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The disproportionate case-fatality ratio of COVID-19 between top vaccinated countries and the rest of the world

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Highlights

- We compared country's vaccination rate and CFR of COVID-19 on 31 December 2022.
- COVID-19 vaccine doses (/100 population) administered in top-20 countries are 260.
- In the rest of the world 152 doses, and in SSA 51 doses are administered.
- The mean CFR of COVID-19 in the top-20 vaccinated countries dropped by 69%.
- The mean CFR dropped by 27% in the rest of the world and 8% in Sub-Saharan Africa.

Keywords: COVID-19, SARS-CoV-2, Case-fatality ratio, Vaccine equity, Variants of Concern (VOC)

Abstract**Objectives:**

We compared the global reported cumulative case-fatality ratio (rCFR) and excess mortality between top-20 countries with COVID-19 vaccination rates, the rest of the world and Sub-Saharan Africa (SSA) before and after commencement of vaccination programmes.

Methods:

We performed time series model to understand the trend of rCFR over time and performed generalized linear mixed model to understand role of vaccination on rCFR.

Results:

By 31 December 2022, on average 260.3 doses of COVID-19 vaccines per 100 people had been administered in the top-20 vaccinated countries, compared to 152.1 doses in the rest of

the world, and 51.2 in SSA. The mean rCFR of COVID-19 had dropped by 69.0% in the top in the top-20 vaccinated countries, 26.5% in the rest of the world and 7.6% in SSA. The excess mortality had dropped by 48.7% in top vaccinated countries compared to 62.5% in the rest of the world and 60.7% in SSA. In a generalized linear mixed model, reported number of vaccine doses administered doses (/100 population) (Odds ratio:0.64) was associated with a steeper reduction of the country's COVID-19 rCFR.

Conclusions:

Vaccine equity and faster roll-out across the world is critically important in reducing COVID-19 transmission and CFR.

Introduction:

In the early stages of the COVID-19 pandemic, the WHO-China Joint Mission on Coronavirus Diseases (COVID-19) 28 February 2020 report indicated a crude Case fatality ratio (CFR) of 3.8% among the first 55,924 laboratory-confirmed cases [1]. Subsequently, systematic reviews on the case-fatality ratio (CFR) of COVID-19 reported an estimated CFR between 2.3-3.6% [2–5]. The global cumulative reported case fatality ratio (rCFR) of COVID-19 increased up until the 17th epidemiological week (April 22–28, 2020) following detection of SARS-CoV-2 in Wuhan China at 7.2, and then started to decline steadily up until 31 December 2021 at 2.2 [6].

Vaccination can reduce the CFR of COVID-19. Several vaccines have been approved for emergency use by the Food and Drug Administration, USA, the European Medicine Agency and the United Kingdom Health Security Agency. The World Health Organization (WHO) also approved use of a few Vaccines across the world. It has been estimated that vaccines

prevent infection by 60-92% [7,8], hospitalizations by 87-94% [7,9] and deaths by 72%-100% [7,10] after 7-28 days of receiving the second dose of the vaccines for Alpha, Beta, or Delta variant of concern (VOC).

COVID-19 Vaccines are not distributed equitably in the world [11]. Although COVID-19 vaccines were developed at an unprecedented rate through the advancement of science and global cooperation, the distribution of the vaccine across the world is questionable [12]. Current global vaccination rates are roughly 6.7 million doses per day and the vaccine distribution is absent or very limited in many low-income countries. Experts anticipated that 80% of the population in low-income countries would not receive a vaccine at the end of 2021 [12], which has been the case.

As the world faces the 3rd year of the COVID-19 pandemic, globally, as of 31 December 2022, there have been over 660.35 million confirmed cases of COVID-19, including 6.69 million deaths, reported to WHO [13]. COVID-19 vaccination rollout globally has progressed at varying rates and the impact of mass vaccination on case fatality ratio should be explored and inform global access to vaccine. To this end, we compared the global rCFR between the top-20 countries in terms of vaccination rates (minimum vaccination: 196.9 dose/100 people), sub-Saharan Africa (SSA), and the rest of the world, before and after commencement of vaccination programs. We further explored the association between vaccination and other control measures on Covid-19 CFR and excess mortality.

