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The relation between timing of vaccinations and levels of confirmed cases of COVID-19 in society: When to roll out vaccination to minimize infections?

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Abstract. This study analyzes the relations between doses administrated of vaccines for Coronavirus disease-2019 (COVID-19) and confirmed cases from March to May 2021 to find out the optimal level of doses administrated per 100 inhabitants, which can lead to a reduction in the diffusion of COVID-19 cases. Findings reveal that a delay of vaccination in population, it moves up the optimal value of doses administrated per 100 inhabitants from 58.5 to more than 86 per 100 people, with consequential damages and long-run deterioration of socioeconomic systems. This study suggests that the optimal policy to pandemic threats is the early, rapid, nationally vaccination rollout for an effective reduction of the spread of infectious disease that reduces negative effects in society.
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JEL. C52; L25; M14.

1. Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which appeared in late 2019 (Coccia, 2021). COVID-19 is still circulating in 2021 with mutations of the novel coronavirus that generate a constant pandemic threat in manifold countries with higher numbers of COVID-19 related infected individuals and deaths (Johns Hopkins Center for System Science and Engineering, 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, 45.9% female, and 45.1% non-Hispanic white... 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)".

The alarming levels of spread and severity of COVID-19 worldwide has supported the development of vaccines in 2020 based on messenger RNA

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vaccines, known as mRNA vaccines for high levels of protection by preventing COVID-19 among people that are vaccinated (Coccia, 2021a). The mRNA vaccines for COVID-19 are based on accumulated knowledge that the infective process itself is effective in raising an immune response and genetic engineering can be utilized to construct virus-like particles from the capsid and envelope proteins of viruses (Smoot, 2020; Coccia & Finardi, 2012). Moreover, mRNA vaccines eliminate a lot of phases in manufacturing process for the development of new drugs because rather than having viral proteins injected, the human body uses the instructions to manufacture viral proteins itself. In short, mRNA vaccines are produced and manufactured by chemical rather than biological synthesis, as a consequence the process of development is much faster than conventional vaccines to be redesigned, scaled up and mass-produced (Komaroff, 2020). Manifold public agencies for protecting and promoting public health through the control and supervision in the United Kingdom, the USA, Europe and other countries confirm that mRNA vaccines for COVID-19 can be effective and safely tolerated in population (Abbasi, 2020; Cylus *et al.,* 2021; Heaton, 2020; Jeyanathan *et al*., 2020; Komaroff, 2020).

Because of the rapid spread of COVID-19 worldwide, understanding the significance of vaccination is crucial in determining how COVID-19 can be eradicated in the population (Aldila *et al.,* 2021). Vaccination has the potential to eradicate COVID-19, to relax nonpharmaceutical measures, maintaining low basic reproduction number, but it is an important and essential point to clarify the optimal strategy of administration of vaccines and widespread mass vaccinations to constrain COVID-19 pandemic and future variants in society (cf., Anser *et al.,* 2020). Akamatsu *et al.* (2021) argue that to cope with the infectious disease severity that increases considerably, governments have to implement an efficient campaign of vaccination to substantially reduce infections and mortality in society and also avoid the collapse of the healthcare system. Aldila *et al.* (2021) argue that higher levels of vaccination rate can eradicate COVID-19 from the population. The final goal of a plan of vaccination is achieving herd immunity to protect vulnerable individuals (Anderson *et al.,* 2020; de Vlas and Coffeng, 2021, Randolph & Barreiro, 2020; Redwan, 2021). Herd immunity indicates that only a share of a population needs to be immune and as a consequence no longer susceptible (by overcoming natural infection or through vaccination) to a viral agent for epidemic control and to stop generating large outbreaks (Fontanet & Cauchemez, 2020). Scholars can estimate the proportion of a population that needs to be immune to support herd immunity. This threshold level depends on the 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 $1–1/R_0$ — 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, and it depends on changes in susceptibility of the population, mitigation policies, variants, etc. (Aschwanden, 2020, 2021). Kwok *et al.* (2021) estimated the Rt in different countries and a threshold for herd immunity in each country's population. The level of Rt ranges from 85% to 5.66% also because of measures of mitigation and containment to infectious disease and other factors, that if they are relaxed can move up herd-immunity threshold (Buss *et al.,* 2021). Rosen *et al.* (2021) describe socioeconomic and organizational factors associate with success of vaccination campaign in Israel as well as there are some aspects of misinformation and social dynamics that can reduce the effectiveness of a fruitful vaccination in population (cf., Prieto Curiel, *et al.* 2021), and they can be divided into three major groups. Different models explain the spread and impact of COVID-19 considering social distancing and vaccination (Dashtbali *et al.,* 2021).

