Evaluation of concordance in estimation of excess mortality due to Covid-19 pandemic

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(2023) Evaluation of concordance in estimation of excess mortality due to Covid-19 pandemic. Journal of Evaluation in Clinical Practice, 29 (6). ISSN 1356-1294

http://dx.doi.org/10.1111/jep.13866

Evaluation of Concordance in Estimation of Excess Mortality due to Covid-19 Pandemic

Short title: Estimation of Excess Covid-19 Mortality

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Abstract

Background: The World Health Organization (WHO) kept track of Covid-19 data at country level on a daily basis during the pandemic that included the number of tests, infected cases, and fatalities. This daily record was susceptible to change depending on the time and place and impacted by underreporting. In addition to reporting cases of excess COVID-19-related deaths, the WHO also provided estimates of excess mortality based on mathematical models.

Objective: To evaluate the WHO reported and model-based estimate of excess deaths in order to determine the degree of agreement and universality.

Methodology: Epidemiological data gathered from nine different countries between April 2020 to December 2021 are used in this study. These countries are India, Indonesia, Italy, Russia, UK, Mexico, USA, Brazil and Peru and each of them recorded more than 1.5 million deaths from Covid-19 during these months. Statistical tools including correlation, linear regression, intra-class correlation, and Bland-Altman plots are used to assess the degree of agreement between reported and model-based estimates of excess deaths.

Results: The WHO derived mathematical model for estimating excess deaths due to Covid-19 was found to be appropriate for only four of the nine chosen countries, namely Italy, UK, USA, and Brazil. The other countries showed proportional biases and significantly high regression coefficients.

Conclusion: The study revealed that, for some of the chosen nations, the mathematical model proposed by the WHO is practical and capable of estimating the number of excess deaths brought on by COVID-19. However, the derived approach cannot be applied globally.

***Keywords**: Excess deaths, World Health Organization, intra-class correlation, Bland-Altman plots*

1. Introduction

Throughout the course of the pandemic, the World Health Organization (WHO) was monitoring the effects of COVID-19. Countries reported the total number of Covid-19 cases and fatalities in their areas to the WHO, and this data has been made available. The Covid-19 indices that are reported, however, fluctuate with time and place and are influenced or underreported[1] by established biases[2]. Recent studies,[3-7] including those from the WHO,[8-10] have noted that the data given does not give a clear picture of the health burden attributed to Covid-19 or the number of lives lost, both directly and indirectly, as a result of the pandemic. As a result of no testing being carried out before death, some Covid-19-related deaths were not recognised as such[6,11].

Additionally, there have been modifications in the Covid-19[7,10,12-13] death certification laws that some nations have implemented. Excess mortality is seen as a more objective and comparable (cross-country) estimate of the influence of Covid-19 on mortality because using reported Covid-19 data presents certain challenges[14-16]. Covid-19 caused mortality in addition to other causes of death, known as "excess deaths", that occurred in a country during a specific time period.

The ability to effectively implement public health programmes is aided by knowledge of excess mortality, and also helps to clarify the impact of the pandemic on the numbers. Several methodologies[7-8,17-19] have been developed to identify the excess mortality attributable to Covid-19 that take into consideration various assumptions regarding deaths from all causes and those related to Covid-19.

The question of concern is whether the mathematical model-based estimates can be followed universally and will align with reported excess deaths due to Covid-19 where both are subject to variance due to time and location and then further affected due to under-reporting. This study's objective is to assess WHO reported and model-based estimates of excess deaths in order to gauge levels of agreement and universality at nation level. Nine countries, including India, Indonesia, Italy, Russia, UK, Mexico, USA, Brazil, and Peru, recorded more than 1.5 million deaths as a result of COVID-19. The degree of agreement between reported and model-based estimates of excess fatalities has been evaluated using statistical approaches such as correlation, linear regression, intra-class correlation, and Bland-Altman plots.

