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Optimal levels of vaccination to reduce COVID-19 infected individuals and deaths: A global analysis

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ABSTRACT

Coronavirus disease 2019 (COVID-19) continues to be a pandemic threat that is generating a constant state of alert in manifold countries. One of the strategies of defense against infectious diseases (e.g., COVID-19) is the vaccinations that decrease the numbers of infected individuals and deaths. In this context, the optimal level of vaccination for COVID-19 is a basic point to control this pandemic crisis in society. The study here,−using data of doses of vaccines administered per 100 inhabitants, confirmed cases and case fatality ratio of COVID-19 between countries (N=192) from March to May 2021,− clarifies the optimal levels of vaccination for reducing the number of infected individuals and, consequently, the numbers of deaths at global level. Findings reveal that the average level of administering about 80 doses of vaccines per 100 inhabitants between countries can sustain a reduction of confirmed cases and number of deaths. In addition, results suggest that an intensive vaccination campaign in the initial phase of pandemic wave leads to a lower optimal level of doses administered per 100 inhabitants (roughly 47 doses of vaccines administered) for reducing infected individuals; however, the growth of pandemic wave (in May, 2021) moves up the optimal level of vaccines to about 90 doses for reducing the numbers of COVID-19 related infected individuals. All these results here could aid policymakers to prepare optimal strategies directed to a rapid COVID-19 vaccination rollout, before the takeoff of pandemic wave, to lessen negative effects of pandemic crisis on environment and socioeconomic systems.

1. Goals of the investigation

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, 2020, 2020a, 2021). COVID-19 is still circulating in 2021 with mutations of the novel coronavirus[1] that generate continuous COVID-19 infections and deaths in manifold countries (Johns Hopkins Center for System Science and Engineering, 2021; Huang et al., 2021; National Academy of Medicine, 2021; Vicenti et al., 2021). Seligman et al. (2021) show some characteristics of people that are associated with COVID-19 mortality, such as: mean age of 71.6 years, nonwhite race/ethnicity, income below the median and less than a high school level of education. High numbers of COVID-19 related infected individuals and deaths worldwide have supported the development of different types of vaccines based on viral vector, protein subunit and nucleic acid-RNA (Abbasi, 2020; de Vlas and Coffeng, 2021; Jones and Helmreich, 2020). 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 Spike (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 (viral vector vaccines for COVID-19 are by Janssen/Johnson & Johnson and University of Oxford/AstraZeneca). 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 (Novavax, an American biotechnology company, has developed this type of protein subunit vaccine; cf., GAVI, 2021). Instead, the messenger Ribonucleic acid (mRNA) vaccines use genetically engineered mRNA to give to cells

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; COVID-19, Coronavirus Disease 2019; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; CFRs, Case Fatality Ratios.

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[1] The World Health Organization (WHO) considers the following variants of concern: Beta, Gamma, Delta and Delta Plus; Variants of interest (Lambda and Mu) and manifold variants under monitoring (ECDC, 2021).

instructions on how to make the S protein found on the surface of the SARS-CoV-2, creating antibodies to fight this novel coronavirus (Mayo Clinic, 2021). The process of development of mRNA vaccines for COVID-19 is much faster than conventional vaccines to be redesigned and mass-produced (Cylus et al., 2021; Heaton, 2020; Jeyanathan et al., 2020; Komaroff, 2020). The first path-breaking mRNA vaccines for COVID-19 are due to premier biopharmaceutical companies: Pfizer-BioNTech and Moderna (cf., Coccia, 2015, 2017, 2017c, 2020c, 2021a). The investigation of vaccination plans between countries 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 of COVID-19, to relax non-pharmaceutical measures and maintain low basic reproduction number, but an important point is to clarify the levels of administering of vaccines between countries to timely reduce negative effects in society (Anser et al., 2020). Akamatsu et al. (2021) argue the vital role of governments to implement an efficient campaign of vaccination to substantially reduce infections in society, and avoid the collapse of healthcare system (cf., Coccia, 2021a, 2022). 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; Randolph and Barreiro, 2020). Herd immunity indicates that only a share of population needs to be immune and therefore no longer susceptible to a viral agent (by overcoming natural infection or through vaccination) for controlling large outbreaks (Fontanet and Cauchemez, 2020). Scholars estimate the proportion of a population that needs to be vaccinated to support herd immunity, *ceteris paribus* (Redwan, 2021). The threshold level depends on basic reproduction number, R_0— the number of average cases 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 everyone 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 evolves, since it depends on changes in susceptibility of the population, mitigation and restriction policies, circulation of variants, etc. (Aschwanden, 2020, 2021; Coccia, 2021c, 2021d). In addition, the relax of mitigation and containment measures can move up herd-immunity threshold in specific situation (Buss et al., 2021; Dashtbali and Mirzaie, 2021). Kwok et al. (2021) argue that the estimates of effective reproduction number range from 1.06 to 6.64 and the minimum proportion (%) of total population required to confer COVID-19 immunity is 5.66 in Kuwait and 85 in Bahrain. Rosen et al. (2021) describe socioeconomic and organizational factors associated with the vaccination campaign in Israel, a virtuous country in the plan of vaccination for COVID-19 (cf., Prieto Cruriel et al., 2021).

