| 1        | Assessing Excess Mortality Patterns in  |
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| 2        | Argentina over the COVID-19   |
| 3        | Pandemic (2020-2021): A   |
| 4        | Comprehensive National and  |
| 5        | Subnational Analysis  |
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| 7        |   |
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## 18 Abstract

The COVID-19 pandemic has dramatically impacted global health metrics, with the World Health
Organization (WHO) reporting over 732 million cases and 6.7 million deaths by the end of 2021.
Additionally, approximately 14.8 million excess deaths were estimated globally through 2022,
significantly surpassing reported COVID-19 deaths. In Argentina, recorded pandemic-related
fatalities reached nearly 160,000 from March 2020 to December 2022, underlining the necessity
for a detailed examination of excess mortality across national and subnational levels.

This study aims to describe excess mortality in Argentina in 2020 and 2021 and its subnational
geographic areas, and to identify geographic and temporal disparities across sub-regionsusing
publicly available monthly mortality and climate data from Argentina, spanning 2015 to 2021.
Excess mortality was assessed using Generalized Additive Models (GAM) to account for longterm and annual trends, monthly climatic variations, and epidemiological reports of Influenza-like
Illness (ILI). Data across various geographic regions was analyzed to identify temporal and spatial
disparities in mortality.

Our analyses revealed significant regional disparities in mortality, identifying a total of 133,612 excess deaths across Argentina during the study period, with notable peaks coinciding with COVID-19 waves. These insights not only contribute to our understanding of the pandemic's broader effects but also emphasize the critical need for enhanced public health responses informed by mortality data analyses. The development of an open-source, interactive platform further supports this initiative, enabling detailed exploration and informed decision-making to better manage future public health crises.

## 39 Introduction

40 The global epidemiological impact of the COVID-19 pandemic has been profound, with the World Health Organization (WHO) reporting over 732 million confirmed cases and 6.7 million deaths as 41 of December 31, 2022<sup>1</sup>. Additionally, the WHO estimates indicate that there were approximately 42 43 14.8 million excess deaths worldwide through the duration of the pandemic by the end of 2022, 44 a figure 2.7 times greater than the reported COVID-19 deaths during the same period<sup>2</sup>. More 45 recent studies describe that out of 131 million global deaths from all causes combined in 2020 46 and 2021, approximately 15.9 million were attributed to COVID-19, either directly or indirectly due 47 to associated social, economic, or behavioral changes during the pandemic<sup>3</sup>. In Argentina, the 48 pandemic led to around 10 million confirmed cases<sup>1</sup> and nearly 160,000 deaths from March 2020 49 to December 2022, with significant annual variances observed; more than 53,000 in 2020, almost 50 85,000 in 2021, and almost 24.000 in 2022<sup>4</sup>.

51 The most substantial impact on the death toll was noted during 2020-2021. Latin America was 52 particularly hard-hit, emerging as one of the regions most affected during this timeframe and 53 several countries in the region presented the highest number of cases and deaths in the world<sup>56</sup>. 54 Notably, countries like Peru and Mexico experienced enormous excess mortality rates during 55 2020, highlighting the severe regional disparities in the pandemic's impact<sup>7</sup>.

In Argentina, the pre-pandemic general mortality rate remained relatively constant between 809.8
and 757.0 per 100,000 from 2015 to 2019, experiencing dramatic increases to 829.0 and 953.5
per 100,000 in 2020 and 2021, respectively (26.0% increase). However, the assessment of excess
mortality has been primarily focused on the year 2020, with limited comprehensive analysis
extending into 2021<sup>8-10</sup>.

61 The anomalous and sudden nature of the pandemic brought significance to the concept of62 "excess deaths" defined as the number of deaths that occurred in a period exceeding what is

expected as "normal" based on historical records. The concept of "excess mortality" is operationalized as a percentage of the total expected deaths under normal conditions and is used as a comparable indicator across different populations, which is useful for quantifying the impact of a pandemic (or other dramatic situations such as climate disasters, wars or catastrophes) on mortality<sup>11</sup>. Unlike other classic mortality indicators, such as crude, adjusted, or specific mortality rates, estimating excess mortality requires the availability of mortality information for all causes for the period of analysis in a given population and a historical period for the same population.

