

Only vaccinations cannot reduce mortality and stop the COVID-19 pandemic because of manifold environmental and socioeconomic factors driving diffusion

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Research Article

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Abstract

One of the fundamental problems in COVID-19 pandemic crisis is whether vaccinations are a sufficient strategy to reduce mortality and mitigate negative effects of this novel infectious disease in society. This study confronts the problem here by developing an analysis of the relation between people fully vaccinated and mortality between countries to clarify sources and effects of COVID-19 pandemic in society. Methodology applies correlation and regression analyses based on global data of more than 150 countries. Findings reveal a strong positive correlation between share of people fully vaccinated and COVID-19 mortality in January 2022 ($r = .65$, p -value $< .01$). Multiple analysis of regression shows that a 1% higher share of people fully vaccinated, increases the expected deaths per 100 000 people by 0.7% (p -value < 0.001), controlling GDP per capita between countries. These results seem to suggest that COVID-19 vaccinations are not a sufficient strategy to reduce the negative impact of the new infectious disease in society, because socioeconomic and environmental factors, mutations of the novel coronavirus and technological aspects of countries (e.g., equipment of non-invasive ventilators in countries) affect the spread and mortality of this pandemic between countries. Overall, then, a pandemic policy only based on vaccinations cannot cope with the eradication of COVID-19 pandemic because manifold factors drive the transmission dynamics of COVID-19 and generate a lot of negative impacts in economic systems, though high levels of vaccinations in some countries.

Introduction And Goal Of Investigation

We are still in the throes in 2022 of negative socioeconomic effects of the pandemic of Coronavirus Disease 2019 (COVID-19), an infectious illness generated by (novel) mutant viral agent of the Severe Acute Respiratory Syndrome Coronavirus 2/SARS-CoV-2 (Bontempi et al., 2021; Bontempi and Coccia, 2021; Coccia, 2020, 2020a, 2020b, 2021; Johns Hopkins Center for System Science and Engineering, 2022; Vinceti et al., 2021)[1]. Initially, in 2020, countries apply non-pharmaceutical interventions (e.g., lockdown and quarantine) to cope with COVID-19 pandemic crisis; a later time, in 2021 and 2022, the most applied health policy worldwide is the administration of new types of vaccines based on viral vector, protein subunit and nucleic acid-RNA (Abbasi, 2020; Coccia, 2021g, 2022a, 2022b, 2022c; Mayo Clinic, 2021). The vaccination plans have the potential goal to reduce the diffusion of COVID-19, to relax non-pharmaceutical measures and maintain low basic reproduction number, but an important problem is whether these novel types of vaccines are really effective to reduce high numbers of COVID-19 related infected individuals and deaths between countries to control and/or eradicate the pandemic diffusion and to reduce negative effects in society (Aldila et al., 2021; Coccia, 2021a; Prieto Cruriel, et al. 2021; Saadi et al., 2021). 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, 2021b, 2021c, 2022a). Shattock et al. (2021) argue that a rapid vaccination rollout can allow the sooner relaxation of non-pharmaceutical interventions, but emerging viral variants of SARS-CoV-2 create new scenarios and problems for epidemic control (Fontanet et al., 2021; Papanikolaou et al., 2021). Shattock et al. (2021) also find that a gradual phased relaxation can substantially reduce population-level morbidity and mortality and that faster vaccination campaign can offset the size of pandemic wave, allowing more flexibility for non-pharmaceutical control measures to be relaxed sooner. 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; Randolph and Barreiro, 2020). However, Aschwanden (2020, 2021) raised many doubts about the achievement of herd immunity, which is a “false promise” because of manifold factors affecting transmission dynamics of COVID-19 (cf., Moore et al., 2021). Seligman et al. (2021) analyze the COVID-19 pandemic in the United States and show that social determinants can affect COVID-19 mortality at the individual level. Results of demographics of deaths reveal a mean age of 71.6 years, 45.9% female, and 45.1% non-Hispanic white. They found that disproportionate deaths occurred among individuals with nonwhite race/ethnicity, individuals with income below the median, individuals with less than a high school level of education, and veterans