In this context, a fundamental problem in COVID-19 pandemic crisis is the optimal level of vaccination that supports a drastic reduction of COVID-19 infected individuals and deaths. The present study confronts this problem here by developing a statistical analysis to explain, at global level, 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 for vaccination plans to guide effective and timely policy responses for constraining negative effects of COVID-19 pandemic crisis and future epidemics of similar infectious diseases in environment and socioeconomic systems. This study is part of a large 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 in society (Coccia, 2020b, 2021b, 2021e, 2021h, 2021i, 2022a).

2. Materials and methods

2.1. Source and sample

The sample of this study is $N = 192$ countries worldwide. Period under study is from March to May 2021, using data of vaccines, confirmed cases and case fatality ratio of COVID-19. The list of countries under study is in Appendix A.

- Measures
  - Doses of vaccines administered $\times$ 100 inhabitants on March 1, April 1 and May 1, 2021.

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 (on March 21, April 21 and May 21, 2021) divided by population of countries under study. This study considers a time lag of 21 days from doses of vaccines administered (1st day of the month) to confirmed cases of COVID-19 (21 day of the same month) to assure a certain level of protection in population that begins after a variable number of days (Faes et al., 2020; Zhang et al., 2020). Source of data: Johns Hopkins Center for System Science and Engineering (2021).
- Number of COVID-19 deaths is measured with Case Fatality Ratio % (on March 21, April 21 and May 21, 2021). It indicates the severity of an infectious disease and evaluates the quality of health systems (Coccia, 2021e; Lau et al., 2021; WHO, 2020; Wilson et al., 2020). Case Fatality Ratio (CFR) estimates the proportion of deaths among identified confirmed cases of COVID-19:

$$Case\,Fatality\,Ratio\,(CFR)\% = \left(\frac{Number\,of\,deaths\,from\,COVID-19}{Number\,of\,confirmed\,cases\,of\,COVID-19}\right) \times 100$$

Angelopoulos at al. (2020) maintain that Case Fatality Ratios (CFRs) between countries are critical measures of relative risk that guide policymakers to decide how to allocate medical resource to cope with COVID-19 pandemic crisis. This study also calculates the mortality rate per 100 000 people for a comparative analysis with CFRs to assess the effects of vaccination with two indexes. Source of data: Johns Hopkins Center for System Science and Engineering (2021).

2.2. Model and data analysis procedure

Firstly, data are analyzed with descriptive statistics of variables given by arithmetic mean and standard error of the mean. Data concerning doses of COVID-19 vaccines, confirmed cases and CFR in the dataset downloaded the days under study can refer to data of different days because of difficulties in countries associated with gather or transmission of information. Moreover, database here includes different COVID-19 vaccines having a different period of administering between the first and second dose to provide a certain level of protection that begins after a variable number of days (approximately after 10–15 days the first dose) and remains for some months (about six months). In the presence of this just mentioned issue, the study here considers a time lag

of 21 days from date of doses of vaccines and date of confirmed cases. In addition, this study considers a large sample of $N = 192$ countries having a normal distribution that mitigates discrepancies among countries for significant statistical analyses.