Considering the impact of a pandemic, this indicator is crucial in examining the aftermath, as it
considers various factors that can affect fatalities, such as government-driven public health and
social policies to manage the crisis, shifts in social behaviors, and preparedness and response of
healthcare systems.

While there is consensus that excess deaths observed above what is expected (in absolute values or percentages) represent the appropriate indicator to capture this phenomenon, there is no consensus in the literature on how to determine the threshold of what is expected under "normal" circumstances, and consequently, how to calculate the indicator. Two of the most commonly used alternatives are models based on percentiles of the historical distribution of deaths <sup>12 8</sup> and models based on more complex or multivariate methods that can incorporate other variables, such as climate or seasonality <sup>13-20</sup>.

This study aims to describe excess mortality in Argentina in 2020 and 2021 and its subnational geographic areas, and to identify geographic and temporal disparities across sub-regions. Beyond providing detailed analyses and insights, the research aims to extend its utility by developing an open-source, interactive, customizable, and user-friendly platform for estimating jurisdiction-specific excess mortality. This tool is designed to facilitate the exploration and understanding of mortality data by researchers, policymakers, and the general public, enabling informed decision-making and targeted interventions to address public health challenges.

4

# 89 Materials and Methods

This is a descriptive and analytic study. Monthly mortality statistical data from 2015 to 2021 were 90 91 utilized to construct curves representing the monthly number of deaths for all causes at both 92 national and subnational levels. The datasets used were publicly released by the Ministry of 93 Health of Argentina (MoH) and were accessible through its Open Data portal<sup>21</sup>. The available 94 information for excess mortality analysis was temporally disaggregated by month. The 95 geographic areas defined in the dataset encompassed complete jurisdictions in 11 cases (the 96 provinces of Buenos Aires, Chaco, Córdoba, Corrientes, Entre Ríos, Formosa, Mendoza, Misiones, 97 Santa Fe, Tucumán, and the Autonomous City of Buenos Aires). Given the lower event frequency 98 and in order to prevent the indirect identification of deceased individuals, the MoH aggregated the 99 remaining jurisdictions into five regions based on geographic contiguity: Jujuy + Salta (NOA 1), 100 Catamarca + Santiago del Estero (NOA 2), Chubut + Santa Cruz + Tierra del Fuego (Southern 101 Patagonia), La Pampa + Neuquén + Río Negro (Northern Patagonia), and San Juan + San Luis + 102 La Rioja (Rest of Cuyo) (Fig 1).

#### 103 Fig 1. Geographic Division for Excess Mortality Analysis in Argentina

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105 Additionally, monthly data for both minimum and maximum temperatures<sup>22,23</sup> recorded by 106 meteorological stations across various geographical regions for the period spanning from 2015 107 to 2021 were incorporated. Data was obtained from the National Meteorological Service of 108 Argentina<sup>24</sup>. Weekly notifications of Influenza-like Illness (ILI) cases <sup>25,26</sup>, sourced from 109 epidemiological bulletins periodically published by the Ministry of Health<sup>27</sup> and the Open Data 110 portal<sup>28</sup> for years 2015–2021, were also used. Studies cited, employing similar models have 111 demonstrated improved goodness of fit, reinforcing the robustness of our methodological 112 approach.

A generalized additive model (GAM) was identified as the best choice for threshold estimation after evaluating the root mean square error (RMSE) between various models (1) simple linear models, 2) simple linear model with regularization, 3) Poisson regression model, 4) negative binomial generalised linear model, 5) GAM model, and 6) median and percentiles methodology<sup>8</sup>) comparing predicted versus observed mortality within trainning data via cross-validation for the time series over the period 2015-2019. This process was carried out using the R<sup>29</sup> package caret and the function "trainControl", with the method specified as "timeslice" <sup>30</sup>.

120 During model development and selection, long-term (systematic changes observed throughout 121 the entire study period, independent of seasonal variations) and annual trends, monthly average 122 minimum and maximum temperatures, and reports of ILI cases from 2015-2019 were taken into 123 account. Based on the RMSE obtained through cross-validation, the GAM was chosen as the best 124 estimator to predict the expected number of deaths in 2020-2021 (test set) and to estimate 125 excess deaths (the difference between observed and expected deaths) on a monthly and annual 126 basis, both at the national and subnational levels.

