Int J Epidemiol Health Sci 2022;3: e26
doi: http//doi.org/10.51757/IJEHS.3.2.2022.248387

Original Article

Vaccination coverage as a predictor of COVID-19 case fatality rates in Malaysia

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Cite this article: Tang, K.H.D. Vaccination coverage as a predictor of COVID-19 case fatality rates in Malaysia. Int J Epidemiol Health Sci 2022; 3: e26. Doi: 10.51757/IJEHS.3.2.2022.248387.

Abstract

Vaccination has offered the possibility of resuming life as it was before COVID-19. Despite greater vaccine coverage, new COVID-19 cases have continued to occur and have grown in certain places. The goal of this study is to see if there are any links between daily COVID-19 case fatality rates, vaccination coverage, and daily COVID-19 new cases and fatalities in Malaysia. Its purpose is to compare COVID-19 case fatality rates before and after immunization to discover if there is a statistically meaningful change. It also wants to figure out what factors influence COVID-19 case fatality rates. For non-parametric statistical analysis, this study gathered data on daily new cases and fatalities of COVID-19, as well as daily vaccination coverage in Malaysia, from official platforms and government offices. It looked at the Spearman's correlations between daily COVID-19 case fatality rates, daily new COVID-19 cases and fatalities, and Malaysian immunization coverage. The Mann-Whitney U Test was used to compare the rates of daily COVID-19 case fatalities before and after vaccination. It created a multiple regression model to find the significant predictors of case fatality rates on a daily basis. Daily new COVID-19 cases and deaths, as well as vaccination coverage, are all positively associated in this study. It shows that case fatality rates are lower after vaccination than before immunization, and that the difference is statistically significant. The number of people who have been fully vaccinated per 100 people is a strong predictor of daily case fatality rates dropping.

Keywords: COVID-19, Fatality, Vaccination, Hygiene, SARS-CoV-2, Malaysia

Introduction

Since its inception in Wuhan, China in December 2019, the coronavirus disease 2019, also known as COVID-19, has decimated the world (1, 2). COVID-19's rapid spread has prompted a slew of control measures around the world, including self-quarantine, the closure of non-essential services, the prohibition of social gatherings, travel restrictions, physical separation, personal hygiene, and regular sanitization of public spaces and premises (3). These measures, particularly the shutdown of non-essential services and harsh travel restrictions, have resulted in far-reaching socioeconomic consequences, ranging from affected employment, job security, learning, and psychological welfare to economic slowdown at national and global levels (4, 5).

In several countries, lockdown has been adaptively tightened and eased to mitigate the socioeconomic repercussions, as seen in the COVID-19 examples (3). COVID-19 vaccine research and development began shortly after local containment failed and a pandemic appeared likely (6). COVID-19 vaccinations are divided into five categories. The viral vector vaccines combine the genetic material of the virus that causes COVID-19, SARS-CoV-2, with a harmless virus to stimulate immune response and create immunological memory. The genetic vaccines include disease-causing regions of the SARS-CoV-2 genetic material known as messenger RNA, which codes for a viral protein capable of inducing an immune response (7). SAR-CoV-2 is inactivated or killed in inactivated vaccines, and it stimulates an immune response when it enters the human body. Attenuated vaccines are similar to inactivated vaccines, except instead of killing the virus, they carry weakened virus (8). Protein vaccines containing SARS-CoV-2 proteins capable of generating immunological memory are the fifth type of vaccine (6). The introduction and licensing of vaccinations provide promise for bringing COVID-19 under control through herd immunity (8).

Currently, the viral vector, genetic, and inactivated types of vaccines are on the market, while attenuated and protein vaccines are still in clinical trials (9). Though vaccines are not a cure for COVID-19, they are widely regarded as the most practical and cost-effective COVID-19 protection available to the general public (6). Vaccination began on February 24, 2021 in Malaysia, but progress was painfully slow until June 2021. (10). In comparison to 1 May 2021, when only 2.8 percent of the population had gotten at least one dose of the vaccine, by 1 July 2021, the percentage had risen to 19.1 (11).