2. Methodology

Data: The "Our World in Data" website (https://ourworldindata.org/coronavirus -source-data; assessed on May, 30, 2022) provided data from dependable sources such as the WHO and the European Centre for Disease Prevention and Control and was used to gather country-by-country reported daily Covid-19 cases and deaths for the current study. This database was used to assess and investigate the excess mortality trend associated with the Covid-19 pandemic from March 2020 (since the WHO proclaimed Covid-19 a pandemic on March 11, 2020) through to December 2021. The WHO website (https://www.who.int/data/sets/global-excess-deaths-associated-with-covid-19-modelled-estimates; assessed on May, 30, 2022) has been used to acquire the mathematical model-based estimates[9] of excess mortality resulting from the Covid-19 pandemic. The top nine countries that have reported more than 1.5 million Covid-19 deaths including India and Indonesia (from Asia), Italy, Russia, and UK (from Europe), Mexico and USA (from North America), Brazil, and Peru (from South America), were taken into account in this study.

Statistical Analysis:

Estimates of the additional mortality brought on by COVID-19 were supplied by the WHO and based on reported data and mathematical models. In this study, three distinct approaches have been used to examine assessments of increased mortality caused by COVID-19 that accord reasonably well. The first step was to determine the correlation (r) between the difference and mean (of reported and estimated excess fatalities) and intra-class correlation (ICC) to see whether there was a pattern of similarity between them on a month-by-month basis. Also to determine whether a correlation coefficient had a high enough value to be considered acceptable in order to measure the degree of linear relationship between two variables. The second step was to look for a linear relationship between reported and model-based estimates of additional deaths caused by COVID-19 as follows:

$$\boldsymbol{Expected(E) = \beta_0 + \beta_1\, Reported(R) + \varepsilon}$$

where $\boldsymbol{\beta_0}$ and $\boldsymbol{\beta_1}$ denotes the regression coefficient and $\boldsymbol{\varepsilon}$ denotes the error. In a case of good linear agreement, the values $\boldsymbol{\beta_0}$ would need to be 0 and $\boldsymbol{\beta_1}$, closer to 1, that is, the regression model is without a constant, and both the variables are equal to zero at the origin. Thirdly, we measured the change in reported and model-based estimates of the additional fatalities caused by Covid-19 using the Bland-Altman plot. This offers a visual representation of the relationship and agreement between two paired observations gathered on the same measurement scale[20-25]. Suppose x_i denotes WHO reported and y_i denotes WHO model-based estimates of excess deaths due to Covid-19 at i^{th} point of time, for all $i = 1,2,\ldots,m$, say months, during a specified period. The Bland-Altman plot is formed by plotting the differences $d_{ij} (= y_{ij} - x_{ij})$ in the j^{th}

month by the i^{th} country on the vertical axis versus the averages, $a_{ij}\left(=\frac{y_{ij}+x_{ij}}{2}\right)$ on the horizontal axis. The mean difference is referred to as the bias ($\bar{d}_i$) that indicates the mean direction of the deviation from reported excess mortality due to Covid-19 of the i^{th} country. The 95% reference range of the mean difference illustrates the magnitude of the systematic difference between reported and mathematical model-based estimates of excess deaths due to covid-19 and is labelled as limits of agreement[26], which is obtained through$\left(\bar{d}_i \pm\ 1.96\, S_{\bar{d}_i}\right)$ where

$$S_{\bar{d}_i} = \sqrt{\frac{\sum_{j=1}^{m}(d_{ij}-\bar{d}_i)^2}{m-1}}$$

The variance is obtained $V\left(\bar{d}_i\right) = \frac{S_{\bar{d}_i}}{m}$, then the 95% confidence interval (CI) has been given by

$$\left(\bar{d}_i \pm t_{\left(1-\frac{\alpha}{2},m-1\right)}\sqrt{V\left(\bar{d}_i\right)}\right)$$

The 95% confidence intervals for the limits of agreement shows error bars, which is obtained as

$$\left(\left(\bar{d}_i \pm\ 1.96\, S_{\bar{d}_i}\right) \pm t_{\left(1-\frac{\alpha}{2},m-1\right)}\sqrt{V\left(\left(\bar{d}_i \pm\ 1.96\, S_{\bar{d}_i}\right)\right)}\right)$$

