

THE PARADOX BETWEEN VACCINATION RATE AND COVID-19 MORTALITY: NUMEROUS SOCIOECONOMIC AND ENVIRONMENTAL ELEMENTS THAT PROMOTE SPREAD

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Abstract

This study examines the effectiveness of vaccination as the primary strategy to reduce COVID-19 deaths in over 150 countries. By analyzing the correlation between full vaccination rates and mortality rates in January 2022, the study initially finds a positive association ($r = 0.65$, $p\text{-value} < .01$). However, further regression analysis reveals a more complex relationship. A 1% increase in full vaccination is unexpectedly linked to a 0.7% rise in expected deaths per 100,000 people ($p\text{-value} < .001$), even when considering GDP differences. This suggests that factors beyond vaccination, such as socioeconomic conditions, virus mutations, and healthcare resources (e.g., ventilators per capita), play a substantial role in determining mortality rates. The study's findings challenge the notion that vaccination alone can eradicate COVID-19. While vaccination is a crucial tool, it's essential to address the broader factors contributing to the virus's spread and its economic impact, particularly in countries with high vaccination rates but persistent mortality. This comprehensive approach is vital for effectively managing the pandemic and minimizing its long-term consequences.

Keywords: COVID-19; Vaccination; Mortality; Correlation; Socioeconomic factors.

Classification: H12, H51, I10, I18

1. INTRODUCTION

Even as we venture into the latter half of 2022, the enduring socioeconomic repercussions of the COVID-19 pandemic remain a paramount concern. This infectious disease, caused by a novel strain of the SARS-CoV-2 virus (Bontempi et al., 2021; Coccia, 2021), continues to exert a significant influence on global well-being [Johns Hopkins Center for System Science and Engineering, JHCSSE, 2022]. The initial response in 2020 leaned heavily on non-pharmaceutical interventions (NPIs) such as lockdowns and quarantines to effectively suppress the outbreak's initial surge (JHCSSE, 2022). However, 2021 and 2022 have witnessed a paradigm shift towards widespread vaccination campaigns, leveraging novel vaccine technologies such as viral vectors, protein subunits, and mRNA (Abbasi, 2020; Coccia, 2022c; Mayo Clinic, 2021). These vaccination programs aim to curtail transmission rates, enabling a gradual relaxation of restrictive measures and the maintenance of a low basic reproduction number (R_0) (Prieto Cruriel et al., 2021; Aldila et al., 2021; Saadi et al., 2021; Coccia, 2021a). Yet, a critical question persists: can these novel vaccines effectively diminish COVID-19 cases and fatalities across diverse populations, ultimately leading to the control and potential eradication of the pandemic, thereby minimizing its detrimental societal impacts (Coccia, 2021b; Saadi et al., 2021; Aldila et al., 2021; Prieto Cruriel et al., 2021)?

Researchers underscore the pivotal role of well-orchestrated vaccination campaigns. Akamatsu et al. (2021) emphasize their significance in demonstrably reducing infection rates and preventing healthcare systems from becoming overburdened (cf., Coccia, 2021c, 2022a; Uçkaç et al., 2023, 2023a). Similarly, Shattock et al. (2021) advocate for expeditious vaccination rollouts to facilitate an earlier relaxation of NPIs. However, the emergence of novel SARS-CoV-2 variants presents renewed challenges for epidemic control efforts (Papanikolaou et al., 2021; Fontanet et al., 2021). Further propose a measured approach to easing restrictions, potentially minimizing morbidity and mortality at the population level. Additionally, a more rapid vaccination campaign can mitigate the peak of the pandemic wave, offering greater flexibility for easing restrictions earlier (Shattock et al., 2021).

Achieving high vaccination rates is proposed as a potential strategy for achieving herd immunity, thereby shielding vulnerable individuals within a population (Aldila et al., 2021; Randolph & Barreiro, 2020; Anderson et al., 2020; de Vlas & Coffeng, 2021). However, Aschwanden (2020, 2021) expresses reservations regarding the attainability of herd immunity for COVID-19, considering it an unrealistic objective due to the intricate interplay of factors influencing transmission dynamics (cf., Moore et al., 2021).

The pandemic has laid bare the stark impact of social determinants on individual mortality rates, as evidenced by research conducted by Seligman et al. (2021) in the United States. Their analysis of COVID-19 deaths revealed an average age of 71.6 years, with a near-equal distribution between females (45.9%) and non-Hispanic whites (45.1%). Notably, the study identified a disproportionate burden of mortality among racial/ethnic minorities, those with lower socioeconomic backgrounds (income and education), and veterans (Wolf et al., 2021; Davies et al., 2021). These findings suggest a clear link between lower socioeconomic status and racial/ethnic minority status with

increased susceptibility to COVID-19 mortality. This vulnerability likely stems from factors such as limited access to quality healthcare and a higher prevalence of underlying health conditions. Garber (2021) reinforces this notion in the context of the US, highlighting a sharp rise in COVID-19 mortality with advancing age, mirroring the overall mortality pattern. This trend translates to a widening mortality gap, with pre-existing disparities in life expectancy at birth further exacerbated for groups like non-Hispanic Black individuals.