The daily COVID-19 instances were increasing in lockstep with the increased immunization rate. Most Malaysian states removed mobility limitations on March 5, 2021, leading to an upsurge in daily cases and the nationwide restoration of movement controls from May 12 to June 28. (12, 13). A four-phase National Recovery Plan was established on June 15, 2021, to allow for a more varied implementation of COVID-19 control measures in different states with different COVID-19 prevalence, and thus in different phases of the National Recovery Plan (14). The number of new COVID-19 cases and deaths increased daily as the number of new COVID-19 cases and deaths climbed (15). Vaccination efforts in the country have gained traction in the meanwhile. This raises the question of whether immunization is effective enough to protect the population from COVID-19. Furthermore, COVID-19 was contracted by people who had been partially and fully immunized (16).

While official data revealed that the majority of daily new COVID-19 cases were asymptomatic or moderate, the rising number of new cases and deaths was clearly a blow to hopes that immunization may bring COVID-19 under control, if not eradicate it entirely (17). The development of the delta variation adds to the skepticism. Few research has looked into whether vaccination affects COVID-19 case fatality rates in Malaysia, or whether it contributes to any differences in case fatality rates before and after vaccination. In the absence of non-pharmaceutical interventions, a greater vaccination rate with lower efficacy vaccines could result in a much lower risk of COVID-19 occurrences than a lower vaccination rate with better efficacy vaccinations, according to a simulated research (18). Real-world data has yet to be used to validate the simulation. Furthermore, research has linked BCG immunization to COVID-19 deaths (19, 20). However, no research has compared COVID-19 case fatality rates in different regions before and after immunization. The goal of this study is to evaluate daily case fatality rates before and after vaccination, as well as to see if daily new cases of COVID-19, vaccination coverage, and daily COVID-19 deaths are all linked to case fatality rates.

Methods

The Center for System Science and Engineering (CSSE) at John Hopkins University provided data on new COVID-19 cases per million population and new deaths per million population on a daily basis (15). Data on total vaccinations per 100 population, persons vaccinated per 100 population, and people fully vaccinated per 100 population in Malaysia was obtained from the global database of COVID-19 vaccines developed by Mathieu et al. (11). The ratios of cumulative new fatalities owing to COVID-19 to cumulative new COVID-19 cases on a daily basis within the periods of interest, expressed as percentages, were used to construct daily case fatality rates (21).

The case fatality rates after vaccination were compared to the case fatality rates throughout the same time period before vaccination to see if there were any differences in case fatality rates pre- and post-immunization. Vaccination in Malaysia began on February 24, 2021, however official data on vaccination rates was not available until February 28, 2021. As a result, the post-vaccination case fatality rates cover a period of 178 days, from February 28, 2021, to August 24, 2021, the cut-off date for data analysis in this study. The pre-vaccination case fatality rates were acquired for the 178 days prior to February 28, 2021 (from September 3, 2020 to February 27, 2021).

To see if the pre-vaccination and post-vaccination case fatality rates in Malaysia were significantly different, statistical analyses were performed. The datasets were subjected to a normality test to decide whether parametric or non-parametric tests will be used in the analysis. The Shapiro-Wilk Normality Test yielded a result of $p < 0.05$, suggesting that the assumption of normally distributed data was rejected (22). As a result, non-parametric analyses were used to see if the datasets were substantially different using the Mann-Whitney U Test. Spearman's correlation was used to see if case fatality rates were linked to vaccination rates, daily new COVID-19 cases, and daily deaths from COVID-19. Following that, a multiple regression analysis was used to determine the primary factors that contributed to the variances in case fatality rates.

