

# The evolution of COVID-19 pandemic wave and optimal levels of vaccination to reduce negative effects in society

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## Research Article

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# THE EVOLUTION OF COVID-19 PANDEMIC WAVE AND OPTIMAL LEVELS OF VACCINATION TO REDUCE NEGATIVE EFFECTS IN SOCIETY

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## **Abstract**

Coronavirus disease 2019 (COVID-19) continues to be a pandemic threat with new mutations of the viral agent (SARS-CoV 2) that are generating a constant state of attention in manifold countries. Innovative drugs, such as vaccines can sustain, as far as possible, immunity of people and decrease negative effects in society. The study here, using data of vaccines and confirmed cases of COVID-19 between countries from March to May 2021, clarifies different optimal levels of vaccination associated with the growth of pandemic wave for reducing infected individuals in society. Findings reveal that a vaccination campaign in the initial phase of pandemic wave has a lower optimal level of doses administered per 100 inhabitants, but the growth of pandemic wave moves up the optimal level of vaccines from 58.5 in March to more than 86 doses per 100 people in May 2021. This study suggests that the optimal strategy and response to pandemic crisis is a rapid vaccination rollout, before the takeoff of pandemic wave, for an effective response to reduce numbers of COVID-19 related infected individuals and deaths and negative effects of pandemic crisis on environment and socioeconomic systems.

**Keywords:** Pandemic diseases, SARS-CoV-2, Coronavirus, Virus transmission, COVID-19 vaccines, Rollout, Vaccination campaigns, Public health, Health planning, Herd immunity, Epidemiology, Crisis management.

## **Declaration of competing interest**

The author declares that he is the sole author of this manuscript and he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious illness caused by the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which appeared in late 2019 (Anand et al., 2021; Bontempi et al., 2020, 2021; Bontempi and Coccia, 2021; Coccia, 2021). COVID-19 is still circulating in 2021 with mutations of the novel coronavirus<sup>1</sup> that generate continuous COVID-19 infections and deaths in manifold countries (Johns Hopkins Center for System Science and Engineering, 2021; Vicenti et al., 2021). Seligman et al. (2021) show some characteristics of people that are significantly associated with COVID-19 mortality, such as: " mean age 71.6 years, ... disproportionate deaths occurred among individuals with nonwhite race/ethnicity (54.8% of deaths ...  $p < 0.001$ ), individuals with income below the median (67.5% ...  $p < 0.001$ ), individuals with less than a high school level of education (25.6% ...  $p < 0.001$ ), and veterans (19.5% ...  $p < 0.001$ )". High numbers of COVID-19 related infected individuals and deaths worldwide have supported the development of innovative products<sup>2</sup> given by different types of vaccines from 2020 based on viral vector, protein subunit and nucleic acid (RNA). In vector vaccines, genetic material from the COVID-19 virus is placed in a modified version of a different virus (called, viral vector). When the viral vector gets into human cells, it delivers genetic material from the COVID-19 virus directed to instruct the cells to make copies of the S protein (the main protein used as a target in COVID-19 vaccines). After that, human cells display the S proteins on their surfaces and immune system responds by creating antibodies and defensive white blood cells to fight the novel coronavirus (Janssen/Johnson & Johnson and University of Oxford/AstraZeneca have generated viral vector vaccines for COVID-19). Protein subunit vaccine includes only the parts of a virus that best stimulate immune system. This type of COVID-19 vaccine has harmless S proteins. The immune system recognizes S proteins and creates antibodies and defensive white blood cells to fight the viral agent (e.g., American biotechnology company Novavax has developed this type of vaccine; cf., GAVI, 2021). Instead, the Messenger RNA (mRNA) vaccines use genetically engineered mRNA to give to cells instructions for how to make the S protein found on the surface of the COVID-19 virus, creating antibodies to fight the novel coronavirus (Mayo Clinic, 2021). The process

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1 WHO considers the following variants of concern: Beta, Gamma and Delta; Variants of interest (Lambda and Mu) and manifold variants under monitoring (ECDC, 2021).

2 About the sources and evolution of innovation cf., Coccia, 2015, 2016, 2016a; 2017a, 2017c, 2017d, 2019a, 2019b, 2020d, 2020e; Coccia and Watts, 2020.

of development of mRNA vaccines for COVID-19 is much faster than conventional vaccines to be redesigned and mass-produced (Abbasi, 2020; Calabrese et al., 2005; Cylus et al., 2021; Heaton, 2020; Jeyanathan et al., 2020; Komaroff, 2020). The first mRNA COVID-19 vaccines are due to premier biopharmaceutical companies: Pfizer-BioNTech and the Moderna (cf., Coccia, 2021a). In the presence of COVID-19 pandemic crisis, the investigation of vaccination plans is a crucial aspect to determine how the novel infectious disease can be controlled and/or eradicated in the population (Aldila et al., 2021). Vaccination has the potential effect to reduce the diffusion COVID-19, to relax nonpharmaceutical measures and maintain low basic reproduction number, but an important point to clarify is the optimal strategy of administering the vaccines during the evolution of COVID-19 pandemic wave to reduce negative effects in society (cf., Anser et al., 2020). Akamatsu et al. (2021) argue the vital role of governments is directed to implement an efficient campaign of vaccination to substantially reduce infections and mortality in society and also avoid the collapse of healthcare system. Aldila et al. (2021) maintain that higher levels of vaccination rate can eradicate COVID-19 in population by approaching herd immunity to protect vulnerable individuals (cf., Anderson et al., 2020; de Vlas and Coffeng, 2021; Jones and Helmreich, 2020; Randolph and Barreiro, 2020; Redwan, 2021). Herd immunity indicates that only a share of population needs to be immune and as a consequence no longer susceptible to a viral agent (by overcoming natural infection or through vaccination) for control of large outbreaks (Fontanet and Cauchemez, 2020). Scholars can estimate the proportion of a population that needs to be immune to support herd immunity, *ceteris paribus*. The threshold level depends on basic reproduction number,  $R_0$ — the number of cases, on average, spawned by one infected individual in an otherwise fully susceptible (Coccia, 2020; Kwok et al., 2020). In particular, the formula for calculating the herd-immunity threshold is  $1-1/R_0$  and it indicates that the more people who become infected by each individual who has the virus, the higher the proportion of the population that needs to be immune to reach herd immunity. The index  $R_0$  assumes that everyone is susceptible to the virus, but the level changes as the epidemic proceeds, since it depends on changes in susceptibility of the population, mitigation policies, circulation of variants, etc. (Aschwanden, 2020, 2021). Kwok et al. (2021) estimated the  $R_t$  and threshold level for herd immunity in different country's population. The estimates of effective reproduction number ( $R_t$ ) range from 1.06 to 6.64 and the minimum proportion (%) of total population required to recover from COVID-19 to confer immunity ( $P_{crit}$ ) is 5.66 in Kuwait and 85 in Bahrain. The estimates of  $R_t$  also depend on measures of