(cf., Davies et al., 2021; Wolf et al., 2021). In general, substantial inequalities in COVID-19 mortality are due to racial/ethnic minorities and poor people having less education. Garber (2021) for the US case study maintains that mortality from COVID-19 rises steeply with advancing age, in a pattern that largely parallels overall mortality. Age specific mortality rates increased in the US more for groups that already experienced greater mortality, such as non-Hispanic Black people, as reflected in projections of life expectancy at birth. Ackley et al. (2022), investigating the impact of the COVID-19 pandemic in the US, show that a significant percentage of excess deaths associated with the pandemic were not directly assigned to COVID-19. Across the U.S.A., the estimates of model indicate about 438,386 excess deaths occurred in 2020, among which 87.5% were assigned to COVID-19. Some regions of Mideast, Great Lakes, New England, etc. had the most excess deaths in large central metropolitan areas, whereas other regions (Southwest, Southeast, Rocky Mountains, Great Plains, etc.) reported the highest excess mortality in non-metropolitan areas. Stokes et al (2021) found that direct COVID-19 death counts in the US in 2020 are substantially underestimated total excess mortality attributable to COVID-19. Racial and socioeconomic inequities in COVID-19 mortality also increased when excess deaths not assigned to COVID-19 were considered (cf., Stokes et al., 2021a). Sanmarchi et al. (2021) argue that many countries experienced an increase in mortality during 2020. Several Latin American and East European countries exhibit a large gap between Excess Mortality (EM) and COVID-19 Confirmed Mortality (CCM), such as Mexico; other countries showed a moderate EM beyond CCM (e.g., Greece). Countries with negative EM also had very low CCM and were mainly located in East Asia. Islam et al. (2021) point out that about one million excess deaths occurred in 2020 in many high-income countries. Age standardized excess death rates were higher in men than women in almost all countries. Excess deaths substantially exceeded reported deaths from COVID-19 in many countries, indicating that determining the full impact of the pandemic on mortality requires assessment of excess deaths. Kiang et al. (2020) argue that the true number of deaths resulting from COVID-19, both directly and indirectly, is likely to be much higher, and correct analysis and evaluation of excess mortality are critical goals to understanding this pandemic and its effect on human life and overall society. In general, these studies clearly show that the mortality of COVID-19 pandemic is a critical indicator associated with manifold factors (Barnard et al., 2021; Garber, 2021; Islam et al., 2021; Stokes et al., 2021, 2021a; Woolf et al., 2021). In this context, this study develops a statistical analysis to explain some relations between the level of vaccinations and mortality rate of COVID-19 between countries to clarify complex factors determining pandemic diffusion and negative impact in society. These results can support the design of best practices of crisis management to cope with current and future pandemic crisis similar to COVID-19 (cf., Coccia, 2019g). This study is part of a large research project 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, 2020, 2020a, 2020l, 2021, 2022a).

[1] Cf. also Coccia, 2020c, 2021a, 2021d, 2021e, 2021f, 2021g, 2022.

Study Design

1.1 Sample

The total sample of this study is $N=151$ countries worldwide. For some statistical analyses based on different confounding factors, the sample can be lower for missing data of some variables.

1.2 Measures for statistical analyses

- Vaccination is measured by percent share of people fully vaccinated against COVID-19 over 11 January 2022. Data refer mainly to January 2022 but some countries, because of difficulty in the gather and transmission of information, can have data of December 2021. Of course, this small temporal gap of some countries does not

affect the statistical analyses based on a large sample >100 units. The data here consider 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. Source: Our World in Data (2022).

- Gross Domestic Product (GDP) per capita in 2020. GDP per capita (constant 2010 US\$). GDP per capita is gross domestic product divided by midyear population. GDP is the sum of gross value added by all resident producers in the economy plus any product taxes and minus any subsidies not included in the value of products. It is calculated without making deductions for depreciation of fabricated assets or for depletion and degradation of natural resources. Data are in constant 2010 U.S. dollars. Source: The World Bank (2022).
- Population Total 2020. Total population is based on the de facto definition of population, which counts all residents regardless of legal status or citizenship. The values are midyear estimates. Source: The World Bank (2022a).
- COVID-19 Deaths. Total number of deaths in January 2022. It indicates the severity of this novel infectious disease in socioeconomic systems. This study also calculates the mortality rate per 100 000 people for a comparative analysis between countries. Source of data: Johns Hopkins Center for System Science and Engineering (2022).

