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The True Human Cost of the Novel Coronavirus 2019 (COVID-19) Pandemic

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As of 6th June 2021, 3:00 PM, there were 174,893,444 worldwide reported cases of the novel coronavirus disease 2019 (COVID-19), with 3,774,138 deaths attributed to this pandemic.[1,2] Infection fatality rate (IFR) i.e., the fraction of deaths reported from all laboratory-confirmed cases for the disease, for COVID-19 has thus far been estimated in a broad range from 0.5 to 1.0%.[3,4] The IFR for any disease is influenced by the accuracy of two metrics: the death reporting mechanism and its attribution to the disease, and testing every possible individual who may have contracted the disease.

Both COVID-19 death reporting and testing are contentious issues, with many countries suspected to be underreporting deaths because of errors of omission and/or commission.[5] This is because, in almost all countries, deaths outside the hospital system are inaccurately reported. Many individuals who die from COVID-19-like symptoms do not get a laboratory confirmatory test. Moreover, asymptomatic individuals constitute a large proportion of COVID-19 cases,[6] accounting for as much as 40 to 45% of total SARS-CoV2 infections.[7,8] Many countries with low resources or with limited testing availability do not even test mildly symptomatic individuals due to scarce availability of RT-PCR testing,[9,10] leading to weak attributable death reporting systems. Thus, estimating IFR accurately is extremely challenging.

So just how many people have died of COVID-19 is a question with huge ramifications for public health policy-making.[11,12] Unfortunately, given the times we live in, this is also a question fraught with political overtones, whose answer depending on whom you ask, range from a benign infection no deadlier than the common seasonal influenza to the deadliest disease since the black plague. As always, the truth lies somewhere in between. Recent newspaper and magazine articles in The New York Times (NYT)[13] and The Economist[14] estimating excess COVID-19 deaths for the period March 2020 to May 2021 have received widespread media coverage. However, both are deficient in scientific rigor. The NYT analysis is a simple linear regression model of varying ranges of COVID-19 mortality as extrapolated from hypothesized rates of IFR, one conservative (496,000 excess deaths in India), and the other, an extreme (4.5 million excess deaths in India), with a mid-point spread estimate (2.1 million excess deaths).[15] The Economist analysis, in contrast, while using the same method as that of NYT at its core, also uses certain assumptions to fit its model, using a machine learning methodology,[16] many of which simply do not hold true in the real world. The analysis suggests a point estimate spread of 7 million (conservative scenario) to 13 million (worst case scenario) excess COVID-19 deaths worldwide, 1 million of these from India alone (worst case scenario).[17]

One underreported analysis that has received lesser coverage but is perhaps one of the most credible, is by the Institute for Health Metrics and Evaluation (IHME), at the University of Washington.[18] IHME has perfected and implemented a long-standing methodology for measuring the burden of diseases on a global scale since 1990 through its *Global Burden of Disease* (GBD) study.[19] The GBD estimates worldwide deaths annually due to aging, communicable

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diseases, non-communicable diseases (including psychiatric disorders), and accidental deaths (traffic, personal injuries, occupational etc.). This is thus far the most comprehensive modeling of all-cause mortality worldwide.

In its special COVID-19 mortality analysis, IHME has used the data from its annual GBD modeling methodology from the period of March 1, 2020, to May 13, 2021, to estimate and predict the global burden of deaths specifically due to COVID-19 during this period. Their methodology is broadly as follows:

1) Using their GBD models, they first estimated the expected all-cause mortality in the period March 1, 2020, to May 13, 2021, based on pre-pandemic deaths, i.e., how many people would have died in this period if there was no COVID-19 pandemic.
2) They then collected the total deaths that were actually reported by countries during this period from all-cause mortality.
3) This was subtracted from the total expected deaths in this period in the absence of the COVID-19 pandemic.
4) The excess mortality thus arrived at was further modeled to identify variables including a lag in death reporting, decrease in mortality due to COVID-19, and increase in mortality directly and indirectly due to COVID-19.