In this context, a key problem in current COVID-19 pandemic crisis is how herd immunity can be achieved with an effective vaccination campaign that supports a drastic reduction of numbers of COVID-19 related infected individuals and deaths. The study here confronts this problem here by developing a modelling and statistical analysis to explain, whenever possible, how change, at global level, optimal threshold that triggers a drastic reduction of COVID-19 infections and support herd immunity. Results can suggest best practices of optimization in the vaccination strategy, considering global data of more than 190 countries, in order to guide effective and timely policy responses that trigger the sharply reduction of confirmed cases in society for combatting the novel coronavirus and constraining negative effects of current COVID-19 pandemic crisis and future pandemics of similar infectious diseases in society. In fact, in the presence of COVID-19 pandemic crisis, it is more and more important to determine efficient strategies of vaccinations, rather than full lockdown that paralyze economic and social activities, to contain and/or prevent negative effects of pandemics on health people and economy (Coccia, 2021c). Lessons learned from this study could be of benefit to countries as they grapple to plan their COVID-19 vaccine programmes to reduce state of emergency of pandemic crisis and negative effects on socioeconomic system. This study is part of a large body of research 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, 2021).

2. Materials and methods

2.1. Source and sample

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 and confirmed cases of COVID-19.

- **Measures**

– Doses of vaccines administrated × 100 inhabitants on 15 March 2021, *N*=114 countries; on 14 April 2021 with *N*=154 countries, on 26 April 2021, *N*= 190 countries . The number of countries tends to increase over time with the diffusion of vaccines across countries. 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). 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).

2.2. Model and data analysis procedure

Firstly, data are analyzed with descriptive statistics of variables given by arithmetic mean (M) and standard error of the mean (SEM). In addition, the normality of the distribution of variables to apply correctly parametric analyses is analyzed with skewness and kurtosis coefficients. Variables of the doses of COVID-19 vaccines and confirmed cases are considered in two different periods of time because studies by Canada's National Advisory Committee on Immunization (NACI) show that Pfizer-BioNTech and Moderna vaccines started providing some level of protection 12 to 14 days after the first dose. By the time the second dose was administered —19 to 42 days after the first — the first shot was shown to be 92 per cent effective (CBC, 2021; CDC, 2021; Rossman *et al.*, 2021).

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

The specification of model is given by:

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

where:

- $y_{i,t}$ = Number of COVID-19 infected individuals/population, dependent variable
- $x_{i,t-1}$ = Doses of vaccines administrated × 100 inhabitants, explanatory variable
- $u_{i,t}$ = Error term
- country *i=1, …, n;* *t=time*

Remark: Model [1] has a time lag effect between explanatory (t-1) and dependent variables (t) to logically include in the relations under study the period from the administration of vaccines doses to the level of protection in population and reduce the endogeneity for providing reliable (estimated) parameters.

Remark: The square of the doses of vaccines administrated × 100 inhabitants in model [1] is introduced to consider, as hypothesized, 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 administrated × 100 inhabitants that support a consequential drastic reduction of confirmed cases /population of COVID-19 over time to constraint negative effects of infectious disease in society and overcome pandemic crisis. 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 level of doses of vaccines administrated × 100 inhabitants at the time *t* that reduces the spread of confirmed cases in society, and stop COVID-19 pandemic crisis for a general herd immunity.