Furthermore, the pandemic has exposed and exacerbated existing socioeconomic inequalities. Research suggests a correlation between lower socioeconomic status and a higher risk of COVID-19 infection, hospitalization, and mortality (Seligman et al., 2021; Wolf et al., 2021). Individuals from lower socioeconomic backgrounds often have limited access to quality healthcare, preventative measures, and healthy living environments (Davies et al., 2021). Additionally, certain occupations associated with lower socioeconomic status, such as essential service jobs, may have necessitated continued in-person work throughout the pandemic, increasing exposure risk (Seligman et al., 2021). These factors contribute to a heightened vulnerability to COVID-19 among lower socioeconomic groups.

The pandemic's economic fallout has further compounded these social disparities. Business closures, job losses, and disruptions in the global supply chain have disproportionately impacted on low-wage earners and minority communities (ILO, 2020). This economic downturn has led to increased poverty and financial insecurity, potentially hindering access to nutritious food, healthcare services, and safe housing – all factors that can influence susceptibility to COVID-19 and overall health outcomes (Seligman et al., 2021).

In conclusion, the COVID-19 pandemic has cast a long shadow, not only on global health but also on socioeconomic well-being. While vaccination campaigns offer a glimmer of hope for controlling the pandemic, achieving equitable access to vaccines and addressing underlying social determinants of health remain crucial challenges. Mitigating the long-term socioeconomic consequences of the pandemic will necessitate comprehensive strategies that target not only public health interventions but also social and economic policies aimed at reducing existing inequalities.

Expanding on the prior discussion regarding social determinants and mortality, a closer examination of excess deaths provides a more holistic understanding of COVID-19's lethality. Ackley et al. (2022) offer a detailed analysis of the US case, revealing a significant number of pandemic-related deaths not directly attributed to COVID-19. Their model estimates suggest that in 2020, the US experienced an estimated 438,386 excess deaths, with only 87.5% officially classified as COVID-19 deaths. Notably, there was variation in the geographic distribution of these deaths; the regions with the highest excess mortality in major metropolitan areas were the Mideast, New England, and Great Lakes; on the other hand, the regions with the lowest concentration of deaths in non-metropolitan areas were the Southeast, Southwest, Rocky Mountains, and Great Plains (Ackley et al., 2022). These results, when combined with those of Stokes et al. (2021), demonstrate how the total COVID-19 mortality rate may have been underestimated when only deaths that are directly ascribed are taken into account. Their research suggests a substantial discrepancy between official death counts and actual excess mortality attributable to COVID-19 (Stokes et al., 2021). Furthermore, Stokes et al.

(2021a) emphasize that racial and socioeconomic disparities in mortality are amplified when incorporating excess deaths not directly attributed to COVID-19.

Sanmarchi et al. (2021) expand the view by looking at mortality patterns in different nations in 2020. A number of Latin American and Eastern European nations, including Mexico, show a notable difference between confirmed COVID-19 mortality (CCM) and excess mortality (EM), according to their data. Some nations, such as Greece, showed a moderate excess mortality rate over COVID-19 confirmed deaths. It's interesting to note that East Asian nations showed negative excess mortality, which may indicate a combination of factors leading to reduced total death rates (Sanmarchi et al., 2021).

An estimated one million excess deaths were reported in high-income countries in 2020. Their findings also highlight a consistent trend of higher age-standardized excess death rates in men compared to women across most countries (Islam et al., 2021). These studies collectively underscore the importance of analyzing excess mortality to gain a comprehensive understanding of the pandemic's true impact on mortality rates, considering that reported COVID-19 deaths often underestimate the full picture (Garber, 2021; Islam et al., 2021; Barnard et al., 2021; Woolf et al., 2021; Stokes et al., 2021, 2021a; Kargi et al., 2023, 2023a, 2023b). Kiang et al. (2020) further emphasize this point, arguing that accurate assessment and analysis of excess mortality are crucial for comprehending the pandemic's full impact on human life and society.

In light of these compelling findings regarding the multifaceted nature of COVID-19 mortality, the present study aims to explore the potential associations between vaccination levels and COVID-19 mortality rates across different countries. By delving into this intricate interplay of factors, the research seeks to illuminate the dynamics of pandemic diffusion and its negative societal consequences. These observations may ultimately aid in the creation of crisis management best practices, better preparing us to deal with pandemics like COVID-19 both now and in the future (cf., Coccia, 2019, 2019a). This study expands on a larger effort to identify the factors that contribute to the spread of COVID-19 and to create efficient policy solutions that would lessen and possibly even eliminate pandemic risks in the future (Coccia, 2020, 2020a, 2021, 2022; Coccia & Benati, 2018, 2018a).

