

Article

Covid-19 vaccines work but other factors play a relevant role: A data analysis on spread and mortality in 24 countries

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Abstract

Background: The aim was to outline a methodology to monitor the impact of vaccinations in different countries comparing in two different time within countries and between countries the frequency of new cases and Covid-19 related deaths and the percentage of vaccinations conducted.

Design and methods: The 25 countries with the largest increase in SARS-CoV-2 cases on 8 August 2021 were evaluated. In each nation was calculated the proportion of Covid-19 deaths divided per new cases x 100 and the proportion of new cases per 1.000 inhabitant on 10 January 2021 (before vaccinations' distribution) and 8 August 2021 (when large percentage of the population had been vaccinated in many countries).

Results: The study shows that in the countries with the highest number of cases as of 8 August 2021, the proportion of vaccinations carried out in the population correlates negatively with both the proportion between Covid-19 dead people x100 infected people and with the rate of new cases. However, the proportion of vaccinations does not correlate with the differences in the two same indicators considered in the weeks observed, thus additional factors seem to play an important role.

Conclusions: This work indicates that mass vaccination is associated with a lower spread of the pandemic and, to greater extent, with a lowering of mortality in infected people.

Introduction

The Covid-19 pandemic has been effectively impacted by the development and dissemination of vaccines.¹ Despite initial promising data,² subsequent publications suggest that all vaccines, including mRNA vaccines- appear to be less effective against the new variants of the virus,^{3,4} but they continue to provide protection against the worst SARS-CoV-2 clinical outcomes and therefore strong effective lower mortality,⁵ with possible different efficacy for the different types of vaccines on different variants.⁶ Furthermore, since new variants, particularly the Delta variant, have a greater ease of spread,⁷ the theoretical threshold needed to achieve herd immunity has now increased.⁸ While this evidence has further stimulated research on vaccines, it has nevertheless suggested that a greater attention to epidemiological factors is needed to develop synergic strategies. Furthermore, there is a growing need to understand the impact and limitations of vaccination campaigns.⁹

A hypothesis on discussion in this framework was that a non-homogeneous distribution of vaccines (also linked to different socio-economic factors), within large pockets of unvaccinated fragile populations, could constitute a favorable ground for the development of new variants.¹⁰⁻¹² These considerations underline the importance of a correct monitoring of the response to vaccines in the different geographies.

The aim of this work is to outline a possible methodology to monitor the impact and effectiveness of vaccinations in different contexts. The analysis will be conducted at two time points: the first in early 2021, when vaccination distribution had not achieved significant proportions of the population and the second in the sec-

Significance for public health

The Covid-19 pandemic has been effectively impacted by the development and dissemination of vaccines. Despite initial promising data subsequent publications suggest that all vaccines, including mRNA vaccines- appear to be less effective against the new variants of the virus but they continue to provide protection against the worst SARS-CoV-2 clinical outcomes and therefore strong effective lower mortality, with possible different efficacy for the different types of vaccines on different variants (e.g., Delta variant). A greater attention to epidemiological factors is needed to develop synergic strategies. Furthermore, there is a growing need to understand the impact and limitations of vaccination campaigns.

ond half of summer 2021 when large percentage of the population had been vaccinated in many countries, including those with the largest number of new cases during August 2021. The observations were conducted both in relation to the frequency of new cases and to the ratio between total number of COVID-19 confirmed cases and COVID-19 related deaths.

Design and methods

The twenty-five countries with the largest increase in SARS-CoV-2 cases as of 8/8/2021 were evaluated for ascertaining new cases and number of deaths recorded in the weeks prior to 1/10/2021 (at the initial phase of vaccination campaigns) and in the week before 8/8/2021 (Johns Hopkins Coronavirus Resource Center, COVID-19 Map). Additionally, the number of vaccines administered, and the proportion of doses delivered per inhabitant in each nation as of 8/8/2021 was also analyzed. This manuscript does not include data from Cuba, as data were not provided.¹³

Data analysis for each nation included: the proportion of Covid deaths divided per new cases x 100 in the weeks preceding 10/1/2021 and 8/8/2021; the proportion of new cases per 1.000 inhabitant in the weeks preceding 10/1/2021 and preceding 8/8/2021; the difference between the proportions in the weeks 10/1/2021 and 8/8/2021 was then calculated; the proportion of deaths at 10/10/2021 and the difference on deaths 10/1/2021 versus

8/8/2021 were therefore correlated by means of a linear Persons coefficient to the proportion of vaccines delivered / inhabitant for each state; the proportion of new cases per 1.000 inhabitant in the weeks preceding 8/8/2021 and the difference 10/1/2021 and 8/8/2021 were also correlated by means of a linear Persons coefficient to the proportion of vaccines delivered / inhabitant for each country.