mitigation and containment that if they are relaxed can move up herd-immunity threshold (Buss et al., 2021; Dashtbali and Mirzaie, 2021). Rosen et al. (2021) describe socioeconomic and organizational factors associated with the success of vaccination campaign in Israel as well as they show some aspects of misinformation that can reduce the effectiveness of a fruitful vaccination plan over time (cf., Prieto Cruriel, et al. 2021). In this context, a vital problem in current COVID-19 pandemic crisis is the effective level of vaccination that supports a drastic reduction of COVID-19 infected individuals and deaths. The study confronts this problem here by developing a statistical analysis to explain, whenever possible at global level, the different optimal levels of vaccination during the evolution of COVID-19 pandemic wave that trigger a reduction of infected individuals in society. Results can suggest best practices of optimization in the vaccination strategy in order to guide effective and timely policy responses for combatting the novel coronavirus and constraining negative effects of COVID-19 pandemic crisis and future epidemics of similar infectious diseases in society. Findings of this study could be also of benefit to countries as they grapple to plan their vaccine programmes for COVID-19 pandemic crisis to minimize negative effects of pandemic crisis on environment and socioeconomic systems. This study is part of a large body of research project directed to explain drivers of transmission dynamics of COVID-19 and design effective policy responses to cope with and/or to prevent pandemic threats (Coccia, 2020, 2020a, 2020b, 2020c, 2021, 2021c, 2021d, 2021e, 2021i, 2022).

## **DATA AND STUDY DESIGN**

### *1.1 Sample and period*

The sample of this study is based on  $N=192$  countries worldwide. Period under study is from March to May 2021, using data of vaccines, confirmed cases and fatality rate of COVID-19.

#### ▪ *Measures of variables*

- Doses of vaccines administered  $\times 100$  inhabitants on 15 March 2021 with  $N=114$  countries; on 14 April 2021 with  $N=154$  countries and on 26 April 2021 with  $N= 190$  countries. The number of sample tends to increase over time with the diffusion of vaccines across countries worldwide. Doses of vaccines refer to the total number of vaccine doses, considering that an additional dose may be obtained from each vial (e.g., six doses for Pfizer BioNTech® Comirnaty), whereas number of doses administered refers to any individual receiving any dose of the vaccine (cf., Freed et al., 2021; Oliver et al., 2020). The data here considers all types of COVID-

19 vaccines used in different countries, i.e., vaccines by Johnson & Johnson, Oxford/AstraZeneca, Pfizer/BioNTech, Sinopharm/Beijing, Sinovac, Sputnik V and Moderna (Ritchie et al., 2020). Of course every country has been using a different combination of these COVID-19 vaccines to protect the population (CBC, 2021; CDC, 2021; Rossman et al., 2021). Source: Our World in Data (2021).

- Number of COVID-19 infected individuals (%) is measured with confirmed cases of COVID-19 divided by population of countries under study on 20 March 2021 ( $N=192$  countries), 25 April 2021 ( $N=192$ ) and 19 May 2021 ( $N=216$  countries). Source of data: Johns Hopkins Center for System Science and Engineering (2021).
- Number of COVID-19 deaths is measured with fatality rate (%) given by deaths on 25 April 2021 divided by total infected individuals in each countries. Source of data: Johns Hopkins Center for System Science and Engineering (2021).

## 1.2 Data analysis procedure and scenarios

Firstly, data are analyzed with descriptive statistics of variables given by arithmetic mean (M) and standard error of the mean (SEM). Data concerning doses of COVID-19 vaccines and confirmed cases of a specific day in the dataset can refer to different days because of the difficulty in countries associated with gather or transmission of information. Moreover, database here includes different COVID-19 vaccines having a different period of administration between the first and second dose to provide a certain level of protection that begins after a variable number of days (approximately after 12 - 14 days the first dose) and remains for some months (about six months). The intrinsic problems of the database, just mentioned, based on data of different countries lead to not consider in the statistical analyses here a specific interval between the date of vaccination of people and date of confirmed cases to detect the optimal levels of vaccination, because we consider the sample of countries as a whole having a normal distribution that mitigates discrepancies among countries (cf., Coccia, 2018).