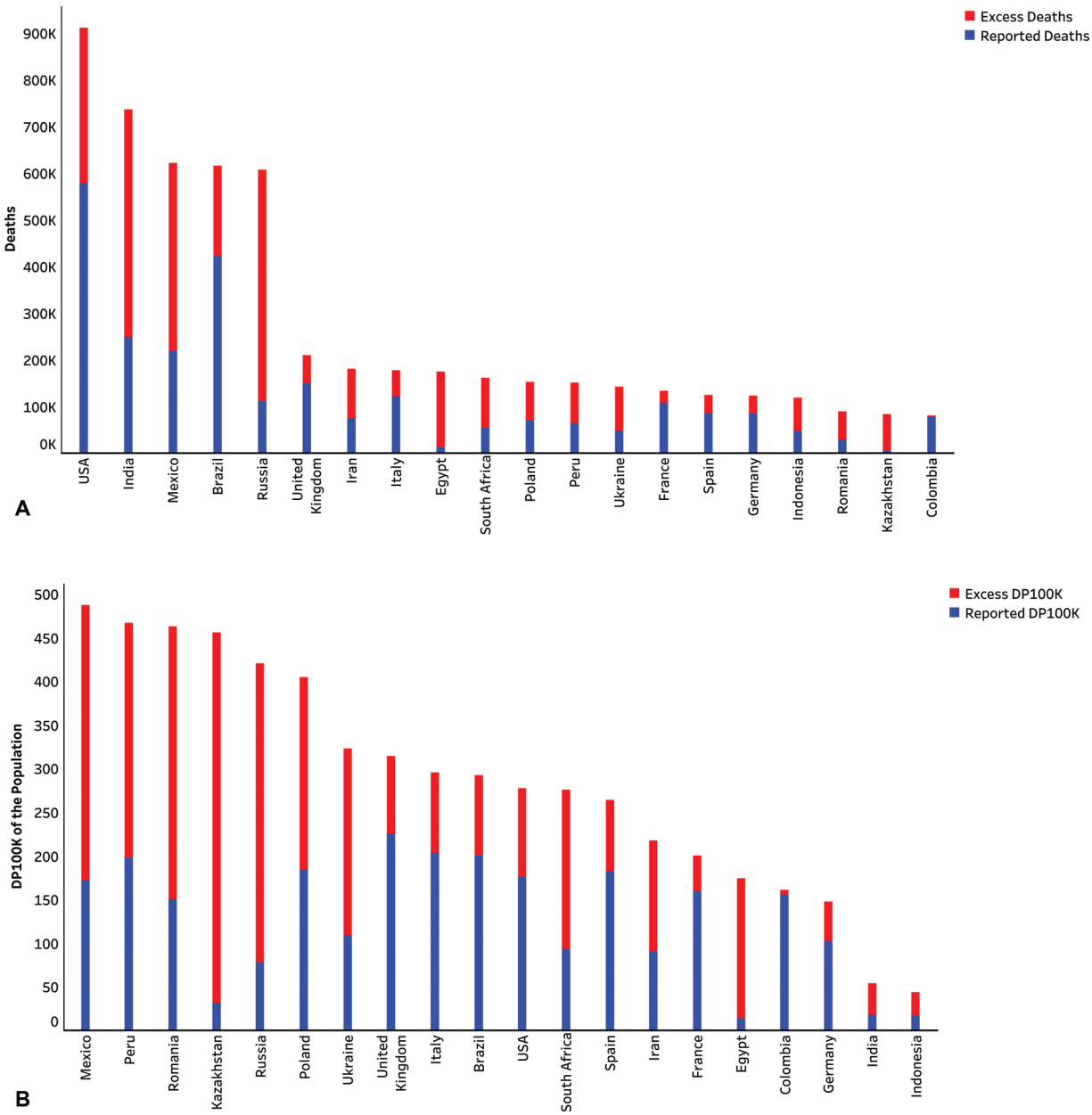

Fig. 1 (**A**) Blue bar indicates absolute number of reported deaths due to COVID-19. Red bar represents the imputed excess deaths due to COVID-19 in the studied time period. Red and blue bars together constitute cumulative deaths due to COVID-19 in the studied time period for that country (X-axis). (**B**) Blue bar indicates reported deaths per 100,000 of the population (DP100K) due to COVID-19. Red bar represents the imputed deaths per 100,000 of the population (DP100K) due to COVID-19 in the studied time period. Red and blue bars together constitute cumulative deaths per 100,000 of the population (DP100K) due to COVID-19 in the studied time period for that country (X-axis). DP100K: Deaths per 100,000 population.