1.3 Model and data analysis procedure

Firstly, data are analyzed with descriptive statistics given by arithmetic mean and standard error of the mean. The normality of distribution of variables under study is checked with skewness and kurtosis coefficients and if distribution of variables is not normal, they are transformed in logarithmic scale for having normality and performing appropriate parametric analyses (Coccia, 2018).

This study focuses on the following ratio of COVID-19 deaths calculated for all countries:

$$\text{Mortality rate per 100 000 people} = \left(\frac{\text{Total number of deaths from COVID-19 at January 2022}}{\text{Total population in 2020}} \right) \times 100\,000$$

Secondly, variables under study are analyzed with the bivariate Pearson Correlation that produces a sample correlation coefficient, r , which measures the strength and direction of linear relationships between pairs of continuous variables, given by share of people fully vaccinated against COVID-19 and mortality rate (deaths / population ´ 100 000) between countries. This study also calculates the partial correlation that indicates the strength and direction of a linear relationship between continuous variables just mentioned whilst controlling for the effect of GDP per capita.

The strength of correlation can be assessed by these general guidelines:

0.1 < | r | < 0.3 ... small / weak correlation

0.3 < | r | < 0.5 ... medium / moderate correlation

0.5 < | r | large / strong correlation

Thirdly, the analysis of multiple regression is applied to predict the value of mortality rate (dependent or response variable) on the value of two explanatory variables: share of people fully vaccinated against COVID-19 and GDP per

capita (independent variables or predictors).

The specification of *log-log* model is given by:

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

where:

1. $y_{i,t}$ = Mortality rate of COVID-19 in January 2022.
2. $x_{i,t}$ = Share % of people fully vaccinated against COVID-19 in January 2022
3. $z_{i,t-1}$ = GDP per capita in 2020
4. $u_{i,t}$ = Error term

country $i=1, \dots, n$; $t=time$

Results of regression analysis are the R^2 and the standard error of the estimate, which determine how well regression model fits the data. R^2 value (also called the coefficient of determination) is the proportion of variance in the dependent variable that can be explained by independent variables. The *F*-ratio in the ANOVA table tests whether the overall regression model is a good fit for the data. Unstandardized coefficients of partial regression indicate how much the dependent variable varies with an independent variable when the other independent variable is held constant and finally the statistical significance of each of the independent variables with *t*-test. Statistical analyses are performed with the Statistics Software SPSS version 26.

Results

Table 1. Descriptive statistics

Variables	N	Mean	Std. Error of Mean	Skewness	Kurtosis
GDPPC 2020, GDP per capita \$	151	14,457.69	1,716.74	2.68	9.64
MOR2022, Mortality rate per 100 000 people (number)	151	111.43	9.75	1.33	1.69
VAC2022, Share % of people fully vaccinated	144	44.14	2.26	-0.13	-1.29
Log GDPPC2020	149	8.68	0.12	0.07	-0.90
LogMOR2022	151	3.82	0.13	-0.58	-0.68
LogVAC2022	144	3.40	0.09	-1.44	1.39

Table 1 shows descriptive statistics and that variables with logarithmic transformation have a normal distribution (coefficients of skewness and kurtosis have values in the correct range) to perform appropriate and robust parametric analyses.

Table 2. Bivariate correlation

	Pearson Correlation	LogVAC2022	LogMOR2022
LogVAC2022		1	.646**
N		144	144

Note: MOR2022, Mortality rate per 100 000 people in 2022, VAC2022, Share % of people fully vaccinated in 2022.

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

The bivariate Pearson Correlation produces, in the sample of $N=144$ countries, a positive coefficient $r=.65$ (p -value <0.01), which indicates a strong correlation between mortality rate per 100 000 people and share % of people fully vaccinated. This finding is confirmed in table 3 with the partial correlation that indicates the moderate linear relationship between continuous variables just mentioned, controlling for the effect of GDP per capita ($r_{\text{partial}} = .44$, p -value $=.001$).

Table 3. Partial correlation

Control variable: GDPPC2020	Partial Correlation	LogVAC2022	LogMOR2022
	LogVAC2022	1	.443***
	N	135	135

Note: GDPPC 2020, GDP per capita; MOR2022, Mortality rate per 100 000 people in 2022; VAC2022, Share % of people fully vaccinated in 2022.

