Evaluation of excess mortality in European all-cause mortality data

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Summary

1. All-age, all-cause mortality data from 24 European countries for the period 2015-2020 was analysed using EuroMOMO Z-scores (number of standard deviations from expected mortality).
2. Z-scores greater than four, signifying high excess mortality and reason for concern, were identified in 13/24 countries during 2020-H1.
3. Six-month rolling average Z-scores showed past mortality did not predict 2020 mortality.
4. All combinations of 2018-2019 high/low mortality followed by 2019-2020 high/low mortality were identified in European countries.
5. Maximum 2018-H1 mortality was positively correlated with 2020-H1 mortality, implying past high excess mortality predicts high 2020-H1 excess mortality.
6. Lower per capita spending on healthcare, increased residential care and high previous excess mortality are significant predictors of countries with high 2020-H1 excess mortality.

Introduction

Official weekly mortality data reported to the European monitoring group EuroMOMO (https://www.euromomo.eu) is analysed routinely using a Poisson regression model, adjusting for an annual sinusoidal periodicity. A Z-score measuring the number of standard deviations from expected deaths for each country is calculated for standard age ranges and all-ages. Normal variation is implied by Z-scores in the range ±2, with a threshold for concern over excess mortality of +4 units. Standardized mortality scores can be used as a measure of mortality to compare European countries and help identifying those with excess 2020 all-cause mortality. In this white paper we consider whether past all-age all-cause mortality is a predictor of excess 2020 mortality and identify useful predictors of whether a country is likely to have experienced excess 2020 all-cause mortality (Z-score > 4).

Methods

All-age Z-scores for 24 countries for the period 2015-1 to 2020-35 were entered manually from https://www.euromomo.eu/graphs-and-maps/ on 23/SEP/2020 in wide format. Data was transformed and a 26-week rolling mean calculated for each country to investigate robust mortality trends. Weeks were subdivided into H1 (up to and including Week 26) and H2 (after Week 26). Maximum Z-score for each half-year was calculated.

Raw and summary Z-score data was plotted by year and country. Individual country 26-week rolling mean Z-score data (as a proxy for average number of deaths in the previous half-year period) was plotted against median, inter-quartile (IQR, P25-P95) and inter-decile (IDR, P10-P90) ranges for all other countries (i.e., N = 23). Maximum 2020-H1 Z-score was plotted against previous H1 and H2 values, with linear regression used to identify correlations. Countries were classified as having high excess 2020 COVID19 mortality (maximum 2020-H1 Z-score > 4) or not, "BIG4" (France, Italy, Spain, England – note Germany submits regional data only), UK only (England, Northern Ireland, Scotland, Wales), Mediterranean (Greece, Italy, Malta, Portugal, Spain), Benelux (Belgium, Luxembourg, Netherlands), Germanic (Germany – Berlin and Hesse regions, Austria Switzerland), and Other (Estonia, Hungary, Ireland).

Explanatory healthcare covariates were collated from ONS information, including OECD per capita spending, where healthcare is provided as a percentage of total care (ONS report: How does UK healthcare spending compare with other countries?, Data Source Figures 1, 6 and 7). Mean and maximum Oxford COVID19 Government Response Tracker (OxCGRT) were also calculated for consideration as a measure of government intervention.

The probability of a country having high excess 2020 COVID19 mortality (maximum 2020-H1 Z-score > 4) was modelled using logistic regression with continuous healthcare spending, healthcare utility, average lockdown stringency and epidemic size covariates. The impact of past epidemics history was included by addition of maximum Z-scores for past years. Odds ratios for high excess 2020 COVID19 mortality were calculated for unit increases in significant covariates identified by automated forward selection based on Bayes Information Criteria.

All analyses were conducted using SAS9.4. Data and SAS code are available on request.

Results

All-cause mortality Z-score data

Baseline all-cause mortality for 24 countries as of 23/SEP/2020 is shown in Figure 1 for the period 2015-1 to 2019-52. The shaded band shows the typical normal range (±2) and a level of concern (Z = 4) is also indicated. Significant excess mortality is noted from seasonal influenza epidemics in 2014-2015, 2016-2017 and 2017-2018. The period 2018-2019 shows a lower peak (maximum Z = 8, compared with >10 for previous influenza seasons). Also, of note is excess summer mortality during the summer of 2018 which recorded a heatwave (Z = 6).