Results

Table 1 shows the number of cases during the second wave of the spread (week preceding 10/1/2021), the number of deaths and the proportion deaths / cases x 100 in the same week; the number of cases during the III wave of the spread (week preceding 8/8/2021), the number of deaths and the proportion deaths / cases x 100 in the same week; the total doses of vaccine in each country at 8/8/21, the doses of vaccines per inhabitants in each country as of 8/8/2021 and the difference in proportion (deaths/cases) as of 10/1/21 and 8/8/21 in each country. A strict inverse correlation between the proportion of cases/death x 100 in the week before 8/8/2021 and the percentage of people with one dose of vaccine in a done country was found ($R=-0.5569$, 46 df, $p=0.004785$). In contrast the invers correlation between the doses of vaccine per inhabitants in a given country and the difference in proportion (cases/deaths) at week 0/1/20 and week 8/8/20 was not statistically

Table 1. Proportion of cases of Covid-19 and deaths in the 2nd and 3rd wave and correlation with vaccines in each country.

Country	Number of cases in 2 nd wave week 10/1/2021	Deaths 2 nd wave week 10/1/2021	Proportion deaths/cases x 100	Number of cases in 3 rd wave - week 8/8/21	Deaths 3 rd wave week 8/8/21	Proportion deaths/cases x 100	Total doses of vaccine in the country at 8/8/21	Doses x inhabitants	Difference in proportion deaths/cases at 10/1/20 and 8/8/20
USA	1,723,000	23,101	1.3	760,368	3,537	0.5	355,310,018	1.1	-0.8
India	126,126	1,511	1.2	273,996	3,536	1.3	543,846,290	0.4	0.1
Brasile	372,044	7,082	1.9	227,214	6,317	2.7	65,011,009	0.3	0.8
Indonesia	62,676	1,395	2.2	225,635	11,373	5.0	81,800,407	0.3	-1.7
Iran	42,972	6,31	1.5	255,210	3019	1.2	16,213,714	0.2	-0.3
UK	418,669	6,430	1.5	190,523	616	0.3	88,616,134	1.3	-1.2
Russia	162,972	3,233	2.0	155,128	5,383	3.4	73,362,254	0.5	1.4
France	127,889	2,721	2.1	161,415	1,334	0.8	80,059,800	1.2	-1.3
Spain	122,095	1,037	0.8	141,088	520	0.4	60,919,867	1.3	-0.4
Turkey	84,344	1,610	1.9	147,906	660	0.8	83,934,599	1.0	-1.1
Thailand	2,108	2	9.4	141,191	1,214	0.9	23,192,221	0.3	-8.5
Malaysia	33,833	114	0.3	264,236	3,450	1.3	28,312,631	0.9	1
Mexico	85,254	6,493	7.6	116,825	3,386	2.9	77,573,476	0.6	-4.7
Japan	43,525	435	1.0	94,732	84	0.1	111,989,059	0.9	-0.9
South Africa	130,849	3,586	2.7	77,282	2,622	3.4	9,753,938	0.2	0.7
Argentina	81,499	1,013	1.2	83,048	1,607	2.0	37,234,819	0.8	0.8
Bangladesh	6,434	155	2.4	89,367	1,736	1.9	21,432,342	0.1	-0.5
Iraq	5,164	61	1.2	76,716	469	0.6	2,102,550	0.1	-0.6
Philippines	9,883	148	1.5	61,227	1,106	1.8	28,308,493	0.3	0.3
Vietnam	20	0	0	58,053	2,091	3.6	15,271,562	0.2	3.6
Morocco	18,722	516	2.8	133,130	1,004	0.8	30,030,540	0.8	-1.6
Colombia	222,160	4,298	1.9	89,140	2,920	3.2	33,005,580	0.6	1.3
Italy	242,090	6,846	2.8	82,138	304	0.4	7,5194,688	1.2	-2.4
Kazakhstan	11,612	80	0.7	112,240	1,664	1.5	1,1347,235	0.6	0.8
Cuba	2,192	4	0.2	63,876	593	0.9	No data	No data	