*** Correlation is significant at the 0.001 level (1-tailed).

Table 4. Regression analyses of mortality rate in 2022 on people fully vaccinated in 2022 (and GDP per capita 2020), *log-log* model [1]

	Simple Regression	Multiple regression
Constant a	0.754*	-0.542
(St. Err)	(0.325)	(0.665)
VAC2022, Coefficient b_1	0.917***	0.713***
(St. Err.)	(0.091)	(0.132)
GDPPC2020, Coefficient b_2	–	0.228*
(St. Err.)		(0.103)
R^2	.42	.43
(St. Err. of Estimate)	(1.23)	(1.22)
F	101.70***	52.80***

Note: Dependent (response) variable is: MOR2022, Mortality rate per 100 000 people in 2022; Explanatory variables are: VAC2022, Share (%) of people fully vaccinated against COVID-19 in 2022 and GDPPC2020, Gross Domestic Product per capita in 2020. Significance: *** p -value <0.001 ; p -value <0.05

Table 4 shows results of simple and multiple regression. Since results are rather similar, we describe estimated multivariate relationship based on Eq. [1] with two explanatory variables (i.e., Share % of people fully vaccinated against COVID-19 in 2022 and Gross Domestic Product per capita in 2020). The partial coefficient of regression b_1 of the model indicates that a 1% higher share of people fully vaccinated (controlling GDP per capita), increases the expected mortality rate of COVID-19 per 100 000 people by 0.7% (p -value < 0.001), whereas the partial coefficient of regression b_2 of the model indicates that a 1% higher level of GDP per capita (controlling share % of people fully vaccinated), increases the expected mortality rate of COVID-19 per 100 000 people by 0.2% (p -value < 0.05). F -test (the ratio of the variance explained by the model to the unexplained variance) is significant at 1 ‰ (i.e., p -value < 0.001), such that overall regression model is a good fit for the data. R^2 of the model of multiple regression indicates that about 53% of the variation in mortality rate of COVID-19 can be attributed (linearly) to share (%) of people fully vaccinated against COVID-19 in 2022 and Gross Domestic Product per capita in 2020. Figure 1 shows regression line of COVID-19 deaths per 100 000 people on share of people vaccinated against COVID-19 (%) based on *log-log* model.

Hence, these critical findings suggest that increasing the share of people vaccinated against COVID-19 is a necessary but not sufficient condition to mitigate the negative impact of COVID-19 in society in terms of reduction of mortality. In fact, the diffusion of the mutant novel coronavirus has complex aspects, and the increasing level of vaccinations seems not to a health policy enough to control the pandemic and reduce mortality because the transmission dynamics is driven by manifold environmental and socioeconomic factors that are discussed in the following section.

Discussions

The critical findings of this study are a strong correlation between mortality rate per 100 000 people and share % of people fully vaccinated against COVID-19 (also controlling for the effect of GDP per capita). This result can be explained with the fact that COVID-19 vaccinations are a necessary but not sufficient strategy to reduce the negative impact of the novel coronavirus in society, because there are manifold factors that support the diffusion and mortality of this pandemic, also in countries having a high level of fully vaccinated people.

Determinants of the pervasive diffusion of COVID-19 in society, which vaccinations cannot stop, are: new variants, high air pollution and density of people in cities, intensive commercial activities of countries, low investments in healthcare sectors and little new technology (such as non-invasive medical ventilation), etc.[2] (Figure 2).

