The World's Deadliest Outbreak During the COVID-19 Pandemic: A Proposed Analytical Approach to Estimate Excess Mortality in Ecuador During the First Year of the Pandemic.

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Research

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The world’s deadliest outbreak during the COVID-19 Pandemic: A proposed analytical approach to estimate Excess mortality in Ecuador during the first year of the pandemic.

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Abstract

**Background:** Latin America is the most affected region by the COVID-19 pandemic in terms of excessive mortality. Diagnostic and health care capabilities are limited in this region, deficiencies resulting in poor contact tracing, insufficient medical treatment and an unprecedented number of deaths. One of the key issues to estimate the pandemic's actual impact is to track deaths as one of the most reliable indicators when SARS-CoV-2 under-diagnosis is evident.

**Objective:** This study's objective was to estimate the number of deaths attributed to COVID-19 based on excess mortality data in Ecuador.

**Methodology:** An ecological study of all-cause mortality recorded in Ecuador during the year 2020. In order to calculate the total excess death relative to the historical average for the same dates in 2017, 2018 and 2019, a Poisson fitting analysis was used to identify trends on officially recorded all-caused deaths and those attributed to COVID-19. A bootstrapping technique based on central tendency measures was used to emulate the sampling distribution of our expected deaths estimator $\hat{\mu}_{\text{deaths}}$ by simulating the data generation and model fitting processes.

**Results:** In Ecuador, during the first year of the pandemic, at least 115,070 deaths were recorded. At least 42,453 of those were catalogued as excessive mortality when comparing with the last 3-years average (2017-2019). Ecuador is the country with the highest recorded excess mortality in the world with $6 / 100,000$ deaths per capita in one single day while Peru had $2 / 100,000$. This value represents an additional $408\%$ of the expected fatalities. The province with the highest number of excess deaths was Santa Elena on Ecuador's coast, with more than $154\%$ increment versus previous years.

**Conclusions:** Adjusting for population size and time, the hardest-hit country due to the COVID-19 pandemic was Ecuador. The mortality excess rate shows that the SARS-CoV-2 virus spread rapidly in the country, especially in the coastal province of Santa Elena and Guayas. Our results and the new proposed methodology could help to address the actual death toll situation during the early phase of the pandemic in Ecuador.
Introduction:

The coronavirus disease 2019 (COVID-19) pandemic continues to put unprecedented pressure around countries and their health system. As of April 2021, more than 137 million cases have been reported worldwide, and at least 3 million deaths have been officially registered as COVID-19 (1,2). The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus has mutated several times since the first genome was sequenced[1–3]. Nowadays, the predominant circulating variants have increased their transmissibility and their virulence, resulting in a continuous state of overwhelmed emergency departments and intensive care wards, while healthcare workers are progressively showing signs of fatigue[4, 5]. Latin America is one of the most affected regions in the world, with more than 16.4% of the total number of COVID-19 confirmed cases and 20.6% of the total number of confirmed COVID-19 deaths globally, while sharing only 5.5% of the global population[6]. Although these figures are alarming themselves, there is a hidden reality about the actual number of deaths from COVID-19 in several countries from Latin America, As the region has limited diagnostic capabilities and struggle to manage the number of daily cases, the unprecedented pressure is overwhelming health systems, tending to under-report COVID-19 related deaths as occurred in Peru, Honduras or Ecuador, where excess mortality is more representative than COVID-19 officially reported deaths[7]. Several research groups have sought to determine the pandemic's real impact using historical records and average deaths in previous years as a good approximation of the reality experienced by the pandemic, especially in developing countries[8–10].

According to demographers, the best tool available during a pandemic or a massive natural disaster to estimate the number of deaths is excess mortality, defined as the difference between the observed number of deaths in specific periods and the expected number of deaths in the same period[11–13]. Excessive mortality may provide a more complete and timely indirect measure of mortality [14–16] by encompassing deaths from all causes; excess mortality exceeds the variation between countries in reporting and proof of COVID-19 and misclassification of cause of death-on-death certificates[17].
The use of excessive mortality is now widely used as a reporting tool. For instance, in England, a study by Sinnathamby et al. 2020 showed higher excess mortality from all causes during the current COVID-19 pandemic[18]. An analysis including variations in the number of excessive mortalities among countries showed that in the United States and Spain, around 25% and 35% excessive mortality is not reflected in the official COVID-19 statistics, respectively[11]. Some of the most significant and crude evidence comes from South America, where countries such as Mexico, Peru, Brazil and Ecuador have suffered a massive surge in cases that have left thousands of deaths behind, not all registered as COVID-19[7, 19–21]. In Ecuador, and while official statistics reported 474 COVID-19 deaths during the first 54 days of the outbreak, the excess mortality data registered at least 4,780 deaths attributed to COVID-19, as previously mentioned[21]. Estimating excess all-cause mortality using a standard approach in all countries provides a powerful tool to quickly obtain unbiased estimates of the COVID-19 mortality burden and how it affects different age groups and different countries and areas[15].