In order to decide the best strategy to prevent future pandemics using lessons learned from COVID-19, this study presents four scenarios, using global data in different periods:

- ☐ *Vaccination campaign and confirmed cases in March 2021*
- ☐ *Vaccination campaign in March 2021 and confirmed cases in April 2021*
- ☐ *Vaccination campaign and confirmed cases in April 2021*
- ☐ *Vaccination campaign in April 2021 and confirmed cases in May 2021*

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

3. Results

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 14 April 2021	154	14.50	1.65
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)

☐ *Case A: Vaccination campaign and confirmed cases of COVID-19 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 α	2.09 ***
(St. Err)	(.38)
Coefficient β_1	.234 ***
(St. Err.)	(.05)
Coefficient β_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:

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

The polynomial function is given by

$$z = 2.09 + 0.234h - 0.002\ h^{2}$$

the necessary condition to maximize is:

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

The first derivative equal to 0 is:

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

h^*= 58.5 per 100 people indicates the optimal level of doses of vaccines, 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.

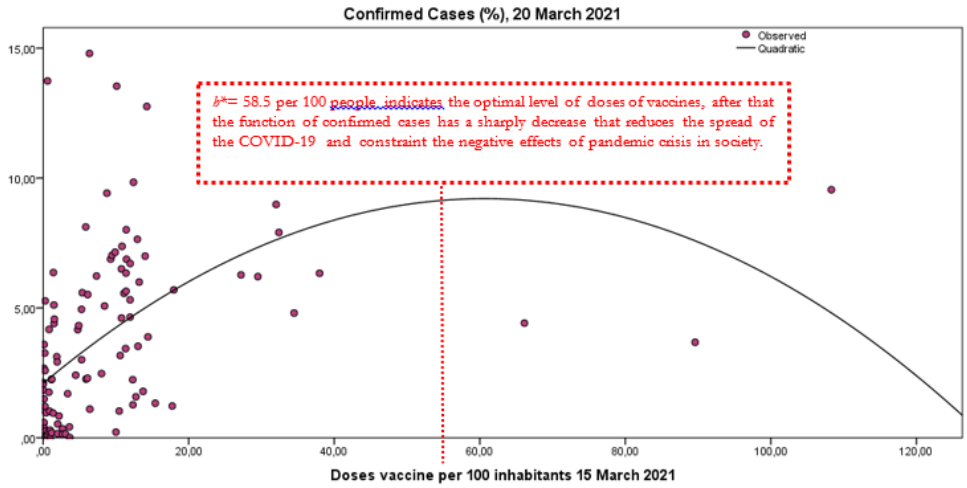

Figure 1. *Relation of confirmed cases/population (%) of 20 March 2021 on doses of vaccines on 15 March 2021 based on quadratic model [1]*

☐ *Case B: Vaccination campaign in March 2021 and confirmed cases in April 2021*

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 α	2.47 ***
(St. Err)	(.43)
Coefficient β_1	.281 ***
(St. Err.)	(.05)
Coefficient β_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:

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

The function to optimize is given by

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

the necessary condition to maximize is:

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

The first derivative equal to 0 is:

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

x^*= 70.25 per 100 people indicates the optimal level of doses of vaccines, 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.

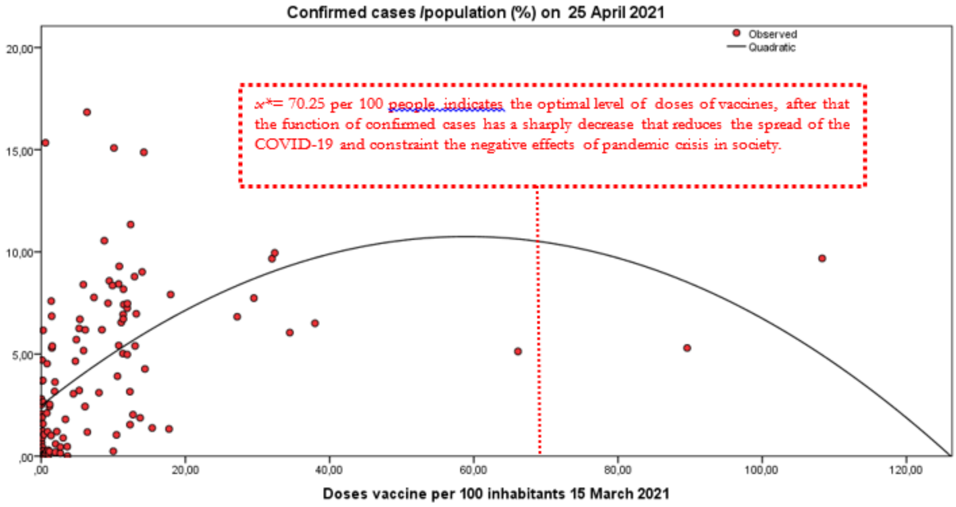

Figure 2. *Relation of confirmed cases/population (%) of 25 April on doses of vaccines 15 March 2021 based on quadratic model [1]*