Results

Table 1 displays descriptive statistics for new COVID-19 cases and deaths in the post- and pre-vaccination periods, with the post-vaccination period running from 28 February 2021 to 24 August 2021 and the pre-vaccination period spanning from 3 September 2020 to 27 February 2021. New cases and deaths per million population in the post-vaccination period averaged 224.83 and 2.33, respectively, compared to 50.16 and 0.17 in the pre-vaccination period. The mean case fatality rates after and before immunization are 0.55 and 0.69, respectively. In terms of vaccination coverage, an average of 23.37 vaccines were administered per 100 people throughout the post-vaccination period of interest. In each 100 persons, 15.30 people were vaccinated and out of which 8.08 people were fully vaccinated (received two doses of vaccines). The number of vaccines provided during that time period was larger than the average number of persons vaccinated, because some of those who were vaccinated also received their second doses of vaccine, resulting in a higher vaccination rate per 100 people. Because not everyone who was vaccinated during that time received their second dosage, the number of people who were fully vaccinated would be smaller. Skewness and kurtosis are measures of normality, with a skewness of 0 indicating a symmetrical dataset and a kurtosis of 3 indicating the sizes of two tails that mimic the normal distribution (22). In other words, perfect normalcy is demonstrated by a skewness of 0 and a kurtosis of 3. Table 1 demonstrates varied degrees of deviation from normality, which agrees with the results of the Shapiro-Wilk Normality Test, which confirms that the data does not have normal distributions. Non-parametric statistical analyses were sought as a result.

Figure 1 shows daily new COVID-19 instances from September 3, 2020, to August 24, 2021, for the pre- and post-vaccination periods of interest. It reveals that daily new COVID-19 cases have been increasing since April 2021, despite a modest decline in June 2021, which was followed by an alarming spike. This happened when the immunization program began in February 2021. This period of upsurge also coincided with the implementation of Conditional Movement Control (CMCO) in some states and Recovery Movement Control Order (RMCO) in a few states, during which a number of restrictions involving interstate travel, religious activities, meetings, and events, as well as non-essential services, were gradually and adaptively lifted (12). However, because the number of daily COVID-19 cases increased, Movement Control Orders (MCO), the foremost severe kind of lockdown, were applied selectively, culminating in an exceedingly national MCO from May 12 to day, 2021. (13). This resulted during a decrease within the number of daily COVID-19 cases by the top of June 2021. Following that, a replacement COVID-19 control referred to as the National Recovery Plan (NRP) was implemented with selective implementation and lockdown relaxation (23). With the deployment of the NRP and enhanced immunization, the daily COVID-19 cases increased.

Figure 2 shows COVID-19-related deaths on a daily basis. Daily deaths fluctuated in lockstep with daily new cases, with the most recent substantial upsurge mirroring the daily COVID-19 cases. Unlike daily deaths, daily case fatality rates followed a distinct pattern, with a downward trend starting on September 3, 2020, followed by a plateau, and then a climb from June 2021 onwards, in line with the increase in daily new cases and new deaths of COVID-19.

Figure 4 shows that vaccination coverage has increased fast after June 2021, albeit it was modest for the first three months after the program began on February 24, 2021. Compared to its neighbouring countries, such as Singapore, which began a COVID-19 vaccination drive on December 30, 2020, and Indonesia, which began the drive on January 13, 2021, Malaysia's vaccination push was slower due to the Ministry of Health's delayed licensing of vaccines (24). The rate of vaccination was painfully slow during the early stages, due to a variety of factors including a lack of vaccine supplies, logistical issues with the digital vaccination appointment and certificate system via a mobile application, a lack of coordination and transparency among vaccine recipients, as well as fake vaccine news and overcrowding of vaccination centers, which were limited at the time. (24) Only 1.72 percent of Malaysia's population was fully vaccinated as of May 1, 2021, compared to 2.79 percent in Indonesia, 5.73 percent in Cambodia, and 23.56 percent in Singapore. Nonetheless, it was greater than Thailand's 0.55 percent and the Philippines' 0.26 percent (11).

From June 2021 onwards, the vaccination rate increased dramatically due to improved logistics, coordination, and the opening of more vaccination centers as a result of the vaccination program's experience. On August 24, 2021, a total of 99.53 vaccines were administered per 100 persons, with 57.57 people receiving vaccinations and 41.96 people receiving full vaccinations (Figure 4). This means that more than half of Malaysia's population has been vaccinated, with the majority of those who have got the second dosage of vaccination. Full vaccine coverage had exceeded Indonesia, with 11.81 percent, and was only slightly behind Cambodia, with 47.52 percent, while Singapore remained at the top of the list with 79.74 percent. In fact, coverage was higher than in industrialized Asian countries like Japan, where 42.92 percent of people were fully vaccinated, and South Korea, where 25.42 percent were fully vaccinated (11).