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

- *Scenario A*. Initial stage of COVID-19 pandemic wave in March 2021. If countries of the sample have the level of vaccination at the time *t* (March 1, 2021) and confirmed cases at *t+21 days* (March 21, 2021), how would be the optimal level of doses of vaccines administered.
- *Scenario B*. Maturity stage of COVID-19 pandemic wave in May 2021. If countries of the sample have the level of vaccination at the time *t'* (May 1, 2021) and confirmed cases of *t'+21 days* (May 21, 2021), how would be the optimal level of doses of vaccines administered.
- *Scenario C*. Overall evolution of COVID-19 pandemic wave from March to May to estimate the optimal level of doses of vaccines administered between countries.

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 for three scenarios just described is given by:

$$y_{i,t} = \alpha_0 + \beta_1 x_{i,t-21} + \beta_2 x^2_{i,t-21} + u_{i,t} \qquad [1]$$

where:

- o $x_{i,t-21}$ = Doses of vaccines administered $\times$ 100 inhabitants on 1st day of the month (Explanatory variable)
- o $y_{i,t}$ = Number of confirmed cases of COVID-19 on 21st day of the month (Response *or* dependent variable)
- o $u_{i,t}$ = Error term
- o country $i = 1, ..., n;$ $t = time$

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

Remark 2. Model [1] has a time lag effect between explanatory (*t*-21 days) and dependent variables (*t*) to reduce the endogeneity of explanatory variable in model and provide reliable (estimated) parameters.

Thirdly, the optimization of the estimated relationships [1] is performed with the perspective of maximization of equation [1] to find the optimal levels of doses of vaccines administered $\times$ 100 inhabitants (during the 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] for three scenarios (A, B, and C) are objective functions of one (real) variable given by polynomial functions of 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 that reduce, subsequently, confirmed cases between countries in a specific stage of COVID-19 pandemic wave as described in scenarios A, B and C.

Finally, the optimal doses of vaccines administered, calculated as described in previous statistical and mathematical analyses, are used as cut-off points. In particular, average Case Fatality Ratios (%) and Mortality rates per 100 000 people are calculated for countries having lower or higher levels of doses of vaccines than cut-off points (i.e., optimal estimated values). This analysis also considers the population of countries in 2020 to assess if the size of countries plays a role in the policy responses to cope with COVID-19 pandemic crisis.

Statistical analyses are performed with the Statistics Software SPSS® version 26.

3. Results

Table 1 shows descriptive statistics of variables in March, April and May 2021.

☐ Scenario A: Initial phase of COVID-19 pandemic wave in March 2021.

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

$$z_{i,t} = 3.25 + 0.187 h_{i, t-21} - 0.002 h^2_{i, t-21}$$

The polynomial function is given by:

$$z = 3.25 + 0.1874h - 0.002\ h^2$$

the necessary condition to maximize is:

$$\frac{dz}{dh} = z'(h) = 0.187\ - 0.004h = 0$$

The first derivative equal to 0 is:

$$z'(h) = 0 \Rightarrow h^* = \frac{0.187}{0.004} = 46.75\ doses\ of\ vaccines\ per\ 100\ inhabitants\ in\ March\ 2021$$

$h^* = 46.75$ doses of vaccine per 100 people; h^* indicates the optimal level in the *initial phase* of pandemic wave (March 2021) between countries to trigger a sharply decrease of confirmed cases and diffusion of COVID-19 leading, whenever possible, to constraint negative effects of the pandemic crisis in society.

☐ *Scenario B*. Maturity phase of COVID-19 pandemic wave in May 2021.

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

$$y_{i,t} = 1.45 + 0.180 x_{i,t-21} - 0.001\ x^2_{i,t-21}$$

The function is given by:

$$y = 1.45 + 0.180x - 0.001\ x^2$$

the necessary condition to maximize the function is:

$$\frac{dy}{dx} = y'(x) = 0.180\ - 0.002x\ = 0 \qquad \qquad 0$$

The first derivative equal to 0 is:

$$y'(x) = 0 \Rightarrow x^* = \frac{0.180}{0.002} = 90\ doses\ of\ vaccines\ per\ 100\ inhabitants\ in\ May\ 2021$$

$x^* = 90$ doses of vaccines per 100 people; x^* indicates the optimal level during the *phase of maturity* of the COVID-19 pandemic in May 2021

Table 1
Descriptive statistics, N=192 countries worldwide.

