Regional excess mortality during the 2020 COVID-19 pandemic: a study of five European countries

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Abstract

The impact of the COVID-19 pandemic on excess mortality from all causes in 2020 varied across and within European countries. Using data for 2015-2019, we applied Bayesian spatio-temporal models to quantify the expected weekly deaths at the regional level had the pandemic not occurred in England, Greece, Italy, Spain, and Switzerland. With around 30%, Madrid, Castile-La Mancha, Castile-Leon (Spain) and Lombardia (Italy) were the regions with the highest excess mortality. In England, Greece and Switzerland, the regions most affected were Outer London and the West Midlands (England), Eastern, Western and...
Central Macedonia (Greece), and Ticino (Switzerland), with 15-20% excess mortality in 2020. Our study highlights the importance of the large transportation hubs for establishing community transmission in the first stages of the pandemic. Acting promptly to limit transmission around these hubs is essential to prevent spread to other regions and countries.

**Introduction**

By December 2020, the World Health Organization (WHO) reported 1,813,188 Coronavirus disease 2019 (COVID-19) related deaths globally [1]. Although COVID-19 related deaths are key to monitoring the pandemic's burden, vital statistics generally suffer from issues related to accuracy and completeness [2]. Additionally, they can be subject to changes in definition and different policies regarding testing and reporting [3, 4]. At the same time, focusing only on COVID-19 deaths does not provide information about indirect pandemic effects due to disruption to health services and wider economic, social and behavioural changes in the population [5]. An effective way to quantify the total mortality burden of the COVID-19 pandemic is through excess mortality [6]. Excess mortality compares the number of deaths from all causes observed during the pandemic, and the number of deaths expected had the pandemic not occurred, using data from recent pre-pandemic years. Preliminary estimates suggest that the total number of global deaths attributable to the COVID-19 pandemic in 2020 is at least 3 million, with approximately 37% of these deaths occurring in the European region [1].

Previous studies have examined excess mortality at the national level reporting a disproportionate mortality burden [7, 6]. In Europe, England and Wales, Spain and Italy experienced the largest increase in mortality during March-May 2020, with excess mortality estimates for the two sexes ranging from 70 to 102 per 100,000 population [7]. In contrast, from October to December 2020, the impact on mortality was great in Switzerland [6]. Studies focusing on the regional level have also found differential effects on mortality [8, 9, 10]. In Italy higher excess mortality was observed in some provinces in the North-west [8, 9]. In England, the highest excess mortality was observed in London and in the West Midlands during March-May 2020 [11, 12]. In Greece, Eastern Macedonia and Thrace, Western Macedonia and Central Macedonia reported more than 10% excess mortality, in contrast to the Aegean islands and Crete for which the excess was smaller than 3% [10]. Studying these variations may help our understanding of the transmission patterns and the effectiveness of policies and measures to contain the pandemic. Other factors that may have also contributed to the varying impact on mortality across regions include differences in demographics [13], the prevalence of comorbidities [13] and environmental factors [12, 14, 15].

In this study of five European countries, we examined the impact of the COVID-19 pandemic on mortality in
2020 using weekly regional all-cause mortality data. We included countries from Northern, Western and Southern Europe (England, Greece, Italy, Spain and Switzerland) and analysed regions defined by Eurostat, which are consistent across different European countries, Supplementary Fig. S1. We used a model-based approach to predict deaths for 2020 by specific age- and sex groups, under the counterfactual scenario that COVID-19 had not occurred. To the best of our knowledge, this is the first international study of the COVID-19 regional impact on mortality.

Results

A total of 565,505 deaths were recorded in 2020 in England, 132,514 in Greece, 756,450 in Italy, 485,536 in Spain and 77,222 in Switzerland (Table 1). The estimated population in 2020 was 56,702,967 in England, 10,718,447 in Greece, 59,641,219 in Italy, 47,332,587 in Spain and 8,681,297 in Switzerland (Table 1). In all countries, the number of deaths in males compared to females was larger for all age groups below 80 years. Comparing the observed number of deaths with the mean number of deaths from 2015 to 2019, there were 40,631 and 27,739 excess deaths in males and in females, respectively, in England, 5,380 and 5,909 in Greece, 59,327 and 52,206 in Italy, 35,868 and 33,208 in Spain and 5,788 and 4,526 in Switzerland (Table 1).

Model validation. Overall the models had good predictive ability in cross validation over 2015 to 2019, Supplementary Table S1. The highest correlation between observed and predicted was observed for age group 80 years or older, with the medians and 95% credible intervals (i.e. 0.95 probability that the true value lies in this interval) ranging from 0.83 (95% CrI 0.82–0.84) in females in England to 0.97 (95% CrI 0.97–0.98) in males in Spain. For the same age group, the coverage (i.e. the probability that the observed number of deaths falls in the 95% credibility interval of the predicted) varied from 0.90 in females in Spain to 0.95 in males in Switzerland, Supplementary Table S1. Although the coverage for the <40 age group is close to 0.95, we excluded this age group from the results reported, as (i) the correlation between observed and predicted values was low, varying from 0.15 in females England to 0.69 in males in Spain, Supplementary Table S1, and (ii) this was the age group least affected by COVID-19 mortality during 2020 [13].