We assume different scenarios considering the evolution of COVID-19 pandemic wave and vaccination over time:

- *Scenario I.* Initial phase of COVID-19 pandemic wave in March 2021. If countries of the sample had the level of vaccination at the time  $t$  (March) and pandemic wave had the confirmed cases  $t'$  of the same month (March), how would be the optimal level of vaccination
- *Scenario II.* Growth phase of COVID-19 pandemic wave in April 2021, whereas level of vaccination is of March

2021. If countries of the sample had the level of vaccination at the time  $t$  (March) and confirmed cases of the following month  $t+1$  (April), how would be the optimal level of vaccination

- *Scenario III.* Maturity phase of COVID-19 pandemic wave in May 2021, whereas the level of vaccination refers to April 2021. If countries of the sample had the level of vaccination at the time  $t$  (April 2021) and confirmed cases of the following month  $t+1$  (May 2021), how would be the optimal level of vaccination.

*Secondly*, the analysis of simple regression applies quadratic models because they fit the scatter of data to detect nonlinear effects of relations understudy.

The specification of model is given by:

$$y_{i,t} = \alpha_0 + \beta_1 x_{i,t-1} + \beta_2 x_{i,t-1}^2 + u_{i,t} \quad [1]$$

where:

- $y_{i,t}$  = Response variable is the number of COVID-19 infected individuals/population
- $x_{i,t-1}$  = Doses of vaccines administered  $\times$  100 inhabitants, explanatory variable
- $u_{i,t}$  = Error term
- country  $i=1, \dots, n$ ;  $t=time$

*Remark:* Model [1] has a time lag effect between explanatory (t-1) and dependent variables (t) to reduce the endogeneity and provide reliable (estimated) parameters.

*Remark:* The square of the doses of vaccines administered  $\times$  100 inhabitants in model [1] is introduced to consider the possibility of non-linear effects in the relation under study.

*Thirdly*, the optimization of the estimated relationship [1] is performed with the following perspective: the *maximization* of the equation [1] to find the optimal levels of doses of vaccines administered  $\times$  100 inhabitants (during the annual cycle of evolution of the COVID-19 pandemic) that support a consequential drastic reduction of confirmed cases of COVID-19 and negative effects in society. In particular, the estimated relationships [1] are objective functions of one (real) variable represented by polynomial functions of an order higher than first order (*i.e.*, second order). These estimated relations [1] are continuous and infinitely differentiable functions. The calculus applied on functional

relation [1] provides the optimal levels of doses of vaccines administered  $\times 100$  inhabitants at the time  $t$  (in a specific stage of COVID-19 pandemic wave as indicated in scenarios A, B and C) that reduces the spread of confirmed cases in society.

Finally, the effects of vaccines on fatality rate are analyzed with a bivariate correlation (1-tailed) and a simple regression analysis given by following *log-log* model:

$$f_{i,t} = \delta_0 + \delta_1 v_{i,t-1} + \varepsilon_{i,t} \quad [2]$$

where:

- $f_{i,t}$  =Fatality rate, dependent variable
- $v_{i,t-1}$  = Doses of vaccines administered  $\times 100$  inhabitants, explanatory variable
- $\varepsilon_{i,t}$  = Error term
- country  $i=1, \dots, n$ ;  $t=time$

In addition, the quartiles of distribution of doses of vaccines administered between countries in April 2021 are used to analyze the average fatality rate (%) from the first quartile (25th percentile) that includes countries having a lower number of doses of vaccine per 100 inhabitants to the fourth quartile including countries with the highest number of doses of vaccine per 100 inhabitants. Statistical analyses are performed with the Statistics Software SPSS® version 26.

## RESULTS

Table 1 shows that number of countries having doses vaccines per 100 inhabitants grows from March to April 2021 because new nations start vaccination campaigns and more data are gathered and transmitted in the progress of vaccination across countries worldwide. The number of countries with confirmed cases of COVID-19 cases also grows over time because other countries gather and transmit new data.

Table 1. Descriptive statistics

| Variables  | N   | Mean  | Std. Error |
|--|-----|-------|------------|
| Doses vaccines per 100 inhabitants 15 March 2021 | 114 | 8.85  | 1.46       |
| Doses vaccines per 100 inhabitants 26 April 2021 | 192 | 22.13 | 2.17       |
| Confirmed Cases /population % 20 March 2021      | 192 | 2.57  | 0.23       |
| Confirmed Cases /population % 25 April 2021      | 192 | 3.04  | 0.26       |
| Confirmed Cases /population % 19 May 2021        | 216 | 2.95  | 0.003      |

N=number of cases (countries)

□ *Phase I (initial) of COVID-19 pandemic wave in March 2021.*

Table 2. Regression analyses of confirmed cases/population of 20 March on doses of vaccines on 15 March 2021 based on quadratic model [1]

|                        |          |
|------------------------|----------|
| Constant $\alpha$      | 2.09 *** |
| (St. Err)              | (.38)    |
| Coefficient $\beta_1$  | .234 *** |
| (St. Err.)             | (.05)    |
| Coefficient $\beta_2$  | -.002*** |
| (St. Err.)             | (.001)   |
| $R^2$                  | .22      |
| (St. Err. of Estimate) | (2.95)   |
| $F$                    | 16.43*** |
| $N$                    | 113      |

*Note:* Dependent variable is Confirmed cases/population (%) of 20 March 2021. Explanatory variable is doses of vaccines on 15 March 2021 per 100 inhabitants.

