	1.09–1.15	<0.001 *	1.05	1.02–1.08	0.001 *
Vaccination						
First dose less than 21 days		Reference			Reference	
Holding the second dose *	0.94	0.91–0.97	0.001 *	0.94	0.91–0.97	<0.001 *
Full vaccination	0.91	0.85–0.97	0.003 *	0.94	0.88–0.99	0.032 *
Observations		1142			1142	
R^2					0.186	
AUC					86.4%	

* The holding the second dose group includes COVID-19 patients who have had their 1st dose for more than 21 days but have not received their 2nd dose. # Lung diseases included chronic obstructive lung disease, asthma, and other lung diseases. * Indicates a statistically significant *p*-value of less than 0.05.

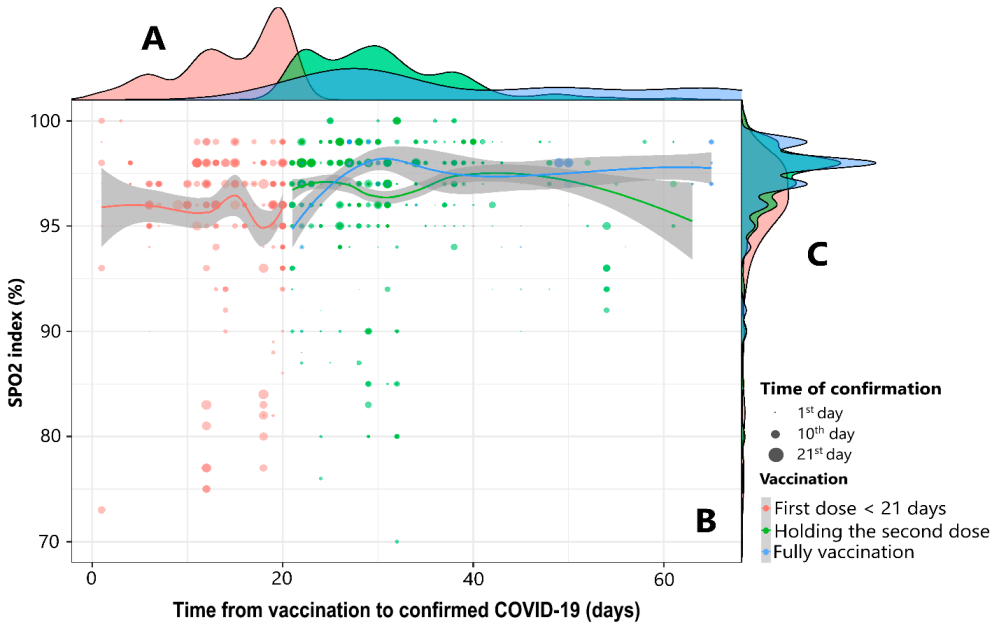

Figure 2. The relationship between the time from vaccination to confirmed COVID-19 and the SPO_2 index by the time of confirmation and vaccination status. Three colors have been used to represent the characteristics of COVID-19 patients, as follows: red represents patients with "first dose < 21 days", green for "holding the second doses", and blue for "fully vaccinated". (**A**,**C**) use density histograms to show the distribution of the study subjects from the time of illness to the time of the survey and the SPO_2 index. (**B**) uses a scatterplot to show the relationship between the duration of illness and the SPO_2 index, and the size of the circle corresponds to the time between the last vaccination and the survey. Loess regression was used to draw smoothing lines according to the SPO_2 index of patients. The time of vaccination refers to the time from the last dose of the vaccine to the time of study participation.