Methods:

COVID-19 data

The necessary COVID-19 related data, including daily reported new cases, daily reported new deaths, reported total deaths, reported total deaths per million inhabitants and vaccination (number of doses of any COVID-19 vaccine administered/100 people), were collected from the WHO daily COVID-19 situation reports of 210 countries from Jan 01, 2020, to December 31, 2022 [14]. On 8th December 2020, the first human in the world received an approved COVID-19 vaccine [15]. We considered the 28th day of receiving the first vaccine in the world as a cut-off to compare the pre-vaccine period (Jan 1, 2020 – Jan 5, 2021) and the post-vaccine period (Jan 6, 2021- December 31, 2022). Altogether, we had data from 159 countries for analysis after excluding countries with population size less than 1 M. Of the 159 countries, 44 were from SSA (doses/100 People): Angola (66.6), Benin (31.7), Botswana (118.7), Burkina Faso (22.6), Burundi (0.2), Cameroon (14.3), Central African Republic (42.2), Chad (22.0), Democratic Republic of Congo (17.6), Congo (14.0), Cote d'Ivoire (84.4), Djibouti (30.2), Equatorial Guinea (29.2), Eritrea (0.0), Ethiopia (42.6), Gabon (24.0), Gambia (30.2), Ghana (63.9), Guinea (63.1), Guinea-Bissau (32.0), Kenya (42.7), Lesotho (54.6), Liberia (84.1), Madagascar (8.0), Malawi (31.2), Mali (19.2), Mauritania (85.6), Mauritius (201.1), Mozambique (88.4), Namibia (37.9), Niger (27.4), Nigeria (46.8), Rwanda (189.5), Senegal (15.7), Sierra Leone (71.6), Somalia (48.4), South Africa (63.5), South Sudan (21.2), Sudan (29.3), Tanzania (55.0), Togo (38.4), Uganda (55.7), Zambia (62.9), and Zimbabwe (74.9).

Identifying top-20 vaccinated countries

We considered top-20 countries that consistently remained on top of weekly vaccination rate (/100 population) during the period 5 Jan 2021- 31 December 2022. We utilized a count variable to identify the top-20 vaccinated countries each week, which adds a score of one if a country is listed in the top-20 countries in a week and zero otherwise. We repeated the

procedure for each week until 31 August 2022. Finally, we selected top-20 countries with higher aggregated score for weekly vaccination rate. The top-20 countries by COVID-19 vaccination rate were (doses/100 people) : Argentina (247.4), Bahrain (236.2), Belgium (253.8), Cambodia (269.0), Canada (250.4), Chile (319.5), China (243.9), Cuba (381.0), Denmark (223.9), Ireland (220.8), Israel (196.9), Italy (242.9), Japan (300.0), Portugal (270.3), Qatar (282.0), Singapore (261.3), South Korea (250.2), United Arab Emirates (264.0), United Kingdom (224.0), and Uruguay (256.4).

Reported case-fatality ratio (rCFR)

We calculated daily cumulative rCFR COVID-19 as we have described in our earlier paper Hasan et al [6]. as the number of reported COVID-19 attributed deaths per 100 COVID-19 confirmed cases expressed as $rCFR = (\text{weekly reported COVID-19 attributed deaths} / \text{weekly reported COVID-19 confirmed cases}) \times 100$. As the number of cases and deaths both are a fraction of total cases or deaths globally, we considered the term as reported CFR (or to make a simplified version as rCFR [6]).

Excess mortality

Excess mortality is used to describe the number of deaths from all causes during a particular period that is higher than expected under "normal" circumstances [16]. The excess mortality was calculated as the difference between the recorded number of fatalities in a certain week or month (depending on the country) between Jan 2021 and December 2022 and an estimate of the projected deaths for that time period if the COVID-19 pandemic had not happened [17,18]. There are great difficulties associated with obtaining excess mortality data from many countries, however, 'Our World In Data' tracked data from different sources and we

could extract excess mortality data from 159 countries for the period of 5 Jan 2021 to 31 December 2022 [19].

Time series model to predict the trend

Three time-series models (i.e., auto-regressive integrated moving average (ARIMA), automatic time-series forecasting model also known as ‘Prophet model’, and simple exponential smoothing (SES), were used to identify the global trend of COVID-19 rCFR and excess mortality. The details of the SES, ARIMA, and Prophet models are discussed in an earlier article on COVID-19 [6].

Outcome and predictor variables

We collected data on selected predictors variables from the World Bank or other UN sources and from “Our World in Data” including population density [20], percentage of people above 65 years of age [21], Gross Domestic Product (GDP) [22], worldwide governance indicators (WGI) [23], and Global Health Security Index (GHSI) [24], the prevalence of obesity [25,26] for our analyses. We also included the country-specific prevalence of diabetes [26] and cardiovascular disease (26) to explain the variation of COVID-19 rCFR. We used ‘stringency index’ from the Oxford COVID-19 Government Response Tracker [27].

Empirical evaluation

We assessed the ARIMA and Prophet models by comparing their results to benchmarks model, the SES [28]. The SES also allows the most appropriate non-seasonal model for each series, allowing for any kind of error or trend component. We, then, analysed and compared the performance of the time series models with some of the commonly used measures to

evaluate the prediction significance including coefficient of determination (R^2), root mean square error (RMSE), and mean absolute error (MAE).