The daily case fatality rates before and after immunization were compared using the Mann-Whitney U Test to see if they were statistically different in both times. The asymptotic significance, p, of the data pair was < 0.05, according to the Mann-Whitney U Test results in Table 2. Pre-vaccination case fatality rates (N = 178) have a higher mean rank (196.12) than post-vaccination case fatality rates (N = 178) with a mean rank of 160.88, according to the Mann-Whitney U Test. There is a statistically significant difference (U = 12706.00, $p < 0.05$).

To determine how the values of the variables vary in relation to one another and whether the changes are statistically significant, a Spearman's correlation was used. Table 3 shows that all of the variables are strongly, positively, and statistically associated. New cases of COVID-19 per million population are significantly correlated with new fatalities (rs = 0.905), showing that an increase in new cases is substantially linked to an increase in new deaths. Similarly, because vaccination was rampant during the period when new cases of COVID-19 and deaths connected with them skyrocketed, the associations were likewise quite high (Table 3). The number of vaccines administered was reported as the number of vaccinations per 100 population. As a result, as the number of vaccinations per 100 people grew, the value of the other two variables increased as well, resulting in strong positive associations (Table 3). In reality, the number of persons vaccinated per 100 population (rs = 1.000) is proportional to the number of vaccinations per 100 population. New cases of COVID-19 per population (rs = 0.907), new deaths per million population (rs = 0.877), vaccinations per 100 population (rs = 0.913), people fully vaccinated per 100 population (rs = 0.914), and people vaccinated per 100 population (rs = 0.913) are all positively correlated with case fatality rates. All of these variables' post-vaccination uptrends reflect this as well (Figures 1, 2, 3, and 4). However, despite demonstrating an upward trend (Figure 3), the post-vaccination daily case fatality rates were statistically significantly lower than the pre-vaccination rates (Table 2).

To see how well the independent factors predicted the daily case fatality rates, multiple regression was used. Due to collinearity (rs = 1.000) between vaccinations per 100 population and people vaccinated per 100 population (Table 3), vaccinations per 100 population was excluded from the regression model (25). The regression model has a R = 0.971, showing a high level of prediction, and an $R^2 = 0.943$, suggesting that the independent variables account for 94.3 percent of the variability in the dependent variable, i.e., daily case fatality rates. The coefficients of three independent variables, namely new fatalities per million population, persons completely vaccinated per 100 population, and people vaccinated per 100 population, are statistically significant ($p < 0.05$) in the regression results shown in Table 4. The unstandardized coefficients demonstrate that the daily case fatality rates rise as new deaths per million population (B = 0.009) and individuals vaccinated per 100 population (B = 0.019) rise. The positive link between vaccination rates per 100 individuals and daily case fatality rates is likely owing to the rising momentum of vaccination, which coincided with an increase in new deaths due to COVID-19 and daily case fatality rates. However, the drop in daily case fatality rates with an increase in completely vaccinated people per 100 population (B = -0.016) is noteworthy. This means that for every additional completely vaccinated person per 100 population, the daily case fatality rate drops by 0.016 percent.