- *High level of air pollution*

Coccia (2020, 2021) finds out, based on a case study of Italy, that the number of infected people was higher in cities with >100 days per year exceeding limits set for PM_{10} or ozone and cities located in hinterland zones (i.e., away from the coast). In hinterland cities (mostly those bordering large urban conurbations) with a high number of days exceeding PM_{10} and ozone limits, coupled with low wind speed, the average number of infected people in April 2020 more than doubled that of more windy coastal cities in Italy that had also exceeded the air pollution limits. These findings provide valuable insight into geo-environmental factors that may accelerate the diffusion of COVID-19 and similar viral agents. Studies show that sustainable environment plays a vital role for reducing COVID-19 related infected individuals and deaths; in particular, a low rate of fatality is associated with a low level of air pollution (cf., Coccia, 2020a, 2020b, 2020c). In fact, average population exposed to levels exceeding WHO guideline value (% of total) is 72% in countries with a lower level of fatality rate, whereas in countries with a higher incidence of mortality of the COVID-19 is almost 98%. Coccia (2020a; 2022b, 2022c) maintains that a proactive strategy to cope with future epidemics should concentrate on reducing levels of air pollution in hinterland and polluted cities. Copat et al. (2020), considering different studies about the relation between air pollution and the spread of COVID-19, suggest that

PM_{2.5} and NO₂ can support the spread and lethality of COVID-19, but additional analyses are needed to confirm this relation concerning transmission dynamics and negative effects of the SARS-CoV-2 in society (cf., Coccia, 2021).

- *Climate factors: low wind speed and temperature, high humidity*

Studies suggest that the concentration of atmospheric pollutants is a main driver of the spread of SARS-CoV-2 (Coccia, 2020a), but a high wind speed sustains clean days from air pollution, reducing whenever possible the spread of COVID-19 (cf., Coccia, 2020b, 2021, 2021a, 2021f; Caliskan et al., 2020). To put it differently, a low wind speed in cities prevents the dispersion of air pollutants that can include bacteria and viruses, such as SARS-CoV-2, and can increase the incidence of COVID-19, such as in some European regions (Coccia, 2020a, 2020b, 2020c; 2021). Rosario et al. (2020, p. 4) suggest that wind improves the circulation of air and increases the exposure of the novel coronavirus to the solar radiation effects, a factor having a negative correlation in the diffusion of COVID-19. Nicastro et al. (2021) also analyze the spatial aspects of SARS-CoV-2 in response to UV light and solar irradiation measurements on Earth. The results of study show that UV-B/A photons have a powerful virucidal effect on the single-stranded RNA virus of the COVID-19. Moreover, the solar radiation that reaches temperate regions of the Earth at noon during summers, it is a sufficient condition to inactivate 63% of virions in open-space concentrations in less than 2 minutes.

- *High density of cities and intensive commercial activities*

Coccia (2020a, 2020b) showed, with a case study of Italy, that average number of infected individuals increases with average density of people/km². In fact, the density of population per km² is an important factor for transmission dynamics of infectious diseases and studies confirm that high population density increases the probability of interpersonal contacts and viral transmission of COVID-19 in cities (Coccia, 2020a, 2021). Moreover, Bontempi and Coccia (2021) and Bontempi et al. (2021) find out that an intensive commercial activity, measured with the level of import and export, can be a main predictor of the diffusion of COVID-19 in society. In particular, the study suggests that total import and export of Italian provinces has a high association with confirmed cases over time (average $r > .78$, p -value $< .001$). Another study based on three large countries in Europe (Italy, France, and Spain) suggests the positive association between trade and pandemic diffusion. In general, international trade data is supposed to be a complex parameter of the transmission dynamics of the COVID-19 that includes many factors related to economic, demographic, environmental, and climate aspects.

- *New SARS-CoV-2 variants of concern*

The novel coronavirus in environment and human ecosystem constantly changes through mutations. A new mutation generates a variant of the original virus of SARS-CoV-2. Fontanet et al. (2021) argue that in December 2020, an unexpected rise in reported COVID-19 cases was attributed to the emergence of new SARS-CoV-2 variants (Alfa, B.1.1.7) in the UK and (Beta, B.1.351) in South Africa. Both variants had a mutation in the receptor-binding domain of the spike protein that is reported to increase transmission, ranging between 40% and 70%. Davies et al. (2021) show that Alpha variant (B.1.1.7) of SARS-CoV-2 is more transmissible than pre-existing variants. This study estimates that the hazard of deaths associated with B.1.1.7 is 61% higher than pre-existing variants. In short, analysis suggests that B.1.1.7 is not only more transmissible than previous SARS-CoV-2 variants but may also cause more severe illness. Other two variants of the novel coronavirus (SARS-CoV-2) that cause coronavirus disease 2019 (COVID-19) and subsequent health and socioeconomic problems are (Mayo Clinic, 2022):

- Delta (B.1.617.2). This variant is nearly twice as contagious as earlier variants and might cause more severe illness. The greatest risk of transmission is among unvaccinated people. People who are fully vaccinated can get vaccine breakthrough infections and spread the virus to others. However, it appears that vaccinated people spread

COVID-19 for a shorter period than do unvaccinated people. While research suggests that COVID-19 vaccines are slightly less effective against the delta variant.