Generalized Linear Mixed Models

We developed a generalized linear mixed model (GLMM) with beta distribution to identify whether the explanatory variables have any relationship with the country's rCFR of COVID-19 and excess mortality. The GLMM is an extension of the Generalized Linear Models (GLM) that allows the analysis of clustered categorical data, as in the case of repeated responses from different subjects [29]. One of the key advantages of GLMM is that it separates the levels of the models to account for the group effect nesting the lower-level observations. In this study, we have several observations within the variable 'locations (country or territory)'. While the location data are assumed to be time-invariant, the independent data are assumed to be universal over the whole study area at a certain time point. The model describes a beta distribution family that has a logit link.

Although we have selected variables carefully and kept consistency with our previous publications on the subject [6], we were not able to add some potential confounding variables including the median age of cases in each country. All analyses were carried out using the statistical software R version 3.5.2.2 [30].

Statistical analysis

We performed summary statistics of vaccine doses/100 inhabitant and rCFR by country in the top-20 countries in terms of vaccination rate (**Fig. 1**), in SSA, and in the rest of the world pre- and post-vaccination programme and reported the mean and standard error (SE). We

observed that the rCFR and excess mortality of COVID-19 has changed over time (**Fig. 2**). Using time-series models alone would not allow us to identify the reason behind the increasing and decreasing trend of COVID-19 rCFR/excess mortality.

RESULTS:

More than 660.35 million cumulative confirmed COVID-19 cases and 6.69 million COVID-19 related deaths had been documented globally by 31 December 2022. More than 165.40 doses of COVID-19 vaccines have been given per 100 population on average globally as of 31 December 2022. On average, for every 100 people, 260.33 doses of vaccines have been given in the top-20 COVID-19 vaccination countries. In the rest of the world (including SSA), 152.12 doses of COVID-19 vaccines have been given, whereas the number is just 51.21 in Sub-Saharan Africa (SSA) (**Table 1**). The rCFR is estimated as 1.89 in the top-vaccinated countries on 5 Jan 2021, which has dropped by 69.31% at 0.58 on 31 December 2022. In the rest of the world, the rCFR dropped from 2.34 on 5 Jan 2021 to 1.72 on 31 December 2022, which represents a reduction of only 26.50% (**Table 1**). In SSA, the rCFR has decreased by 7.61% over the period (1.97 vs. 1.82). Between 5 Jan 2021 and 30 December 2022, the excess mortality had dropped by 48.65% in top vaccinated countries compared to 62.50% in the rest of the world and 60.71% in SSA (**Table 1**). The correlation coefficient between vaccination rate (/100 people) and rCFR in different countries of the world on 31 December 2022 is estimated as -0.363 ($p < 0.001$) and with excess mortality as -0.321 ($p < 0.001$) (**Fig 3**).

Factors associated with rCFR and excess mortality:

In the GLMM, the estimated effect of each variable is presented as odds ratio (OR). The reported number of vaccine doses administered (/100 population) (0.64 [0.62–0.65]) and

(0.96 [0.95–0.98]), GDP (0.79 [0.68–0.91]) and (0.92 [0.89–0.96]), and stringency index (0.88 [0.87–0.89]) and (1.13 [1.11–1.15]) were negatively significantly associated with the COVID-19 rCFR and excess mortality, respectively (**Table 2**).

Table 2 includes various covariates and the random intercept in the model. The intraclass correlation coefficient (ICC) of 0.682 was calculated by dividing the variance of the random effect by the total variance. Thus, the spatial unit effects account for approximately 68.2% of the total variance of weekly rCFR, which suggests moderate reliability on location effects on weekly rCFR. It is also to be noted that with the introduction of a random intercept, “vaccination”, “population density”, “GDP”, “weeks” and “stringency index” had significant negative effects on weekly rCFR and “the percentage of people aged 65 and above” have significant positive effects.

The Trend of global rCFR of COVID-19:

In the ARIMA and Prophet models, we found a strong declining trend of rCFR of COVID-19 between observed and predictive global rCFR of COVID-19 with an R^2 , RMSE, and MAE value of 99.97% and 99.50%, 0.029 and 0.113, and 0.008 and 0.059, respectively (**Table 3**). The observed and predicted rCFR and observed and predicted excess mortality had a fair agreement (**Fig 4**). In terms of accuracy, the ARIMA model performed better over Prophet and SES model (with better R^2 , RMSE, and MAE value). The coefficient of determination of the ARIMA model was larger and errors are lower than in the Prophet and SES models. According to the forecast in both models, the ratio of COVID-19 rCFR is expected to decrease considerably in the coming 10 days (**Fig 1**).