Country-level trends and overall excess mortality. Temporal patterns differed across countries, with England and Spain experiencing a larger death toll during March-May 2020 and Switzerland and Greece during November-December 2020, Fig. S2-3 and S5-6. Mortality was high in Italy during both periods, Fig. S4. Across the five nations, the median relative excess mortality together with the 95% credible intervals for the entire 2020 (relative to what is expected had the pandemic not occurred) ranged from 6% (95% CrI -1%–13%) in Greece to 12% (95% CrI 6%–19%) in Spain in men. For women, it ranged from 6% (95% CrI -2%–13%) in Greece to 12%
(95% CrI 6%–19%) in Spain, Fig. 2 and Supplementary Tables S2-6. For the country-level weekly trends see Supplementary Fig. S2 to S6.

**Sub-national level trends: NUTS2 regions.** Excess mortality was evident for most regions, but with large intra-country variability, as shown in Fig. 1. Across the five countries, Madrid, Castile-La Mancha, Castile-Leon (Spain) and Lombardia (Italy) are the regions with the highest excess mortality in 2020, ranging from 28% (95% CrI 22%–34%) to 33% (95% CrI 27%–39%) for males and 25% (95% CrI 17%–38%) to 32% (95% CrI 23%–40%) for females (Fig. 1 and Supplementary Table S4-5). Ceuta (Spain) experienced a similar median excess for females (31%: 95% CrI 14%–54%), albeit associated with larger uncertainty, Fig. 1 and Supplementary Table S5. For males, the regions most affected in England, Greece and Switzerland were Outer London and the West Midlands, Eastern, Western and Central Macedonia, and Ticino, with the median excess mortality varying from 15% (95% CrI 8%–24%) to 21% (95% CrI 15%–28%), Fig. 1 and Supplementary Table S2-3 and S6. For females, the median excess mortality varied from 18% for the Ticino to 19% in Western Macedonia and 15% in East-North East outer London, Fig. 1 and Supplementary Table S2 and S6. The regions that show the lowest excess mortality are Cornwall and Isle of Scilly and Devon in England, Crete, and North and South Aegean in Greece for males, Lazio in Italy for females and Canary and the Balearic islands in Spain, Fig. 1 and Supplementary Table S2-6.

**Finer sub-national level trends: NUTS3 regions.** The higher resolution maps in Fig. 2 and 3 show the median relative excess mortality and the posterior probability of a positive excess, allowing appreciation of patterns missed by the lower resolution. In England, the high excess experienced by the West Midlands was driven by Birmingham, the largest urban area in the region, which recorded values above 20%. In Greece, the municipality of Drama, with an excess >20% was responsible for the high excess in Eastern Macedonia and Thrace. For Italy, outside the Northern regions, the model highlights localised excess in the provinces of Rimini, Pesaro-Urbino and Foggia, on the Eastern coast, while central Spain and Catalonia had the highest excess in Spain. In Switzerland, all regions had a relative excess of <20% but the French and Italian speaking regions experienced a posterior probability of a positive excess above 0.95. In contrast, the German-speaking regions were more diverse, Fig. 2 and 3. In Supplementary Fig. S7 to S16 we report the spatial trends by age and sex at the higher geographical resolution. The spatial trends differ depending on the age group, but are similar for men and women for age groups over 60 years.

**Spatio-temporal trends at the regional level.** Fig. 4 shows the relative excess mortality and the posterior probability that the excess mortality is greater than 0 for the different NUTS2 regions, for each week in 2020. Across the five countries, relative excess larger than 200% is observed only during the first epidemic period
of 2020 (March-May 2020) in England (Greater London), Italy (Lombardia) and Spain (Madrid, Castille-La Mancha, Catalonia), Fig. 4. In Switzerland, during the first epidemic period, the geographical patterns of excess mortality were highly localised, with Ticino experiencing the highest excess mortality. In contrast, the geographical variability in Greece was more diffuse. During the second epidemic period (October-December 2020), the excess mortality in Italy and Switzerland was similar across the country, whereas in Greece it was highly localised, with Central Macedonia experiencing a relative excess mortality between 100-200% during November 2020, Fig. 4.

Discussion

To the best of our knowledge, this is the first multi-country study examining excess mortality in 2020 across five European countries at the sub-national level. We found that excess mortality in 2020 varied widely both between countries and within countries. Spain experienced the largest excess mortality among the five countries studied. Within Greece and Italy the northern regions were more affected than other regions. The temporal trends at the sub-national level showed patterns of localised excess mortality in England, Italy, Spain and Switzerland during the first wave, whereas in Greece the excess mortality was homogeneous. During the second wave, excess deaths were overall lower in magnitude and their distribution more homogeneous in England, Italy and Spain. In contrast, in Greece and Switzerland, the second wave was more severe than the first one.

Our study has several strengths. It quantifies the short term, direct effect of the COVID-19 pandemic and indirect effects on mortality due to other life-threatening conditions, such as myocardial infarction [16], in five European countries. Reduced access to or uptake of medical care due to COVID-19 leading to delays in cancer screening, cancer diagnosis, rescheduling of surgery or cancellation of outpatient visits in patients with chronic conditions may have increased mortality during the pandemic, particularly in countries with weaker health systems [17, 18, 19]. Our modelling approach incorporated spatial and temporal mortality trends, factors such as temperature and public holidays, and the different population temporal trends across space, age and sex groups. We carefully validated the model employing a cross-validation approach and found that it had high predictive accuracy. In contrast to previous studies, we stratified by age and sex, thus allowing the spatial and temporal mortality trends to vary across these groups. Weaknesses include the lack of detailed data on the causes of death, which would have allowed insights into the sources of the observed variation in excess deaths.