To test the hypothesis (H_0) that there is no difference among WHO reported and mathematical model-based estimates of excess mortality, the Kolmogorov-Smirnov test for comparing distributions was carried out. If this test confirmed distributional homogeneity, high positive values of the correlation coefficient (*r*), and ICC, and the value of the regression coefficient $\boldsymbol{\beta_1}$ was closer to 1 and free from proportional bias, then the agreement between WHO reported and expected values of excess mortalities due to Covid-19 for any country could be established. The statistical analysis was conducted using R-software version 4.1.3 and SAS university edition.

3. Results

Table 1 displays a summary of statistics (mean of standard deviation - SD) and their 95% confidence intervals of WHO reported and estimated Covid-19 related excess deaths and their differences in the selected nine countries. The correlation coefficient (*r*), ICC and linear regression coefficient (**β_1**) are displayed and their 95% tolerance limits, corresponding to each of the 95% limits of confidence intervals known as level of agreements, are also shown. The measures considered, analysing the accord between WHO reported and mathematical model-based estimates, are statistically significant for their differences or biases to values of r, ICC and **β_1,** respectively.

The results showed that differences (d_{ij}) or biases in WHO reported and estimated excess deaths, and the associated 95% lower and upper confidence intervals and tolerance limits, were significantly different and higher in four out of the nine countries. These countries were India (259927±324884), and Indonesia (50279±34653) in Asia; among European countries, only in Russia (34770± 24249), and in Mexico from North America (17426±18425). The data suggest that, on average, the estimated excess deaths measures in India, Indonesia, Russia, and Mexico were significantly higher (ranges from 17.5 thousand to 2.6 lakhs) than the reported excess death counts, which shows that there is consistent bias. On the other hand, in the remaining five countries of Italy, UK, USA, Brazil and Peru, the difference in reported and estimated Covid-19 related excess deaths were statistically insignificant, and, on average, the estimated excess deaths measures were closer (ranging from one thousand to six thousand) than the reported excess death counts.

A high positive correlation ($r>0.80$) among mean and differences of reported and estimated Covid-19 related excess deaths were observed in eight of the nine countries. Italy, UK, USA, Brazil and Peru provided excellent consistency ICC($\geq$ 0.70) among values of reported and estimated Covid-19 related excess deaths. Single score intra-class correlation between both the reported and estimated mortality counts showed excellent consistency between both values in Italy (0.75), UK (0.81), USA (0.76), Peru (0.88) and Brazil (0.93). To measure the accord among reported and estimated mortality patterns due to Covid-19, the value of the regression slope coefficient (**β_1**) must be closer to one and was only found in Italy (1.18), UK(1.10), USA(1.12) and Brazil(1.1).

Figure 1 provides a graphic demonstration of the Bland-Altman plot to show the agreement between WHO reported and expected values of excess mortalities due to Covid-19 for all the selected nine countries. The Bland-Altman plot was used to calculate the mean and difference (deviation) of estimated and reported excess deaths due to covid-19, as measures of agreement. The 95% confidence interval for difference limits included '0' in Italy (-460, 4298), UK(-2708,4434), USA(-3146,13528) and Brazil(-1120,6283), with no proportional bias.

4. Discussion

The COVID-19 pandemic, one of the most significant global catastrophes in centuries, has had significant and far-reaching effects on health systems, economies, and civilizations[27]. Different populations have been impacted by COVID-19 and governmental responses to it in different ways. Government decisions frequently exacerbated pre-existing structural disparities in income and poverty as well as socioeconomic inequalities in education and skill levels, and in intergenerational inequalities[28]. Social constraints caused by the pandemic[29] compelled people to acclimatize themselves for solitude, that then led to increases in the prevalence of familial violence[30], depression[31-32], anxiety[31-32], and post-traumatic stress disorder[33-34]. COVID-19 deaths acted as an indicator for policymakers and medical professionals to take necessary decisions and proper infrastructural developments to try and control the pandemic[35-37].
The excess mortality rate, due to Covid-19, created additional burdens on countries in terms of healthcare, finance, and life expectancy[38-39]. However, due to differences in time zones, geographical composition, implementation and duration of lockdowns[40-41], along with socio-economic conditions in different countries, exact reporting of cases and deaths due to Covid-19 was not possible throughout the globe.[42] Considering the different methods employed in reporting Covid-19 figures, some mathematical models have been formulated to approximate excess mortality.[9-10,12-15]