Discussion:

The global rCFR of COVID-19 has been declining since May 2020, stabilizing or increasing slightly with the emergence of different variants of concern, particularly Delta VOC [31,32]. Following the rollout of COVID-19 vaccines, the rCFR started to decline, although, at a different rate in top-20 vaccination rate countries (69% drop), and the rest of the world (27% drop). In SSA, where the vaccine rollout has not yet reached a satisfactory mark, the rCFR of COVID-19 remained roughly unchanged (dropped by 8%). The excess mortality, on the other hand, dropped by 49% in top-vaccinated countries, 62.5% in the rest of the world and 60.71% for Sub-Saharan Africa. Many factors affect the reduction of rCFR, however, our results are compatible with vaccination and stringency of control measures contributing to the reduction of rCFR. A study on global impact of COVID-19 vaccination showed that the vaccination averted 14.4 million reported deaths (or 19.8 million excess deaths) due to COVID-19 in the first year of vaccination (8 Dec 2020-8 Dec 2021) [11]. This analysis complements previous findings showing a disproportionate decline of rCFR and excess mortality in countries with various vaccination coverage indicating the importance of equitable distribution of COVID-19 vaccine.

We found an overall decreasing trend of excess mortality post vaccination period. In contrast to the negligible decline of the rCFR, SSA countries experienced a marked drop of the excess mortality. Excess mortality during this pandemic was affected by different factors, and not merely by transmission of COVID-19 and vaccination coverage. Some of these factors (e.g. shielding the elderly people) may have even contributed to reduction in excess mortality. The differential impact of these factors made the use of excess mortality an unpredictable estimator of COVID-19 severity [33]. We did not compare the excess mortality data at country level. Although differences in data and methodology preclude direct comparisons between our results and those of the above studies, it should be noted that none of the top

ranked countries according to excess mortality are from SSA. Although increasing vaccination where possible is beneficial, it may not be the only reason why the mortality rate in SSA, where the majority of the population is under 65 years, has dropped markedly since 2021. It is known that survival from COVID-19 infection is higher in younger age groups [6,34]. The positive association between stringency index and excess mortality is surprising and needs further study. An earlier study showed a chaotic behaviour of COVID-19 data when compared with stringency index [35] or weaker relationship with the mortality rate [36]. The excess mortality has decreased 48.6% in the top-20 vaccinated countries, 62.5% in the rest of the world and 60.7% in Sub-Saharan Africa. Excess mortality had a different pattern than the rCFR of COVID-19. This change might be because of the differences of the age structure of population between high-income countries and the rest of the world including SSA rather than the actual impact of lockdown related control measures estimated in the stringency index which need further exploration in a well-designed study.

The negative correlation between doses of COVID-19 vaccines given per hundred populations, rCFR and excess mortality indicate the benefit of vaccines. Thus, the vaccine has been considered as a pathway out of this pandemic, but strong, innovative policies that ensure fast and equitable distribution are absent [11,12]. Vaccinating the world serves global interests of protecting each other's health, and economy [12]. Our analysis showed a great disparity in vaccine roll out between top vaccinated countries (260 doses/100 people) and low-income countries (e.g., 51 doses/100 people in SSA) by 31 Dec 2022. In high-income countries, the administration of a third or even fourth COVID-19 vaccine dose is ongoing [37] whereas more than 60% of the population in SSA have not yet received a single dose of vaccine (as of 31 Dec 2022).

We found COVID-19 vaccination, stringency index, and GDP as significantly associated with the reduction of rCFR of COVID-19. The major vaccines (mRNA, or adenovirus vectored) have all been found to be highly effective in reducing hospital admission and death, even though some of the vaccines were not very effective in limiting the infection [38]. Thus, the vaccine rollout helped high-income countries quickly reduce the burden of patients in hospitals limiting COVID-19 fatalities. However, in the rest of the world where vaccine rollout is still far from reaching a satisfactory level (70-85% of people receiving full doses of vaccines) [12], the case-fatality ratio has not declined markedly in comparison to the top vaccinated countries. On the other hand, the results from different surveys suggest that in many SSA countries, the natural immunity had reached a state where it is limiting spread and reducing the overall burden of the pandemic [39]. In the Republic of Congo 66% of people in Brazzaville [40] in Malawi, 64.9% of blood donors [41] and in the Central African Republic, 74% of community residents have been found to have antibodies to SARS-CoV-2 [42]. The country's GDP is another indicator associated with the reduction of COVID-19 rCFR. Countries with higher national income deployed vaccines at a faster rate, which reduced the local transmission and rate of hospitalization, allowing them to concentrate on the vulnerable population, all synergistically helped them reduce the fatalities due to COVID-19. Earlier studies have also identified these variables as a risk factor for mortality/fatality ratio of COVID-19 [6,43,44].

Equitable distribution of SARS-CoV-2 vaccines is crucial to ending the COVID-19 pandemic [11,45]. The circulation of SARS-CoV-2 across the world among the large unvaccinated populations might allow the virus to reassort and become a new VOC. Furthermore, many animal species are susceptible to SARS-CoV-2 including mink, primates, rodents, cats, and dogs [46]. Several animal species have been linked with emergence of SARS-CoV-2 VOC

including dogs for Alpha variant [47] and rodents for Omicron variant [48]. Thus, this is important to reduce the circulation of SARS-CoV-2 in the human and animal populations to avoid further epidemics caused by emergence of new VOC. Equitable and faster vaccine rollout is the key to reducing the circulation of SARS-CoV-2 across the world [11].