significant ($R = -0.1242$, $df 46$, $p=0.563751$). The higher discrepancies between an inverse correlation were found in: Argentina with dose of vaccine / inhabitants 0.8; and difference in proportion (cases/ deaths) at 10/1/2021 and 8/8/2021, increased of 0.8; Malesia with dose of vaccine / inhabitants 0.9; and difference in proportion (cases/deaths) at 10/1/2021 and 8/8/2021, increasing of 1.0; Indonesia with dose of vaccine / inhabitants of 0.3; and difference in proportion (cases/deaths) at 10/1/2021 and 8/8/2021, decreasing of -1.7; Thailand with dose of vaccine / inhabitants 0.3; ND difference in proportion (cases/deaths) at 10/1/2021 and 8/8/2021, decreasing of -8.5; Mexico with dose of vaccine /inhabitants of 0.6; and difference in proportion (cases/deaths) at 10/1/2021 and 8/8/2021, decreasing of -4.7; Bangladesh dose of vaccine / inhabitants of 0.1; and difference in proportion (cases/deaths) at 10/1/2021 and 8/8/2021, decreasing of -0.5; Iraq with dose of vaccine / inhabitants of 0.1; and difference in propor-

tion (cases/deaths) at 10/1/2021 and 8/8/2021, decreasing of -0.6.

Table 2 shows the trend in cases/death week ratio (10/1/2021 vs 8/8/2021) in countries with more than 1 dose of vaccine x inhabitant and in countries without. The countries with at least 1 dose of vaccine x inhabitant were: France, Spain, Turkey, US, UK, Italy, all these countries show a decrease in new cases/death week ratio comparing the week 10/1/2021 vs 8/8/2021 against 8 out of 18 countries without 1 dose of vaccine x inhabitant (100% vs 44.4%, Fisher Exact Test $p=0.024$).

Table 3 shows the difference in new cases of SARS-CoV-2 x 1,000 inhabitants in the two weeks data window in each country. The correlation in each country between this indicator and the doses/inhabitants reach a weak statistical significance ($R=0.4128$, 46 GL, $p=0.044988$). In contrast the correlation between difference in new cases in the two weeks considered and doses x inhabitants of vaccine in a done country didn't reach the statistical significance

Table 2. Trend in cases/death week ratio (10/1/2021 vs 8/8/2021) in countries with more than 1 dose x inhabitant and countries without.

	Countries with more than 1 dose x inhabitant	Countries with less than 1 dose x inhabitant
Countries with decreasing trend in cases/death week ratio	6 (France, Spain, Turkey, US, UK, Italy)	8
Countries with increasing trend in cases/death week ratio	0	10

Fisher Exact test $p=0.024$.

Table 3. Difference in new cases x 1,000 inhabitants in the two weeks evaluated, correlation with doses/inhabitants in each country and correlation between difference in new cases in the two weeks considered and doses x inhabitants of vaccine in a done country.