As illustrated in Fig 2, the data was segmented into training, validation, and test sets. The training and validation sets were split sequentially in chronological order, using the last year of each sequence as the validation set. RMSE was used as the metric for selecting the best performing model. The test set (2020-2021) was used for the final performance evaluation.

#### 131 Fig 2. Time series split for k-fold cross validation: training and validation set.

The final selected model was a quasi-Poisson regression model that relates the logarithm of the monthly number of deaths to various time-dependent predictors, including annual trends, longterm trends, climatic variables such as average monthly maximum and minimum temperatures, monthly reports of Influenza-like Illness cases, and the month of the year. The models were fitted to the data using the GAM function in R statistical software's *mgcv* library<sup>31</sup>. A separate model was fitted for each geographical area and one at the national level. A second-order autoregressive

correlation structure was specified in the model to account for temporal correlation in the data.
This allows the modeling of the dependence of errors over time. An examination of the residuals
of the models showed a good fit to the data, including all lag autocorrelations. The annual trend
was modeled using a cyclic B-spline with predefined smoothing levels.

142 Excess mortality percentage indicators were calculated using the selected GAM. As elaborated 143 in this section, multivariate models and their corresponding prediction intervals were developed 144 for each deographic area or jurisdiction to estimate expected deaths on a monthly basis for the 2020-2021 period. The excess percentages for 2020 and 2021 were calculated using the 145 146 thresholds generated by this model, involving the summation of the monthly estimates for each 147 year. Unlike previous methods, which were based solely on the mean and median of the past five 148 years, this approach enables distinct estimations for different years. Additionally, a prediction 149 interval was constructed from which the confidence intervals for the excess indicator were 150 derived. These intervals were calculated using the model's statistical estimates and the 151 properties of the residual distribution with the predict() function from mgcv library.

The number of excess deaths was calculated on a monthly basis as the difference between the total observed deaths from all causes and the expected deaths based on the model. The confidence interval for the number of excess deaths was determined by using the prediction interval of the fitted model. Annual summary indicators were constructed by summing the monthly values. The p-score, or percentage of excess mortality, was calculated as the ratio of excess deaths to expected deaths per 100 per month, year, and geographic region.

Values for the entire country were computed using a stratified approach as described by Nielsen
et al.<sup>32</sup>. Unlike the summarized approach, this approach assumes statistical independence
among geographic regions and has the advantage of mitigating discrepancies between the
national and regional levels.

- 162 During the development of our study, an interactive visualization was created using the R
- 163 programming language, utilizing the Shiny package<sup>33</sup> for the user interface and the Highcharter
- **164** package<sup>34</sup> for graphical representations..
- 165 The codes used to fit the models are publicly available and are accessible in the GitHub repository
- 166 (https://github.com/agsantoro/excesoMortalidad). The results of this study can be visualized at
- 167 <u>https://iecs.shinyapps.io/excesomortalidad</u>.

# 168 Results

Figs 3, 4, and 5 present a comprehensive graphical representation of the data utilized as covariates in our models, described by province/region. Figure 3 displays the temperature variables. Figure 4 depicts the number of reported cases of Influenza-Like Illness , providing insights into the epidemiological trends across different provinces. Figure 5 charts the mortality data from all causes. These figures collectively facilitate a nuanced understanding of the interplay between environmental factors, disease incidence, and mortality outcomes.

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- Fig 3. Monthly Average of Maximum (orange) and Minimum (cyan) Temperatures by
  Geographic Region. Period 2015-2021.
- **Fig 4. Monthly Reported Cases of Influenza-like Illness (ILI).** Period 2015-2021.
- **Fig 6. Monthly All-causes Deaths by Geographic Region.** Period 2015-2021.