The present study is an attempt to analyse the extent, accuracy, credibility, and uniformity of agreement among the WHO reported and WHO estimated[9] excess mortality rates using the top nine countries that reported more than 1.5 million Covid-19 deaths. Statistically, significant proportional bias was found in five countries out of the nine, that is, India, Indonesia, Russia, Mexico and Peru. There was no proportional bias with closure (ranges from one to six thousand) with estimated values of excess deaths found in the other four countries of Italy, UK, USA, and Brazil. High positive correlation among mean and differences of reported and estimated Covid-19 related excess deaths were observed in all of the selected countries, except Indonesia, but it could not be confirmed[43] whether this was due to a better alignment among estimated and reported values. High ICC values in Italy, UK, USA, Brazil and Peru showed similarities among reported and estimated mortality counts. The value of regression coefficient for the null intercept regression model was found to closure to one for Italy, UK, USA, and Brazil, that defined a more reliable and significant agreement of excess mortality due to Covid-19 in terms of reported and estimated mortalities in these countries only. The Bland-Altman plot revealed that for India, Indonesia, Russia, Mexico and Peru the distributional pattern of mean and difference of estimated and reported Covid-19 related excess deaths showed proportional bias, as the values increased in proportion to the average values. The Bland-Altman plot confirmed that the reported and estimated mortality counts in Italy, UK, USA and Brazil are free from proportional bias.

According to the study, only Italy, UK, USA, and Brazil demonstrated agreement between WHO reported and expected values of excess mortalities resulting from Covid-19. The Kolmogorov-Smirnov test confirmed their distributional homogeneity, having high positive values of correlation coefficient (*r*) and ICC, value of regression coefficient ($\boldsymbol{\beta_1}$) (closer to 1), and free from proportional bias.

This study shows that proper reporting and estimation are both necessary in order to develop and/or update policy measures in order to address any pandemics in the future. The mathematical models that were developed to estimate the extra mortality must be validated and take into account the geographic makeup, pattern of incidences, healthcare infrastructures, governmental initiatives, and the socioeconomic conditions of different countries.

5. Conclusion

The WHO published estimated excess mortality rates attributable to COVID-19, as well as reported excess mortality rates, and it recommended using the estimated figures to describe the pandemic's state in various countries. The aim of this study is to describe the consistency and assumption of universality of the model-based estimates of excess mortality in the top nine countries that have reported more than 1.5 million Covid-19 deaths. To do this, excess mortality estimates from the WHO were compared with those from our model, in order to determine how well they both aligned. Results obtained indicate that only four of the nine countries, that is, Italy, UK, USA, and Brazil, were appropriate for using the WHO's mathematical approach for predicting excess mortality caused by COVID-19. The study comes to the further conclusion that larger correlation values or ICC, as well as linear associations among reported and estimated excess mortality attributable to COVID-19, do not always explain the applicability of any approach. Before claiming to be a universally accepted model and making the corresponding remark about its implications for policy, any mathematical models created to estimate the extra deaths must be validated.

Acknowledgments

Authors would like to thank all of the anonymous reviewers and editorial board for their valuable comments and suggestions to improve the quality of this manuscript.

Disclosure Statement: No potential conflict of interest was reported by the authors.

Conflict of Interest Statements: No potential conflict of interest was reported by the authors.