We have adjusted the model with number of test/100 population in each country. Some countries do not report the daily testing number while some countries share test number irregularly. Testing is an important variable that if not adjusted for it might result in the identification of spurious relationships. The denominator of the rCFR, the cases of COVID-19 is entirely predicated on the number of tests that a country has reported. As such, it is possible that the lower rCFRs in higher vaccination countries is simply reflective of greater testing capacity and thus a bigger denominator for the same number of deaths. Thus, only those countries that regularly reported test data were kept in the analysis.

This study has several limitations. The main limitation is the dependence of number of cases on the intensity of testing thus countries with under testing had missed the fatal cases due to COVID-19. In countries where people undergo swabs for travelling, working, moving, accessing to healthcare etc., which tend to be higher income countries where vaccine roll out was faster, large numbers of asymptomatic people are tested daily, which may result in the identification of large numbers of asymptomatic infections. These are then counted as COVID cases but are merely clinically ill. Thus, only some individuals in these countries actually are cases, because a large fraction of positives is asymptomatic and are, therefore, infected. This might cause an expansion in the denominator of the proportion artificially lowering the case fatality ratio. In contrast, it is likely that in Saharan African countries the proportion of apparently healthy individuals who are tested is much lower leading to

apparently lower rCFR in these countries. The associations we reported between COVID-19 rCFR/excess mortality and explanatory variables are statistical associations and should not be interpreted as causal. Finally, different VOCs of SARS-CoV-2 have different rCFR and the VOCs circulated at different times in different countries [32], we could not adjust those in our analysis.

Conclusion:

More than 260 doses of COVID-19 vaccines have been given per 100 people in the top-20 countries with higher vaccination rates, compared to 152 doses in the rest of the world and 51 doses in Sub-Saharan Africa as of 31 December 2022. Vaccination is negatively correlated with reported CFR ($r=-0.36$) and with excess mortality ($r=-0.32$) which is likely to reflect a contribution of vaccines to the reduction of COVID-19 related deaths. The excess mortality and COVID-19 rCFR continued to decline since February 2021, although at a disproportionate rate between top vaccinated countries and the rest of the world. However, the rCFR has dropped dramatically (69.3%) in the group of 20 countries with highest vaccination rates (70%), quite markedly in the world (30.0%), whereas only 7.6% in in Sub-Saharan Africa. The COVID-19 vaccination, stringency index, and country's GDP were associated with reduction of rCFR of COVID-19. Vaccine equity and faster roll-out across the world is critically important in reducing COVID-19 transmission and CFR.

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Author contribution statement: NH and RK originally planned the study, MNH collected the data, NH and MNH, MJU analyzed the data. NH prepared the first draft manuscript and MNH, JG, RAK, DM, FN, OD, RA, MJU, AZ and RK reviewed the draft manuscripts. All authors approved the submission of the manuscript.

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Ethical approval: This study does not include any individual-level data and thus does not require any ethical approval.

Data availability statement: All the data presented in this manuscript are publicly available in "Our World in Data", "WHO" or "United Nations" webpages. However, the corresponding author can be reached to specific queries on the data sources.

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Figure legends:

Fig 1: The top-20 countries with COVID-19 vaccination rate (reported number of vaccine doses administered/100 people) and the reported case-fatality ratio due to COVID-19.