Significance: \*\*\*  $p$ -value < 0.001

The estimated relationship, based on results of table 2, is:

$$z_{i,t} = 2.09 + 0.234h_{i,t-1} - 0.002 b_{i,t-1}^2$$

The polynomial function is given by

$$z = 2.09 + 0.234h - 0.002 b^2$$

the necessary condition to maximize is:

$$\frac{dz}{dh} = z'(b) = 0.234 - 0.004b = 0$$

The first derivative equal to 0 is:

$$z'(b) = 0 \Rightarrow b^* = \frac{0.234}{0.004} = 58.5 \text{ per 100 inhabitants}$$

$b^* = 58.5$  per 100 people indicates the optimal level of doses of vaccines in the initial phase of pandemic wave, after that the function of confirmed cases has a sharply decrease that reduces the negative impact and diffusion of COVID-19 leading, whenever possible, to constraint the pandemic crisis in society.

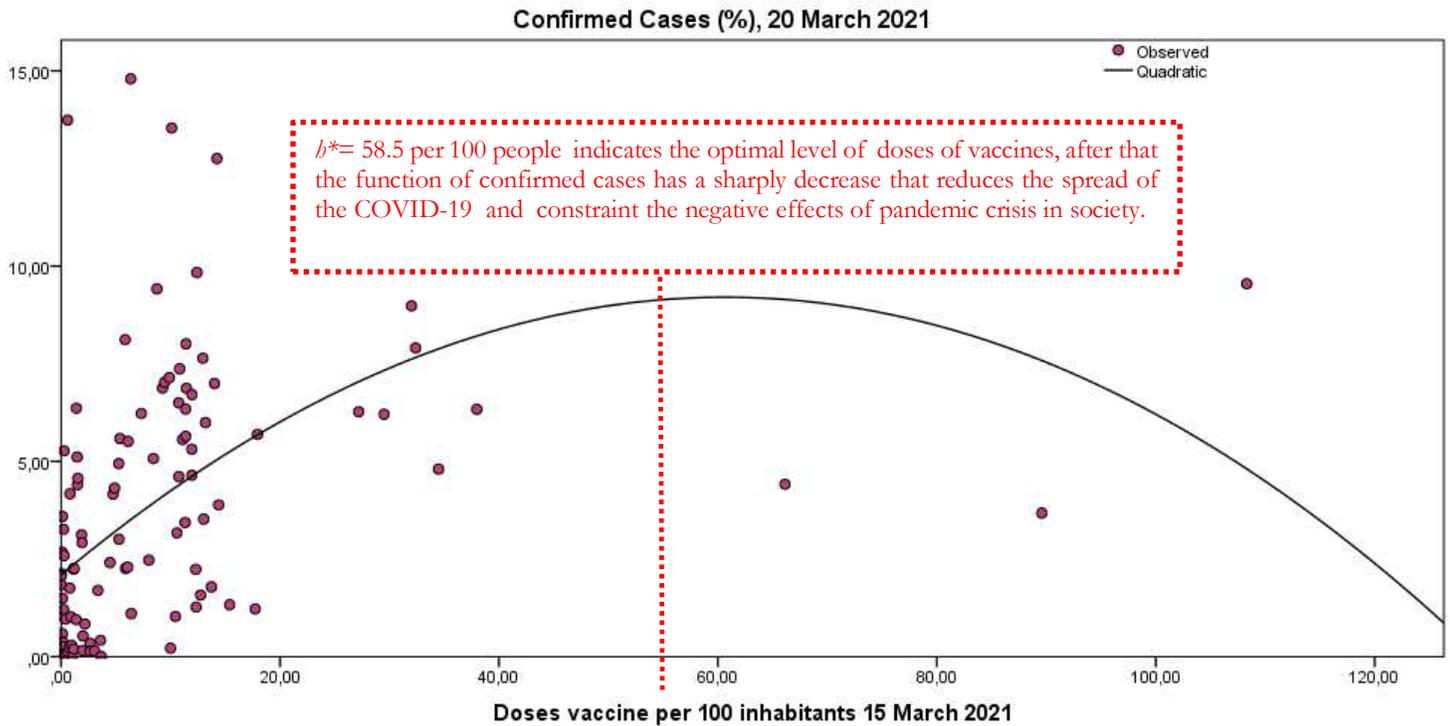


Figure 1. Relation of confirmed cases/population (%) of 20 March 2021 on doses of vaccines on 15 March 2021 based on quadratic model [1]

□ Phase II, the growth of COVID-19 pandemic wave in April 2021 and level of vaccination in March.

Table 3. Regression analyses of confirmed cases/population (%) of 25 April on doses of vaccines on 15 March 2021 based on quadratic model [1]

|                        |          |
|------------------------|----------|
| Constant $\alpha$      | 2.47 *** |
| (St. Err)              | (.43)    |
| Coefficient $\beta_1$  | .281 *** |
| (St. Err.)             | (.05)    |
| Coefficient $\beta_2$  | -.002*** |
| (St. Err.)             | (.001)   |
| $R^2$                  | .23      |
| (St. Err. of Estimate) | (3.35)   |
| $F$                    | 17.58*** |
| $N$                    | 113      |

*Note:* Dependent variable is Confirmed cases/population (%) of 25 April 2021. Explanatory variable is doses of vaccines on 15 March 2021 per 100 inhabitants.

Significance: \*\*\*  $p$ -value < 0.001

The estimated relationship, based on results of table 3, is:

$$y_{i,t} = 2.47 + 0.281x_{i,t-1} - 0.002 \times x_{i,t-1}^2$$

The function to optimize is given by

$$f = 2.47 + 0.281x - 0.002 \times x^2$$

the necessary condition to maximize is:

$$\frac{df}{dx} = f'(x) = 0.281 - 0.004x = 0$$

The first derivative equal to 0 is:

$$f'(x) = 0 \Rightarrow x^* = \frac{0.281}{0.004} = 70.25 \text{ per 100 inhabitants}$$

$x^* = 70.25$  per 100 people indicates the optimal level of doses of vaccines during the phase of growth (April) of pandemic wave, after that the function of confirmed cases has a sharply decrease that reduces the negative impact and diffusion of COVID-19 leading, whenever possible, to constraint the pandemic crisis in society.