Variables	Mean	Std. Error
Doses vaccines per 100 inhabitants March 1, 2021	7.547	1.506
Doses vaccines per 100 inhabitants April 1, 2021	12.750	1.573
Doses vaccines per 100 inhabitants May 1, 2021	19.514	1.957
Confirmed Cases/population % March 21, 2021	2.640	0.234
Confirmed Cases/population % April 21, 2021	3.062	0.265
Confirmed Cases/population % May 21, 2021	3.421	0.288
Case Fatality Ratios % March 21, 2021	2.182	0.186
Case Fatality Ratios % April 21, 2021	2.138	0.176
Case Fatality Ratios % May 21, 2021	2.271	0.215
Mortality rates per 100 000 people March 21, 2021	51.131	4.773
Mortality rates per 100 000 people April 21, 2021	58.046	5.369
Mortality rates per 100 000 people May 21, 2021	63.443	5.741

Table 2
Regression analyses of confirmed cases of March 21, 2021 on doses of vaccines on March 1, 2021 based on quadratic model [1].

Constant α (St. Err)	3.25 *** (.47)
Coefficient β₁ (St. Err.)	.187 ** (.07)
Coefficient β₂ (St. Err.)	−.002* (.001)
R² (St. Err. of Estimate)	.10 (3.24)
F	4.79**
Total cases	192

Note: Dependent variable is: Confirmed cases/population (%) of March 21, 2021. Explanatory variable is: doses of vaccines per 100 inhabitants on March 1, 2021.
*Significance: *** p-value < 0.001,** p-value < 0.01, * p-value < 0.05.*

Table 3
Regression analyses of confirmed cases (%) of May 21, 2021 on doses of vaccines on May 1, 2021 based on quadratic model [1].

Constant α (St. Err)	1.45 *** (.40)
Coefficient β₁ (St. Err.)	.180 *** (.03)
Coefficient β₂ (St. Err.)	−.001*** (.000)
R² (St. Err. of Estimate)	.33 (3.35)
F	38.46***
Total cases	192

Note: Dependent variable is: Confirmed cases/population (%) of May 21, 2021. Explanatory variable is: doses of vaccines per 100 inhabitants on May 1, 2021.
*Significance: *** p-value < 0.001.*

between countries to support, after this threshold, a sharply decrease of infections that reduces negative effects of COVID-19 pandemic in society.

☐ *Scenario C*: Overall evolution of COVID-19 pandemic from March to May 2021 between countries

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

$$j_{i,t} = 2.33 + 0.161 w_{i,\,t-21} - 0.001 \; w^2_{i,\,t-21}$$

The function is given by:

$$j = 2.33 + 0.161 w - 0.001 \; w^2$$

the necessary condition to maximize the function is:

$$\frac{dj}{dw} = j'(w) = 0.161 \; - \; 0.001 w \; = 0$$

The first derivative equal to 0 is:

$$j'(w) = 0 \Rightarrow w^* = \frac{0.161}{0.001} = 80.5 \; doses \; of \; vaccine \; per \; 100 \; inhabitants$$

Table 4
Regression analyses of confirmed cases of March 21, April 21, May 21, 2021 on doses of vaccines on March 1, April 1 and May 1, 2021 based on quadratic model [1].

Constant α (St. Err)	2.33 *** (.24)
Coefficient β₁ (St. Err.)	.161 *** (.020)
Coefficient β₂ (St. Err.)	−.001*** (.000)
R² (St. Err. of Estimate)	.21 (3.40)
F	50.45***

Note: Dependent variable is: Confirmed cases/population March 21-Apri 21l-May 21, 2021. Explanatory variable is: Doses of vaccines per 100 inhabitants on March 1, April 1 and May 1, 2021.
Significance: ***p-value<0.001.

$w^* = 80.5$ doses of vaccine per 100 people; w^* indicates the optimal target between countries for a policy response to support a sharply decrease of confirmed cases of COVID-19 leading, whenever possible, to constraint the negative societal effects of pandemic crisis in society (Fig. 1).

Fig. 1 shows the regression line and optimal level of doses of vaccines to trigger the reduction of confirmed cases. Some countries close to this optimal level are mainly small countries, such as Israel and United Arab Emirates.

☐ Effects of vaccination in society measured with level of Case Fatality Ratios (CFRs) and mortality rates per 100 000 people of COVID-19

In general, these results suggest that countries with levels of vaccination above the optimal level of doses of vaccines have lower average values of CFR % and mortality rate, whereas the confirmed cases have a higher level likely because of pro-active testing activity across countries. Finally, results reveal that countries best performers in the administering of high levels of doses of vaccines per 100 inhabitants are mainly smaller countries, such as Israel (cf., Fig. 1).