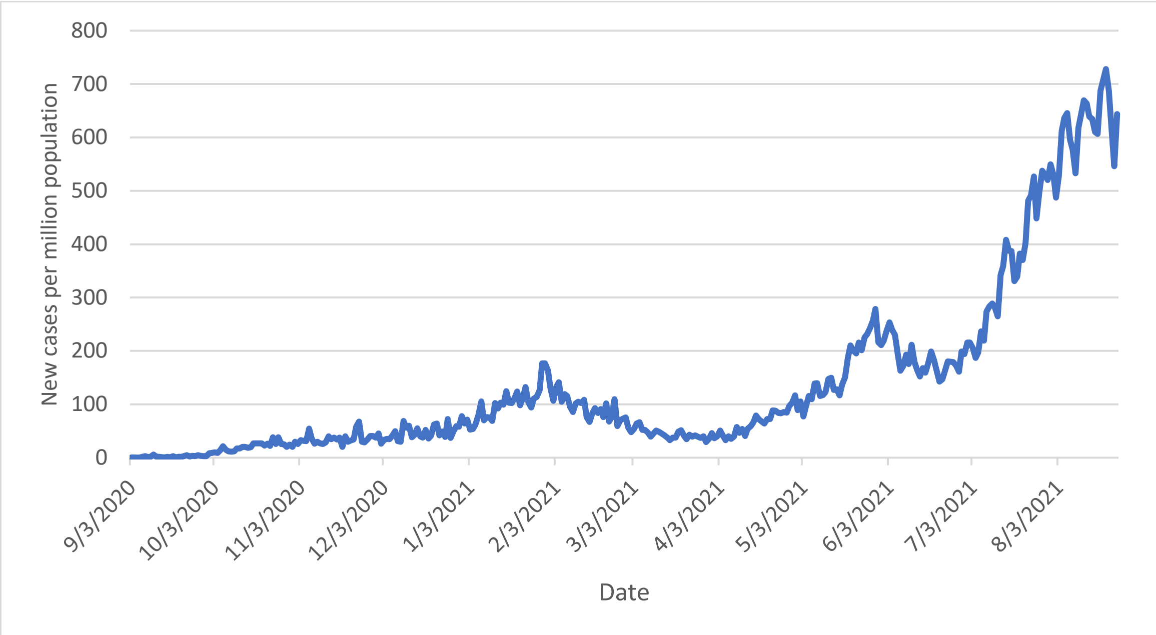

Figure 1. New Cases of COVID-19 per Million Population from 3 September 2020 to 24 August 2021

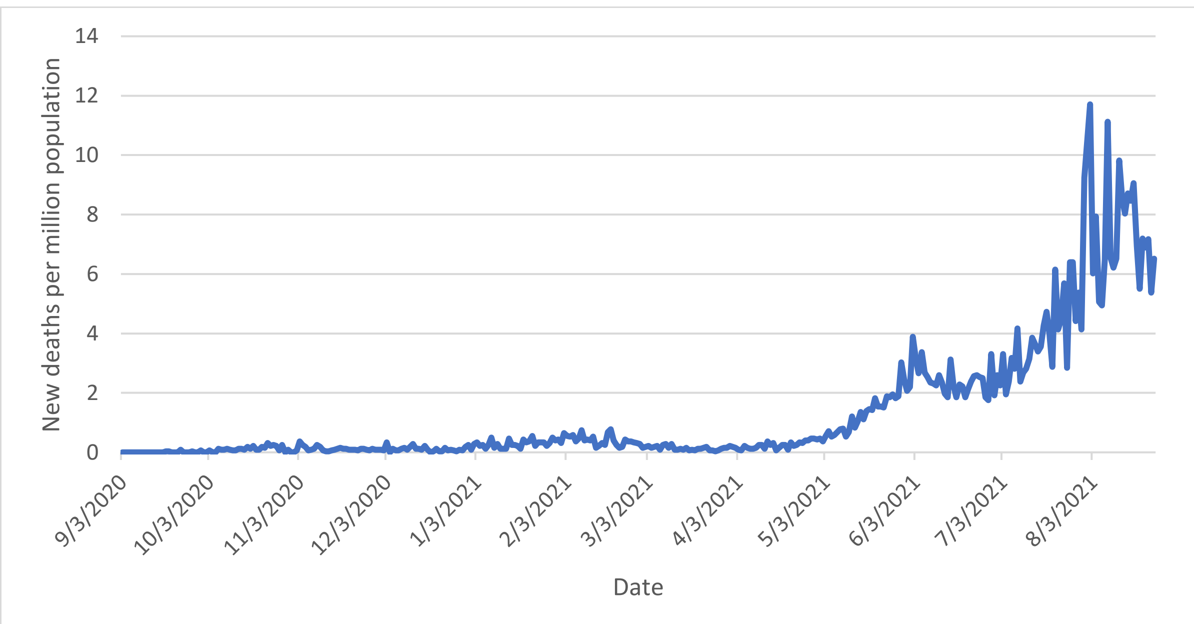

Figure 2. Daily Deaths due to COVID-19 per Million Population from 3 September 2020 to 24 August 2021