We propose an innovative approach that uses mean in the context of bootstrapped simulations in order to replicate the data generation mechanism of death time series and obtain more robust estimations of expected deaths in order to quantify excess mortality in Ecuador.

Methods and Data

Study design

An ecological study of all-cause mortality recorded in Ecuador during 2020 was performed. All deaths recorded within the national registry database in Ecuador was used to COVID-19 and non-COVID-19 related deaths during the first year of the pandemic in Ecuador.

Setting

The study was carried out in Ecuador, one of the smallest Latin-American country located in the equatorial line and bordering the Pacific Ocean. Ecuador shares borders with Peru and Colombia and its current population is estimated to be 17,577,116 inhabitants. The country has four regions (Coast, The Highlands, The Amazonian and the Galapagos Islands) 24 provinces and 221 political subdivisions called cantons (cities).
Population

Our study included all nationwide recorded deaths during 2017 to 2020. A total number of 115,070 deaths in 2020 were analysed and 42,453 of those were catalogued as excessive deaths.

Variables:

The data retrieved regarding deaths in Ecuador had the following variables: jurisdiction (canton, province and region), date, and total absolute and relative number of deaths from 2017-2020. Total deaths represent the number of deaths in each specific period considered in the analysis. For other complementary analyses, variables such as region or contagious cases were used, which were obtained from the same official websites.

Data sources/ measurement:

Data for this study was obtained using the free information available over historical databases of the National Institute of Statistics and Census (INEC)(20) (https://www.ecuadorencifras.gob.ec/nacimientos-y-defunciones-informacion-historica/) and the National Civil Registry of Ecuador[22] (https://www.registrocivil.gob.ec/cifras/) with data from January 2017 to December 2020.

The complexity of algorithms in computational time is around 5 minutes for the classic method and around 3 hours for the bootstrapped method. The measure studied in this document was the mean. Mean was computed at different periods, and then the difference of values between deaths in the year 2020 was compared against average deaths in years 2017-2019. The same method was applied for the bootstrapped concept. However, in this case, we simulate deaths' behaviour considering what would happen in other years having an extreme event such as a pandemic to model the generation mechanism of data for 2020.
The excess deaths were computed with built-in algorithms applied to that data using R software version 3.6.1. Algorithms were developed for each time stage at daily, weekly and monthly levels.

**Bias:** To reduce the risk of bias or involuntary errors, two researchers retrieved the data separately. Once data was downloaded, both investigators analysed the dataset separately. The researchers resolved any questions or doubts after reaching consensus with a third researcher including in the analysis. Means and confidence intervals were computed independently, instead of using the same R data code used for the entire analysis as a way to confirm the homogeneity of the dataset used by both researchers.

**Study Size:**

Excess deaths were calculated with a daily, weekly and monthly resolution. Data of death cases at the monthly level was composed of a time series of 1,152 observations across 24 provinces of the country. At the weekly level, the time series of deaths was composed of 5,088 observations for 24 provinces. At the daily level, the time series of deaths was composed of 35,064 observations for 24 provinces. The time series starts on January 1, 2017 and ends on December 31, 2020. For cantons, the time series of deaths had 323,611 observations.

**Statistical methods:**

Descriptive statistics were applied to describe differences among provinces and cantons. To analyze the evolution of deaths, we initially applied dynamic statistical tests to the daily death series in each province as well as across the whole of Ecuador in order to identify on which days there were changes in the behavior of the number of reported cases.

In all provinces, we have $n$ daily observations. Each $i$ observation from two to $n$ was be used as a change point. With this reference point, the previous and subsequent observations constitute different datasets. Then, a variance test was applied to identify the variability and test the following hypothesis:

$$H_0: \text{Deaths before } i \text{ are equal to Deaths after } i$$
$H_1$: Deaths before $i$ are different to Deaths after $i$

As no data was available before the first day in the death series, we start from $i = 2$. We obtained a series of $p$-values for each $i$ and therefore selected the minimum of those where $H_0$ is rejected. This point highlights where an important change occurred.