4. Discussion

Our study aimed to determine the factors associated with low SPO_2 in Vietnamese post-vaccination COVID-19 patients treated at home to evaluate the effects of delaying the second dose or administering only one dose of vaccination. Through a multivariable logistic regression model, nine factors that affected COVID-19 patients' SPO_2 index were identified. A 10-year increase in age, developing sneezing, shortness of breath, coughing, and fainting as COVID-19 symptoms, co-living with an additional one person above the reported average, and having a history of lung disease were all associated with a higher risk of developing low SPO_2. Contrastingly, COVID-19 patients belonging to the group of stable immunity (full vaccination group or holding second dose group) and female gender were found to be linked to a lower risk of developing low SPO_2. Furthermore, vaccination was associated with an increased proportion of asymptomatic patients, with 15.3%, 25.1%, 28.8%, and 39.3% asymptomatic rates in patients who did not receive any dose, first dose less than 21 days, holding the second dose, and full vaccination, respectively.

In 2021, Moghadas et al. evaluated the optimal time for the administration of the second dose of the Moderna and Pfizer-BioNTech vaccines. They found a significant reduction in infection, hospitalization, and death rates when the second dose was deferred 12–15 weeks from the first dose less than 21 days [20]. Similarly, Silva et al. studied the ideal delay between COVID-19 dose administration and its effect on ICU admission rates. As in our study, they reported that a minimum of a 4-week delay in second dose administration is expected to decrease ICU admission rates, as it gives time to the first dose less than 21 days to achieve a higher efficacy [21]. An Oxford study carried out to assess the reactogenicity and the immunogenicity following the delay in the administration of the ChAdOx1 nCoV-19 included participants with 8–12, 15–25, and 44–45-week intervals between the doses. Antibody levels measured 6 months (median = 3738, IQR = 1824–6625) after the administration of the second dose were found to be significantly higher ($p < 0.001$) than those with a 15–25-week interval between the first and second doses (median = 1860, IQR = 917–4992), showing that the delay in the administration of the second dose of AstraZeneca vaccine increases its efficacy [22].

Regarding the factors associated with worse COVID-19 outcomes, a systematic review was conducted to determine the factors associated with higher mortality risk following SARS-CoV-2 infection. Consistent with our study, old age, male gender, and previous lung diseases had a positive correlation with COVID-19 mortality. A prolonged inflammatory response following the weakening of immunity and the excessive release of type 2 cytokines was found to be the reason behind worse outcomes in elderly patients [23]. Moreover, hypoxia in COVID-19 patients is associated with viral lung injury, with alternating regions of hyperventilation and hypoventilation [24]. Therefore, sneezing influences airflow and ventilation pressure change [25], which may be responsible for the more common occurrence of low SPO_2 in this group of patients.

Our findings suggest that several benefits can be obtained from holding the second dose of vaccination, which are comparable to the benefits seen in the full vaccination group. Achieving the full effectiveness of the first dose in less than 21 days was shown to be associated with higher asymptomatic rates, and less severe outcomes. A longer interval between vaccination and COVID-19 infection was further associated with improved SPO_2 rates, which indicates that a second dose delay could contribute to lowering ICU admissions and mortality rates. However, our findings should be cautiously interpreted on a global scale, due to various reasons including the higher use rate of AstraZeneca and the lower BMI when compared to higher-income countries, as well as the statistically significant differences between the two groups, detected in Table 2.

Although, as far as we know, this is the only study investigating the delay in the administration of COVID-19 vaccines in Vietnam, better results could have been obtained by investigating individual vaccines rather than unspecified vaccines as was carried out by Payne et al. in the UK [26]. As for the analysis of individual COVID-19 vaccines, a study in Canada by Hall et al. reported that extending the interval between the two doses

of the Pfizer-BioNTech vaccine from 3–6 weeks to 8–16 weeks leads to a better antibody response in female healthcare workers [27,28]. The same results were reported earlier for the AstraZeneca vaccine for both the second and the booster dose [22]. However, we were not able to do so due to the limited variability of sample sizes for each vaccine type. Another limitation of this study is the study design, which did not allow for a follow-up. Moreover, we were not able to assess more detrimental clinical features and outcomes, choosing to analyze only the SPO_2. Lastly, it is important to consider the findings of this study in the context of wider public health in Vietnam, where nearly a quarter of the population is hesitant to receive the vaccine or offer it to their children [29,30]. Moreover, people with medical or allergic history are more likely to decline vaccination, further contributing to the health inequalities gap related to vaccination [29].