2. THEORETICAL FRAMEWORK

2.1. Sample

This research investigates the potential link between vaccination levels and COVID-19 mortality rates across a global sample of 151 countries. It's acknowledged that the sample size might fluctuate slightly for specific statistical analyses due to missing data in certain variables.

2.2. Measures for Statistical Analyses

Vaccination Coverage: The study focuses on vaccination coverage, defined as the proportion of a population fully immunized against COVID-19. The data primarily reflects January 2022 figures, with some countries potentially having December 2021

data due to reporting challenges. This minor timeframe variation is considered negligible due to the large sample size (over 100 countries). The research encompasses all types of COVID-19 vaccines used globally, including those developed by Johnson & Johnson, Oxford/AstraZeneca, Pfizer/BioNTech, Sinopharm/Beijing, Sinovac, Sputnik V, and Moderna [1]. Each country has understandably adopted a unique combination of these vaccines to protect its citizens (Data: Our World in Data, 2022).

Measuring Economic Well-Being: Gross Domestic Product (GDP) per capita for the year 2020 serves as an indicator of economic well-being in this study. This metric represents GDP adjusted for inflation and expressed in constant 2010 US dollars. It is calculated by dividing the total value of goods and services produced within a country (gross value added) by its mid-year population. GDP encompasses the market value of all final goods and services produced within a nation, including product taxes but excluding subsidies not factored into product value. Importantly, depreciation of physical assets or depletion of natural resources isn't considered when calculating GDP per capita [2]. The data is presented in constant 2010 US dollars to enable consistent comparison across countries (Data: World Bank, 2022).

Population Considerations: According to the de facto definition, population data for 2020 represents a nation's whole population. All residents are taken into account by this definition, irrespective of their citizenship or legal status. The population estimates given are for the middle of the year (Source: World Bank, 2022a).

Examining COVID-19 Mortality: The total number of COVID-19-related deaths in January 2022 is included in the analysis. This measure shows how seriously this new infectious disease is affecting socioeconomic structures. Furthermore, the study computes the death rate per 100,000 individuals to enable cross-national comparisons (Source of data: JHCSSE, 2022).

2.3. Data Analysis and Model

The analysis commences with a foundational step: exploring and summarizing the data through descriptive statistics. The arithmetic mean, often referred to as the average, provides a central tendency indicator, offering a single value that represents the typical magnitude within the dataset. To complement this measure of central tendency, the standard error of the mean is calculated. This statistic reflects the variability around the mean, quantifying how much individual data points tend to deviate from the average value (Coccia, 2018).

Following the calculation of these initial statistics, the researchers delve into the normality of the data distribution for the variables under investigation. Skewness and kurtosis coefficients serve as valuable tools in assessing this characteristic. Skewness gauges the asymmetry of the distribution, indicating whether the data is skewed towards one tail (positive skew) or the other (negative skew). Kurtosis, on the other hand, sheds light on the distribution's "tailedness," revealing whether it's flatter or more peaked compared to a normal distribution (bell curve). If the data exhibits a non-normal distribution, a transformation technique is employed to rectify this issue. The text suggests a logarithmic transformation as a potential solution (Coccia, 2018). This transformation method involves applying the logarithm function to each data point, effectively compressing the larger values and stretching the smaller ones. The result is

a distribution that more closely resembles a normal curve, making it suitable for subsequent parametric analyses.

By incorporating the details you provided earlier, it can be inferred that this study most likely centers on a ratio of COVID-19 deaths calculated on a country-by-country basis. The application of descriptive statistics, normality assessment, and potential logarithmic transformation suggests a rigorous approach to data preparation, paving the way for reliable and statistically sound analyses.

$$MRp = \left(\frac{Tnd}{Tp} \right) \times 100000$$

MRp= Mortality rate per 100000 people; Tnd= Total number of deaths from COVID-19 in January 2022; Tp= Total population in 2020.

Bivariate Pearson correlation is the initial method used in the study to evaluate the associations between the variables. The strength and direction of any linear link between two continuous variables are reflected in the sample correlation coefficient (r), which is computed using this method. In this context, the variables being examined are:

Bivariate Pearson Correlation for Initial Analysis:

Vaccination Rate: The proportion of a population that has received all COVID-19 vaccinations. The **COVID-19 Mortality Rate** is the number of deaths per 100,000 persons due to the virus (derived by dividing deaths by the population and multiplying the result by 100,000). The correlation coefficient (r) that is obtained will have a range of -1 to +1. Higher vaccination rates may be linked to decreased death rates; a value closer to +1 denotes a positive linear relationship. On the other hand, a number nearer -1 indicates a negative linear relationship, which could indicate that fewer people die from vaccinations (though this wouldn't necessarily be a causative relationship). A result that is close to zero suggests that there is little to no linear correlation between the two variables.