The Poisson adjustment makes it possible to identify what the trend in the evolution of the cases of death will be like[23]. Based on a Poisson distribution, it measures the increase or decrease considering the change rate in death cases by days.

To calculate the excess deaths at the country and province level, we developed a bootstrap method based on central tendency measure, mean, which is being used for many research and news clinical investigation centres to calculate excessive mortality.

Statically, the mean is used to make exploratory analysis, and the measure is sensitive to extreme values[24]. As a consequence, this might impact over the quality of results. Moreover, due to the current pandemic, all countries are having many deaths per day and comparing them with the traditional values of the deaths series of previous years could inflate the excess deaths indicator.

To avoid extreme estimates in the expected deaths, we use a bootstrapping approach. The essential concept of bootstrapping is to emulate the repetition of certain experiments by simulating new data, followed by a statistical measure's recalculation using such simulated data [25].

The bootstrap emulates the sampling distribution of our expected deaths estimator $\hat{\mu}_{deaths}$ by simulating the data generation and model fitting processes. It does this by generating artificial data $y^{(b)} = (y_1^{(b)}, ..., y_n^{(b)})$ from a distribution that approximates the true unknown sampling distribution of the actual data. This is repeated a number of times, $B$, resulting in an extensive collection of bootstrap estimators $\mu_{deaths}^{(b)}, b = 1, ..., B$. The distribution of these artificially generated bootstrap estimators can be used to infer the sampling distribution of $\hat{\mu}_{deaths}$.
As the true sampling distribution of the death time series is unknown, we will use nonparametric bootstrapping. Suppose the death data \( y_i, i = 1, \ldots, n \), are independent and have an identical distribution. In that case, the empirical cumulative distribution (ecdf) can be used as a discrete approximation of the true cumulative function.

\[
\hat{F}_{ecdf}(y) = \frac{1}{n} \sum_{i=1}^{n} I(y_i \leq y)
\]

The general algorithm we define is as follows:

1. Generate a bootstrap sample from death data \( y^{(b)} = (y_1^{(b)}, \ldots, y_n^{(b)}) \) \( \hat{F} \).
2. \( \hat{\mu}_{deaths}^{(b)} \) using \( y^{(b)} = (y_1^{(b)}, \ldots, y_n^{(b)}) \).

With the results of simulations, we obtained \( \hat{\mu}_{deaths} \) and defined bootstrap confidence intervals at \( \alpha = 0.05 \) using the percentile method. We completed 1,000 bootstraps in order to retrieve robust estimates (25). Because data are available at the daily level, we produced monthly, weekly, and daily time-scale estimates for the country and its provinces.

**Results**

In Ecuador since the beginning of the pandemic, at least 42,453 people have died in excess when compared with the previous year's averages. The previously mentioned value comes from the classic mean definition for calculating excess deaths.

**Maximum number of deaths per day**

The maximum number of deaths in one single day in Ecuador occurred on 04/04/2020, with at least 1,120 deaths, having an excess in mortality in at least 921 deaths. In the case of Provinces of the Ecuadorian region, for Guayas, the maximum occurred on the same day with 848 total deaths and 795 excess. In contrast, for the second national wave, Pichincha suffered the worst part, having a total of 97 deaths in excess on 17/20/2020. As of the last update of our analysis (December 31, 2020), there were 101,439 deaths in Ecuador, with 42,453 excesses.
Our methodology based on bootstrap simulations derives an estimate of 30,213, which, compared with the classical method, calculated total excess deaths in 2020 at 42,453, which implies a difference of 12,240 death cases (Figure 1).

*Figure 1 Maximum number of deaths per date in Ecuador.*

**Excessive mortality per province**

In terms of provinces below our formulation, the cumulative excess on December 31, 2020 for Guayas was 10,727 deaths, with a maximum daily excess of 795, whereas for Pichincha was 1,785 deaths, with a maximum daily excess of 72 deaths (Figure 2).
According to the provinces, the classical estimation for excess mortality was compared to the bootstrapped estimation up to December 31, 2020. The differences in values, compared with the classical excess approach, demonstrated that our method was more consistent than just using the mean as a measure to quantify excess deaths. For instance, Santa Elena had an increase of 87% regarding monthly excess deaths and an increase of 92% daily excess deaths (Table 1).
Table 1 Excessive mortality per time comparing the classic estimation and the bootstrapped estimation (new).