Ethics Approval: The database considered for the present study does not contain any individual identifiable information. Due to the unidentified nature of the dataset and no human subject were directly involved in the present study; therefore, this study was exempt from any ethical or Institutional Review Board clearance.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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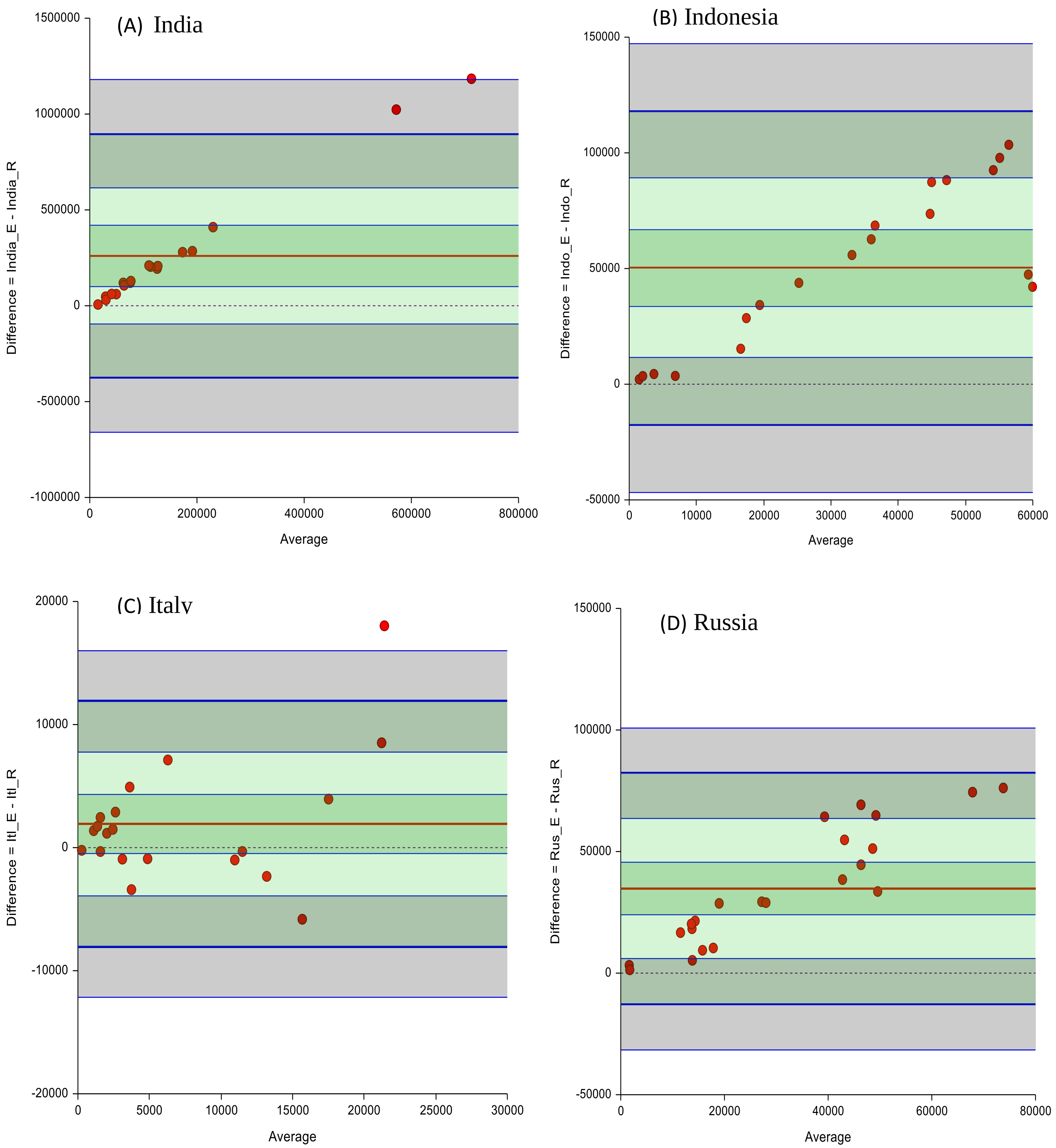
Table 1: Descriptive statistics for WHO reported and expected values of excess mortalities due to Covid-19