Several previous studies reported nationwide excess mortality for 2020. The Office for National Statistics in England reported a 17.9% increase in male mortality and 11.2% in females [11]. A recent study of 40 industrialised countries covered the period from February 2020 to February 2021 and found an excess mortality of 15% to 20%
in England and Wales, Spain and Italy [20]. Our estimates are lower but credibility intervals include the figures from both studies. Reasons for the discrepancies include the different periods used to train the model, different data sources, different prediction periods and the exclusion of Wales from our data [21]. Our results are in line with estimates from the Hellenic Statistical Authority, which reported a 7.3% increase in the relative excess in Greece during 2020 [10], a Swiss study reporting a 10.6% increase in excess mortality in males and a 7.2% increases in females relative to 2019 [22] and the estimates from the Italian National Institute of Statistics [23]. The latter reported a 15.6% excess for 2020 compared to the average number of deaths 2015 to 2019 [23]. In Spain, the relative excess mortality varied from 26.8% to 77.9% across the different age groups for the period March to May 2020 and from 10.0% to 18.9% during the period July to December 2020 [24].

At the regional level, our findings align with the Office for National Statistics in England, which reported a 20% increase in the relative excess mortality in London, the largest relative excess observed nationwide in 2020 [11]. Our estimates are also in line with the Hellenic Statistical Authority reports suggesting that Macedonia and Thrace experience the largest relative increase in excess deaths in Greece (14.9% in males and 12.9% in females) [10]. The observed north-to-south geographical gradient in the impact of COVID-19 in Italy is in line with previous studies [9, 8]. The Italian National Institute of Statistics reported that the provinces with the highest excess of mortality in Northern Italy were Bergamo (51.5%), Cremona (47.5%), Lodi (39.9%) and Piacenza (35.7%) [23]. In central and southern Italy, Pesaro-Urbino (21.1%) and Foggia (16.1%) were the most affected provinces [23]. The Instituto de Salud Carlos III together with the European mortality monitoring initiative (EuroMOMO) reported the highest excess mortality in Madrid, varying from 17.6% for age group 65 to 74 years during August 2020 to January 2021 to 21.6% for those aged 74 years or older during the period March to May 2020 [24]. Similarly to our study, Madrid, Castile-La Mancha, Castile-Leon, and Catalonia had the highest excess mortality [24].

Several factors may have contributed to the differences in excess mortality we observed during the COVID-19 pandemic across countries and regions. Mortality depends on the probability of being infected and mortality among those infected. Both probabilities vary depending on the country’s demographic and socio-economic characteristics, including age structure, ethnicity, level of deprivation, and environmental factors [14]. Further, the timeframe of non-pharmaceutical interventions in countries and regions and the resilience and capacity of health care systems have played a role [7]. The mobility of populations across borders and between regions and the timeliness of lockdowns have probably been the most important factors [25, 26].

The first wave of the pandemic was mainly exogenous, with international airports and transport routes serving as main entry points. Thus, the highest number of excess deaths during the first wave was observed in
the areas affected first, i.e., big transit hubs like London, Madrid, Lombardia and Ticino, and Geneva. From the initial point of introduction, SARS-CoV-2 spread to nearby large urban areas where community transmission was established and increased exponentially, spreading to the entire country in the absence of mobility restrictions [27]. Furthermore, during the first wave stochastic super-spreader events like the Champion’s League football game between Atalanta and Valencia on February 19, 2020 [28] played an important role in establishing community transmission [29]. The lockdowns in Italy, England and Spain were introduced after community transmission was established in the areas first affected. On the day of the national lockdown 1,797 new cases were reported in Italy, 1,159 in Spain and 2,349 in the UK. The lockdown reduced mobility, allowing some areas to maintain lower levels of community transmission and, for example, leading to the north-south divide in Italy. In Greece, a nationwide lockdown was imposed on March 13, 2020, before the country reached 100 reported cases per day, probably explaining the lack of a spatial gradient excess mortality during the first six months of 2020.

The spatial distribution of excess mortality during the second wave of the pandemic was more homogeneous, reflecting multiple routes of entry and transmission. Factors contributing to this situation included the relaxation of non-pharmaceutical interventions with the reopening of schools, retail and other activities, domestic and international travel, and the public’s loosening of preventive behaviours [30]. The timeliness of the lockdowns and population mobility again played a crucial role. Lockdowns during the second wave were slower to be implemented and less rigorous [31]. In Italy and Switzerland, the geographical distribution of the excess deaths was equal nationwide, whereas it was more variable in England, Greece and Spain. In Greece, where community transmission was not established during the first epidemic wave, the patterns observed were highly localised, mimicking the patterns observed in the other countries during the first epidemic wave. Central Macedonia (with the transit hub Thessaloniki), Eastern Macedonia and Thrace, and Western Macedonia which border on Bulgaria and Turkey, are the hardest-hit regions. On November 3, 2020, the Greek nationwide lockdown limited transmission in the rest of the country, resulting in lower excess mortality in areas in the south. In Switzerland, the area hit hardest during the second wave was the lake of Geneva region, potentially influenced by the French second wave [30].

In conclusion, this study provides the first comprehensive analysis of weekly sub-national excess mortality for 2020 across five countries, disaggregated by sex and age groups. Our findings highlight how excess mortality varied largely across countries, within countries and over time. They suggest that a timely lockdown led to reduced community transmissions and, subsequently, lower excess mortality. However, lockdowns have adverse short and long-term health, psychosocial and economic effects that need to be considered [7, 32]. Community transmission was established in the transit hubs and nearby large metropolitan areas during the first stages of
the pandemic. Therefore, rapid action to limit transmission around these hubs is essential to prevent spread to other regions and countries.