- Omicron (B.1.1.529). This variant might spread more easily than other variants, including delta. But it's not yet clear if omicron causes more severe disease. It's expected that people who are fully vaccinated likely can get breakthrough infections and spread the virus to others. However, the COVID-19 vaccines are expected to be effective at preventing severe illness. This variant also reduces the effectiveness of some monoclonal antibody treatments.

The alpha, gamma and beta variants of SARS-CoV-2 continue to be monitored but are spreading at much lower levels. The mu variant is also being monitored. Of course, these variants of the novel coronavirus change the transmissions dynamics and negative effects in society.

- *Health investments and new technology of medical ventilators*

Coccia (2021e) reveals that countries with lower fatality rates have a high average level of health expenditure given by 7.6% of GDP and average government health expenditure per capita of about \$2,300, whereas countries with higher fatality rates of COVID-19 have an average health expenditure of roughly 6% of GDP and very low government health expenditure per capita (a mere average value of about \$243 per inhabitants) that indicates a weak healthcare sector to cope with pandemics and also other diseases in society. In the context of COVID-19, a main technology to cope with a serious illness of people admitted in Intensive Care Units (ICUs) is mechanical ventilator (it is an artificial breathing device that is used for patients who are not able to breathe naturally due to a critical illness, such as COVID-19). Some of the most used products include positive and negative mechanical ventilators that are utilized in ICUs, neonatal care centers and ambulances. These devices consist of a hollow tube that is inserted into the patient's trachea to create a stable airway. They also assist in maintaining adequate levels of oxygen and carbon dioxide in the body to relieve respiratory distress, reverse respiratory muscle fatigue and initiate lung healing (IMARC, 2022). However, invasive ventilation can create problems to lung and infection in case of prolonged utilization, such as to treat COVID-19 patients. Ventilator-associated lung injury, sometimes referred to as ventilator-induced lung injury, is damage to the alveolar and / or small airways related to mechanical ventilation. Possible mechanisms include alveolar over distension and shear forces created by repeated opening and collapsing of the alveoli, leading to the release of inflammatory mediators that result in increased alveolar permeability and fluid accumulation. New technology is more and more based on Non-Invasive Ventilation (NIV) that refers to the administration of ventilatory support without using an invasive artificial airway (endotracheal tube or tracheostomy tube). The use of NIV has markedly increased over the past two decades, and NIV has now become an integral tool in the management of both acute and chronic respiratory failure, in both the home setting and in the critical care unit. Non-invasive ventilation is a new technology that is generating a replacement for invasive ventilation, and its flexibility also allows it to be a valuable complement in patient management (Soo Hoo, 2020, 2010). New technology of NIV accurately measures patient's airway pressure, moreover the respiratory abdominal sensor and transducer allow patient-triggered pressure assists with breath rate monitoring. New technology of NIV allows an adequate humidification to maintain airway clearance, optimize ventilation and improve patient comfort (in fact, normal functions of the nose and air passages of the respiratory tract are to warm, moisten and filter the inhaled gases before they reach the lungs. In normal respiration, the nasal mucosa and upper airways provide 75% of the heat and moisture supplied to the smaller airways and alveoli. By the time air reaches the alveoli, the inspired gas warms to 37°C at 100% relative humidity). In short, benefits of NIV are due to both the patient and the facility using it, such as cost-effective, no need for sedation, comfortable for the patient, intubation and airway skills not required and time-efficient for facility. In the presence of pandemic crisis some countries, such as Germany had a high number of medical ventilators: about 30,000 in 2020 (Our World in Data, 2022a) and though a population of 83.24 million, COVID-19 deaths (117 318) are lower than for instance Argentina that has 120 019 deaths

with about 45 million of people (The World Bank, 2022a; Johns Hopkins Center for System Science and Engineering, 2022). Other scholars, such as [Kapitsinis \(2020\)](#), argue that investments in health sector are a critical public policy to mitigate mortality rate of COVID-19. Hence, countries should support healthcare investments in the expansion of hospital capacity and R&D investments in new technology to develop effective vaccines, antivirals, innovative drugs and high-tech devices that can counteract future public health threats of new epidemics like COVID-19 (Ardito et al., 2021; Coccia, 2017c, 2017d, 2019f, 2020).