☐ *Case C: vaccination campaign in April 2021 and confirmed cases in April 2021*

Table 4. *Regression analyses of confirmed cases/population (%) of 25 April on doses of vaccines on 14 April 2021 based on quadratic model [1]*

Constant α	1.71 ***
(St. Err)	(.37)
Coefficient β_1	.197 ***
(St. Err.)	(.03)
Coefficient β_2	–.001***
(St. Err.)	(.000)
R^2	.28
(St. Err. of Estimate)	(3.23)
F	30.04***
N	153

Note: Dependent variable is Confirmed cases/population (%) of 25 April 2021. Explanatory variable is Doses of vaccines on 14 April 2021 per 100 inhabitants; Significance: *** *p*-value <0.001

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

$$g_{i,t} = 1.71 + 0.234k_{i,t\text{-}1} - 0.002\ k^2_{i,t\text{-}1}$$

The function is given by

$$z = 2.09 + 0.197k - 0.001\ k^2$$

the necessary condition to maximize is:

$$\frac{dg}{dk} = g'(k) = 0.197 - 0.001k = 0$$

The first derivative equal to 0 is:

$$g'(k) = 0 \qquad \Rightarrow k^* = \frac{0.197}{0.002} = 98.5\ per\ 100\ inhabitants$$

k^*= 98.5 per 100 people indicates the optimal level of doses of vaccines, 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.

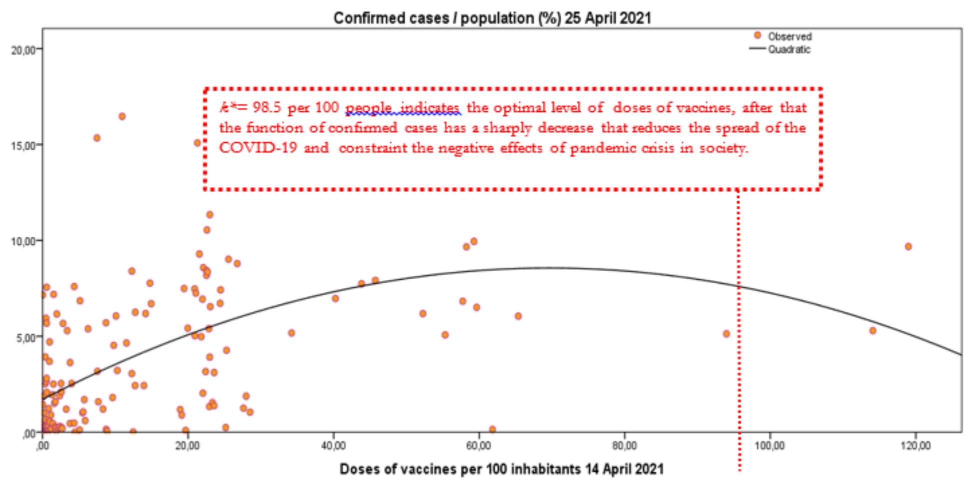

Figure 3. *Relation of confirmed cases/population (%) of 25 April on doses of vaccines 14 April 2021 based on quadratic model [1]*

☐ *Case D: Vaccination campaign in April and confirmed cases in May 2021*

Table 5. *Regression analyses of confirmed cases/population of 19 May 2021 on doses of vaccines on 26 April 2021 based on quadratic model [1]*

Constant α	.020 ***
(St. Err)	(.004)
Coefficient β_1	001 ***
(St. Err.)	(.000)
Coefficient β_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 5, is:

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

The function to optimize is given by

$$j = 0.02 + 0.001w \quad - 0.000005789\ w^{2}$$

the necessary condition to maximize is:

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

The first derivative equal to 0 is:

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

w^*= 86.37 per 100 people indicates the optimal level of doses of vaccines, 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.