| Province      | Monthly Excess | Weekly Excess | Daily Excess | Monthly Excess | Weekly Excess | Daily Excess | Excess against Deaths (%) |
|---------------|----------------|---------------|--------------|----------------|---------------|--------------|--------------------------|
| Classic Estimation |                |               |              | Proposed new Estimation |                |               |                          |
| Azuay         | 299            | 83            | 21           | 284            | 81            | 24           | 45%          | 50%          | 69%          |
| Bolivar       | 52             | 20            | 9            | 46             | 20            | 8            | 38%          | 54%          | 80%          |
| Cañar         | 72             | 31            | 12           | 79             | 31            | 12           | 45%          | 58%          | 80%          |
| Carchi        | 69             | 29            | 8            | 74             | 27            | 7            | 54%          | 66%          | 78%          |
| Chimborazo    | 245            | 69            | 15           | 230            | 66            | 16           | 51%          | 57%          | 70%          |
| Cotopaxi      | 142            | 39            | 13           | 147            | 40            | 14           | 48%          | 53%          | 74%          |
| El Oro        | 470            | 139           | 26           | 431            | 132           | 27           | 60%          | 67%          | 75%          |
| Esmeraldas    | 198            | 50            | 12           | 176            | 49            | 12           | 55%          | 60%          | 71%          |
| Galapagos     | 4              | 0             | 2            | 3              | 2             | 2            | 43%          | 67%          | 100%         |
| Guayas        | 10,727         | 4,926         | 795          | 10,383         | 4,860         | 787          | 83%          | 91%          | 92%          |
| Imbabura      | 209            | 66            | 13           | 209            | 63            | 14           | 54%          | 61%          | 70%          |
| Loja          | 191            | 57            | 12           | 179            | 53            | 12           | 46%          | 53%          | 63%          |
| Los Ríos      | 610            | 164           | 36           | 589            | 152           | 34           | 64%          | 67%          | 76%          |
| Manabí        | 1,266          | 367           | 75           | 1,180          | 348           | 68           | 66%          | 72%          | 77%          |
| Morona Santiago | 41            | 12            | 5            | 34             | 13            | 5            | 44%          | 57%          | 83%          |
| Provincia      | Total  | 931 | 14,057 | 5,764 | 889 | 67% | 79% | 79% |
|---------------|--------|-----|--------|-------|-----|-----|-----|-----|
| Napo          | 56     | 16  | 6      | 52    | 16  | 6   | 60% | 67% | 86% |
| Orellana      | 52     | 23  | 7      | 49    | 21  | 6   | 58% | 72% | 86% |
| Pastaza       | 38     | 12  | 6      | 38    | 12  | 6   | 58% | 67% | 86% |
| Pichincha     | 1,785  | 453 | 72     | 1,658 | 408 | 67  | 58% | 60% | 63% |
| Santa Elena   | 1,047  | 339 | 59     | 1,012 | 330 | 57  | 87% | 91% | 92% |
| Santo Domingo | 266    | 77  | 18     | 238   | 67  | 18  | 55% | 60% | 75% |
| Sucumbíos     | 134    | 36  | 9      | 123   | 30  | 8   | 68% | 70% | 80% |
| Tungurahua    | 384    | 107 | 24     | 362   | 98  | 24  | 59% | 63% | 75% |
| Zamora Chinchipe | 31 | 10  | 5      | 34    | 11  | 4   | 60% | 69% | 80% |
| **Ecuador**    | **15,009** | **5,826** | **931** | **14,057** | **5,764** | **889** | **67%** | **79%** | **79%** |
**Confirmed deaths against daily excess deaths by region**

As an additional insight, using excess deaths below the classical estimation method as reported by the National Institute of Statistics and Census (INEC) in Ecuador, we compared the impact of daily excess deaths by regions, an analysis not previously performed in Ecuador (Figure 3).

![Figure 3 Daily Excess Deaths in Ecuadorian Regions.](image)

Excessive mortality is higher in the coast than in the highlands and the amazon region and the percentage increased during 2020 reached almost the double than the previous years (Table 2).