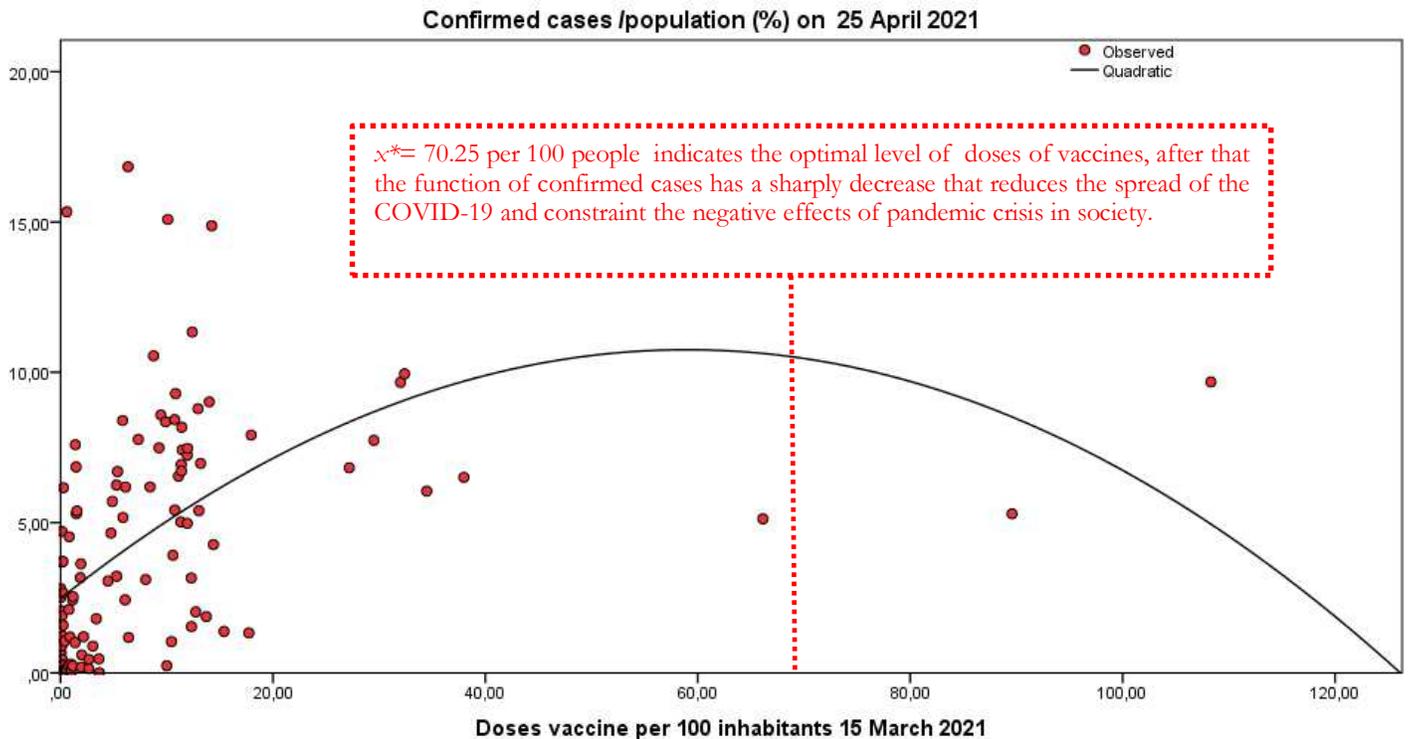


Figure 2. Relation of confirmed cases/population (%) of 25 April on doses of vaccines 15 March 2021 based on quadratic model [1]

□ Phase III, maturity of COVID-19 pandemic wave in May 2021 and level of vaccination in April 2021.

Table 4. Regression analyses of confirmed cases/population of 19 May 2021 on doses of vaccines on 26 April 2021 based on quadratic model [1]

|                        |                |
|------------------------|----------------|
| Constant $\alpha$      | .020 ***       |
| (St. Err)              | (.004)         |
| Coefficient $\beta_1$  | 001 ***        |
| (St. Err.)             | (.000)         |
| Coefficient $\beta_2$  | -.000005789*** |
| (St. Err.)             | (.000)         |
| $R^2$                  | .11            |
| (St. Err. of Estimate) | (.037)         |
| $F$                    | 12.16***       |
| $N$                    | 191            |

Note: Dependent variable is Confirmed cases/population of 19 May 2021. Explanatory variable is Doses of vaccines on 26 April 2021 per 100 inhabitants.

Significance: \*\*\* $p$ -value<0.001

The estimated relationship, based on results of table 4, is:

$$j_{i,t} = 0.02 + 0.001w_{i,t-1} - 0.000005789 w_{i,t-1}^2$$

The function to optimize is given by

$$j = 0.02 + 0.001w - 0.000005789 w^2$$

the necessary condition to maximize is:

$$\frac{dj}{dw} = j'(w) = 0.001 - 0.000011578w = 0$$

The first derivative equal to 0 is:

$$j'(w) = 0 \Rightarrow w^* = \frac{0.001}{0.000011578} = 86.37 \text{ per 100 inhabitants}$$

$w^* = 86.37$  per 100 people indicates the optimal level of doses of vaccines in the phase of maturity of pandemic wave (May 2021), after that the function of confirmed cases has a sharply decrease that reduces the negative impact and

diffusion of COVID-19 leading, whenever possible, to constraint the negative societal effects of pandemic crisis in countries.