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Based on the method employed for the entire period, 133,612 excess deaths were identified in Argentina, while 137,736 deaths are reported due to COVID-19 for the full period (2020-2021). This discrepancy yields an undercount ratio of 0.97. The undercount ratio highlights the percentage by which reported disease-specific deaths deviate from excess deaths estimated from all-cause mortality data, which in this instance suggests a 3% underreporting of COVID-19 deaths. Upon annualized assessment for the year 2021, 91,125 excess deaths are described alongside 84,190 COVID-19 deaths, resulting in a higher undercount ratio of 188 1.08.

#### 189 Waves identified

190 When observing by geographical area, it is noteworthy that in the province of Buenos Aires and 191 the City of Buenos Aires (CABA), three peaks of deaths above expected levels were identified, with 192 elevated mortality levels between each one. These events occurred in July, August, and 193 September 2020; January 2021; and May 2021. Given that the province of Buenos Aires is the 194 largest and most populated jurisdiction in the country, the same pattern of three peaks of excess 195 deaths is found when analyzing the total for Argentina. However, in the jurisdictions of Córdoba, 196 Entre Ríos, Santa Fe, Corrientes, Chaco, Tucumán, Mendoza, and the NOA 1, Resto Cuyo, and 197 Patagonia Norte regions, two peaks were identified, one in 2020 and another in 2021 (months 198 from May to June). In these geographic areas, the level of mortality did not return to the expected 199 value during any period of the study (figure 6).

#### 200 First Half of 2020

During the first half of 2020, four geographical areas were identified with mortality levels below
expected levels (Santa Fe, Córdoba, Tucumán, and Patagonia Norte, see Table 1). The rest of the
areas studied did not show significant excess mortality, as the percentage excess presented a
confidence interval that included zero.

#### 205 **Table 1**.

|                                    |                      | Year                | 2020                              |      |  |      |
|------------------------------------|----------------------|---------------------|-----------------------------------|------|--|------|
|                                    | Semestre 1           |                     | Semestre 2                        |      | Year 2021                                  |      |
| Region                             | Excess Deaths (%)    | COVID Deaths<br>(%) | Excess Deaths (%) COVID Deaths (% |      | COVID Deaths<br>) Excess Deaths (%)<br>(%) |      |
| Total Country                      | -3.4 ( -8.6 - 2.5 )  | 1.5                 | 27.8 ( 20.2 - 36.5 )              | 23.3 | 26.8 ( 17.8 - 37.3 )                       | 19.5 |
| Buenos Aires                       | -3.5 ( -7.5 - 0.9 )  | 1.8                 | 26.2 ( 21.2 - 31.6 )              | 25.5 | 28.4 ( 22.9 - 34.5 )                       | 19.8 |
| Chaco                              | -5.1 ( -10.9 - 1.5 ) | 3.4                 | 19.6 ( 12.1 - 28.3 )              | 14.7 | 32.2 ( 23.1 - 42.7 )                       | 21.6 |
| Ciudad Autónoma de<br>Buenos Aires | 5.8 ( -2.1 - 14.9 )  | 5.3                 | 38.3 ( 26.3 - 52.8 )              | 26.4 | 21.6 ( 8.2 - 38.8 )                        | 17.4 |
| Corrientes                         | -4.6 ( -11.9 - 4.1 ) | 0.0                 | 6.1 ( -4.1 - 18.8 )               | 9.3  | 20.4 ( 6.3 - 38.9 )                        | 18.0 |
| Córdoba                            | -6.9 ( -12.11 )      | 0.9                 | 18.9(11.1 - 27.7)                 | 21.8 | 15.7 ( 6.4 - 26.7 )                        | 15.8 |
| Entre Ríos                         | -4.6 ( -11.2 - 3 )   | 0.1                 | 12.2 ( 1.6 - 25.2 )               | 12.1 | 25.4 ( 10.3 - 45.3 )                       | 17.1 |
| Formosa                            | -0.8 ( -9.4 - 9.6 )  | 0.1                 | -9.3 ( -19.1 - 3.3 )              | 0.5  | 26 ( 8.9 - 49.6 )                          | 24.5 |
| Mendoza                            | -3.6 ( -8.2 - 1.5 )  | 0.1                 | 41 ( 34.2 - 48.5 )                | 22.6 | 26.1 ( 19.7 - 33.2 )                       | 20.7 |
| Misiones                           | 1.9 ( -7 - 12.6 )    | 0.1                 | -1.9 ( -14.1 - 14.2 )             | 1.6  | 30.4 ( 9.8 - 60.6 )                        | 19.2 |
| NOA 1                              | -0.7 ( -7 - 6.4 )    | 0.2                 | 73.5 ( 59.6 - 90.1 )              | 30.4 | 30.9 ( 17.1 - 48.4 )                       | 15.1 |
| NOA 2                              | 3.9 ( -3.9 - 13.1 )  | 0.0                 | 16.4 ( 5.4 - 29.9 )               | 9.6  | 46.9 ( 28.9 - 70.8 )                       | 24.5 |
| Patagonia Norte                    | -7.1 ( -11.81.9 )    | 1.3                 | 34.2 ( 24.4 - 45.5 )              | 30.3 | 29.8 ( 17.9 - 44.3 )                       | 27.1 |
| Patagonia Sur                      | -5.5 ( -10.9 - 0.5 ) | 0.3                 | 44.1 ( 35.4 - 54 )                | 32.6 | 32.9 ( 24.6 - 42.5 )                       | 25.0 |
| Resto Cuyo                         | -0.7 ( -6 - 5.3 )    | 0.4                 | 22.4 ( 15.6 - 29.9 )              | 18.1 | 33.1 ( 25.6 - 41.6 )                       | 20.2 |
| Santa Fe                           | -10.4 ( -163.9 )     | 0.1                 | 30.9 ( 22.7 - 40.2 )              | 21.6 | 25.1 ( 16 - 35.6 )                         | 17.7 |
| Tucumán                            | -4.3 ( -7.90.4 )     | 0.6                 | 40.2 ( 35.1 - 45.7 )              | 25.1 | 26.6 ( 21.8 - 31.9 )                       | 21.7 |