**Table 2 Confirmed deaths against daily excess deaths by region in a year**

| Region    | Population | Total Deaths | Expected Deaths | Excess deaths | % increase | Rate per 100,000 |
|-----------|------------|--------------|-----------------|---------------|------------|-----------------|
| Highlands | 7,847,136  | 41,140       | 26,925          | 14,215        | 53%        | 181.1           |
| Coast     | 8,631,859  | 57,293       | 30,042          | 27,251        | 91%        | 315.7           |
Confirmed deaths against daily excess deaths rates by province

Guayas was the province with the highest excess deaths at 17,582, representing an increase of 103% over the expected deaths in comparison to previous years. This represented an excess mortality rate of 400.7 per 100,000 inhabitants. However, considering the variability of population density, the province of Santa Elena had the highest excess mortality rate with 412.4 per 100,000 inhabitants. (Table 3)

Table 3 Confirmed deaths against daily excess deaths rates by province.

| Region   | Province          | Population | Total Deaths | Expected Deaths | Excess Deaths | % increase | Rate per 100,000 |
|----------|-------------------|------------|--------------|-----------------|---------------|------------|-----------------|
| Highlands| Azuay             | 881,394    | 4,425        | 3,266           | 1,159         | 35%        | 131.5           |
|          | Bolívar           | 209,933    | 951          | 673             | 278           | 41%        | 132.4           |
|          | Cañar             | 281,396    | 1,313        | 892             | 421           | 47%        | 149.7           |
|          | Carchi            | 186,869    | 850          | 576             | 274           | 48%        | 146.8           |
|          | Cotopaxi          | 488,716    | 2,240        | 1,403           | 837           | 60%        | 171.3           |
|          | Chimborazo        | 524,004    | 2,972        | 1,950           | 1,022         | 52%        | 195.0           |
|          | Imbabura          | 476,257    | 2,325        | 1,628           | 697           | 43%        | 146.2           |
|          | Loja              | 521,154    | 2,481        | 1,925           | 556           | 29%        | 106.6           |
|          | Pichincha         | 3,228,233  | 17,224       | 10,684          | 6,540         | 61%        | 202.6           |
|          | Tungurahua        | 590,600    | 3,618        | 2,216           | 1,402         | 63%        | 237.3           |
|          | Santo Domingo     | 458,580    | 2,741        | 1,712           | 1,029         | 60%        | 224.5           |
| Coast    | El Oro            | 715,751    | 4,422        | 2,439           | 1,983         | 81%        | 277.0           |
|          | Esmeraldas        | 643,654    | 1,871        | 1,279           | 592           | 46%        | 92.0            |
|          | Guayas            | 4,387,434  | 34,661       | 17,079          | 17,582        | 103%       | 400.7           |
|          | Los Ríos          | 921,763    | 4,465        | 2,962           | 1,503         | 51%        | 163.1           |
| Departamento      | Población 1 | Población 2 | Población 3 | Población 4 | Población 5 | Población 6 | Población 7 | Población 8 |
|-------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Manabí            | 1,562,079   | 9,147       | 5,210       | 3,937       | 76%         | 252.0       |
| Santa Elena       | 401,178     | 2,727       | 1,073       | 1,654       | 154%        | 412.4       |
| **Amazon**        |             |             |             |             |             |             |             |             |
| Morona            | 196,535     | 541         | 396         | 145         | 37%         | 73.6        |
| Santiago          |             |             |             |             |             |             |             |             |
| Napo              | 133,705     | 477         | 306         | 171         | 56%         | 127.6       |
| Pastaza           | 114,202     | 340         | 253         | 87          | 34%         | 76.47       |
| Zamora            | 120,416     | 313         | 207         | 106         | 51%         | 88.3        |
| Chinchipe         |             |             |             |             |             |             |             |             |
| Sucumbíos         | 230,503     | 807         | 494         | 313         | 63%         | 135.6       |
| Orellana          | 161,338     | 487         | 326         | 161         | 50%         | 99.9        |
| **Galapagos Islands** |          |             |             |             |             |             |             |             |
| Galápagos         | 33,042      | 41          | 37          | 4           | 11%         | 13.1        |
| **Ecuador**       | 17,510,643  | 101,439     | 58,986      | 42,453      | 72%         | 242.4       |
As observed in figure 4, those provinces located in the coastal region on Ecuador have higher mortality per capita than those provinces and regions from the amazon and the highlands.

**Figure 4 Excess mortality rate per province**
**Confirmed deaths against daily excess deaths by cantons**

The cantons with the highest excess mortality rate were located in the coastal region, being the province of Santa Elena and Guayas Provinces the most affected (Table 4).