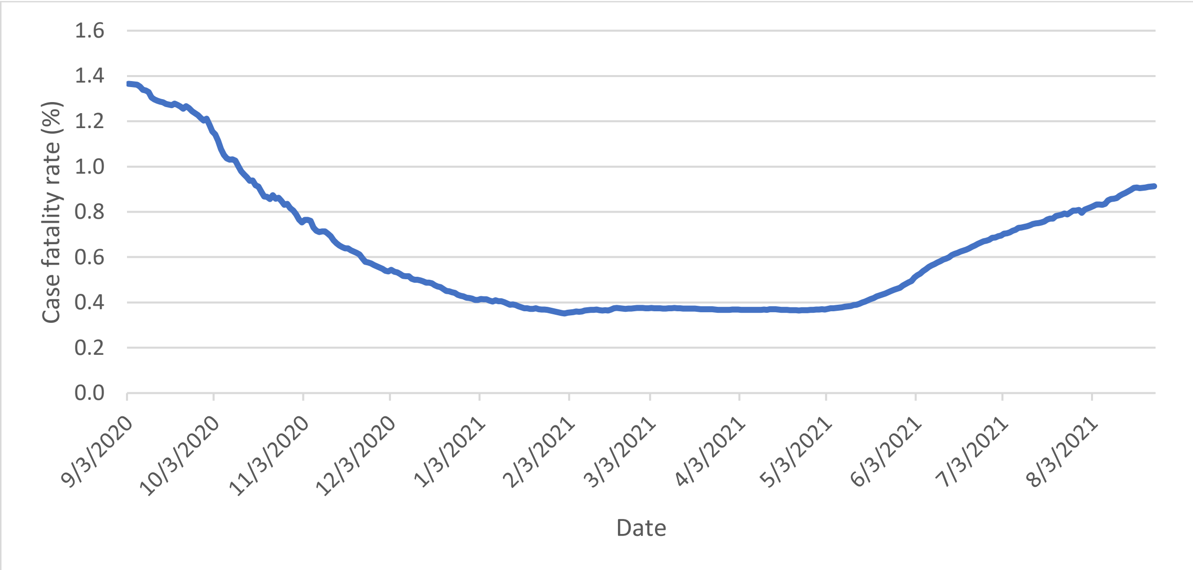

Figure 3. Daily Case Fatality Rates from 3 September 2020 to 24 August 2021

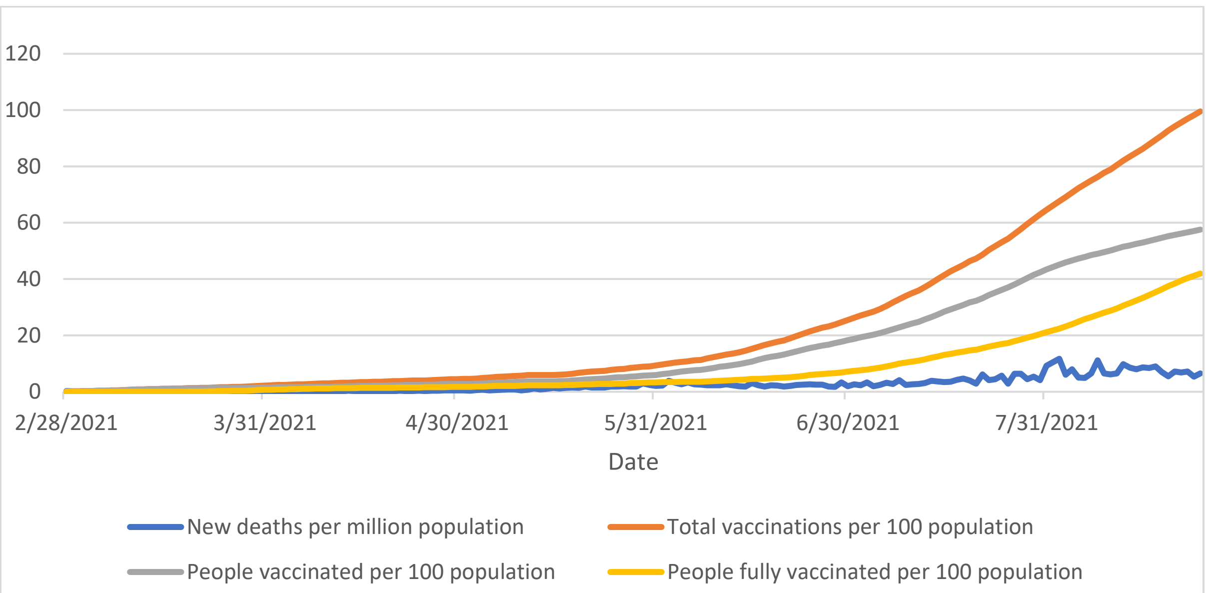

Figure 4. Vaccination Coverage and Daily Deaths After the Initiation of Vaccination (28 February 2021 to 24 August 2021)

Table 1. Descriptive Statistics of the Post- and Pre-vaccination New COVID-19 Cases and Deaths, and Vaccination Coverage

Variable	N	Mean ± SD	Skewness	Kurtosis
Pre-vaccination (3 Sep 2020 – 27 Feb 2021)				
New cases per million population	178	50.16 ± 40.45	0.825	0.059
New deaths per million population	178	0.17 ± 0.16	1.265	1.352
Daily case fatality rates	178	0.69 ± 0.33	0.775	-0.831
Post-vaccination (28 Feb 2021 – 24 Aug 2021)				
New cases per million population	178	224.83 ± 196.98	1.098	-0.025
New deaths per million population	178	2.33 ± 2.57	1.405	1.515
Vaccinations per 100 population	178	23.37 ± 28.42	1.304	0.415
People vaccinated per 100 population	178	15.30 ± 17.87	1.132	-0.152
People fully vaccinated per 100 population	178	8.08 ± 10.70	1.653	1.735
Daily case fatality rates	178	0.55 ± 0.19	0.498	-1.342

Table 2. Mann-Whitney U Test results for COVID-19 daily case fatality rates pre- and post-vaccination

Data Pair	Mann-Whitney U	Wilcoxon W	Z	Asymptotic significance (2-tailed)
Daily case fatality rates*	12706.00	28637	-3.230	0.001

* Pre-vaccination and post-vaccination

Table 3. Spearman's Correlation between New COVID-19 Cases and the Associated Deaths, Vaccination Coverage and Case Fatality Rate

	New cases per million population	New deaths per million population	Vaccinations per 100 population	People fully vaccinated per 100 population	People vaccinated per 100 population	Daily case fatality rates