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#### 207 Second Half of 2020

| 208         | During the second half of 2020, following the multivariate modeling methodology, three               |
|-------------|--|
| 209         | geographical areas were identified with no significant excess mortality (Misiones, Corrientes, and   |
| 210         | Formosa). The rest of the areas studied showed significant excess mortality, with the three most     |
| 211         | affected being Noa 1 (73.5% CI 59.6 - 90.1), Patagonia Sur (44.1% CI 35.4 - 54), and Mendoza         |
| 212         | (41% CI 34.2 - 48.5). The regions with the lowest levels of excess for the second half of 2020 were  |
| 213         | Entre Rios (12.2% CI 1.6 - 25.2), NOA 2 (16.4% CI 5.4 - 29.9), and Córdoba (18.9% CI 11.1 - 27.7).   |
|             |  |
| 214         | In comparing the indicator of the percentage of COVID-19 related deaths to the percentage of         |
| 215         | excess mortality, it was observed that in all the studied regions exhibiting significant excess, the |
| 216         | excess mortality surpassed the percentage of deaths attributed to COVID-19. However, this trend      |
| 217         | was not observed in the provinces of Córdoba and Corrientes (fig 6)                                  |
| 210         | Fig 6 COVID Deaths and Example Deaths per Month by Congraphic Design Deried 2020 2021                |
| <b>∠</b> 10 | rig o. Covid dealis and Excess dealis per wondin by deographic region. Penou 2020-2021.              |

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#### 220 Year 2021

221 The year 2021 showed significant levels of excess mortality in all studied geographical areas. The 222 highest levels of the p-score indicator were observed in the NOA 2 area, which reached values of 223 46.9% (CI 28.9 - 70.8), Resto de Cuyo (33.1% CI 25.6 - 41.6), Patagonia Sur (32.9%, CI 24.6 - 42.5), 224 and Chaco (32.2, CI 23.1 - 42.7). Fig 6 illustrates the magnitude of the excess in these 225 geographical areas. It can also be observed that, unlike 2020, excess mortality in these areas was 226 distributed between January and September, in contrast to 2020, where it was mainly 227 concentrated between August and December. The regions of Córdoba (15.7% (CI 6.4 - 26.7), 228 Corrientes (20.4% (CI 6.3 - 38.9), and CABA (21.6%; CI 8.2 - 38.8) showed lower levels of excess

229 mortality. In 2021, all geographical regions displayed higher mortality rates than those presented230 by COVID-19 deaths.