Partial Correlation to Isolate Effects, with control variables:

The study notes that the observed association between vaccination rates and mortality rates may be influenced by other factors, such as a nation's economic standing. Partial correlation is used in the study to take this possible confounding influence into consideration. Using a statistical method of "controlling for" the impact of a third variable (in this case, GDP per capita), this technique calculates the linear relationship's strength and direction between the two main variables (the mortality rate and vaccination rate). Scholars can enhance their comprehension of the direct correlation between vaccination rates and mortality rates, irrespective of economic differences among nations, by contrasting the outcomes of the bivariate correlation and the partial correlation. This may offer stronger proof of the efficacy of immunization campaigns in reducing COVID-19-related mortality.

These broad recommendations can be used to evaluate the correlation's strength:

- 0.1 < a| r |b < 0.3 small /a weak correlation
- 0.3 < a| r |b < 0.5 medium /a moderate correlation
- | r | > 0.5b.... large /a strong correlation

Thirdly, examining many relapses is linked to predicting the value of death rate (a subordinate or response variable) on the value of two representative factors: the percentage of people fully inoculated against COVID-19 and GDP per capita (free factors or indicators). The following provides the log-log show determination:

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

where:

- 1. $ay_{i,2t}$ = COVID-19 mortality rate as of January 2022
 - 2. $ax_{i,2t}$ = percentage of individuals who had all COVID-19 vaccinations in January 2022
 - 3. $az_{i,2t-1}$ = GDP per capita in 2020
 - 4. $au_{i,2t}$ = Error term
- country $i=1, \dots, n$; t = time

R^2 and the gauge's standard error are the two results of relapse analysis that indicate how well a relapse display corresponds with the data. The amount of the dependent variable's variance that the independent variables can account for is expressed by the coefficient of assurance, or R^2 value. Whether or not the usual relapse matches the data is indicated by the F-ratio in the ANOVA table. Lastly, the t-test reveals the quantitative importance of each of the autonomous components through the unstandardized coefficients of midway relapse, which represent the extent to which the subordinate variable changes with a free variable while the other autonomous variable stays constant. Measurements Quantifiable study is carried out using SPSS program version 26.

3. RESULTS

In order to facilitate appropriate and reliable parametric analyses, Table 1 shows logarithmic transformation of variables under study to have a normal distribution appropriate for robust statistical analyses (coefficients of skewness and kurtosis are in the correct range for the normality of distribution).

Table 1. Descriptive statistics

Variables	N	Mean	Std. Error of	Skewness	Kurtosis
GDP per capita, GDPPC 2020 \$	151	14,457.69	1,716.74	2.68	9.64
MOR2022, the death rate per 100,000 individuals	151	111.43	9.75	1.33	1.69
VAC2022, Percentage of Immunized Individuals	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

In short, all results in following tables consider the variables in logarithmic scale because they have normality to provide robust statistical analyses.

Table 2. Correlation bivariate

Pearson Correlation	LogVAC2022	LogMOR2022
LogVAC2022	1	.65**
N	144	144

Notes: ** VAC2022, Death per 100,000 persons in 2022, MOR2022, Percentage of individuals fully immunized in 2022At the 1-tailed 0.01 significance level, the relationship is noteworthy.

The bivariate Pearson connection produces a positive coefficient $r=.65$ ($p\text{-value}<0.01$) in the sample of $N=144$ countries, suggesting a significant correlation between the death rate per 100,000 individuals and the percentage of people who are fully vaccinated. Table 3's partial correlation (r partial $=.44$, $p\text{-value}=.001$), which displays a modest linear link between the previously described continuous variables after correcting for the impact of GDP per capita, supports this result.

Table 3. Correlation partial

Control variable: GDPPC2020	Partial Correlation	LogVAC2022	LogMOR2022
	LogVAC2022	1	.44***
	N	135	135

Note: GDPPC 2020 represents gross domestic product (GDP), MOR2022, the number of deaths per 100,000 people in 2022, and VAC2022, the percentage of the population that will be fully immunized in 2022. *** At the significance level of 0.001 (1-tailed), a substantial correlation is found.

The number of cases can change in statistical analyses of table 2 and 3 because when we use multiple variables, missing data in one variables, present in the original dataset, reduces the cases under study in cross-sectional data, but robustness of results is maintained because of our large sample.