4. Discussion and policy implications

The findings of the study here 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 support the reduction of infected individuals, but the growth of pandemic wave moves up the optimal level of vaccines from 46.75 (in March 2021) to about 90 doses of vaccines in May 2021. This study also reveals that high levels of vaccination can reduce case fatality ratios and mortality rates of COVID-19 associated with other factors of health, environmental and economic system.

This study suggests that the optimal strategy and policy response to pandemic crisis are a rapid vaccination rollout to reduce timely numbers of infected individuals and deaths, before the takeoff of pandemic wave. These results may be interpreted through the lens of different studies that focus on many factors contributing to the success of implementing a rapid roll out of COVID-19 vaccination for reducing confirmed cases and negative social impact (Coccia, 2021a, 2021e, 2022). In fact, Sim et al. (2021) compare the COVID-19 pandemic in Israel and the UK, showing the importance of factors influencing the early days of the rollout of vaccination. Rosen et al. (2021) indicate three groups of facilitating factors the success of 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
- specific factors of the health-system, such as the organizational, IT and logistic 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 effective 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 for population, the use of simple, clear and easily criteria for determining who had priority for receiving vaccines in the early phases of the distribution process, demanding cold storage requirements of the Pfizer-BioNTech COVID-19 vaccines, and outreach efforts to

Table 5

Negative effects of COVID-19 between countries having doses of vaccine below or above the optimal (estimated) level, used as cut-off point.

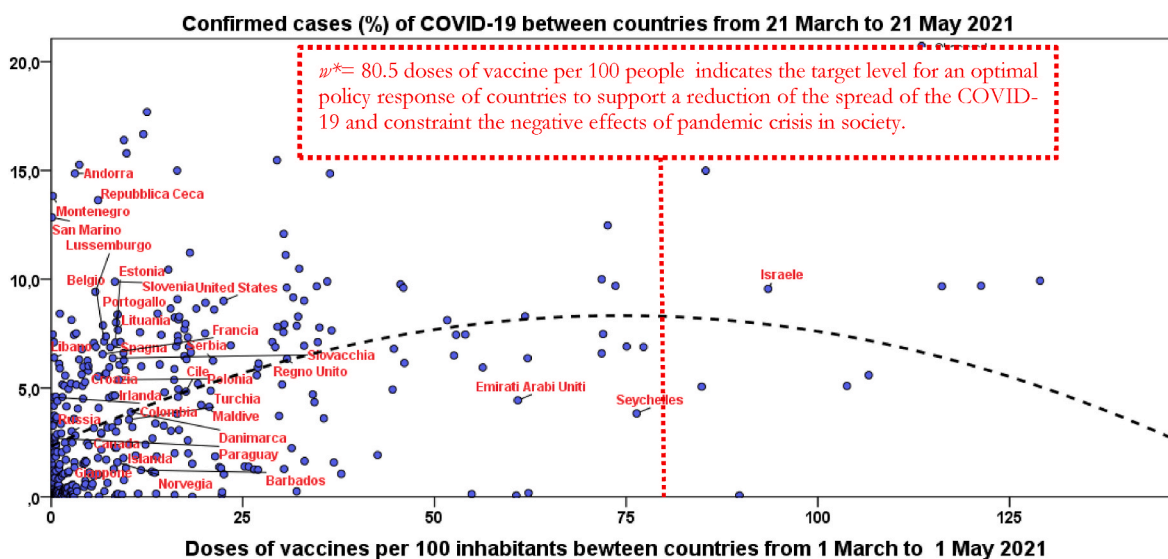|		Scenario A	Scenario B	Scenario C
Variables	Below or above the cut-off point = optimal level (estimated)	*Optimal level in March 2021 (Initial phase of pandemic) Doses of vaccines per 100 inhabitants = 46.8* Average value*	*Optimal level in May 2021 (Maturity phase of pandemic) Doses of vaccines per 100 inhabitants = 90* Average value*	*Optimal level over March–May 2021 (Evolution of COVID-19 pandemic) Doses of vaccines per 100 inhabitants = 80.5* Average value*
Confirmed Cases/	Below	4.15	3.88	3.82
population %	Above	5.94	8.41	7.74
Case Fatality Ratios	Below	1.94	1.84	1.86
(CFR) %	Above	0.50	0.47	0.75
Mortality per 100	Below	75.00	67.93	67.90
000 people	Above	32.74	41.11	63.20
Population	Below	65 495 630.45	51 009 497.76	51 777 286.42
	Above	6 401 920.67	6 401 920.67	6 642 840.00

Fig. 1. Relation of confirmed cases/population (%) on doses of vaccines from March to May 2021 between countries based on quadratic model [1].

encourage people to sign up for vaccinations and then show up to get vaccinated (cf., McKee and Rajan, 2021).