[2] For role of science, technology, research labs, leading firms and institutions for economic and social change see: Ardito et al., 2021; Coccia, 2003, 2005, 2005a; Coccia, 2008, 2013, 2014, 2015, 2016, 2107, 2017a, 2017b, 2017c, 2017d, 2017e, 2018a, 2018b, 2018c, 2018d, 2018e, 2018f, 2019, 2019a, 2019b, 2019c, 2019d, 2018e, 2019f; 2018g, 2019h, 2019i, Coccia, 2020d, 2020e, 2020f, 2020g, 2020h, 2020i; Coccia, 2021h, 2021i, 2020l; Coccia, 2022d; Coccia and Bellitto, 2018; Coccia and Benati, 2018; Coccia and Cadario, 2014; Coccia and Finardi, 2012, 2013; Coccia and Rolfo, 2000, 2008; Coccia and Watts, 2020; Pagliaro and Coccia, 2021; Pronti and Coccia, 2020.

Conclusions

Lau et al. (2021) argue that in the presence of a continuous global COVID-19 pandemic threat, the mortality rate is a main indicator to evaluate the real effects of COVID-19 in society (cf., Liu et al., 2021). In this context, one of the goals of nations to cope with COVID-19 pandemic crisis is to mitigate mortality and case fatality rate (cf., Coccia, 2020a, 2021e). Initially, in 2020, countries apply non-pharmaceutical interventions (e.g., lockdown) to cope with COVID-19 pandemic crisis; a later time, in 2021 and 2022, the most applied health policy worldwide is the administration of vaccinations on a vast population (Coccia, 2022b). Findings here reveal that the increase of vaccinated people (%) against COVID-19 is not associated with a reduction of mortality of COVID-19 between countries because manifold factors can affect the complex dynamics of diffusion of COVID-19 pandemic in environment and society. 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 total vaccinations in manifold countries. Second, not all the possible confounding factors that affect the diffusion of vaccination and mortality of COVID-19 are taken into consideration and in future these factors deserve to be controlled for supporting results here. Third, the lack of integration of data with socioeconomic aspects of countries may influence the results of mortality, making comparative analyses a problematic approach (Angelopoulos et al., 2020; Coccia, 2018). Fourth, country-specific health investments may affect the vaccination, management of healthcare and mortality of people and have to be controlled in future development of this study. Finally, the estimated relationships in this study focus on variables in specific months (based on recent data available) but an extension of the period under study is needed to reinforce results here. Thus, the generalization of this results 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 the interaction between vaccination, mortality and other socioeconomic factors between countries. Despite these limitations, results presented here suggest that the vaccination is a health policy not enough to reduce mortality of COVID-19, control and stop the pandemic diffusion and subsequent negative effects in society. Hence, there is need for much more detailed research in these topics and this study encourages further investigations to clarify complex factors driving pandemics in environment and ecosystems also considering the interaction between restrictions, vaccinations and general investments in healthcare. To conclude, different factors between countries that are not only parameters related to medicine but also to social, economic and innovation studies can explain the mortality of COVID-19 pandemic in society and should be accurately considered to control future negative impact of pandemic crisis on public health, economy and society. Hence, results here have to be reinforced with much more

follow-up investigation concerning detailed research into the relations between negative effects of pandemic in society, health system, public health capacity and pandemic response of countries.

Overall, then, this study suggests that an effective strategy to reduce the negative impact (in terms of mortality) of future pandemic threats similar to COVID-19, it has to be based on high investments in health system and design of comprehensive health, social and economic policy responses of crisis management, not only vaccination-based approach, considering that complex environmental and socioeconomic factors guide transmission dynamics of COVID-19 and negative effects in society. To conclude, this study here suggests analyzing further socio-economic factors that may shape and support general health strategy, beyond vaccinations, to cope with future pandemic crises by creating appropriate ecosystems and socioeconomic systems of countries that improve public health and overall wellbeing of people.