Methods

All-cause mortality. We retrieved data for all-cause deaths and population counts from the Office for National Statistics in England (derived from the national mortality and birth registrations and the Census), the Hellenic Statistical Authority in Greece, the Italian National Institute of Statistics in Italy, the National Centre of Epidemiology at the Carlos III Health Institute and the Daily Monitoring Mortality System and also the National Statistics Institute and Ministry of Justice in Spain and the Federal Statistical Office in Switzerland, Supplementary Table S8. We selected the current Nomenclature of Territorial Units for Statistics (NUTS) and in particular NUTS3 (small regions for specific diagnoses) as the main spatial unit of our analysis [33]. We also show results at the NUTS2 level, which is defined to reflect basic regions for the application of regional policies (https://ec.europa.eu/eurostat/web/nuts/background/). The number of deaths from all-causes and the population denominator was available by sex, age, week and NUTS3 region defined as areas with a population varying from 150,000 to 800,000, for 2015-2020. We used the International Organization for Standardization (ISO) week calendar, i.e. the seven consecutive days beginning with a Monday and ending with a Sunday. We aggregated mortality and population data by age groups <40, 40-59, 60-69, 70-79 and 80 years and above to maintain consistency between countries and the literature [12].

Population at risk. Population estimates for the years 2014-2020 are available for Greece, Italy and Spain for the January 1 of every year, whereas for Switzerland for December 31, Supplementary Table S7. To obtain weekly 2020 population figures we performed a two-step linear interpolation. In a first step, using the years 2015-2020, we predicted population counts by age, sex and NUTS3 regions for January 1, 2021. In a second step, we calculated weekly 2020 population figures by linear interpolation of the estimates on January 1, 2020, and January 1, 2021, by age, sex and NUTS3 regions. For England, mid-year population figures were available, Supplementary Table S7, which for 2020 were affected by COVID-19 deaths during the first wave. We, therefore, used the data for 2015 to 2019 and estimated the midyear population of 2020 through linear interpolation for England. We estimated population numbers for January 1 2020, and then used linear interpolation to obtain the weekly population of 2019, which we used as a proxy for 2020.

Covariates. As ambient temperature influences death rates [34], we retrieved data on temperature from the ERA5 reanalysis data set of the Copernicus climate data [35]. Using data from global in situ and satellite measurements, ERA5 provides hourly estimates of a large number of atmospheric, land and oceanic climate
variables, spatially and temporally compatible with our analysis [35]. For each centroid of the grid cells (at 0.25° × 0.25° resolution) that fall into the NUTS3 regions, we calculated the daily mean temperature during 2015-2020 and then the weekly mean, align temperature and mortality data. Additionally, as mortality from all causes can be different during national holidays, we also included a binary variable taking the value 1 if the week contains a public holiday and 0 otherwise.

**Statistical methods.** We used Bayesian hierarchical models to predict deaths in 2020, under the scenario of absence of the pandemic. Let $y_{jtsk}$ be the number of all-cause deaths, $P_{jtsk}$ be the population at risk and $r_{jtsk}$ the risk in the $j$-th week of the $t$-th year ($t = 1, \ldots, 5$ with year 1 corresponding to 2015), for the $s$-th spatial unit ($s = 1, \ldots, S$) and $k$-th age-sex group ($k = 1, \ldots, 10$) (male-female and <40, 40-59, 60-69, 70-79, ≥80). The models in the main analysis excluded the age group below 40 years, based on the cross-validation exercise.

We assume a Poisson distribution for the number of deaths $y_{jtsk}$ and modeled the risk $r_{jtsk}$ using the following specification:

$$y_{jtsk} \sim \text{Poisson}(r_{jtsk} P_{jtsk})$$

$$\log (r_{jtsk}) = \beta_0 t + \beta_1 Z_j + f(x_{jts}) + b_s + w_j,$$

where $\beta_0 t$ is the year specific intercept given by $\beta_0 t = \beta_0 + \epsilon_t$, with $\beta_0$ being the global intercept and $\epsilon_t \sim \text{Normal}(0, \tau_{\epsilon}^{-1})$ an unstructured random effect representing the deviation of each year from the global intercept, with $\tau_{\epsilon}$ denoting the precision of $\epsilon_t$. The term $\beta_1$ represents the effect of public holidays (i.e. $Z_j = 1$ if week $j$ contains a public holiday and 0 otherwise). The linear predictor includes also a non-linear effect $f(\cdot)$ of the average weekly temperature in each area, $x_{jts}$; in particular, we assume the following second-order random walk (RW2) model:

$$x_{jts} \mid x_{(j-1)ts}, x_{(j-2)ts}, \tau_x \sim \text{Normal} \left( 2x_{(j-1)ts} + x_{(j-2)ts}, \tau_x^{-1} \right),$$

with $\tau_x$ denoting the precision.