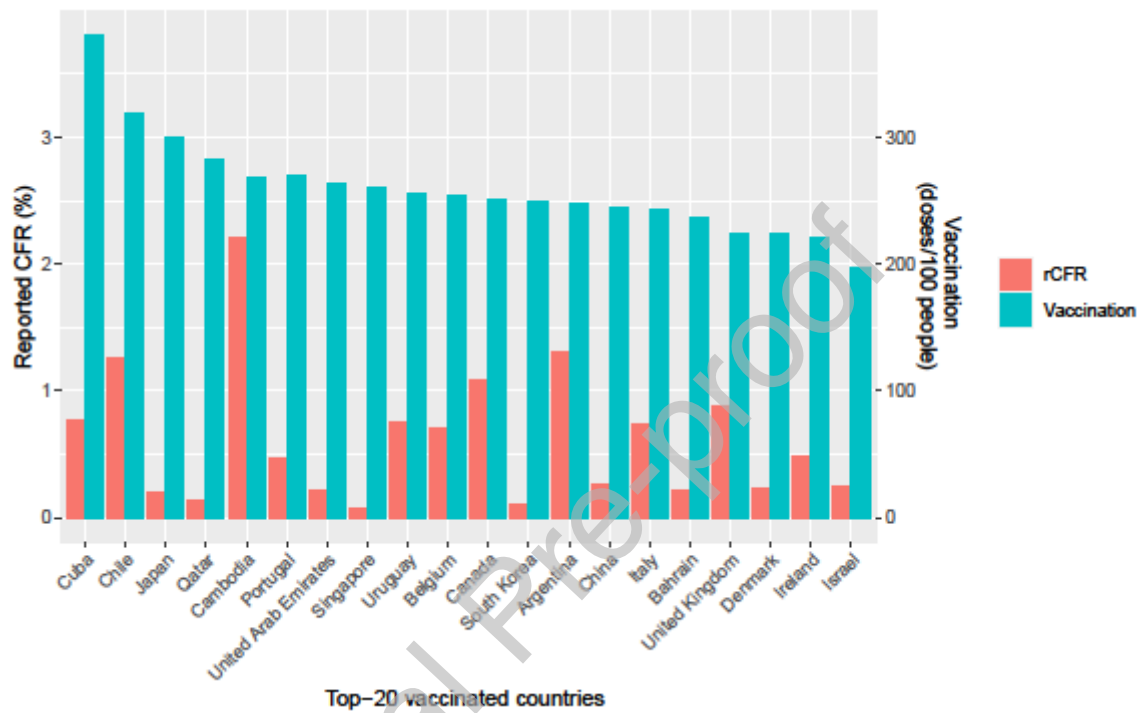


Fig 2. Top: Observed and predicted global daily reported Case-Fatality ratio (rCFR) using Simple Exponential Smoothing (SES) model. Middle: Observed and predicted daily worldwide daily cumulative rCFR using Auto-Regressive Integrated Moving Average (ARIMA) model. Bottom: Observed and predicted daily worldwide daily cumulative rCFR using Automatic Forecasting time-series model (Prophet model). The black dots indicate observed data, the blue line indicates the predictive CFR, and the shaded area indicates the 95% confidence interval of predicted CFR.