### Table 4 Confirmed deaths against daily excess deaths by cantons.

| Rank | Canton         | Total Deaths | Expected Deaths | Excess Deaths | % Increase | Population   | Rate x 100,000 |
|------|----------------|--------------|-----------------|--------------|------------|--------------|---------------|
| 1    | Santa Elena    | 1,821        | 727             | 1,094        | 150%       | 188,821      | 579.2         |
| 2    | Guayaquil      | 29,262       | 15,881          | 13,381       | 84%        | 2,723,665    | 491.3         |
| 3    | Machala        | 2,812        | 1,516           | 1,296        | 85%        | 289,141      | 448.2         |
| 4    | Manta          | 2,601        | 1,448           | 1,153        | 80%        | 264,281      | 436.3         |
| 5    | Milagro        | 1,768        | 1,033           | 735          | 71%        | 199,835      | 368.0         |
| 6    | Daule          | 1,145        | 516             | 629          | 122%       | 173,684      | 362.2         |
| 7    | Santa Lucía    | 396          | 238             | 158          | 67%        | 45,004       | 351.8         |
| 8    | Portoviejo     | 2,820        | 1,725           | 1,095        | 64%        | 321,800      | 340.4         |
| 9    | Jipijapa       | 638          | 406             | 232          | 57%        | 74,645       | 310.8         |
| 10   | Quevedo        | 1,591        | 940             | 651          | 69%        | 213,842      | 304.3         |
| 11   | Ambato         | 3,200        | 2,032           | 1,168        | 57%        | 387,309      | 301.6         |
| 12   | Durán          | 1,299        | 476             | 823          | 173%       | 315,724      | 260.6         |
| 13   | Riobamba       | 2,147        | 1,492           | 655          | 44%        | 264,048      | 247.9         |
| 14   | Latacunga      | 1,462        | 956             | 506          | 53%        | 205,624      | 246.2         |
| 15   | La Libertad    | 635          | 348             | 287          | 83%        | 117,767      | 244.0         |
| 16   | Pedro Carbo    | 411          | 288             | 123          | 43%        | 51,802       | 236.8         |
| 17   | Santo Domingo  | 2,988        | 1,934           | 1,054        | 55%        | 458,580      | 229.9         |
| 18   | Quito          | 18,017       | 11,880          | 6,137        | 52%        | 2,781,641    | 220.6         |
| 19   | Azogues        | 696          | 508             | 188          | 37%        | 86,276       | 218.3         |
| 20   | Ibarra         | 1,594        | 1,133           | 461          | 41%        | 221,149      | 208.3         |
| 21   | Esmeraldas     | 1,397        | 949             | 448          | 47%        | 218,727      | 205.0         |
| 22   | Pasaje         | 514          | 339             | 175          | 51%        | 87,723       | 199.1         |
| 23   | Salinas        | 528          | 348             | 180          | 52%        | 94,590       | 189.9         |
| 24   | Babahoyo       | 1,407        | 1,081           | 326          | 30%        | 175,281      | 186.2         |
|   | Cantón         | Población | Casos | Letalidad | Población 100,000 | Mort. % |
|---|----------------|-----------|-------|-----------|-------------------|---------|
| 25 | Lago Agrio     | 650       | 428   | 222       | 119,594           | 52%     |
| 26 | Rumiñahui      | 537       | 338   | 199       | 115,433           | 59%     |
| 27 | Sucre          | 409       | 306   | 103       | 62,443            | 34%     |
| 28 | Salitre        | 370       | 264   | 106       | 65,765            | 40%     |
| 29 | Tucán          | 591       | 431   | 160       | 102,395           | 37%     |
| 30 | Samborondón    | 431       | 271   | 160       | 102,404           | 59%     |
| 31 | Chone          | 767       | 566   | 201       | 131,002           | 36%     |
| 32 | Montecristi    | 450       | 291   | 159       | 107,785           | 54%     |
| 33 | Colta          | 312       | 247   | 65        | 44,838            | 26%     |
| 34 | Cuenca         | 3,977     | 3,064 | 913       | 636,996           | 30%     |
| 35 | Playas         | 373       | 288   | 85        | 59,628            | 29%     |
| 36 | Guaranda       | 596       | 458   | 138       | 108,763           | 30%     |
| 37 | Otavalo        | 582       | 441   | 141       | 125,785           | 32%     |
| 38 | Tena           | 360       | 272   | 88        | 79,182            | 33%     |
| 39 | Loja           | 1,699     | 1,403 | 296       | 274,112           | 21%     |
| 40 | Empalme        | 395       | 303   | 92        | 86,073            | 30%     |

Some cantons reached unprecedented high mortality rates. For instance, Santa Elena (A canton with the same name as the province) had 579.2 deaths per every 100,000 inhabitants, followed by Guayaquil with 491.3 per 100,000 inhabitants. At the same time, other cantons have significantly lower mortality rates, such as those located in the amazon region or Galapagos (figure 5).
Figure 5 Excess Deaths Rate in Ecuador by canton.