Their final model thus was able to predict the following different causes of mortality

1) all deaths directly on account of a laboratory-confirmed COVID-19 infection
2) increase in mortality due to
   i. life-saving health care (including disease screening) being delayed or deferred during the pandemic.
   ii. mental health disorders (depression) due to COVID-19 isolation/lockdowns, loss of earnings, and resulting opioid use.
   iii. excessive alcoholism.
3) reduction in mortality due to:
   i. decreased mobility associated with social distancing mandates
   ii. reduced transmission of other viruses (influenza, respiratory syncytial virus, and measles)
   iii. individuals at immediate risk of dying from chronic conditions, such as cardiovascular disease and chronic respiratory disease, dying instead from COVID-19.

The IHME reports the largest number of cumulative deaths worldwide accounting for underreported deaths are from the USA (912,345), India (736,811), Mexico (621,962), Brazil (616,914), and Russia (607,589) (►**Fig. 1A**). This is not surprising because these countries have had the largest epidemics to date. Interestingly, but not unexpectedly, some countries with relatively smaller epidemics saw a large increase in the death rate when accounting for unreported deaths, most of these in South America, Central Asia, and Eastern Europe (►**Fig. 1B**). We divided the excess death count for each country (as estimated by the IHME), with the reported death counts for that country. The excess death ratio thus arrived at revealed that 12 countries had undercounted their deaths by at least as much as their total reported deaths, 6 countries had undercounted by close to half the total reported deaths, while 2 countries had undercounted by a low proportion (►**Table 1**). The IHME estimates the global COVID-19 death rate is 91.7 per 100,000. Vietnam has the lowest total COVID-19 death rate at 0.1 per 100,000, while a staggering 15 countries have total COVID-19 death rates per 100,000 (DP100K) higher than 200 (►**Table 1**, ►**Fig. 1B**). These findings, besides shedding light on the true human cost associated with this pandemic, also reveal an important detail: some countries have done exceedingly well at preventing deaths, while for unknown reasons that we can only speculate upon at this point of time, other countries have been less nimble.[12] Clearly, only data based public health interventions will help formulate policies that can tackle this pandemic to prevent further loss of life.

Table 1 Country-wise reported and excess deaths as per IHME estimates (columns 1–4) and estimated total deaths including per 100 thousand population as estimated by us based on data from the IHME analysis (columns 5–7)

Country	Reported COVID-19 deaths	Excess deaths	Total COVID-19 deaths	Reported COVID-19 deaths per 100K	Total COVID-19 deaths per 100K	Increase in deaths per 100K
Kazakhstan	5,810	78,643	84,453	31.39	456.16	424.77
Russia	111,909	495,680	607,589	77.52	420.85	343.33
Mexico	219,372	402,590	621,962	171.96	487.53	315.57
Romania	29,020	60,599	89,619	149.93	463	313.07
Peru	64,511	87,428	151,939	198.44	467.36	268.92
Poland	69,954	83,672	153,626	184.24	404.59	220.35
Ukraine	48,393	95,022	143,415	109.03	323.12	214.09
South Africa	54,746	106,758	161,504	93.49	275.81	182.32
Egypt	13,970	161,620	175,590	13.92	174.92	161
Iran	75,547	104,940	180,487	91.12	217.69	126.57
USA	578,555	333,790	912,345	176.27	277.96	101.69
Brazil	423,307	193,607	616,914	200.58	292.31	91.73
Italy	122,851	55,293	178,144	203.75	295.45	91.7
United Kingdom	150,815	59,261	210,076	225.66	314.33	88.67
Spain	85,822	38,627	124,449	182.31	264.36	82.05
Germany	84,807	38,170	122,977	102.02	147.93	45.91
France	106,874	27,526	134,400	159.38	200.42	41.04
India	248,016	488,795	736,811	18.16	53.93	35.77
Indonesia	47,150	71,646	118,796	17.43	43.9	26.47
Colombia	78,216	2,752	80,968	155.38	160.85	5.47

Statement of Integrity

The manuscript has been read and approved by all authors and the requirements for authorship have been met, and that each author believes that the manuscript represents honest work.

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Conflict of Interest

None declared.

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