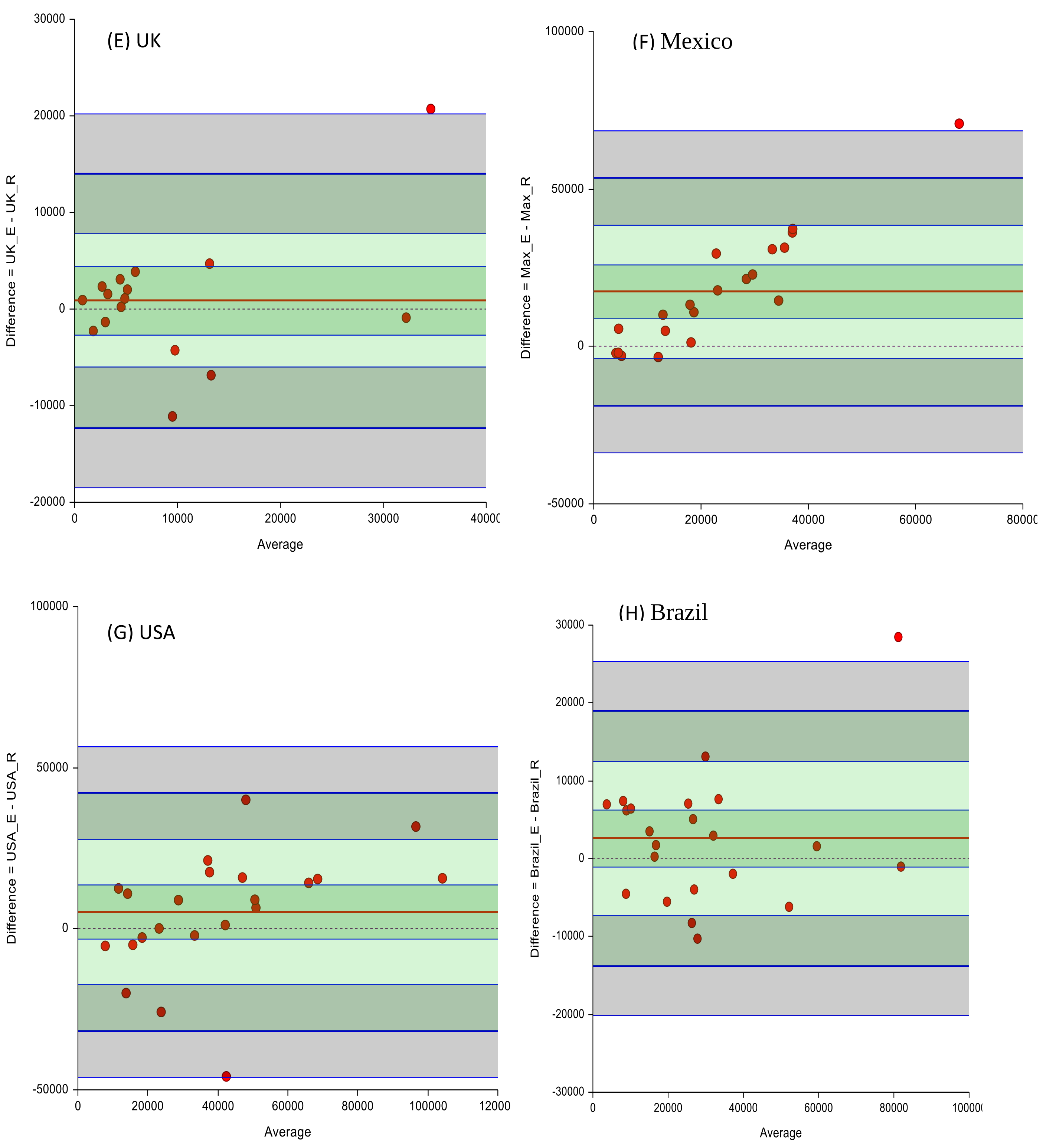
Parameters	**Asia**		**Europe**			**North America**		**South America**	
	India	**Indonesia**	**Italy**	**Russia**	**UK**	**Mexico**	**USA**	**Brazil**	**Peru**
Months	18	19	20	22	16	20	22	22	22
Expected (E) (M±SD)	285449± 350303	57778± 36536	8261± 8432	48528± 32023	9738± 11971	31769± 24486	42659± 31289	30732± 23056	12999± 10383
95% CI	111247, 459650	40169, 75388	4315, 12207	34330, 62726	3359, 16117	20309, 43229	28786, 56532	20510, 40955	8395, 17602
Reported (R) (M±SD)	25521± 28020	7499± 10794	6342± 6433	13758± 10532	8875± 9198	14343± 7606	37468± 23340	28151± 21234	9245± 7812
95% CI	11587, 39455	2296, 12702	3331, 9353	9088, 18428	3974, 13776	10783, 17902	27119, 47817	18736, 37566	5781, 12709
Diff (E-R) or Bias(Diff) (M±SD)	259927± 324884	50279± 34653	1919± 5083	34770± 24249	863± 6702	17426± 18425	5191± 18803	2581± 8349	3753± 2770
95% CI	98366, 421488	33577, 66981	-460, 4298	24019, 45522	-2708, 4434	8803, 26049	-3146, 13528	-1120, 6283	2525, 4982