In general, optimal strategies to pandemic shocks should be based on a strong public governance driven by adequate and effective leadership that engages with the communities and adjusts to population needs (Williams et al., 2020). In fact, good governance can support the preparedness of nations for performing efficient campaigns of vaccination to reduce infections, mortality, morbidity, mental stress among the population and support economic recovery (Ardito et al., 2021; Coccia, 2017a, 2018a, 2019, 2021e, 2021f, 2021g, 2022; (Coccia, 2021l), Coccia and Bellitto, 2018; Coccia and Benati, 2018; Kluge et al., 2020). The public governance supporting efficient plans of vaccination is not limited to health system, but it involves other functions of public administration to work properly for strengthening health, economic and social systems (Sagan et al., 2020). As a matter of fact, effective crisis management of COVID-19 pandemic, supported by multi-level governance, should implement timely vaccine programmes to achieve, whenever possible, the goal of proposed scenarios (Abuza, 2020; Anttiroiko, 2021; Coccia, 2021a, 2021f; DeRoo et al., 2020; Frederiksen et al., 2020; Harrison and Wu, 2020; Ritchie et al., 2020, 2020a). Nevertheless, the optimal level of vaccination in the initial phase of pandemic has to face distribution and allocation hurdles, and in the presence of delays, governments have to cope with changes into the equation of herd-immunity with a strategy of vaccination directed to increase the thresholds of immunization in population to reduce infected individuals and negative effects in society (Callaway, 2021; Dooling et al.,

2020; Vignesh et al., 2020). In fact, the study here clearly shows that a delay of effective vaccination plan from March to May 2021, considering the evolutionary growth of pandemic wave, it moves forward the optimal threshold between countries from about 47 to 90 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 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 have delayed, the progress of pandemic wave may generate additional health and socioeconomic issues. Overall, then, the policy response based on an optimal level of vaccination, according to suggested scenarios, is a significant challenge associated with manifold socio-cultural and political-administrative factors, and enormous public investments in health system of countries (Ethgen et al., 2018; Coccia, 2017b, 2019, 2021g, 2022). Hence, countries can adequately prepare to prevent, detect and respond to both epidemics and pandemics, over the next ten years, with a better governance, innovative partnerships, high public investments, and efficient utilization of economic resources in health and other sectors (U.S. Department of Health and Human Services, 2021).

5. Conclusions and prospects

COVID-19 and future epidemics of novel viruses pose, more and more, a serious threat to security and public health of nations. An influenza pandemic, similar to COVID-19, 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; Huang et al., 2021).

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 negative impact of novel viral agent in society. These results here can help policymakers to design satisfying goals to cope with current pandemic applying effective vaccination strategies to prevent and/or cope with future outbreaks of the COVID-19 and similar epidemics. 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 global level (in the medium run) because of the inequality in the distribution of vaccines, the uncertainty if and how new vaccines prevent or not the transmission, the duration of immunity in vaccinated people, hesitancy of people to vaccination and new variants that modify the herd-immunity equation and transmission dynamics (cf., Aschwanden, 2020, 2021). In fact, on November 2021 about 52% of the world population has received at least one dose of a COVID-19 vaccine and in poor countries a mere 5% of people have received at least one dose (Our World in Data, 2021).