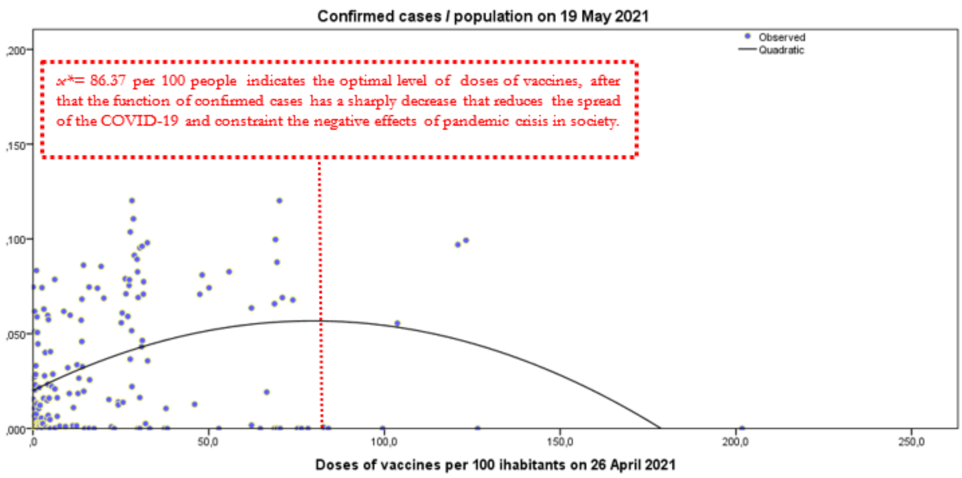

Figure 4. *Relation of confirmed cases/population (%) of 19 May 2021 on doses of vaccines 26 April 2021 based on quadratic model [1]*

4. Discussion

The novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that caused the Coronavirus Disease 2019 (COVID-19), as said, continues to be a constant pandemic threat in 2021 with mutations of novel coronaviruses[1], such that the state of emergency remains in manifold countries because of high numbers of COVID-19 related infected individuals and deaths in society. The COVID-19 pandemic crisis needs rapid pandemic

[1] WHO considers the following variants of concern: Alpha, Beta, Gamma and Delta; Variants of interest (Eta, Epsilon, Theta, Kappa) and manifold variants under monitoring, such as Iota and Zeta (ECDC, 2021).

responses in several areas, including health systems, development of new drugs and vaccine research associated with development, manufacturing, distribution, allocation, and administration (National Academy of Medicine, 2021, 2021a).

The main findings of statistical analysis and optimization can be summarized in the following table 6. In particular, the findings of this study reveal that a delay of vaccination plan in population, from March to April 2021, it moves forward the optimal level of doses administrated per 100 inhabitants, prolonging the state of emergency and exit from COVID-19 pandemic crisis with consequential damages and long-run deterioration of socioeconomic systems. Hence, the strategy and optimal response to pandemic threats is, first start vaccination, first I can go out from emergency and crisis, synthetized with the acronym *FirstS, FirstO*: a timely start of the vaccination plan, it leads countries to anticipate the exit from the emergency and pandemic crisis.

Table 6. *Optimal level of vaccination based on relation of confirmed cases on doses of vaccines over time to constrain the diffusion of COVID-19*

Scenarios	Doses vaccines per 100 inhabitants administrated	Confirmed cases/population	Optimal* level of doses per 100 inhabitants that triggers the sharply decline of confirmed cases
A	15 March 2021	20 March 2021	58.50
B	15 March 2021	25 April 2021	70.25
C	14 April 2021	25 April 2021	98.25
D	26 April 2021	19 May 2021	86.37

A large number of factors can contribute to the success of implementing the optimal level of scenario A (Table 6), which is lower level of doses per 100 people than other scenarios, to maximize of the positive social impact, reducing confirmed cases, for achieving early the final goal of herd immunity and as a consequence to constrain negative socioeconomic effects. Rosen *et al.* (2021) indicate three groups for a case study of Israel, driven by a combination of facilitating factors and organizational synergies: a) 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; b) health-system specific factors, such as the organizational, IT and logistical capacities of community-based health care providers, the availability of a cadre of well-trained, salaried, 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, c) 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, a creative technical response that addressed the demanding cold storage requirements of the Pfizer-BioNTech COVID-19 vaccine, and well-tailored outreach efforts to encourage people to sign up for vaccinations and then show up to get vaccinated (cf., McKee & Rajan, 2021). Sim *et al.* (2021) analyze the response to the global 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.