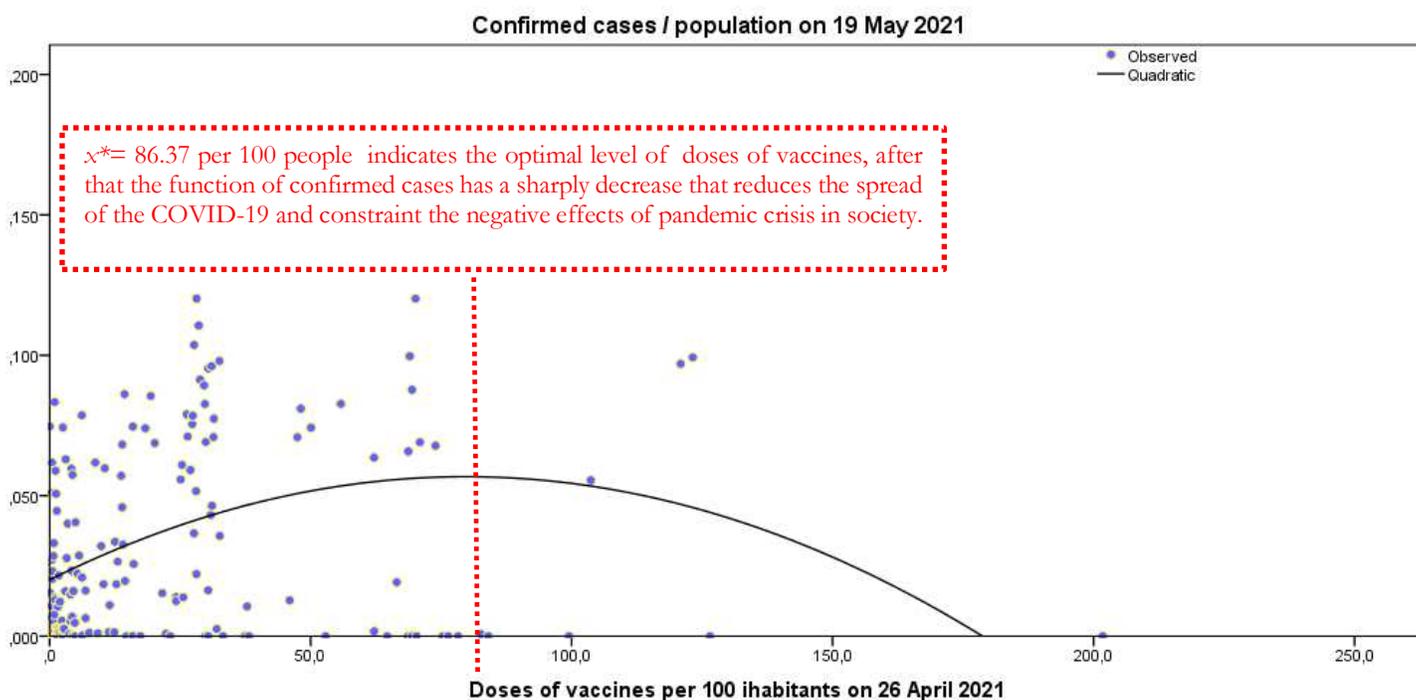


Figure 3. Relation of confirmed cases/population (%) of 19 May 2021 on doses of vaccines 26 April 2021 based on quadratic model [1]

□ *Effects of vaccination on fatality rate of COVID-19*

Table 5. Correlation

|  | Log Doses vaccines per100 inhabitant 15 March 2021 | Log Doses vaccines per100 inhabitant 14April 21 | Log Fatality Rate 25 April 21 |
|--|--|---|-------------------------------|
| Log Doses vaccines per100 inhabitant 15 March 2021 | 1  | .932**<br>0.001                                 | -.185*<br>0.026               |
| Log Doses vaccines per100 inhabitant 14 April 2021 |  | 1   | -.236**<br>0.002              |
| Log Fatality Rate 25 April 2021                    |  |   | 1                             |

\*\* Correlation is significant at the 0.01 level (1-tailed).

\* Correlation is significant at the 0.05 level (1-tailed).

Table 5 shows bivariate correlation of variables under study: fatality rates have a moderate negative association with doses vaccines per100 inhabitant on 15 March 2021 ( $r = -.19$ ,  $p$ -value  $< .05$ ) and doses vaccines per100 inhabitant on 14 April 2021 ( $r = -.24$ ,  $p$ -value  $< .01$ ).

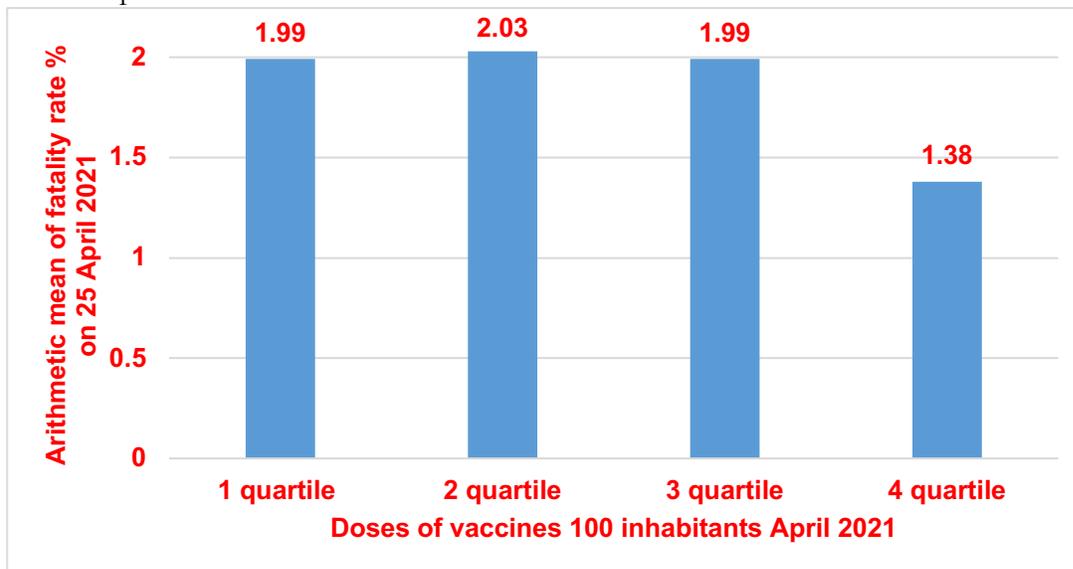
Table 6. Regression analyses of log fatality rate of the 25 April 2021 on log doses of vaccines per 100 inhabitants of the 14 April 2021 based on liner model [2]