The interactive visualization <u>https://iecs.shinyapps.io/excesomortalidad</u>) displaying the results was developed to enable users from various levels and jurisdictions to conduct their own analyses, select indicators, and easily obtain results. It allows for comparisons between regions and the disaggregation of indicators at different levels. Although the models underlying the visualization are sophisticated, the platform facilitates straightforward interpretation and can be customized to meet the needs of specific users.

#### 237 Limitations

238 It is important to note that the excess mortality measures employed in this study (both the 239 quantity and percentage of excess deaths) do not account for the differences in the 240 demographic structures of the compared populations. While there are precedents for studies 241 that have used age-adjusted indicators to estimate excess mortality, most of the studies did 242 not incorporate this adjustment. In future approaches, it is crucial to evaluate whether to 243 prioritize demographic structure as a determinant of the magnitude of excess (older 244 populations tend to exhibit a higher proportion of excess deaths due to the overrepresentation 245 of older age groups) or regarding this structure as a bias, prioritizing interpretations based on 246 the comparative impact of the anomalous phenomenon. Additionally, it is worth noting that the 247 excess mortality measures used in this study are not based on differences between age-248 adjusted mortality rates and therefore possess inherent interpretability.

The lack of mortality data for 2022 at the time this study was conducted is another limitation. In Argentina, the temporal criteria for the statistical recording of deaths are based on the date of registration; therefore, the release of 2022 data will also include deaths that occurred in 2021 (primarily towards the end of the year) but were reported to the MoH in 2022. This circumstance is evident in Fig 6, where a noticeable decrease in excess mortality is observed in November and December 2021. It should also be considered that the inclusion of these deaths will elevate the annual figures for excess deaths and excess mortality for 2021, particularly in the final months of the year, as the vast majority of deaths registered in the subsequent year, originate in November and December of the preceding year.

We should take into account some idiosyncrasies of the data used. Deaths have been tabulated by their "underlying cause of death"<sup>35</sup> which was selected for each death based on rules among the multiple causes of death indicated in the death certificate. However, due to the novelty of the COVID-19 event, the WHO established new rules for its registry in 2020<sup>36</sup>, prioritizing COVID-19 over other causes, which could constitute a bias of over-representation of mortality due to COVID-19 and, consequently, an under-representation of mortality from other causes. In other words, deaths with COVID-19 rather than deaths by COVID-19.

## 265 Discussion

266 First, based on the methodology employed in this study for the entire period, we identified 267 133,612 excess deaths in Argentina, while 137,736 COVID-19 deaths were reported for the entire period (2020-2021). This discrepancy yields an undercount ratio of 0.97. However, when 268 269 examining each year individually, 2021 shows 91,125 excess deaths and 84,190 reported 270 COVID-19 deaths, leading to an undercount ratio of 1.08. Argentina's estimated undercount 271 ratio for the entire period of 2020-2021 aligns closely with those of Chile (0.99) and Panama 272 (1.01) for 2020, and is lower than those of Brazil (1.11), Paraguay (1.15), and Peru (1.07) for 273 the same period<sup>7</sup>.

The GBD 2021 provides vital demographic estimates spanning 204 countries, including Argentina, emphasizing pandemic-period changes in mortality and life expectancy, underscoring the need for timely data to grasp COVID-19's impact on population health trends.<sup>3</sup>

Notably, the excess deaths estimated for Argentina in this study are also in line with figures
 from other sources. The Institute for Health Metrics and Evaluation (IHME)<sup>37</sup> estimates
 141,488 excess deaths, while The Economist<sup>38</sup> reports a figure of 132,470 for the entire period.

281 The challenges associated with analyzing excess mortality in Argentina are significant due to 282 the absence of a digital death registry<sup>8</sup>, which impedes real-time pandemic response and 283 delays the provision of vital statistics. Studies by Rearte et al. (2020)<sup>8</sup> reveal a 10.6% increase 284 in excess mortality in 2020 compared with the 12.7% obtained in this study, although the 285 methodology may oversimplify outcomes by not accounting for environmental, and long -term trend and annual trends. Regional insights provided by Sarrouf et al. (2020)<sup>10</sup> and Pesci et al. 286 287 (2021)<sup>39</sup> highlight disparate impacts across the country, with notable increases in areas like 288 Patagonia and Buenos Aires province, reflecting healthcare saturation and altered public 289 behaviors. Additionally, a reported decline in non-COVID-19 mortality among the elderly 290 suggests significant behavioral and healthcare engagement changes during the pandemic.