Table 4. Analysis of death rate in 2022 based on GDP per capita in 2020 and the number of persons who received all recommended vaccinations in 2022 using a 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: The response variable, or dependent variable, is MOR2022, or the mortality rate per 100,000 people in 2022; the explanatory variables are VAC2022, or the percentage of people who receive the full COVID-19 immunization in 2022, and GDPPC2020, or the gross domestic product per capita in 2020. *** $p\text{-value}<0.001$; significance is indicated by a $p\text{-value}<0.05$.

This section delves into the intricate interplay between COVID-19 mortality rates and two critical determinants: national wealth and vaccination coverage. The research

team leverages a statistical approach known as multiple regression analysis to elucidate these complex relationships, as presented in Table 4 and Figure 1 [Eq. 1]. Results of table 4 are presented also verifying problems of heteroscedasticity that in this case are not present because the variance is the same for all the errors in model (homoscedasticity). As far as autocorrelation is concerned, it is not considered here because we do not use time series.

The analysis focuses on a model that incorporates two explanatory variables: the proportion of a nation's population fully vaccinated against COVID-19 in 2022 and the Gross Domestic Product (GDP) per capita for the year 2020. This specific model offers intriguing insights (Field, 2013). The partial regression coefficient (b_1) of the model suggests a counterintuitive finding: a statistically significant (p -value < 0.001) increase of 0.7% in the predicted mortality rate per 100,000 individuals for every 1% rise in the fully vaccinated population (while controlling for the effects of GDP per capita). This seemingly paradoxical association necessitates further investigation to unearth potential underlying explanations. Conversely, the model reveals that a 1% increase in GDP per capita, after accounting for vaccination rates, is associated with a more modest but statistically significant (p -value < 0.05) increase of 0.2% in the predicted death rate.

The strength of the overall model is corroborated by the statistically significant F-test (p -value < 0.001). This metric signifies that the model effectively captures a substantial proportion of the variation observed in COVID-19 mortality rates across the study population. Furthermore, the R-squared value of the multiple regression analysis indicates that approximately 43% of the variance in COVID-19 deaths per 100,000 individuals can be attributed to the combined effects of vaccination coverage in 2022 and national wealth in 2020. The goodness of fit in this model, measured with coefficient of determination, is good considering that the variables under study in model hold main assumptions concerning the distribution of the ϵ s.

Figure 1 provides a visual representation of this relationship through a log-log regression line, highlighting the observed trend between vaccination rates and COVID-19 deaths.

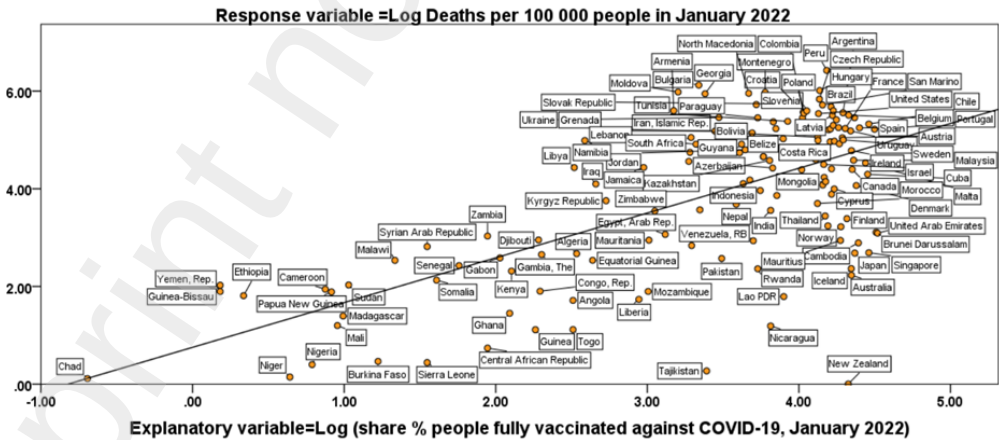


Figure 1. Relationship, using a loglog model, between the percentage of the population immunized against COVID-19 and the number of COVID-19 deaths per 100,000 persons.

These findings present a critical message: while increasing COVID-19 vaccination rates remains an essential public health strategy, it might not be the sole solution for reducing mortality. The emergence of new COVID-19 variants adds another layer of complexity. Simply achieving high vaccination levels cannot be viewed as a one-size-fits-all solution for controlling the pandemic and minimizing deaths. As the following section will explore, numerous environmental and socioeconomic factors significantly influence COVID-19 transmission dynamics. A comprehensive approach that addresses these multifaceted aspects is likely necessary to effectively manage the pandemic and its associated mortality burden.

The text emphasizes the counterintuitive finding regarding the association between vaccination rates and mortality rates, acknowledging the need for further exploration. It elaborates on the statistical tests (F-test and R-squared) and their interpretation. The importance of considering factors beyond vaccination rates, such as emerging variants and socioeconomic conditions, is highlighted.