Although this study has provided 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 and transmission of data and information. Second, not all the possible confounding factors that affect the efficacy of vaccination are taken into consideration (such as, length of lockdown, mitigation measures, etc.) and in future these factors 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. In addition, structure of population and characteristics of patients (e.g., ethnicity, age, sex, and comorbidities) may vary between countries making comparative analysis in some cases a problematic approach (Angelopoulos et al., 2020; Coccia, 2018; WHO, 2020). 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) also argue that the similarity of symptoms between COVID-19 and influenza can have generated under-reported 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 under study 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, to examine also other variables between countries to explain dynamic relationships under study over time and space. Despite these limitations, the results presented here suggest the critical aspect of the relationship between the evolution of pandemic wave and timing of the vaccination rollout to achieve the goal of optimal threshold of vaccination at national (and global) level for reducing negative effects of pandemic crisis in society. However, there is need for much more detailed research in these topics and this study encourages further investigations for supporting optimal strategies of vaccination, using lessons learned of COVID-19, also considering the temporal interaction between the evolution of pandemic wave and vaccination plan. To conclude, different factors between countries that are not only parameters related to medicine but also to other sciences can improve the preparedness of countries for an effective and a rapid roll out of vaccination to control negative impact of pandemic crisis on public health, economy and society.

Author's contributions

Single author, Mario Coccia.

Declaration of competing interest

The author, Mario Coccia, declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. List of countries $N = 192$

Countries 1-46	Countries 47-92	Countries 93-138	Countries 139-184	Countries 185-192
Afghanistan	Danimarca	Kuwait	Qatar	Uruguay
Albania	Diamond Princess	Laos	Regno Unito	Uzbekistan
Algeria	Dominica	Lesotho	Repubblica Ceca	Vanuatu
Andorra	Ecuador	Lettonia	Repubblica Centrafricana	Venezuela
Angola	Egitto	Libano	Repubblica democratica del Congo	Vietnam
Antigua e Barbuda	El Salvador	Liberia	Repubblica Dominicana	Yemen
Arabia Saudita	United Arab Emirates	Libia	Romania	Zambia
Argentina	Eritrea	Liechtenstein	Ruanda	Zimbabwe
Armenia	Estonia	Lituania	Russia	
Australia	Etiopia	Lussemburgo	Saint Kitts and Nevis	
Austria	Figi	Macedonia del Nord	Saint Lucia	**TOTAL = 192**
Azerbaigian	Filippine	Madagascar	Saint Vincent e Grenadine	
Bahamas	Finlandia	Malawi	Samoa	
Bahrein	Francia	Maldive	San Marino	
Bangladesh	Gabon	Malesia	Sao Tome and Principe	
Barbados	Gambia	Mali	Senegal	
Belgio	Georgia	Malta	Serbia	
Belize	Germania	Marocco	Seychelles	
Benin	Ghana	Mauritania	Sierra Leone	
Bhutan	Giamaica	Mauritius	Singapore	
Bielorussia	Giappone	Messico	Siria	

(*continued on next page*)

(*continued*)

Countries 1-46	Countries 47-92	Countries 93-138	Countries 139-184	Countries 185-192
Bolivia	Gibuti	Micronesia	Slovacchia	
Bosnia ed Erzegovina	Giordania	Moldavia	Slovenia	
Botswana	Grecia	Monaco	Somalia	
Brasile	Grenada	Mongolia	Spain	
Brunei	Guatemala	Montenegro	Sri Lanka	
Bulgaria	Guinea	Mozambico	United States of America	
Burkina Faso	Guinea Equatoriale	MS Zaandam	Sudafrica	
Burundi	Guinea-Bissau	Myanmar	Sudan	
Cambogia	Guyana	Namibia	Sudan del Sud	
Camerun	Haiti	Nepal	Suriname	
Canada	Honduras	Nicaragua	Sweden	
Capo Verde	India	Niger	Svizzera	
Ciad	Indonesia	Nigeria	Swaziland	
Cile	Iran	Norvegia	Tagikistan	
Cina	Iraq	Nuova Zelanda	Taiwan*	
Cipro	Irlanda	Oman	Tanzania	
Città del Vaticano	Islanda	Paesi Bassi	Thailandia	
Colombia	Isole Marshall	Pakistan	Timor Est	
Comore	Isole Salomone	Palestina	Togo	
Congo	Israel	Panama	Trinidad e Tobago	
Corea del Sud	Italy	Papua Nuova Guinea	Tunisia	
Costa d'Avorio	Kazakistan	Paraguay	Turchia	
Costa Rica	Kenya	Perù	Ucraina	
Croazia	Kirghizistan	Polonia	Uganda	
Cuba	Kosovo	Portugal	Ungheria	

Appendix. ASupplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.112314.

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