Country	Number of cases in 2 nd wave = week 10/1/2021	New cases in week 10/1/21 x inhabitants x 1000	Number of cases in 3 rd wave = week 8/8/21	New cases in week 8/8/21 x inhabitants	Difference in the two weeks evaluated	Doses x inhabitants	Number of inhabitants
USA	1,723,000	5.1	760,368	2.3	-3.8	1.1	332,732,331
India	126,126	0.1	273,996	0.2	0.1	0.4	1,394,306,208
Brasile	372,044	0.3	227,214	1.1	0.8	0.3	213,908,708
Indonesia	62,676	0.2	225,635	0.8	0.6	0.3	276,122,198
Iran	42,972	0.5	255,210	3.0	3.8	0.2	84,820,190
UK	418,669	6.1	1,905,233	2.8	-3.3	1.3	68,168,033
Russia	162,972	1.1	155,128	1.1	0	0.5	145,989,705
France	255,778	3.9	332,830	5.1	1.2	1.2	65,388,646
Spain	122,095	2.6	141,088	3.0	0.4	1.3	46,769,864
Turkey	84,344	1.0	147,906	1.7	0.7	1.0	85,037,969
Thailand	2,108	0.03	141,191	2.0	2.0	0.3	69,938,626
Malaysia	33,833	1.0	264,236	8.0	7.0	0.9	32,716,130
Mexico	85,254	0.7	116,825	1.0	0.3	0.6	129,976,073
Japan	43,525	0.3	94,732	0.7	0.4	0.9	126,136,695
South Africa	130,849	2.2	77,282	1.3	0.9	0.2	59,902,511
Argentina	81,499	1.8	83,048	1.8	0	0.8	45,540,268
Bangladesh	6,434	0.04	89,367	0.5	0.5	0.1	166,161,194
Iraq	5,164	0.1	76,716	1.9	1.8	0.1	40,968,539
Philippines	9,883	0.1	61,227	0.5	0.4	0.3	110,703,120
Vietnam	20	0.001	58,053	0.6	0.6	0.2	98,013,529
Morocco	18,722	0.5	133,130	3.6	3.1	0.8	37,273,622
Colombia	222,160	4.3	89,140	1.7	-2.6	0.6	51,322,788
Italy	242,090	4.0	82,138	1.4	-2.6	1.2	60,370,002
Kazakhstan	11,612	0.6	112,240	5.6	5.0	0.6	19,724,856
Cuba	2192		63,876			No data	

($R = 0.294$, $df 46$, $p=0.1631$).

Table 4 shows the trend in new cases x 1.000 inhabitants (10/1/2021 vs 8/8/2021) in countries with more than 1 dose of vaccine x inhabitant and in countries without. The countries with at least 1 dose of vaccine x inhabitant were: France, Spain, Turkey, US, UK, Italy, 3 out of these countries show a decrease of incidence of new cases of SAR-CoV-2 comparing the week 10/1/2021 vs 8/8/2021 against 1 out of 18 countries without 1 dose of vaccine x inhabitant (50% vs 5.5%, Fisher Exact test $p=0.035$).

Discussion

The study shows that in the 24 countries with the highest number of SARS-CoV-2 cases as of 8/8/2021, the proportion of vaccinations carried out in the population correlates negatively in the week 8/8/2021 with both the proportion between dead people x100 people infected in that week and with the rate of new cases in the same week. However, the proportion of vaccinations carried out in the population does not correlate with the differences in the two same indicators considered in the weeks 10/1/2021 (when vaccinations had not yet started on a large scale) and 8/8/2021.

The study therefore confirms that vaccination plays an important role in fighting the pandemic; it also highlights that other factors might play a role since the difference in the two indicators in the two time points considered did not correlate with the percentage of the vaccinated population (aka, before the start of vaccination in January 2021 and when the vaccination was administered, although with a degree of variability in different countries, to relevant portions of the population August 2021).

In fact, it is necessary to consider multiple interacting factors that can have an impact on the vaccine's efficacy as it relates to the two indicators considered. First, the new variants involved do not have a homogeneous geographical distribution;^{7,14} additionally, different vaccines (whose precise distribution is not easy to establish) could have different efficacy on the different variables.^{6,15} Finally, data quality especially around the incidence of new cases, as data might be collected and verified differently in different countries and therefore might not have the same accuracy.

A factor that undoubtedly comes into play is the climate which, according to past studies, appears to affect lethality more than diffusivity.¹⁶⁻²⁰ In fact, when we consider those countries in which the trend towards the evolution of the infected / ratio was more optimistic than expected (aka, it anticipated a lower mortality / new case ratio), these are all countries of the equatorial, sub equatorial or tropical belt (Indonesia, Thailand, Mexico, Bangladesh, Iraq). Therefore, during the months considered, we have limited elements to draw any conclusion as it relates to those countries where temperatures are significantly higher than in countries with a temperate climate; during our second evaluation, in August, we observed an opposite trend in Malaysia, which has a relative high percentage of vaccine per inhabitant but a higher mortality / new