5. Conclusions

The study shows that holding the second dose of vaccination against COVID-19 is as effective as obtaining a full vaccination in terms of increasing the asymptomatic rate and reducing the rate of low SPO_2. Moreover, the SPO_2 rate was different in the unvaccinated patients and the group receiving the first dose of the vaccine less than 21 days following SARS-CoV-2 infection. Our study provides further evidence for policymakers about how vaccine distribution ensures maximum protection for the community in the face of limited vaccine supply. However, the study also suggests the need for policies to limit the process of cross-contamination during vaccination, helping to improve the effectiveness of patient protection and avoid outbreaks related to an infection at the vaccination site. Although it has not been given sufficient attention yet, sneezing was present in 21.4% of our sample and was associated with a 10% increased risk of low SPO_2 together with an increased risk of disease transmission.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/vaccines11020293/s1, Supplementary Table S1: STROBE Statement—Checklist of items that should be included in reports of cross-sectional studies, Supplementary Table S2: Univariable and multivariable logistic regression model to predict low SPO_2, sub-grouped by gender.

Author Contributions: V.T.T.T. and L.V.T. were principally responsible for formulating the study idea and design. All authors wrote and revised the protocol and the manuscript. All authors reviewed and approved the final version of the manuscript under the supervision of A.M.M. and N.T.H. The Nagasaki University Collaborative authors were in charge of data collection. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Our study used registry data from Ho Chi Minh City's COVID-19 home care program according to ethical approval decision No. 980/UBND-VP issued on 14 August 2021 by the People's Committee of District 5, Ho Chi Minh City, Vietnam. The data extracted from the records did not include personal information such as the patient's name, telephone number, or home address. Written informed consent was obtained from all participants after explaining all aspects of the study, including the non-monetary benefits and the probable risk of increased anxiety during the study. All consent forms were kept in a safe place by the first author.

Informed Consent Statement: Written informed consent was obtained from all participants after explaining all aspects of the study, including the non-monetary benefits and the probable risk of increased anxiety during the study. All consent forms were kept in a safe place by the first author.

Data Availability Statement: All the data used in this study are available upon contacting the corresponding author (Nguyen Tien Huy) at tienhuy@nagasaki-u.ac.jp.

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Acknowledgments: The authors would like to thank Truong Minh Kieu (Chairman of District 5, Ho Chi Minh City), Trinh Thi Phuong Thao (Deputy Health Department of District 5, Ho Chi Minh City), and Khuong Le Thuy Anh (Chairman of Ward 14, District 5, Ho Chi Minh City) for authorizing the authors to approach patients and supporting human resources to monitor patients during the treatment of patients with COVID-19 at home. We would also like to thank the medical staff of District 5, along with the members who followed the patients, including Nguyen Thanh Trung (Ninh Diem General Hospital); Nguyen Thi To Van (Ward 12 medical station), Duong The Vinh, Lam Hoang Tinh, Le Huynh Tam, Nguyen Huu Thang (University of Medicine and Pharmacy at Ho Chi Minh), Luong Thi Huyen Trang (Thuong Tin General Hospital), Dinh Van Dung (Traditional Medicine Hospital, Thanh Hoa, Vietnam), Diep Thi Thanh Hang; Nguyen Quoc Anh, Dang Xuan Thang (Duy Tan University, Danang, Vietnam), Nguyen Quy Vu (Vietnam Military Medical University), Nguyen Tuan Anh; Nguyen Thuy Diem, Ngo Thanh Trung (local volunteers), and Nguyen Xuan Giang (Vietnam National University of Forestry; Hai Phong University of Medicine And Pharmacy, Hai Phong, Vietnam).

Conflicts of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Abbreviations

ANOVA	analysis of variance
BMI	body mass index
COPD	chronic obstructive lung disease
COVID-19	coronavirus disease 2019
HIV/AIDS	human immunodeficiency virus/acute immunodeficiency syndrome
LMICs	low- and middle-income countries
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SPO_2	saturation of peripheral oxygen

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