However, some rich countries are lacking several of these factors of governance, reducing the pace of vaccination to combat the spread of COVID-19. Williams *et al.* (2020) argue that effective responses to public health emergencies should rely on translating rapidly emerging research into timely, evidence-informed policies and best practices. Optimal strategies of vaccinations to pandemic shocks must have strong governance structures driven by adequate and effective leadership that engages with the communities, listens and adjusts to population needs. Efficient governance can support health system preparedness for performing efficient campaign of vaccinations in the presence of turbulent scenarios and new population needs. Moreover, countries with constant investment in health sector and preparedness can apply effective policy responses, vaccination-based, to reduce infections, mortality, morbidity and stress among the population as well as promote health of people and economic recovery (Coccia, 2021f; Kluge *et al.*, 2020). In general, efficient strategies of vaccinations have to be based on effective governance and technical capacity to respond in a short period of time to pandemic crisis (Sagan *et al.*, 2020; Kluge *et al.*, 2020). Sagan *et al.* (2020) consider a broad concept of governance that is not limited to health system alone but also directed to support other functions of nation and its government to work properly for strengthening health, economic and social systems in the presence of emergency. In general, crisis management of COVID-19 pandemic to implement effective vaccine programmes is based on effective multi-level governance, combining both national and local strategies to support vaccination campaign, achieve herd immunity and improve health safety in society (Anttiroiko, 2021; Ritchie *et al.*, 2020). Abuza (2020) argues that effective policy responses are due to leadership and competence, rather than regimes of countries.

Overall, then, in the presence of pandemic threat, mass vaccination is the most credible option to cope with the COVID 19 pandemic but it has to be applied properly and timely (DeRoo *et al.*, 2020; Frederiksen *et al.*, 2020; Harrison & Wu, 2020). The implementation of a mass vaccination campaign is a significant challenge for all countries globally because it is associated with manifold economic, socio-cultural and political-administrative factors. Economic factors are a relevant component since mass vaccination campaign involves enormous public investment to be organized (Ethgen *et al.*, 2019). The wealth of nations, in this sense, becomes a discriminating factor for success of vaccination plan. In fact, higher-income countries perform better than low-income ones in vaccine programmes of their citizens (Ataguba *et al.*, 2016). Other factors that affect vaccinations are socio-cultural factors, such house living conditions (Kusuma *et al.* 2010; Mitchell *et al.* 2009), education, religious beliefs (Soura *et al.* 2013), gender based inequity (Pande, 2003) and information (Logan *et al.* 2018). A vital role is due to good governance that provides effective organizational aspects of decision support for effective campaign of vaccinations (Glatman-Freedman & Nichols, 2012). Good governance has a whole range of positive effects on institutional change, organizational behavior, economic growth and as well as improvement of public services (Coccia, 2019, 2020a; Glatman *et al.*, 2010; Glatman-Freedman & Nichols, 2012; Kaufmann *et al.*, 1999). The ability to organize a vaccination campaign to cope with COVID-19 pandemic crisis can be compared to the organization of public service in a short period of time in a context of crisis management and factors described above play a critical role for achieve herd immunity (Coccia, 2020b, 2021b). In addition, country-level governance may also affect the infrastructure required for the successful implementation of vaccine programs, such as the ability to reach distant locations, to manage cold chain, to support safe disposal of used syringes and needles, and sustain training of human resources. In fact, country-level governance was found to be a stronger predictor of the initial introduction of new vaccines to poor African nations than healthcare-related financial indicators (cf., Glatman *et al.* 2010; Glatman-Freedman & Nichols, 2012).