New cases per million population	1.000					
New deaths per million population	0.905**	1.000				
Vaccinations per 100 population	0.944**	0.903**	1.000			
People fully vaccinated per 100 population	0.947**	0.905**	0.999**	1.000		
People vaccinated per 100 population	0.944**	0.903**	1.000**	0.999**	1.000	
Daily case fatality rates	0.907**	0.877**	0.913**	0.914**	0.913**	1.000

**Correlation is significant at the 0.01 level (2-tailed)

Table 4. Multiple Regression Results of the Predictor Variables of Daily Case Fatality Rates

	Unstandardized coefficients		Standardized coefficients	t	P-Value
	B	Standard error	Beta		
(Constant)	0.382	0.007		57.159	0.000
New cases per million population	-9.235×10^{-5}	0.000	-0.094	-1.238	0.217
New deaths per million population	0.009	0.003	0.124	2.958	0.004
People fully vaccinated per 100 population	-0.016	0.002	-0.860	-9.845	0.000
People vaccinated per 100 population	0.019	0.001	1.773	16.993	0.000

Discussion

Vaccination has long been thought to be one of the most efficient ways to guard against COVID-19 (9). Vaccines, on the other hand, do not prevent COVID-19 from spreading. The steady increase in daily COVID-19 new cases and deaths (Table 1, Figures 1 and 2) over the post-vaccination period, when vaccination was started and reached a high level of coverage, reflects this. This period coincides with a more relaxed control of COVID-19 transmissions in Malaysia, characterized by a gradual relaxation of non-essential sector operations, such as dine-in, religious activities, and travel restrictions, though precautionary measures, locally known as standard operating procedures, such as physical distancing, hand hygiene, and mask wearing were widely practiced (12, 26).