The term $b_s$ is a spatial field defined as an extension of the Besag-York-Mollié model given by the sum of an unstructured random effect, $v_s \sim \text{Normal}(0, \tau_v^{-1})$, and a spatially structured effect $u_s$ [36, 37, 38]. In particular $b_s$ is defined as follows:

$$b_s = \frac{1}{\tau_b} \left( \sqrt{1 - \phi} v_s + \sqrt{\phi} u_s^* \right),$$

where $u_s^*$ and $v_s^*$ are standardised version of $u_s$ and $v_s$ to have variance equal to 1 [39]. The term $0 \leq \phi \leq 1$ is a mixing parameter which measures the proportion of the marginal variance explained by the structured effect.
To account for seasonality, we included in the linear predictor a non-linear weekly effect $w_j$, common to all the areas, with a first order random walk (RW1) structure:

$$w_j \mid w_{j-1}, \tau_w \sim \text{Normal}(w_{j-1}, \tau_w^{-1})$$

where $\tau_w$ is the precision of $w_j$.

We specified minimally informative prior distributions, i.e. $\text{Normal}(0, 10^3)$ for the fixed effects $\beta_0$ and $\beta_1$. For the spatial field hyperparameters $\phi$ and $\tau_b$ we adopted priors that tend to regularise inference while not providing too strong information, the so-called penalize complexity (PC) priors introduced in [39]. In particular, for the standard deviation $\sigma_b = \sqrt{1/\tau_b}$ we selected a prior so that $\Pr(\sigma_b > 1) = 0.01$, implying that it is unlikely to have a spatial relative risk higher than $\exp(2)$ based solely on spatial or temporal variation. For $\phi$ we set $\Pr(\phi < 0.5) = 0.5$ reflecting our lack of knowledge about which spatial component, the unstructured or structured, should dominate the field $b$. Finally, PC priors are also adopted for all the standard deviations $\sigma_e = \sqrt{1/\tau_e}$, $\sigma_x = \sqrt{1/\tau_x}$ and $\sigma_w = \sqrt{1/\tau_w}$ such that for each hyperparameter $\Pr(\sigma > 1) = 0.01$.

We train the model using the years 2015-2019 and predict area level weekly mortality for 2020 assuming that the pandemic did not take place. To summarise the results we retrieve samples by age, sex, week and NUTS3 regions for 2020 from the posterior predictive distribution:

$$p(y_{jsk6} \mid \mathcal{D}) = \int p(y_{jsk6} \mid \theta)p(\theta \mid \mathcal{D})d\theta,$$

where $\theta$ is the vector of the model parameters and $\mathcal{D}$ the observed data. We report the weekly observed number of deaths in 2020 together with $p(y_{jsk6} \mid \mathcal{D})$ at the weekly resolution. We also compare $p(y_{jsk6} \mid \mathcal{D})$ with the observed number of deaths in 2020 and retrieve the posterior of the relative (percent) increase in mortality (i.e. relative to what is expected had the pandemic not occurred). We summarise the above posterior reporting medians, 95% credible intervals and posterior probability that the relative excess mortality is larger than 0.

**Model validation.** We perform a cross-validation like procedure to examine the validity of our predictions. Using the years 2015-2019, we fit the proposed model multiple times, leaving out one year at a time and predicting the weekly number of deaths by NUTS3 regions for the year left out. We repeat for the different age and sex groups, and different countries. We assess the agreement between the predicted and observed deaths at the year $t$. We use the following metrics: a) the correlation between the predicted and observed deaths and b) the 95% coverage, defined as the probability that the observed deaths lie within the 95% interval estimated from the model.
Data availability statement

We provide at https://github.com/gkonstantinoudis/ExcessDeathsCOVID the final version of the datasets for Italy and Switzerland as their mortality data is available online.

Raw mortality data files for Switzerland are provided at https://www.bfs.admin.ch/bfs/en/home/statistics/population/births-deaths/deaths.assetdetail.19184461.html and https://www.bfs.admin.ch/bfs/en/home/statistics/population/births-deaths/deaths.assetdetail.13187299.html, whereas for Italy at https://www.istat.it/it/archivio/240401. Access to mortality data for Greece, England and Spain is subject to requests. For England, the data were obtained from the Small Area Health Statistics Unit (SAHSU), which does not have permission to supply data to third parties. The data can be requested through the Office for National Statistics (https://www.ons.gov.uk/). For Greece, mortality data can be requested from ELSTAT (https://www.statistics.gr) and for Spain from the National Centre of Epidemiology at the Carlos III Health Institute (https://eng.isciii.es/eng.isciii.es/Paginas/Inicio.html).

Population data is available at the following locations:

England: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland

Greece: The selected aggregation by age, sex and NUTS3 regions is subject to a request at: https://www.statistics.gr/en/statistical-data-request

Italy: http://demo.istat.it/ricostruzione/download.php?lingua=ita for 2015-2019 and http://demo.istat.it/popres/download.php?anno=2020&lingua=itafor2020

Spain: https://www.ine.es/jaxiT3/Tabla.htm?t=9691

Switzerland: https://www.pxweb.bfs.admin.ch/pxweb/en/px-x-0102010000_102/-/px-x-0102010000_102.px/

Code availability

All models were fitted using the Integrated Nested Laplace Approximation (INLA) using its R software interface [40]. To ensure reproducibility and transparency to our results and approach the code for running the analysis is available at https://github.com/gkonstantinoudis/ExcessDeathsCOVID. Results are also provided in a Shiny app (http://atlasmortalidad.uclm.es/excess/), to facilitate communication with the general public and stakeholders.
Ethics

The analyses for England were covered by national research ethics approval from the London-South East Research Ethics Committee (Reference 17/LO/0846). Data access was covered by the Health Research Authority Confidentiality Advisory Group under section 251 of the National Health Service Act 2006 and the Health Service (Control of Patient Information) Regulations 2002 (Reference 20/CAG/0028). Data access for Greece was approved by the 28th Statistical Privacy Committee and the relevant letter of the president of the Hellenic Statistical Authority (ΤΠ-498/23-12-2020) in accordance with section 5.3 of the Minutes of the Statistical Privacy Committee. The study is about secondary, aggregate anonymised data so no additional ethical permission is required.