Declarations

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 influence the work reported in this paper.

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Figures

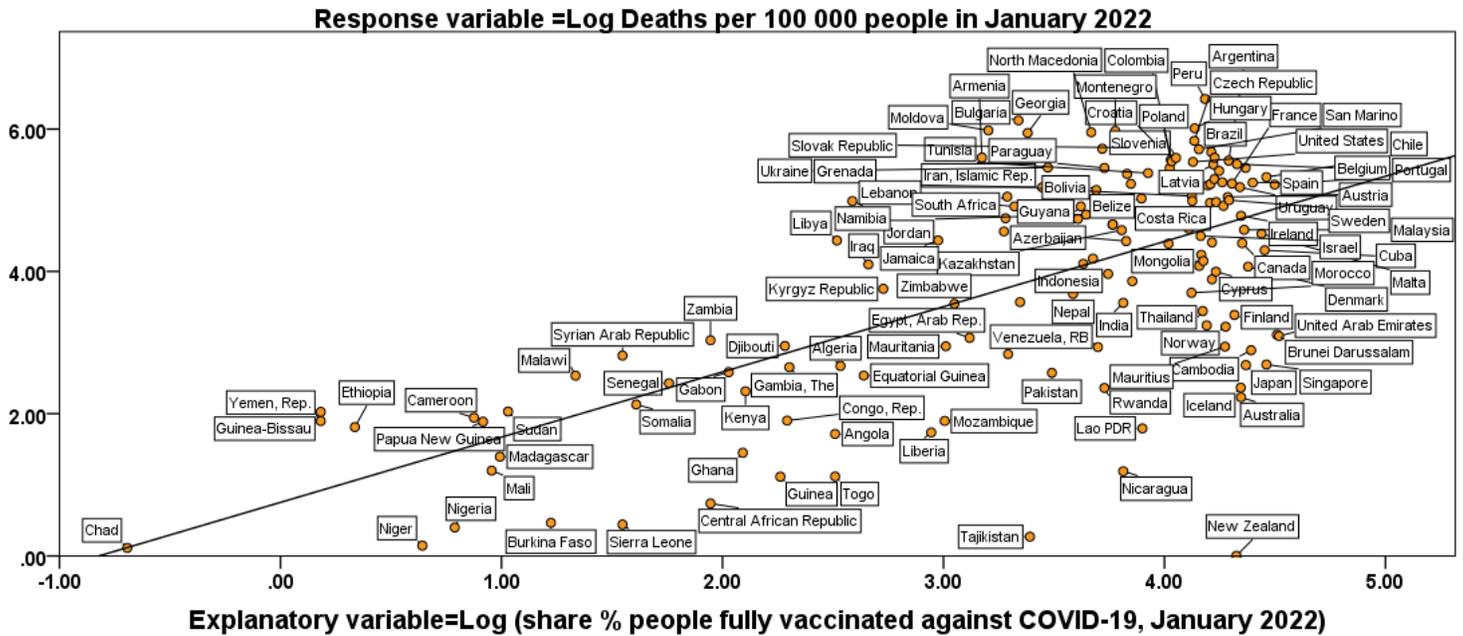


Figure 1

Relation of COVID-19 deaths per 100 000 people on share of people vaccinated against COVID-19 (%) based on *log-log* model.

Factors determining high mortality rates, though a high share of vaccinated people (factors to be considered when shaping general strategies to mitigate case fatality rates of future waves of COVID-19 and similar pandemics)

- High air pollution and exposure of population to days exceeding levels of PM_{2.5} air pollution (e.g., max 50 days of high levels of air pollution per year)
- Low wind speed, low temperature and high atmospheric humidity
- New SARS-CoV-2 variants of concern (e.g., Delta, etc.)
- Low health expenditure as % of GDP
- Low government health expenditure per capita
- Lower investments in new technology, such as high-tech medical ventilators
- Delayed application of containment policies
- Unsustainable policies for economic development
- High density and intensive commercial activity

Figure 2

Factors determining high mortality rates, though a high share of vaccinated people between countries. Factors to be considered to design general guidelines to constrain pandemic crises of novel viral agents like Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).