p-value#	**0.000013**	**0.000156**	0.174533	**0.000674**	0.716412	**0.012299**	0.871679	0.990057	0.218368
r	0.91	0.32	0.80	0.82	0.83	0.85	0.80	0.93	0.99
ICC (95% CI)	0.10 (0.0, 0.45)	0.06 (0.0,0.32)	0.75 (0.48,0.90)	0.24 (0.0, 0.59)	0.81 (0.54,0.93)	0.34 (0.0,0.67)	0.76 (0.52,0.89)	0.93 (0.83,0.97)	0.88 (0.11,0.97)
$\boldsymbol{\beta_1}$**	11.3153	3.3127	1.1761	3.1487	1.0893	2.3273	1.1211	1.0637	1.7240
Lower Level of Agreement (M±SD)	-376845± 133378	-17641± 13833	-8045± 1976	-12758± 8973	-12274± 2925	-18687± 7162	-31662± 6958	-13782± 3089	-1676± 1025
95% CI	-658248, -95442	-46703, 11421	-12181, -3909	-31418, 5902	-18510, -6037	-33678, 3697	-46131, -17193	-20207, 7358	-3807, 455
Upper Level of Agreement (M±SD)	896699± 133378	118199± 13833	11882± 1975	82298± 8973	14000± 2925	53540± 7162	42044± 6957	18945± 3089	9183± 1025
95% CI	615296, 1178102	89138, 147261	7746, 16018	63638, 100959	7764, 20236	38549, 68531	27575, 56513	12520, 25370	7051, 11315