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Department of Health and Social Care.

Author contributions

G.K and M.B. conceived the study. M.B. supervised the study. G.K. developed the initial study protocol and discussed it with M.B., M.C., M.P. and G.B.. G.K. developed the statistical model, prepared the population and covariate data and led the acquisition of mortality data. M.C. validated and modified accordingly the code. G.K. ran the analysis for England, Greece and Switzerland, M.C. for Italy and I.L.G for Spain. G.K. wrote the initial draft and all the authors contributed in modifying the paper and critically interpreting the results. P.V, J.R., M.E. and A.L. commented extensively on previous drafts. V.G.R. developed the Shiny app. All authors read and approved the final version for publication.

Competing interests

The authors declare no competing interests.

References

[1] World Health Organization. The true death toll of COVID-19: estimating global excess mortality, 2021.

[2] Ruiyun Li, Sen Pei, Bin Chen, Yimeng Song, Tao Zhang, Wan Yang, and Jeffrey Shaman. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). Science, 368(6490):489–493, 2020.

[3] Marina Karanikolos and Martin McKee. How comparable is COVID-19 mortality across countries?, 2020.

[4] David Spiegelhalter. Coronavirus deaths: how does Britain compare with other countries?, 2020.

[5] Janusz Kaczorowski and Claudio Del Grande. Beyond the tip of the iceberg: direct and indirect effects of COVID-19. The Lancet Digital Health, 3(4):e205–e206, 2021.

[6] Nazrul Islam, Vladimir M Shkolnikov, Rolando J Acosta, Ilya Klimkin, Ichiro Kawachi, Rafael A Irizarry, Gianfranco Alicandro, Kamlesh Khunti, Tom Yates, Dmitri A Jdanov, et al. Excess deaths associated with COVID-19 pandemic in 2020: age and sex disaggregated time series analysis in 29 high income countries. BMJ, 373, 2021.
[7] Vasilis Kontis, James E Bennett, Theo Rashid, Robbie M Parks, Jonathan Pearson-Stuttard, Michel Guillot, Perviz Asaria, Bin Zhou, Marco Battaglini, Gianni Corsetti, et al. Magnitude, demographics and dynamics of the effect of the first wave of the COVID-19 pandemic on all-cause mortality in 21 industrialized countries. *Nature Medicine*, pages 1–10, 2020.

[8] Marta Blangiardo, Michela Cameletti, Monica Pirani, Gianni Corsetti, Marco Battaglini, and Gianluca Baio. Estimating weekly excess mortality at sub-national level in Italy during the COVID-19 pandemic. *PLOS ONE*, 15(10):1–15, 10 2020.

[9] Matteo Scortichini, Rochelle Schneider dos Santos, Francesca De’Donato, Manuela De Sario, Paola Michelozzi, Marina Davoli, Pierre Masselot, Francesco Sera, and Antonio Gasparrini. Excess mortality during the COVID-19 outbreak in Italy: a two-stage interrupted time-series analysis. *International Journal of Epidemiology*, 49(6):1909–1917, 2020.

[10] Hellenic statistical authority. Data on weekly deaths: Period 1st to last week, 2020, 2021.

[11] Public Health England. Excess mortality in England: weekly reports, 2021.

[12] Bethan Davies, Brandon L Parkes, James Bennett, Daniela Fecht, Marta Blangiardo, Majid Ezzati, and Paul Elliott. Community factors and excess mortality in first wave of the COVID-19 pandemic in England. *Nature Communications*, 12(1):1–9, 2021.

[13] Elizabeth J Williamson, Alex J Walker, Krishnan Bhaskaran, Seb Bacon, Chris Bates, Caroline E Morton, Helen J Curtis, Amir Mehrkar, David Evans, Peter Inglesby, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*, 584(7821):430–436, 2020.

[14] Garyfallos Konstantinoudis, Tullia Padellini, James Bennett, Bethan Davies, Majid Ezzati, and Marta Blangiardo. Long-term exposure to air-pollution and COVID-19 mortality in England: A hierarchical spatial analysis. *Environment International*, 146:106316, 2021.

[15] Julien Riou, Radoslaw Panczak, Christian L Althaus, Christoph Junker, Damir Perisa, Katrin Schneider, Nicola G Criscuolo, Nicola Low, and Matthias Egger. Socioeconomic position and the COVID-19 care cascade from testing to mortality in Switzerland: a population-based analysis. *The Lancet Public Health*, 2021.

[16] Alexander Fardman, Doron Zahger, Katia Orvin, Daniel Oren, Natalia Kofman, Janeiro Mohsen, Or Tsafrir, Elad Asher, Ronen Rubinshtein, Jafari Jamal, et al. Acute myocardial infarction in the COVID-19
era: Incidence, clinical characteristics and in-hospital outcomes—a multicenter registry. *PLOS ONE*, 16(6):e0253524, 2021.

[17] Rachel Riera, Ângela Maria Bagattini, Rafael Leite Pacheco, Daniela Vianna Pachito, Felipe Roitberg, and Andre Ilbawi. Delays and disruptions in cancer health care due to COVID-19 pandemic: Systematic review. *JCO Global Oncology*, 7(1):311–323, 2021.