5. Conclusions and prospects

COVID-19 and future epidemics of novel influenza viruses pose, more and more, a serious threat to national security and public health. 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). The global response to COVID-19 pandemic has pushed the studies for detecting factors and aspects for rapid pandemic response in several areas, including healthcare system, vaccine research, development, manufacturing, distribution, allocation, and administration of doses. These actions could support organizational behavior and human resources to improve preparedness efforts to advance R&D for efficient pandemic vaccines and timely public responses of vaccine plans to constrain the spread of pandemics similar to COVID-19. New strategies of vaccination campaign in the presence of severe pandemic threats have to be highly responsive, flexible, resilient, scalable, and more effective for reducing the impact of pandemic viruses and likely mutations. An efficient strategy of crisis management for pandemic threats can be based on three goals:

- Strengthen and diversify vaccine development, manufacturing, and supply chain;
- Promote innovative approaches and use of new technologies to detect, prevent, and respond to epidemics and pandemics; and
- Timely plan of vaccination to increase vaccine access and coverage across all populations in the presence of unforeseen pandemic of novel viral agents.

In this context, to adequately prepare for, prevent, detect, and respond to both epidemics and inevitable pandemics, it is important to reinforce the governance of countries, supporting pandemic preparedness efforts by collaborating with domestic and international stakeholders. In fact. execution of this strategic approach over the next ten years will require a better governance, innovative partnerships, financial investments, and efficient utilization of resources (U.S. Department of Health & Human Services, 2021). In short, policies of vaccination having agility and speed of responses have to be based on a better governance of countries that is a vital factor of crisis management to cope with new waves of COVID-19 and future epidemics/pandemics similar to COVID-19 (Chang *et al.*, 2020; Coccia, 2021d; Janssen & van der Voort, 2020; Renardy *et al.*, 2020). In the presence of a good governance, Evans & Bahrami (2020) pinpoint that countries can apply super-flexibility to cope with COVID-19 pandemic in which decision making is oriented to versatility, agility, and resilience.

In general, vaccine rollout plans have to face distribution and allocation hurdles, and new mutations of SARS-CoV-2, likely more transmissible and resistant to vaccines, can change the equation of herd-immunity and strategy of vaccinations, increasing the thresholds of immunization in population (Callaway , 2021; Dooling *et al.*, 2020; Vignesh *et al.*, 2020). A delay of the plan of vaccinations and of the achievement of optimal threshold within countries, it does not reduce transmission dynamics and it can foster emergence and diffusion of variants, such as in Brazil and India (ECDC, 2021; Mallapaty, 2021; Buss *et al.*, 2021; Whittaker *et al.*, 2021).

In short, the timely achievement of the optimal threshold of doses administered is basic, because a vaccination plan quickly and thoroughly can prevent new mutations of the novel coronavirus and constrain transmission dynamics in society and consequential socioeconomic issues (Akamatsu, 2021). In this context, non-pharmaceutical interventions continue to play a crucial part also during vaccination plans to stop/reduce the transmission paths and maximize the positive societal effects. Even though herd immunity is a difficult goal for manifold countries, the ability to vaccinate vulnerable people seems to be one of the vital factors for reducing hospitalizations, admission to Intensive Care Units and deaths from COVID-19 and similar infectious diseases (Jones & Helmreich, 2020). Engelbrecht & Scholes (2021) argue that COVID-19 can have a seasonal dependence and if herd immunity is not established by effective strategies of vaccination and/or vaccination has delayed diffusion for high demand that generates problems of production, recurring waves may generate additional health and socioeconomic issues.

Overall, then, findings here reveal that the optimal threshold by a timely vaccination can lead to a drastic reduction of COVID-19, though this novel infectious disease might not disappear in the short term. These results here can help policymakers to design satisfying goals to cope with current infectious diseases and to prevent future outbreaks of the COVID-19 and similar viral agents in future. Nevertheless, the proposed results are of course tentative because other factors should be included in future development of this study to design optimal strategy of vaccinations. A limitation of the study is the lack of data about doses administrated and total vaccinations in manifold countries, mainly at the beginning of the year 2021, also for the difficulty of production and distribution of COVID-19 vaccines. Therefore, there is need for much more detailed research using updated data to further verify proposed relations between administration of vaccines and confirmed cases also in the presence of new mutation of the novel coronavirus between countries. To conclude, this study encourages further investigations for developing comprehensive analyses for supporting optimal strategies of vaccination plans, using lessons learned of COVID-19, also considering institutional and socioeconomic factors between countries, and not only parameters related to medicine to prevent future pandemics and/or to contain their negative impact on public health, economy and society.

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