4. DISCUSSION

This study's key finding is a robust positive correlation between a country's mortality rate per 100,000 people and the percentage of its population fully vaccinated against COVID-19. This association remains significant even after accounting for the influence of GDP per capita. However, the results highlight that vaccination, while crucial, is just one piece of the puzzle. Numerous other factors significantly influence the spread and severity of COVID-19, even in nations boasting high vaccination rates.

Mounting evidence underscores the multifaceted nature of COVID-19 transmission, with air pollution, urban density, and geo-environmental factors playing significant roles. Research by Coccia (2020, 2021) suggests a concerning link between high levels of air pollution, particularly in densely populated cities, and increased COVID-19 caseloads. These findings are corroborated by studies demonstrating a correlation between lower air pollution levels and decreased COVID-19 mortality rates (Coccia, 2020a, 2020b, 2020c). Notably, Coccia's (2020) work highlights the disparity observed in case numbers between hinterland cities with limited air circulation and high pollution, and windier coastal areas during the early stages of the pandemic (April 2020).

Further research by Copat et al. (2020) emphasizes the potential influence of specific climatic factors on COVID-19 spread. They posit that low wind speed, temperature, and humidity may create conditions conducive to viral persistence. Conversely, strong winds promote air circulation and dispersal, potentially mitigating viral spread (Coccia, 2021; Caliskan et al., 2020). Additionally, Rosario et al. (2020) suggest that wind exposure also increases viral susceptibility to sunlight, a known detrimental factor for the virus. Nicastro et al. (2021) delve deeper into this concept, exploring the spatial distribution of the virus relative to solar radiation. Their research demonstrates the virucidal effect of UV-B/A photons on the single-stranded RNA of the COVID-19 virus, highlighting the potential benefit of midday sunlight in temperate regions during summers, where it can significantly inactivate the virus within minutes.

These combined findings advocate for a multi-pronged approach to combatting future pandemics. While vaccination remains the cornerstone strategy, proactive measures to reduce air pollution levels, particularly in densely populated urban centers, are crucial. Furthermore, promoting sustainable environmental practices holds promise for mitigating the spread and severity of future infectious diseases.

Furthermore, Bontempi & Coccia (2021) and Bontempi et al. (2021) identify a strong association between intensive commercial activity and the spread of COVID-19. Their research, focusing on Italy as a case study, suggests a statistically significant correlation (average $r > 0.78$, $p\text{-value} < 0.001$) between the total import and export levels of Italian provinces and confirmed COVID-19 cases over time. Similar findings emerge from a study encompassing three major European countries (Italy, France, and Spain), indicating a positive association between international trade and pandemic diffusion. It is important to acknowledge the complexity of international trade data, which reflects a multifaceted interplay of economic, demographic, environmental, and climate factors that all contribute to the transmission dynamics of COVID-19.

The ongoing emergence of novel variants underscores the dynamic nature of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus. Mutations within the viral genome, arising both in the environment and during human host replication, can lead to the formation of new variants with potentially altered characteristics (Fontanet et al., 2021). Notably, the unexpected surge in COVID-19 cases observed in December 2020 was attributed to the emergence of variants like Alpha (B.1.1.7) in the UK and Beta (B.1.351) in South Africa. These variants harbored mutations within the receptor-binding domain of the spike protein, a critical element for viral attachment and entry into host cells. These mutations were estimated to enhance transmissibility by 40% to 70% (Fontanet et al., 2021). Davies et al. (2021) subsequently confirmed the increased transmissibility of the Alpha variant compared to earlier strains. Their research also suggested a concerning 61% higher risk of mortality associated with the B.1.1.7 lineage, implying a potential for not only increased spread but also more severe illness.

The emergence of new SARS-CoV-2 variants poses a significant challenge for global public health efforts aimed at controlling the COVID-19 pandemic. This paper will explore two particularly concerning variants – Delta (B.1.617.2) and Omicron (B.1.1.529).

The Delta Variant (B.1.617.2): A Threat of Heightened Transmissibility and Potential Severity: Mounting evidence suggests that the Delta variant exhibits a significantly increased transmissibility compared to earlier strains. Research indicates that it may be nearly twice as contagious, potentially leading to a rapid rise in case numbers (Mayo Clinic, 2022). Unvaccinated individuals remain at the greatest risk of contracting and transmitting the Delta variant. While full vaccination with approved COVID-19 vaccines offers substantial protection against severe illness and hospitalization, breakthrough infections can still occur. However, data suggests that the duration of infectiousness following a breakthrough infection might be shorter in vaccinated individuals compared to unvaccinated persons. Importantly, COVID-19 vaccines continue to demonstrate effectiveness in preventing severe illness even with the Delta variant.