|                        |         |
|------------------------|---------|
| Constant $\alpha$      | .54 *** |
| (St. Err)              | (.078)  |
| Coefficient $\beta_1$  | -.09 ** |
| (St. Err.)             | (.032)  |
| $R^2$                  | .06     |
| (St. Err. of Estimate) | (.75)   |
| $F$                    | 8.54**  |
| $N$                    | 191     |

Significance: \*\*\* $p$ -value<0.001 \*\* $p$ -value<0.01

Table 6 shows the coefficient of regression that indicates how an increase of 1% of doses of vaccines, it reduces the expected fatality rate by approximately 0.09% ( $p$ -value = .01). However, the coefficient  $R^2$  is rather low.

Figure 4. Average fatality rate at 25 April 2021 in different quartiles of the distribution of doses of vaccines per 100 inhabitants on 14 April 2021



Note: the 1<sup>st</sup> quartile (25th percentile) includes countries having a lower number of doses of vaccines per 100 inhabitants ( $\leq 8.3$ ), 2<sup>nd</sup> quartile (8.3 -5.79), 3<sup>rd</sup> quartile ( $\leq 5.79$ -22.43), 4<sup>th</sup> quartile has countries with the highest number of doses of vaccines per 100 inhabitants >22.43).

In general, these results suggest that the higher levels of vaccination generates a moderate reduction of fatality rate of COVID-19 in society, also considering that COVID-19 pandemic is going towards summer season characterized by a natural reduction of infected people (Figure 4).

## DISCUSSION

The main findings of the study here can be summarized in table 7. In particular, results reveal that optimal level of vaccination is associated with the evolution of COVID-19 pandemic wave: a vaccination in the initial phase of pandemic wave has a lower optimal level of doses administered per 100 inhabitants to reduce infected individuals, but the growth of pandemic wave moves up the optimal level of vaccines from 58.5 (March 2021) to more than 86 doses per 100 people (May 2021) with consequential effects on socioeconomic systems. This study suggests that the optimal strategy and response to pandemic crisis is a rapid vaccination rollout, before the takeoff of pandemic wave, for an effective response to reduce numbers of infected individuals and deaths.

Table 7. Optimal levels of vaccination based on relation between confirmed cases and doses of vaccines in different phases of pandemic wave to constrain the diffusion of COVID-19 in society

| Scenarios based on different phases of COVID-19 pandemic wave in 2021 | Optimal level of doses per 100 inhabitants that triggers the sharply decline of infected individuals |
|---|--|
| I (initial stage, March)  | 58.50  |
| II (growth stage, April)  | 70.25  |
| III (maturity stage, May)   | 86.37  |

These results may be interpreted through the lens of different studies that focus on a large number of factors contributing to the success of implementing the vaccination plan as suggested in the scenario A, having a lower level of doses of vaccines per 100 people for reducing confirmed cases and negative social impact. Sim et al. (2021) compare the coronavirus pandemic in Israel and the UK, showing the importance of factors influencing the early days of the rollout of vaccination and learning processes that can provide main lessons for other countries to plan COVID-19 vaccine programmes. Rosen et al. (2021) indicate three groups of facilitating factors for vaccination plan in Israel:

- extrinsic factors to health care (small size in terms of both area and population), a relatively young population, warm weather in December 2020, a centralized national system of government, and well-developed infrastructure for implementing prompt responses to large-scale national emergencies
- health-system specific factors, such as the organizational, IT and logistical capacities of community-based health care providers, the availability of well-trained cadre, a tradition of effective cooperation between government,

health plans, hospitals, and emergency care providers – particularly during national emergencies; and support tools and decision-making frameworks to support vaccination campaigns

- finally, specific factors to the COVID-19 vaccination effort: the mobilization of special government funding for vaccine purchase and distribution, timely contracting for a large amount of vaccines relative to population, the use of simple, clear and easily implementable criteria for determining who had priority for receiving vaccines in the early phases of the distribution process, technical response that addressed the demanding cold storage requirements of the Pfizer-BioNTech COVID-19 vaccine, and outreach efforts to encourage people to sign up for vaccinations and then show up to get vaccinated (cf., McKee and Rajan, 2021).