[18] Camille Maringe, James Spicer, Melanie Morris, Arnie Purushotham, Ellen Nolte, Richard Sullivan, Bernard Rachet, and Ajay Aggarwal. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. *The Lancet Oncology*, 21(8):1023–1034, 08 2020.

[19] Luigi Ricciardiello, Clarissa Ferrari, Michela Cameletti, Federica Gaianill, Francesco Buttitta, Franco Bazzoli, Gian Luigi de’Angelis, Alberto Malesci, and Luigi Laghi. Impact of SARS-CoV-2 Pandemic on Colorectal Cancer Screening Delay: Effect on Stage Shift and Increased Mortality. *Clinical Gastroenterology and Hepatology: the Official Clinical Practice Journal of the American Gastroenterological Association*, 19(7):1410–1417.e9, 07 2021.

[20] Vasilis Kontis, James E Bennett, Robbie M Parks, Theo Rashid, Jonathan Pearson-Stuttard, Perviz Asaria, Bin Zhou, Michel Guillot, Colin D Mathers, Young-Ho Khang, et al. Lessons learned and lessons missed: Impact of the COVID-19 pandemic on all-cause mortality in 40 industrialised countries prior to mass vaccination. *MedRxiv*, 2021.

[21] Marília R. Nepomuceno, Ilya Klimkin, Dmitry A. Jdanov, Ainhoa Alustiza Galarza, and Vladimir Shkolnikov. Sensitivity of excess mortality due to the COVID-19 pandemic to the choice of the mortality index, method, reference period, and the time unit of the death series. *medRxiv*, 2021.

[22] Isabella Locatelli and Valentin Rousson. A first analysis of excess mortality in Switzerland in 2020. *Plos one*, 16(6):e0253505, 2021.

[23] Istituto Nazionale di Statistica (ISTAT) and Istituto Superiore di Sanità. Impatto dell’epidemia COVID-19 sulla mortalità totale della popolazione residente. Anno 2020 e Gennaio-Aprile 2021 (in Italian). *https://www.istat.it/it/archivio/258463*, 2021.

[24] Centro Nacional de Epidemiología (ISCIII). Vigilancia de los excesos de mortalidad por todas las causas. momo: Situación a 29 de diciembre de 2020, 2020.
[25] Paolo Cintia, Luca Pappalardo, Salvatore Rinzivillo, Daniele Fadda, Tobia Boschi, Fosca Giannotti, Francesca Chiaromonte, Pietro Bonato, Francesco Fabbri, Francesco Penone, et al. The relationship between human mobility and viral transmissibility during the COVID-19 epidemics in Italy. *arXiv preprint:2006.03141*, 2020.

[26] Matt J Keeling and Ken TD Eames. Networks and epidemic models. *Journal of the Royal Society Interface*, 2(4):295–307, 2005.

[27] Miguel AL Nicolelis, Rafael LG Raimundo, Pedro S Peixoto, and Cecilia S Andreazzi. The impact of super-spreader cities, highways, and intensive care availability in the early stages of the COVID-19 epidemic in Brazil. *Scientific Reports*, 11(1):1–12, 2021.

[28] Tales Azzoni and Andrew Dampf. Game zero: Spread of virus linked to champions league match, 2020.

[29] James O Lloyd-Smith, Sebastian J Schreiber, P Ekkehard Kopp, and Wayne M Getz. Superspreading and the effect of individual variation on disease emergence. *Nature*, 438(7066):355–359, 2005.

[30] Mun-Keat Looi. COVID-19: Is a second wave hitting Europe? *BMJ*, 371, 2020.

[31] J Holder, M Stevis-Gridneff, and A Mccann. Europe’s deadly second wave: How did it happen again? *The New York Times*, 2020.

[32] Itai Bavli, Brent Sutton, and Sandro Galea. Harms of public health interventions against covid-19 must not be ignored. *bmj*, 371, 2020.

[33] Regulation (EC) no 1059/2003 of the European Parliament and of the Council of 26 may 2003 on the establishment of a common classification of territorial units for statistics (NUTS), 2019.

[34] Ji-Young Son, Jia Coco Liu, and Michelle L Bell. Temperature-related mortality: a systematic review and investigation of effect modifiers. *Environmental Research Letters*, 14(7):073004, 2019.

[35] Hans Hersbach, Bill Bell, Paul Berrisford, Shoji Hirahara, András Horányi, Joaquín Muñoz-Sabater, Julien Nicolas, Carole Peubey, Raluca Rudu, Dinand Schepers, et al. The ERA5 global reanalysis. *Quarterly Journal of the Royal Meteorological Society*, 146(730):1999–2049, 2020.

[36] Julian Besag, Jeremy York, and Annie Mollié. Bayesian image restoration, with two applications in spatial statistics. *Annals of the Institute of Statistical Mathematics*, 43(1):1–20, 1991.
[37] Andrea Riebler, Sigrunn H Sørbye, Daniel Simpson, and Håvard Rue. An intuitive Bayesian spatial model for disease mapping that accounts for scaling. *Statistical Methods in Medical Research*, 25(4):1145–1165, 2016.

[38] Garyfallos Konstantinoudis, Dominic Schuhmacher, Håvard Rue, and Ben D Spycher. Discrete versus continuous domain models for disease mapping. *Spatial and Spatio-temporal Epidemiology*, 32:100319, 2020.

[39] Daniel Simpson, Håvard Rue, Andrea Riebler, Thiago G Martins, Sigrunn H Sørbye, et al. Penalising model component complexity: A principled, practical approach to constructing priors. *Statistical Science*, 32(1):1–28, 2017.