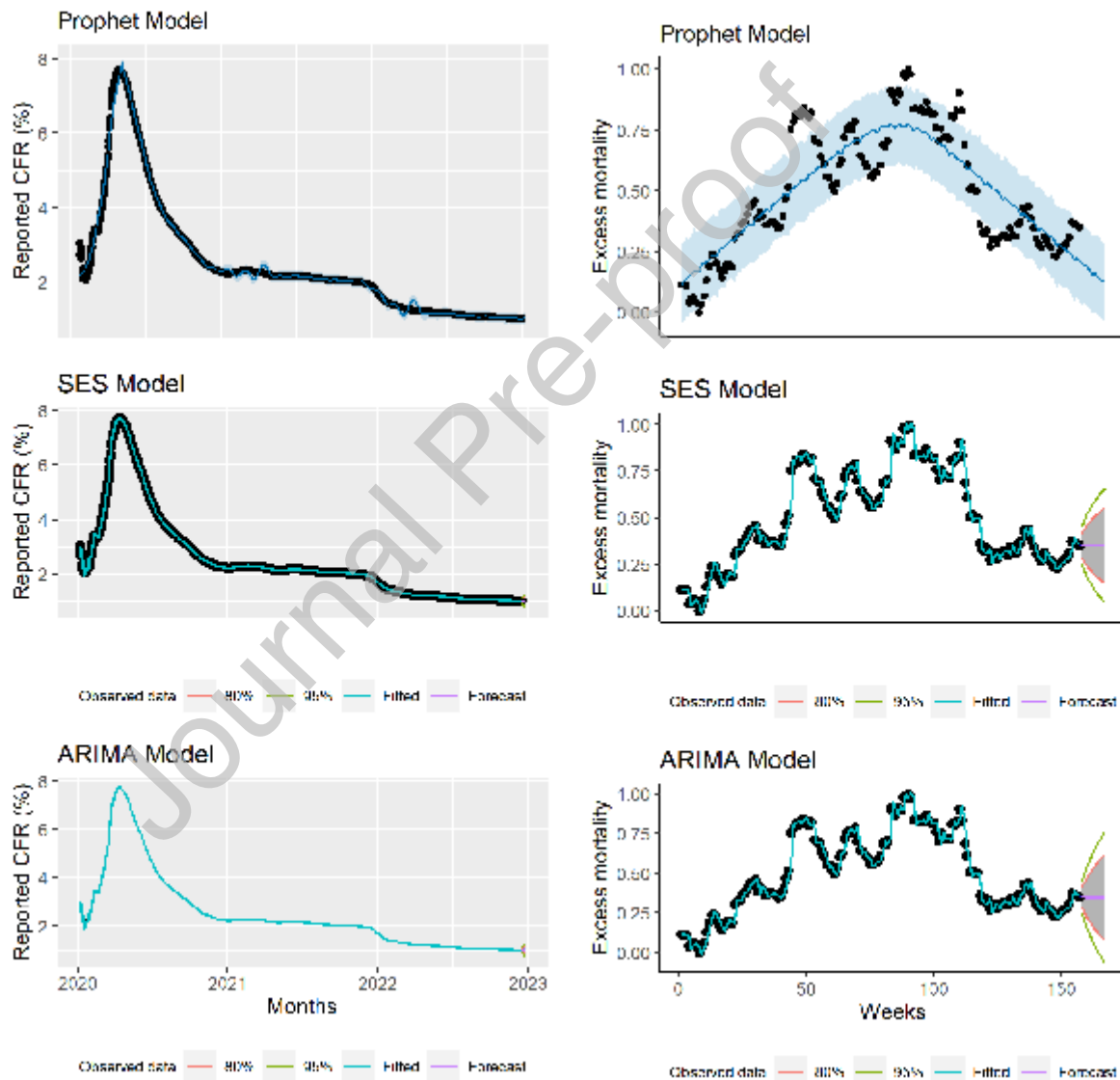


Fig 3: The map shows the COVID-19 vaccination rate (reported number of vaccine doses administered/100 people) and the reported Case-fatality ratio (rCFR) in different countries of the world on 31 December 2022. The darker colour indicates the higher vaccination rates or higher case-fatality ratios. An opposite correlation exists between COVID-19 vaccination rate and rCFR ($r = -0.363$, $p < 0.001$) and excess mortality (-0.321 ($p < 0.001$)).

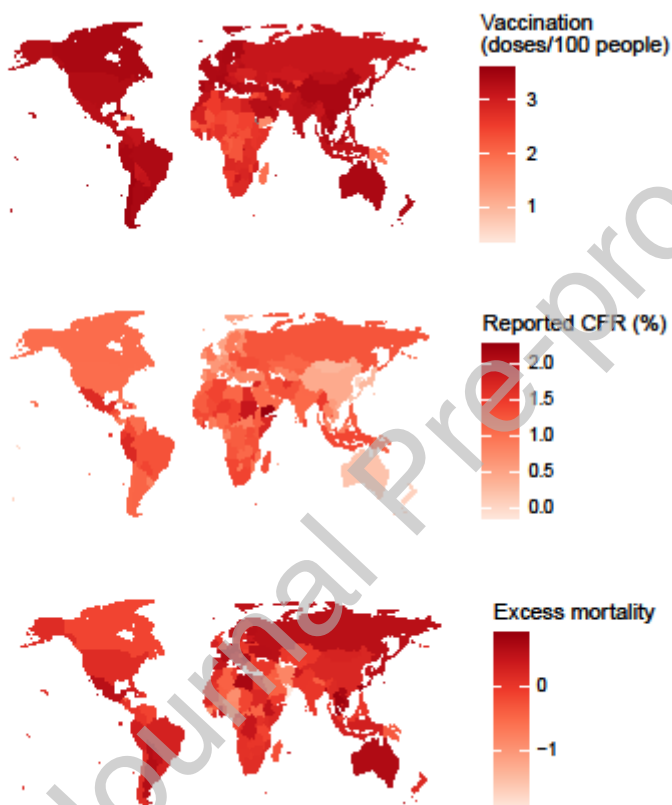
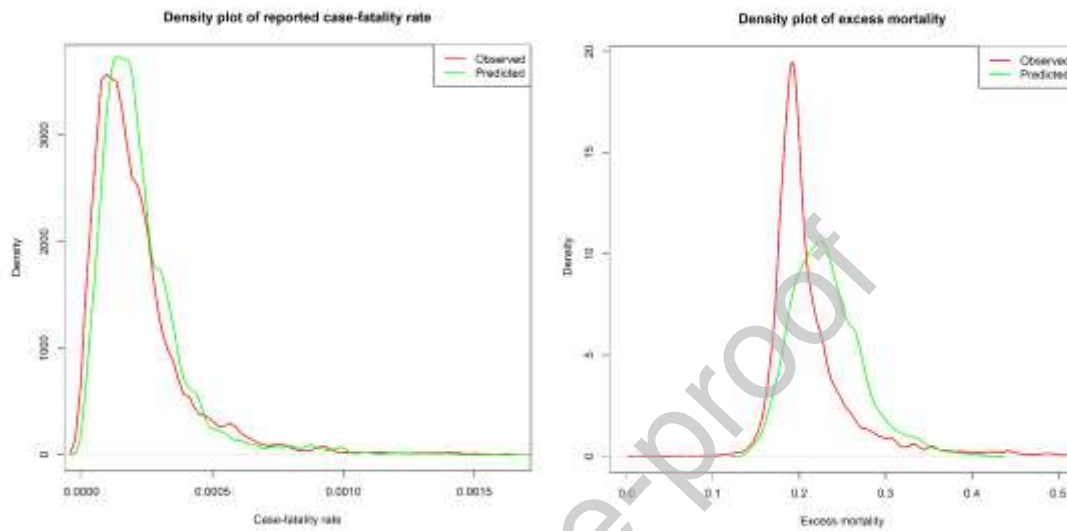


Fig 4: The density plot of observed reported case-fatality ratio (rCFR) and predicted rCFR of COVID-19 (left) and rCFR and Excess mortality (right).