Argentina's struggle to manage mortality data is not unique, as a significant digital divide hinders timely public health interventions globally. The EuroMOMO<sup>40</sup> initiative serves as a model for Argentina to enhance its pandemic response and data analysis capabilities. Comparative analyses by Rossen et al. (2021)<sup>18</sup> highlight universal challenges and the sustained impacts of the pandemic, emphasizing the global scale of the crisis and the common hurdles in pandemic management and response strategies.

Global insights from the WHO (2020)<sup>2</sup> estimate 14.8 million excess deaths worldwide, underscoring the critical need for robust data collection and analysis methodologies. The parallel between global figures and national findings in Argentina highlights the underreporting and challenges in accurately assessing the pandemic's full impact. By aligning Argentina's research approaches with global standards and insights, there is an opportunity to refine public health strategies, enhance real-time monitoring, and ensure a more informed and effective response to current and future public health crises.

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304 During the COVID-19 pandemic, a significant substitution of causes of death was noted, where 305 declines in mortality from non-COVID-19 causes were observed, with diabetes being the 306 notable exception<sup>9</sup>. This phenomenon highlights the complex interplay between the pandemic 307 and other health conditions and deserves a specific approach. In particular, the study 308 showcases that during 2020, there was a notable decrease in mortality across various non-309 COVID-19 categories, illustrating the shift in mortality causes during the pandemic period. 310 However, these changes in the mortality profile must be evaluated taking into account the 311 particularities of each group of causes of death and the historical period (circulation restriction 312 measures, difficulties in accessing health services, etc.).

313 Moreover, the investigation reveals that in 2021, excess deaths estimated by the study 314 exceeded the number of deaths officially recorded as due to COVID-19, suggesting possible 315 underreporting and an increase in deaths from other causes, potentially linked to the 316 pandemic's indirect impacts (REF). This situation aligns with the concept of syndemics, 317 emphasizing the exacerbated mutual impacts of COVID-19 and non-communicable diseases, 318 affecting individuals with chronic conditions. Understanding this dynamic requires a 319 comprehensive approach, integrating the substitution phenomenon observed in 2020, where 320 a reduction in non-COVID deaths, aside from diabetes, coincides with the pandemic's wider 321 implications. This context underscores the need for precise methodologies for estimating all-322 cause excess mortality and understanding non-COVID mortality behaviors, particularly 323 regarding NCDs, to inform public health decisions and address the intertwined challenges of 324 infectious and chronic diseases.

# 325 Conclusions

To conclude, our examination of excess mortality in Argentina during the COVID-19 pandemic provides significant insights into the extensive impact of the pandemic, beyond just the reported infection and mortality rates. These insights greatly contribute to our understanding 329 of the pandemic's broader effects and emphasize the critical need for detailed public health 330 responses. Highlighting how pandemic preparedness and response strategies can be 331 informed by the lessons learned from the COVID-19 mortality rates, we see a clear directive 332 for strengthening health systems and enhancing response mechanisms to better manage 333 future public health crises. Additionally, it is crucial to extend our research by analyzing excess 334 mortality due to different causes of death. Further analysis will improve our comprehension of 335 the pandemic's complex effects and help in crafting focused health interventions. Future 336 studies should track these developments using thorough methods to support the ongoing and 337 future public health efforts.

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431



# Training set





#### Monthly Average of Maximum (orange) and Minimum (cyan) Temperatures by Geographic Region Period 2015-2021



Monthly Reported Cases of Influenza-like Illness (ILI) Period 2015-2021



#### Monthly All-causes Deaths by Geographic Region

Period 2015-2021



COVID Deaths and Excess Deaths per Month by Geographic Region Period 2020-2021



Reference: - Number of COVID Deaths - Number of Excess Deaths

Fig6