[40] Håvard Rue, Sara Martino, and Nicolas Chopin. Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations. *Journal of the Royal Statistical Society: Series B (statistical methodology)*, 71(2):319–392, 2009.
### Table 1: Age and sex-specific number of excess and observed deaths and population for 2020 by country of death.

|          | England | Greece | Italy | Spain | Switzerland |
|----------|---------|--------|-------|-------|-------------|
| **Males** |         |        |       |       |             |
| < 40     | -1,216  | 8,645  | 14,400,221 | -149  | 1,290 | 2,017,962   |
| 40-59    | 2,650   | 27,448 | 7,285,268  | 90    | 5,916 | 1,311,414  |
| 60-69    | 3,807   | 36,749 | 2,660,291  | 773   | 9,151 | 606,322    |
| 70-79    | 12,039  | 72,721 | 2,323,869  | 855   | 15,023 | 455,459    |
| ≥ 80     | 23,551  | 142,090| 1,182,213  | 3,801  | 35,476 | 164,268    |
| **Total**| 40,631  | 255,683| 28,051,858 | 5,380  | 66,856 | 5,215,425  |
| **Females** |         |        |       |       |             |
| < 40     | -488    | 4,142  | 13,913,794 | -86   | 538 | 2,434,019   |
| 40-59    | 1,308   | 17,636 | 7,443,579  | 211   | 3,075 | 1,603,581  |
| 60-69    | 1,403   | 24,300 | 3,009,520  | 485   | 4,502 | 685,346    |
| 70-79    | 7,529   | 54,344 | 2,583,842  | 308   | 9,899 | 548,506    |
| ≥ 80     | 17,987  | 179,400| 1,700,375  | 4,992  | 47,644 | 231,571    |
| **Total**| 27,739  | 279,822| 28,651,110 | 5,909  | 65,658 | 388,134    |

|          | England | Greece | Italy | Spain | Switzerland |
|----------|---------|--------|-------|-------|-------------|
| < 40     | -1,705  | 10,817 | 28,314,021 | -526  | 1,768 | 5,011,590  |
| 40-59    | 4,158   | 45,084 | 14,728,647 | 301   | 9,051 | 3,114,996  |
| 60-69    | 4,869   | 61,049 | 5,669,901  | 1,258  | 13,653 | 1,291,668  |
| 70-79    | 19,568  | 127,065| 4,907,711  | 1,161  | 24,922 | 1,003,965  |
| ≥ 80     | 41,537  | 321,490| 2,682,587  | 8,791  | 83,120 | 355,839    |
| **Total**| 68,368  | 565,505| 56,702,967 | 11,289 | 132,514 | 10,718,447 |

**Excess** = Observed - Expected

**Total**

|          | England | Greece | Italy | Spain | Switzerland |
|----------|---------|--------|-------|-------|-------------|
| < 40     | -1,216  | 8,645  | 14,400,221 | -149  | 1,290 | 2,017,962   |
| 40-59    | 2,650   | 27,448 | 7,285,268  | 90    | 5,916 | 1,311,414  |
| 60-69    | 3,807   | 36,749 | 2,660,291  | 773   | 9,151 | 606,322    |
| 70-79    | 12,039  | 72,721 | 2,323,869  | 855   | 15,023 | 455,459    |
| ≥ 80     | 23,551  | 142,090| 1,182,213  | 3,801  | 35,476 | 164,268    |
| **Total**| 40,631  | 255,683| 28,051,858 | 5,380  | 66,856 | 5,215,425  |

**Excess** = Observed - Expected

**Total**

**Excess** = Observed - Expected
Figures

Fig. 1: Posterior distribution of relative excess deaths (%) across the different countries by NUTS2 region and sex in 2020. The first panel shows the posterior of relative excess deaths in the different NUTS2 regions in England, the second in Greece, the third in Italy, the fourth in Spain and the last in Switzerland. The red line highlight the 0% relative excess deaths, which mean no observed difference in the 2020 mortality compared to the counterfactual scenario that the pandemic did not occur.
Fig. 2: Median relative excess deaths (%) across the different countries by NUTS3 region in 2020. The different panels show the median relative excess deaths in (clockwise) England, Greece, Italy, Spain and Switzerland in categories. Areas in blue indicate areas that observed less deaths than expected had the pandemic not occurred, whereas the different shades of red indicate the higher relative excess mortality. The black solid lines correspond to the NUTS2 region borders.
Fig. 3: Probability that the relative excess deaths is higher than 0% across the different countries by NUTS3 region in 2020. The different panels show the probability that the relative excess deaths is higher than 0% in (clockwise) England, Greece, Italy, Spain and Switzerland in categories. Areas in blue indicate weak evidence of an increased relative excess, areas in white insufficient evidence, whereas areas in red strong evidence. The black solid lines correspond to the NUTS2 region borders.
Fig. 4: Weekly median relative excess deaths (%) across the different countries by NUTS2 region in 2020 (left) and corresponding probability that the weekly relative excess is larger than 0% (right). The first panel shows the weekly median relative excess deaths and posterior probability form England, the second for Greece, the third for Italy, the fourth for Spain and the fifth for Switzerland. Different shades of red on the left panels indicate higher relative excess mortality, whereas the white relative excess mortality lower than 0. The white colour on the right panel indicate insufficient evidence of a relative excess larger than 0%, whereas the red strong evidence.