The most important policy implications of findings here are that, though high vaccination efforts of most advanced countries worldwide, the theoretical threshold for vanquishing COVID-19 seems to be out of reach at national and global level because of the accelerated diffusion of COVID-19 pandemic that changes the optimal level every month, the inequality of speed and distribution of vaccines, the ambiguities if and how vaccines prevent or not the transmission, the duration of immunity of vaccinated people and new variants that modify the herd-immunity equation (cf., Aschwanden, 2020, 2021). This study also reveals that high levels of vaccination can reduce slightly fatality rates of COVID-19 but optimal strategies to pandemic shocks should be based on strong governance structures driven by adequate and effective leadership that engages with the communities and adjusts to population needs (Williams et al., 2020). In fact, an organized public governance can support preparedness of nations for performing efficient campaigns of vaccination to reduce infections, mortality, morbidity, stress among the population and support economic recovery (Ardito et al., 2021; Coccia, 2005; Coccia, 2017, 2019, 2021e, 2021f, 2022; Kluge et al., 2020). The public governance supporting efficient vaccination plans is not limited to health system but it involves other functions of nation and its government to work properly for strengthening health, economic and social systems (Sagan et al., 2020). In general, effective crisis management of COVID-19 pandemic should implement timely vaccine programmes (as indicated in scenario A described before) supported by effective multi-level governance to improve health and social safety (Abuza, 2020; Anttiroiko, 2021; DeRoo et al., 2020; Frederiksen et al., 2020; Harrison and Wu, 2020; Ritchie et al., 2020). In addition, plans to achieve optimal levels of vaccination in the initial stage of pandemic have to face distribution and allocation hurdles, and in the presence of delays, they have to cope with

changes into the equation of herd-immunity with a strategy of vaccination directed to increase the thresholds of immunization of population to reduce, whenever possible, infected individuals in society (Callaway , 2021; Vignesh et al., 2020). In fact, the study here clearly shows that a delay of vaccinations from March to April 2021, in the presence of an evolutionary growth of pandemic wave, it moves forward the optimal threshold between countries from about 59 to 86 doses of vaccines per 100 people to trigger the reduction of the transmission dynamics of COVID-19 (Buss et al., 2021; ECDC, 2021; Mallapaty, 2021; Whittaker et al., 2021). In short, the timely achievement of the optimal threshold of doses administered is a basic aspect of crisis management, because a quickly and thoroughly vaccination plan can reduce mutations of the novel coronavirus, constrain transmission dynamics and consequential socioeconomic issues (Akamatsu, 2021; Byun et al., 2021; Liu et al., 2021). Engelbrecht and Scholes (2021) argue that if effective strategies of vaccination and/or vaccination plans have delayed, the progress of pandemic wave may generate additional health and socioeconomic issues. Overall, then, the implementation of optimal level of vaccination as suggested in scenario A is a significant challenge for all countries globally because it is associated with manifold socio-cultural and political-administrative factors, and enormous public investment in health system and research labs (Ethgen et al., 2019; Coccia, 2008, 2018b; 2019, 2021g, 2022; Coccia and Cadario, 2014). Hence, countries can adequately prepare for, prevent, detect, and respond to both epidemics and inevitable pandemics, over the next ten years, with a better governance, innovative partnerships, financial investments, and efficient utilization of economic resources in health and other sectors ( Coccia, 2017b; 2018a; 2019c; Coccia and Bellitto, 2018; U.S. Department of Health & Human Services, 2021).

## **CONCLUDING REMARKS AND RECOMMENDATIONS**

COVID-19 and future epidemics of novel influenza viruses pose, more and more, a serious threat to security and public health of nations. An influenza pandemic can occur at any time with little warning; any delay in detecting a novel influenza strain; sharing of influenza virus samples; and in developing, producing, distributing, or administering a therapeutic or vaccine could result in significant additional morbidity and mortality, and deterioration of socioeconomic systems (Coccia, 2021, 2021e). The global response to COVID-19 pandemic has pushed the research for detecting factors and aspects associated with a rapid pandemic response in several areas, including vaccine development, distribution, allocation, and administration. This study suggests that efficient strategies of vaccination

have to be rapid and responsive in the initial phase of COVID-19 pandemic wave for reducing the impact of novel viral agent in society, though this novel infectious disease might not disappear in the short term because of new variants. These results here can help policymakers to design satisfying goals to cope with current infectious diseases with effective vaccination strategies to prevent future outbreaks of the COVID-19 and similar viral agents.

Although this study has provided some interesting results, that are of course tentative, it has several limitations. First, a limitation of the study is the lack of data about doses administered and total vaccinations in manifold countries, mainly in the spring season of the year 2021, also for the difficulty of production and distribution of COVID-19 vaccines worldwide. Second, not all the possible confounding factors that affect the efficacy of vaccination are taken into consideration (such as, length of lockdown, facemask wearing, etc.) and in future they deserve to be controlled for supporting results here. Third, the lack of integration of data with age of vaccinated people (the priority given in many countries to elderly subjects, with a more compromised immune system) may have influenced the results of infected individuals and deaths across countries. Fourth, country-specific health norms may affect the gather and transmission of data, such that unreported confirmed cases and doses of vaccines in manifold countries may be present in database under study here. Antony et al. (2020) argue that the similarity in presentation between COVID-19 and influenza can have generated underreported data across countries. Finally, the estimated relationships in this study focus on variables in specific months (based on recent data available) but an extension of period is needed in future development of the research here. Thus, generalizing the results of this research should be done with caution. Future research should consider new data, when available, and when possible also to examine time series of variables within countries to explain more dynamic relations of the phenomena and relationships under study over time and space. Despite these limitations, the results presented here clearly illustrate the critical aspect of the relationship between phases of the evolution of pandemic wave and timing of the vaccination rollout to better support the goal of reducing negative effects of pandemic crisis in society. However, to conclude, there is need for much more detailed research in these topics and this study encourages further investigations for supporting optimal strategies of vaccination plans, using lessons learned of COVID-19, also considering the interaction between the evolution of pandemics and vaccination, and different factors between countries that are not only parameters related to medicine

but also to other sciences to improve preparedness of countries to face pandemic crisis and/or to control negative impact on public health, economy and society.

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