Discussion

Ecuador has been the country with the highest number of COVID-19 related excess deaths per capita reported in a single day worldwide. The impact of the pandemic during the early phase of the outbreak in the country was devastating[26].
While we know that some countries worldwide, such as the US, India, or Brazil, have reported higher daily COVID-19 related deaths, Ecuador exceeds those countries greatly when adjusting for its population (Table 5).

Such was the demand for hospital beds, medical attention, and medical supplies that during the first wave of the pandemic in Ecuador, hundreds of critically ill patients were treated in their homes. This action resulted in painful scenes, with dozens of human corpses left on the streets while funeral homes were overwhelmed[21].

| Country    | Total Number of COVID-19 Officially reported deaths | COVID-19 Mortality crude /rate | Maximum Number of Deaths per day | % increases in terms of Excessive mortality | Highest Mortality rate/100.000 per day |
|------------|-----------------------------------------------------|-------------------------------|----------------------------------|-------------------------------------------|--------------------------------------|
| Ecuador    | 17,965                                              | 101                           | 1,120                            | 408%                                       | 6.27                                 |
| Bolivia    | 12,731                                              | 108                           | 84                               | 256%                                       | 0.71                                 |
| Peru       | 58,261                                              | 175                           | 740                              | 178%                                       | 2.21                                 |
| Brazil     | 381,687                                             | 179                           | 4,249                            | 86%                                        | 1.98                                 |
| Colombia   | 69,596                                              | 136                           | 429                              | 83%                                        | 0.83                                 |
| Chile      | 25,532                                              | 133                           | 316                              | 68%                                        | 1.64                                 |
| Mexico     | 214,957                                             | 168                           | 1,584                            | 60%                                        | 1.24                                 |
| Argentina  | 60,083                                              | 132                           | 515                              | 40%                                        | 1.13                                 |
| USA        | 586,152                                             | 178                           | 5,057                            | 47%                                        | 1.54                                 |
| India      | 195,123                                             | 14                            | 2,624                            | -                                          | 0.18                                 |

The government of Ecuador has only reported those deaths that were confirmed COVID-19 cases. For instance, As April 29th, 2021, Ecuador reported 18,470 confirmed deaths due to COVID-19 and for the same date, the excessive mortality has overpassed 55,418 deaths[22]. Thus, 36,948 could represent the actual excess deaths in this period of time, at least 200% more than expected. This difference between excess deaths and the official COVID-19 deaths is similar to the data reported by Benitez et al. in which Ecuador presented 21,990 excess deaths representing an increase of 386% of the deaths reported by COVID-19, as of August 2020[27].
At the provincial level, it can be observed that significant outbreaks showed values higher or lower than those reported by the official method. Cevallos et al. 2021 estimated an interim excess death in Ecuador from March 17 to October 22, 2020; which indicated that excess deaths were estimated at 36,922, and also indicates that the peak in excess all-cause mortality in Ecuador may have occurred on April 4, 2020, with 909 excess deaths[28]; however, this study did not analysed the excess of deaths at the provincial or canton level.

Our study on the other hand, explores the epidemiological dynamics of COVID-19 relates excess mortality with a cantonal resolution. For instance, Santa Elena was one of the most affected jurisdictions in the country, has reached an astonishing 579.2 excess deaths per 100,000, five times more than Italy or Spain during the worst part of their pandemic[9, 29]. It can be seen that most of the affected cantons during pandemics death outbreak belong to the Coastal region. This might be caused by its demographic density or triggered by cultural aspects linked to higher mobility, nevertheless this is still unknow[30]. The opposite situation occurred within the highlands. The pandemic decelerated during the first months of the lock-down and that might be linked to a reduction on the speed of contagium among those cantons. For instance, and even though cumulative mortality in the highlands was critically high, the daily mortality was far below the one seen in the Coast. Quito had less than 100 excessive deaths in a single day, while Guayaquil, the biggest coastal city in Ecuador had more than 600 deaths a day.

Excessive mortality is not only used for developing countries with poorer reporting systems. For example, in the US, a 20% increase in deaths was reported during March-July 2020, and 28% during March-May[14], of which 67% corresponded to COVID-19 confirmed deaths[31].