During the post-vaccination era, the daily case fatality rates grew in tandem with the increase in daily COVID-19 new cases and fatalities, albeit at a slower rate than during the pre-vaccination period (Figure 3). The difference in case fatality rates before and after vaccination was statistically significant (Table 2), showing that vaccination does give some protection to vaccinated people. A study found that single-dose Ad26.COV2.S vaccinations protected vaccine recipients from severe to critical COVID-19 infection (27). Another study found that following the first and second doses, mRNA-1273 (Moderna) gave 81.6 percent and 95.7 percent protection against severe, critical, or deadly COVID-19, respectively (28). According to the research, the decline in post-vaccination daily case fatality rates in Malaysia is consistent. Daily deaths due to COVID-19 grow as daily new COVID-19 cases increase, according to Spearman's correlation. This is consistent with Lai‘s findings that COVID-19 incidence and mortality are related to the daily cumulative index (29). The greater vaccination rate, which coincided with the rise in new COVID-19 cases and fatalities when control measures were loosened, was captured by Spearmen's correlation, which shows that vaccination coverage correlates to daily new COVID-19 cases and deaths (Table 3). Vaccination coverage variables, such as vaccinations per 100 population, persons vaccinated per 100 population, and people completely vaccinated per 100 population, are all closely interconnected (Table 3). The daily COVID-19 case fatality rates are positively and strongly correlated with new COVID-19 cases and deaths, showing that, despite vaccination protection, the case fatality rates could still grow with more new cases and deaths of COVID-19.

In keeping with the strong Spearman's correlation of 1.000, a multiple regression model indicates collinearity between individuals vaccinated per 100 population and vaccinations per 100 population (Table 3). The sole independent variable that contributes to the lowering of daily case fatality rates (B = -0.016) is the number of people fully vaccinated per 100 population, according to the model (Table B). This is consistent with recent data that show that second vaccine doses are more effective against SARS-CoV-2 illness (28, 30).

This study, like previous correlational studies, has the drawback of not providing a causal relationship between the independent factors and daily case fatality rates (31). While the connections are often substantial, they should not be misconstrued for the causes of daily case fatality rate variations. The rise in vaccination rates, for example, coincided with an increase in new COVID-19 cases and deaths, resulting in higher case fatality rates. This is not to say that a higher vaccination rate leads to a higher rate of case fatality. In fact, when the pre-vaccination and post-vaccination case fatality rates were compared, the post-vaccination rates were statistically significantly lower. Despite this, the regression model shows that full vaccination (two vaccine doses) had a small yet significant influence on COVID-19 case fatality rates. Confounding factors such as co-morbidities, age, hygiene practices, and healthcare quality that may contribute to case fatality rates are not taken into account in the model. Furthermore, the data for this study came from official and internet sources, and there was no control over the data's quality, which added to the study's limitations. Future research should look into how daily COVID-19 case fatality rates differ depending on demographic factors including age, gender, education, and access to health-care facilities, as well as health factors like medical history, vaccination history, pregnancy, and current illnesses. This will allow vulnerable populations to be recognized, and appropriate measures to provide more protection can be established. Furthermore, comparative studies of pre- and post-vaccination daily case fatality rates in different nations might be conducted to gain a better understanding of the impact of vaccination on daily case fatality rates (32).

Conclusion

This study shows that the reduction in COVID-19 daily case fatality rates after immunization is statistically significant when compared to those before vaccination. Despite this, case fatality rates changed in response to the daily increase in new COVID-19 cases and deaths, implying that COVID-19 transmission must be controlled through adaptive limits on travel, social, and work activities. Hygiene-related activities and physical separation are also essential. This research backs up previous findings about the effectiveness of vaccination in lowering COVID-19 patients that are severe to critical. It emphasizes that complete vaccination (two doses of vaccine) may result in a decrease in daily COVID-19 case fatality rates. While acknowledging that immunization against COVID-19 provides protection, this study recommends that adaptive constraints on travel and social activities, as well as hygiene-related behaviors and physical separation, be maintained.

Conflicts of interest/ competing interests: None.

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