The Omicron Variant (B.1.1.529): A Highly Transmissible Variant with Uncertainties Regarding Severity and Vaccine Effectiveness. The Omicron variant appears to be even more transmissible than other variants of concern, including Delta. This enhanced spreadability has the potential to significantly impact public health efforts. Even though knowledge about the severity of Omicron-induced sickness is still developing, people who have had the required course of immunizations are likely to have breakthrough infections and perhaps spread the virus to others. Even with the Omicron form, COVID-19 vaccination is probably still going to be able to protect against serious sickness.

One concerning aspect of the Omicron variant is the potential for decreased effectiveness of some monoclonal antibody treatments. This underscores the continuous need for the development and evaluation of potent therapeutic approaches to combat COVID-19 (Wang et al., 2022).

While variants such as Alpha, Beta, and Gamma are still monitored by public health agencies, their current circulation levels are significantly lower compared to previous peaks. The Mu variant (B.1.621) also remains under observation. It is crucial to acknowledge that the emergence of novel SARS-CoV-2 variants can significantly alter the transmission dynamics and disease severity of COVID-19, necessitating continued vigilance and adaptation of public health strategies.

The emergence of non-invasive ventilation (NIV) represents a significant advancement in the realm of respiratory support. Unlike invasive mechanical ventilation, which necessitates the insertion of an endotracheal tube (through the mouth) or a tracheostomy tube (via a surgical incision in the throat), NIV offers a patient-centered alternative. The utilization of NIV has witnessed a remarkable surge in recent decades, solidifying its position as a cornerstone in managing both acute and chronic respiratory failure, applicable in both home settings and intensive care units (Soo Hoo, 2020, 2010).

This innovative technology presents a compelling alternative to invasive ventilation due to its inherent versatility and potential to enhance patient care protocols. NIV advancements include the integration of respiratory abdominal sensors and transducers. These advancements enable patient-triggered pressure support with breath rate monitoring, facilitating a more accurate assessment of a patient's airway pressures. These features contribute to a more comfortable and potentially less invasive approach to respiratory support, promoting improved patient tolerance and potentially accelerating recovery.

One of the key strengths of NIV technology lies in its ability to not only deliver adequate ventilation but also to mimic natural respiratory processes for optimal patient benefit. Maintaining airway clearance, maximizing ventilation, and enhancing patient comfort are the three pillars of this approach. It is well established that the nose and upper respiratory passages play a critical role in naturally warming, humidifying, and filtering inhaled gases before they reach the lungs (Chang et al., 2018). The upper airways and nasal mucosa contribute significantly, providing around 75% of the heat and moisture that reach the smaller airways and alveoli during normal breathing. This intricate system ensures that air typically reaches the alveoli at close to 100% relative humidity and a temperature of approximately 37°C (Gattin et al., 2014). NIV

technology strives to replicate these natural processes to best serve patients and optimize respiratory outcomes.

In essence, the advantages of NIV extend to both the patient and the healthcare facility. For patients, NIV offers several benefits:

- Cost-effectiveness: NIV treatment is generally less expensive compared to invasive mechanical ventilation.
- Reduced need for sedation: Patients on NIV often don't require sedation, allowing for a more conscious and interactive experience.
- Enhanced comfort: NIV is generally considered more comfortable for patients compared to invasive ventilation techniques.
- Elimination of intubation: NIV avoids the need for inserting a tube into the airway, reducing potential complications associated with intubation.
- Time efficiency for healthcare facilities: Implementing NIV can be a more time-efficient approach for healthcare providers compared to setting up and managing invasive ventilation.

The COVID-19 pandemic served as a stark reminder of the critical need for robust preparedness measures to combat large-scale public health emergencies. Data suggests a potential link between ventilator availability and national COVID-19 mortality rates. For instance, Germany, boasting a substantial ventilator stockpile (approximately 30,000 units in 2020) according to Our World in Data (2022a), exhibited a lower COVID-19 death toll (117,318) compared to Argentina (The World Bank, 2022a). Notably, Argentina, with a significantly smaller population (around 45 million) than Germany's (over 83 million), reported a higher death toll (120,019) from COVID-19 (JHCSE, 2022). While this comparison cannot definitively establish causality, it suggests that ventilator availability might be a significant factor in mitigating pandemic severity.

In the context of pandemic preparedness, it's crucial to consider not only traditional invasive mechanical ventilation but also the growing role of non-invasive ventilation (NIV). Unlike invasive techniques that necessitate the insertion of a tube into the airway, NIV offers a patient-centered alternative by delivering respiratory support through a comfortable facial mask or similar interface. This approach holds promise for several reasons. Firstly, NIV can potentially alleviate the strain on intensive care units (ICUs) by providing effective respiratory support to patients who do not require invasive ventilation. This can free up ICU beds for critically ill patients with more severe respiratory failure, ultimately improving overall patient outcomes during a surge in cases. Secondly, NIV offers a generally lower risk of complications compared to invasive ventilation, potentially reducing hospital stay duration and associated healthcare costs.