cases ratio. Considering the climatic differences, it is also possible to partly explain the case of Argentina, which despite reaching a good proportion of vaccine doses per inhabitant (0.8) nevertheless presents, in contrast, an increase in mortality / new case ratio. Among those considered to be in the southern hemisphere, Argentina is in fact is the only country with a temperate climate (at least in its more populated area). While in the other countries the 1/10/2021 measurement took place in the winter and the 8/8/2021 measurement in the summer, for Argentina it was the opposite as the seasons are reversed, being January the hottest month and July the coldest month. Therefore, while in other situations with a high frequency of vaccinations, the climate trend would appear to be synergistic with the effect of the vaccine, in Argentina it would have played an opposite role. If this hypothesis will be confirmed, this would mean that the effect of the vaccination on lethality exists but it is partial. A possibility worth considering is that the proportion of mRNA-acting vaccines was lower in Argentina than in the daredevil countries of the North hemisphere, and that this may have limited the effect of vaccination. From January to July most of the vaccinations took place in Argentina through the Sputnik-V vaccine and only at the end of July 2020 therefore (with an insignificant effect on the data collected in August) did vaccinate large sections of the population with the Moderna vaccine.^{9,21,22}

The data from Malaysia (with good level of vaccination but not decreasing in mortality of infected people) cannot be easily explained as what observed in this state is in contrast with what observed in other nations (with the exception of Argentina) with a good level of vaccination in which mortality decreases; furthermore, data collected contrast with the nations of the same geographical area that record an improvement or a non-worsening of mortality in infected people albeit with a lower rate of vaccinations. It should be noted that Malaysia has started mass vaccinations with AstraZeneca and Chinese vaccines, while the vaccination with mRNA vaccine started at the end of February 2021 but a substantial part of the population started to be vaccinated with Pfizer vaccine at the end of April 2021.²³⁻²⁶ this data perhaps played a role. However, Turkey that had started vaccinating with Sinovac (vaccine with deactivated virus) and only partially with Sputnik-5 (vaccine with vehiculation with adenovirus) and which started vaccinating with Pfizer only in April has obtained a lowering of the mortality.²⁶ Turkey, on the other hand, is one of the countries (with France and Spain, these countries with larger proportion of the people vaccinate by Pfizer) in which, despite the high portions of vaccinations, the difference between cases in January and cases in August was not high as in Italy, UK and USA (high percentage of vaccinated people and all with higher percentage of mRNA vaccines) and Colombia (with low percentage of vaccinated people). These differences are most likely caused by difference in policies and practices as it relates to social distancing, use of masks and other protective elements.²⁷ In fact, if this study confirms the trend towards improvement linked to the vaccine in infections and in mortality linked to the virus, the great variability

Table 4. Difference in new cases x 1,000 inhabitants in the two weeks evaluated in in countries with more than 1 dose x inhabitant and countries without.

	Countries with more than 1 dose x inhabitant	Countries with less than 1 dose x inhabitant
Countries with decreasing less than 1/1.000 inhabitant or increasing	3 (France, Spain, Turkey)	17
Countries with decreasing more than 1/1.000 inhabitant	3 (US, UK, Italy)	1 (Colombia)

Fisher Exact test $p=0.035$.

underlines the probable important effect of other variables that must not be neglected. If the efficacy of the vaccine is still confirmed, the study suggests that we absolutely must not let our guard down in neglecting the other prevention tools as the vaccine cannot solve the problems by itself

Limitations

This work is meant to be an investigative and hypothesis-producing study more than a conclusive one. The biggest limitation is determined by the potential variability in accuracy in the different states surveyed. Another limitation is related to the big number of confounding factors, among which: climate,²⁰ level of pollution,^{18,28} different strategies in the administration of vaccines for age groups^{29,30} and fragile populations,^{31,32} accessibility of vaccines by public health services, different average age of populations, restriction measures adopted and effectiveness in their implementation.

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Conclusions

Despite the considerable limitations described, this work indicates that mass vaccination is associated with a lower spread of the pandemic and, to greater extent, with a lowering of mortality in infected people. The study suggests that not all vaccines may have the same efficacy, but this must be confirmed with further investigations.

Additional factors seem to play an important role and the study confirms that climate mainly affects virus lethality. Our findings suggest that other protective measures such as wearing masks indoor must be observed to contrast the viral spread. This study and other data on Delta transmission show that precautions with synergize the effect of the virus are still needed.

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