In Italy, an increase in pandemic-related mortality has been found, specifically related to an excess of deaths from undetermined respiratory illnesses (31,32). Results consistent with Ortiz-Prado et. al 2021 analysis that reported an increase in the number of deaths registered as acute respiratory distress syndrome during the first months of the pandemic in Ecuador while failing to provide accurate diagnosis [21].

In this sense, countries such as Italy or Spain even though they were also struggling with an early violent COVID-19 first wave that took countries off-guards, diagnosis capabilities were
superior that those reported in Latin America, including Ecuador[32]. Michelozzi et al. 2020 reported that in Italy, 52% of excess deaths were coded as COVID-19[33]. Another study in England showed that 23.6% of all deaths registered from February to June 2020 were registered as COVID-19 (30). Whereas in Ecuador, confirmed COVID-19 deaths only account for 3% of the total number of excess deaths during the first wave of the pandemic in Ecuador.

This difference between excess mortality and reported deaths from COVID-19 may be attributed to the country's SARS-CoV-2 diagnostic testing strategy not being widely distributed, coupled with a congested healthcare system, especially during the highest number of hospitalized patients[34].

The use of excessive mortality can be the most reliable indicator to understand and estimate the real impact of the pandemic. This metric can also be used to imply how many people was actually infected during the early stage of the pandemic using reverse upscaling calculations as a proxy of the early attack rate within the country.

Finally, we believe that acknowledging the real impact of the pandemic using excessive mortality will be useful to create public policy that will ensure future actions towards prevention and health care services responses against future biological threats.

**Limitations**

The main limitation of this study is the use of one dimension to track excess deaths and bootstrapped excess deaths. A vast array of research has been conducted recently where excess deaths are also analysed for other factors like age ranges, gender, and social strata (17). Unfortunately, the lack of data management in the official statistics unit of Ecuador has produced all deaths cases at an aggregated level, so there is not an official source to find more details about the impact of deaths across multiple strata.

Another limitation related to data quality is the level of death underreporting. After data analysis, it was quantified that there are delays between 3-5 days to register a death case at the official statistics unit. Using the common mean as the base for excess deaths tracker, considering this situation, can alter the results for excess because of extreme values that can appear on specific days. On the other side, using the bootstrapped mean helps to control the
phenomenon of underreporting since this measure infers the data generation mechanism for
the death cases series, thus better discriminating outliers.

Additionally, having only the death cases series for the country and provinces can impact the
distribution of excess deaths below traditional mean and bootstrap mean. Despite having data
from 2017 to 2020 in terms of death cases, the absence of covariates like age or gender can
influence the results profoundly. It could produce large, aggregated values, as our results
show a difference of almost 9,000 cases between traditional excess and bootstrapped excess.
This is related to how the distribution of excess deaths is affected because of necessary
elements like socio-demographic variables and classification of death cases in reporting. This
can be connected to the fact that another kind of information is needed, such as similar
illnesses like influenza and the contribution of effects from lockdown like the reduction of
pollution (34). Further work is needed to determine the relative importance of these different
factors on the overall estimates of excess deaths.

Conclusions

Ecuador had the highest numbers of excess deaths per capita in the world in a single day. The
mortality excess rate shows that the SARS-CoV-2 virus spread rapidly in the country,
especially in the coastal provinces of Santa Elena and Guayas during the first wave of the
pandemic. These deaths reflect the number of active cases that were missing diagnosis but
were responsible for the collapse of the health system during March and April 2020 in
Ecuador. Due to the lack of diagnosis capabilities, excessive mortality has demonstrated to
be a good indicator of the real impact of the pandemic and can be used as a proxy to estimate
the real attack rate that was greatly underreported.

Abbreviations

COVID-19: Coronavirus disease 2019
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2
INEC: National Institute of Statistics and Census
Declarations

Ethical Approval and Consent to participate
According to the local and international regulation, this study did no required ethical approval.

Consent for publication
Not applicable.

Availability of data and materials
The datasets generated and/or analysed during the current study are available in the github repository: https://github.com/covid19ec/DataDeathsEC

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
EOP is responsible for the conceptualization of the study. RF and KSR contributed to data collection, data extraction and data visualization. EOP, RF and KSR were responsible for the elaboration of the first draft of the manuscript. EOP, RF, EV and KSR contributed with the descriptive statistical analysis. EOP, AL, EV, SL and RL were responsible for the elaboration of the discussion section of the manuscript. AL, SL added important insights from a public health perspective. EOP and RF and KSR were responsible for editing the final version of the manuscript.

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