As highlighted by scholars like Kapitsinis (2020), robust public policy investments in healthcare infrastructure are essential to mitigate the mortality burden of pandemics like COVID-19. This underscores the need for strong national healthcare systems with adequate capacity to manage large-scale outbreaks. Governments should prioritize strategic investments aimed at expanding hospital capacity, fostering research and development (R&D) efforts for novel technologies, and accelerating the

development of effective vaccines, antivirals, and innovative medical devices (Ardito et al., 2021; Coccia, 2020). These advancements can equip healthcare systems to strategically counter future public health threats posed by emerging epidemics.

5. CONCLUSIONS

Lau et al. (2021) assert that the fatality rate is a critical metric for determining the actual social impact of COVID-19, given the persistent risk of a worldwide pandemic (cf., Liu et al., 2021). Accordingly, lowering the death and case fatality rates has been a major goal for countries fighting the COVID-19 pandemic (cf., Coccia, 2020a, 2022b). Lockdowns and other non-pharmaceutical treatments were used as part of the first reaction to handle the problem in 2020 (Coccia, 2022b). But by 2021 and 2022, the emphasis was on mass immunization campaigns (Coccia, 2022b). It's interesting to note that this study implies there is no clear correlation between a rise in the percentage of vaccinated people and a drop in COVID-19 death rates in various nations. This can be explained by the intricate interactions between many elements that affect how the pandemic spreads in particular settings and communities.

While the study by Lau et al. (2021) presents intriguing, albeit preliminary, findings, it does have limitations. Firstly, there is a lack of comprehensive data on total vaccination rates across a broad range of countries. Secondly, the study does not account for all potential confounding variables that might influence both vaccination rates and COVID-19 mortality. Future research should aim to control these variables to strengthen the study's conclusions. Additionally, the absence of integration between the mortality data and the socioeconomic characteristics of different countries can potentially skew the results, making comparisons problematic (Angelopoulos et al., 2020; Coccia, 2018; Kargi, 2023b). Furthermore, the level of healthcare investment within each country likely plays a role in vaccination rates, healthcare management, and ultimately, mortality rates. Including this factor as a control variable in future studies would be beneficial. Finally, the study focuses on relationships between variables within specific timeframes based on recent data availability. Extending the study period would contribute to more robust results. Consequently, generalizing these findings requires caution.

This study highlights the need for future research to incorporate new data, as it becomes available, to comprehensively examine the interplay between vaccination rates, mortality rates, and various socioeconomic factors across different countries. While the current research acknowledges limitations, the findings suggest that solely focusing on vaccination as a health policy may not be sufficient to effectively reduce COVID-19 mortality, control the pandemic's spread, and mitigate its subsequent negative societal impacts.

More detailed research in these areas is therefore desperately needed. In order to clarify the intricate environmental and ecosystemic elements that impact pandemics, this study advocates for additional research. It also highlights how crucial it is to examine how limitations, immunization campaigns, and total healthcare spending interact.

In conclusion, a broader range of variables beyond purely medical parameters should be meticulously considered to explain the varying COVID-19 mortality rates

observed across different societies. These other elements include societal, economic, and innovation-related aspects in addition to medical aspects. By meticulously examining these factors, we can gain valuable insights to control the negative impacts of future pandemic crises on public health, economic stability, and societal well-being. Building upon the results presented here, further in-depth investigations are necessary. These investigations should focus on the intricate relationships between the negative societal effects of pandemics, the capacity and response of public health systems, and the overall pandemic response strategies implemented by different countries.

Overall, this study emphasizes the value of a multimodal strategy to lessen the harmful effects of pandemic threats like COVID-19 in the future, especially with regard to mortality. Vaccination programs alone should not be the only component of a successful approach. Rather, it ought to be based on large-scale investments in bolstering healthcare institutions and creating all-encompassing health, social, and economic policy solutions for crisis handling. This method recognizes the intricate interactions between socioeconomic and environmental elements that impact the dynamics of COVID-19 transmission and the consequent harm to society. This study's conclusion highlights the necessity of more research on socioeconomic variables that can influence and assist a comprehensive public health approach that goes beyond immunizations. By fostering the development of appropriate ecosystems and socioeconomic systems within countries, we can enhance public health outcomes and improve the overall well-being of people in the face of future pandemic crises.

Ethical Statement:

Ethics committee approval was not required for this study.

Contribution Statement:

The author of the study has contributed to all stages of the study, from writing to drafting, and has approved the final version after reviewing it.

Conflict of Interest Statement:

This study has not led to any individual or institutional/organizational conflict of interest.

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