***** Shapiro-Wilk Test of Normality of Differences;

** Regression equation: ***Expected(E) = β_1 Reported(R)+ε***

pvalue- Based on Kolmogorov-Smirnov test for comparing distributions


(A) India
Difference = India_E - India_R
1500000
1000000
500000
0
-500000
-1000000
0
200000
400000
600000
800000
Average
(B) Indonesia
Difference = Indo_E - Indo_R
150000
100000
50000
0
-50000
0
10000
20000
30000
40000
50000
60000
Average
(C) Italy
Difference = Itl_E - Itl_R
20000
10000
0
-10000
-20000
0
5000
10000
15000
20000
25000
30000
Average
(D) Russia
Difference = Rus_E - Rus_R
150000
100000
50000
0
-50000
0
20000
40000
60000
80000
Average


(E) UK
Difference = UK_E - UK_R
Average
30000
20000
10000
0
-10000
-20000
0
10000
20000
30000
(F) Mexico
Difference = Max_E - Max_R
Average
100000
50000
0
-50000
0
20000
40000
60000
(G) USA
Difference = USA_E - USA_R
Average
100000
50000
0
-50000
0
20000
40000
60000
80000
100000
(H) Brazil
Difference = Brazil_E - Brazil_R
Average
30000
20000
10000
0
-10000
-20000
-30000
0
20000
40000
60000
80000

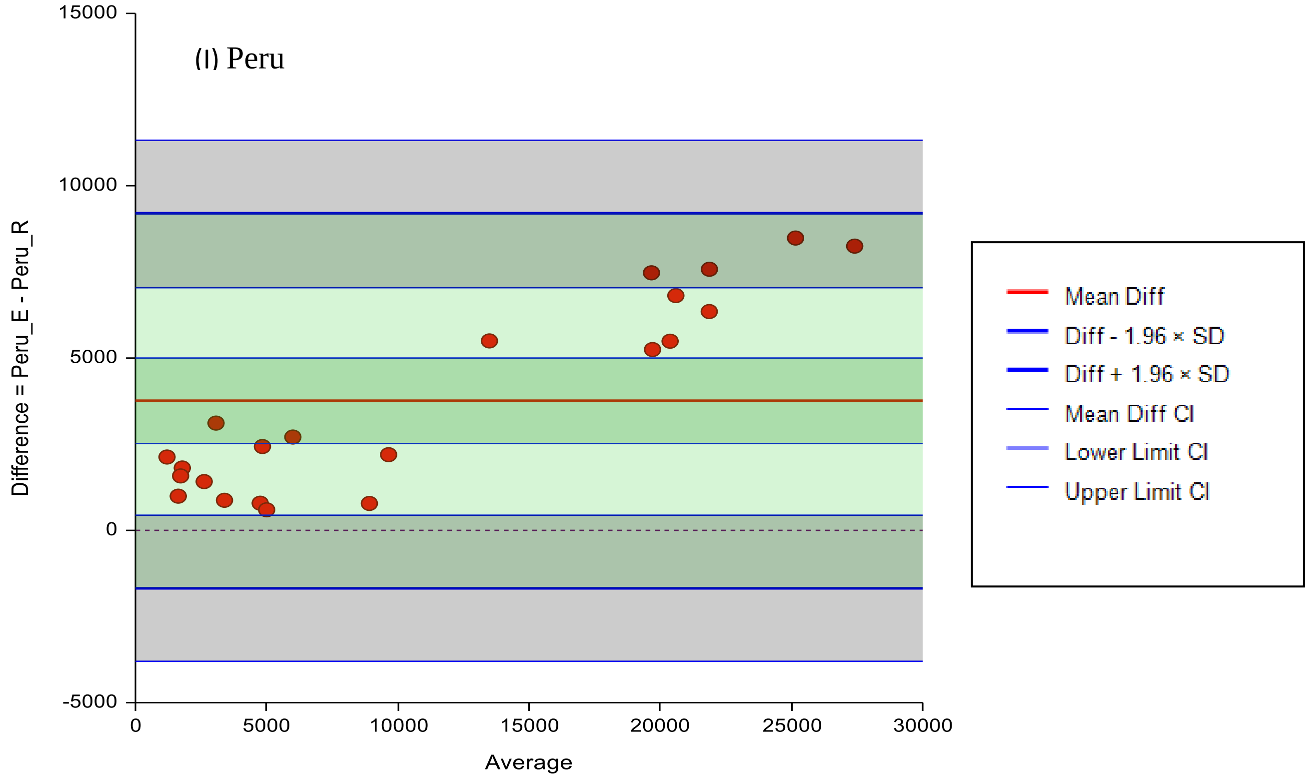


Figure 1 : Bland-Altman plot showing agreement between WHO reported and expected values of excess mortalities due to Covid-19 of the country (A) India, (B) Indonesia (C) Italy, (D) Russia, (E) United Kingdom, (F) Mexico, (G) The United States of America, (H) Brazil, and (I) Peru