The disproportionate case-fatality ratio of COVID-19 between top vaccinated countries and the rest of the world

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Tables:

Table 1: The reported number of vaccine doses administered/100 people and reported case-fatality ratio (rCFR) of COVID-19 in the top-20 vaccinated countries and rest of the world during 5 Jan 2021 and 31 Dec 2022 (for excess mortality 30 Dec 2022).

	Top-20	Rest of the	Global	Sub-Saharan

	countries with vaccination rates Mean \pm SE	world including SSA Mean \pm SE	Mean \pm SE	Africa Mean \pm SE
Vaccination Doses/100 People (31 December 2022)	260.33 \pm 9.35	152.12 \pm 6.97	137.67 \pm 6.87	51.21 \pm 6.26
Reported CFR by 5 Jan 2021	1.84 \pm 0.39	2.34 \pm 0.24	2.27 \pm 0.21	1.97 \pm 0.19
Reported CFR by 31 December 2022	0.58 \pm 0.12	1.72 \pm 0.16	1.59 \pm 0.14	1.82 \pm 0.20
Reported CFR dropped by (%)	69.31	26.50	29.96	7.61
p-value (for the differences of rCFR between 5 Jan 2021 and 31 December 2022)	0.003	0.318	0.008	0.309
Excess mortality (deaths/100,000) by 4 Jan 2021	0.37 \pm 0.12	0.40 \pm 0.05	0.39 \pm 0.04	0.28 \pm 0.07
Excess mortality (deaths/100,000) by 30 Dec 2022	0.19 \pm 0.03	0.15 \pm 0.01	0.16 \pm 0.01	0.11 \pm 0.01
Excess mortality dropped by (%)	48.65	62.50	58.97	60.71
p-value (for the differences of excess mortality between 4 Jan 2021 and 30 December 2022)	0.207	<0.001	<0.001	0.022

Table 2: Factors associated with reported Case-Fatality ratio (rCFR) of COVID-19 and excess mortality in different counties of the world using a generalized linear mixed model during 1 Jan 2020 and 31 Dec 2022.

Variables	Reported case-fatality ratio (rCFR)			Excess mortality		
	Odds	95%	P-value	Odds	95%	P-value

	ratio (OR)	Confidence Interval		ratio [OR]	Confidence Interval	
Vaccination	0.636	0.620 - 0.652	<0.001 ***	0.960	0.943 - 0.977	<0.001 ***
The percentage of people aged 65 and above	1.189	1.020 - 1.387	0.027 *	1.164	1.117 - 1.212	<0.001 ***
Population density	0.878	0.652 - 1.182	0.390	0.994	0.918 - 1.076	0.877
COVID-19 Tests/1000	0.849	0.829 - 0.868	<0.001 ***	1.013	1.002 - 1.023	0.015 **
GDP	0.787	0.682 - 0.908	<0.001 ***	0.923	0.889 - 0.959	<0.001 ***
GHSI	1.221	1.043 - 1.428	0.013 *	0.968	0.928 - 1.010	0.133
WGI	0.986	0.854 - 1.138	0.848	0.932	0.896 - 0.969	<0.001 ***
Obesity (%)	1.186	1.054 - 1.335	0.005 **	1.076	1.042 - 1.111	<0.001 ***
Stringency index	0.880	0.867 - 0.893	<0.001 ***	1.132	1.118 - 1.145	<0.001 ***
Weeks	1.100	1.044 - 1.158	<0.001 ***	1.156	1.124 - 1.187	<0.001 ***
Groups Name	Variance	Standard Deviation		Variance	Standard Deviation	
Location (Intercept)	0.3103	0.5571		0.01998	0.1414	
Weeks (Intercept)	0.0478	0.2186		0.01055	0.1027	
Akaike information criterion (AIC)	-174928.6				-30707.5	
Bayesian Information Criterion (BIC)	-174826.5				-30605.3	
Root Mean Square Error (RMSE)	0.0001				0.062	
Conditional R^2	0.788				0.513	
Marginal R^2	0.333				0.217	
Intraclass correlation (ICC)	0.682				0.378	

Table 3. The summary of Simple Exponential Smoothing (SES), Auto-Regressive Integrated Moving Average (ARIMA), and Automatic forecasting time-series model (Prophet). The SES, ARIMA, and Prophet models used daily cumulative reported case-fatality ratio (rCFR) data.

	Reported case-fatality ratio			Excess mortality		
Method & Period	R^2	RMSE	MAE	R^2	RMSE	MAE
<i>Simple Exponential Smoothing</i>						
Overall	99.94%	0.038	0.014	96.19%	0.049	0.034
<i>Auto-Regressive Integrated Moving Average</i>						
Overall ARIMA	99.97%	0.029	0.008	96.41%	0.048	0.033
<i>Automatic Forecasting time-series model</i>						
Overall	99.50%	0.113	0.059	75.11%	0.126	0.102

Conflict of interest: The authors declare that they have no conflict of interest.