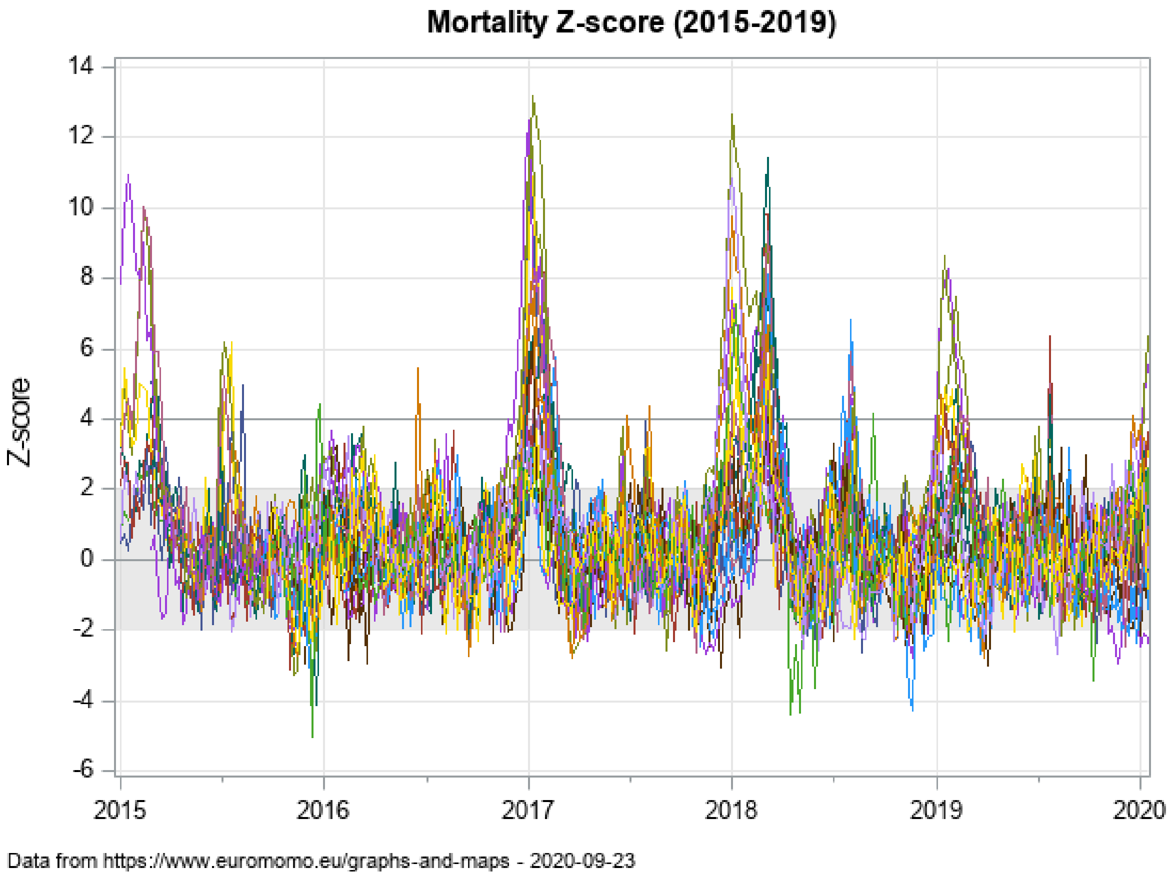

Figure 1

Plotted on the same scale for reference, Figure 2 shows the Z-scores for 2020 for the same 24 countries. Data for the last three weeks should be interpreted with caution since it is subject to reporting delays for which EuroMOMO make a model adjustment. It is immediately clear from the plot that the scale of the 2020 COVID19 epidemic has produced Z-scores in excess of previous years for many countries. It is also evident that other countries have maintained Z-scores below the level of concern, some within the normal shaded bounds of ±2.

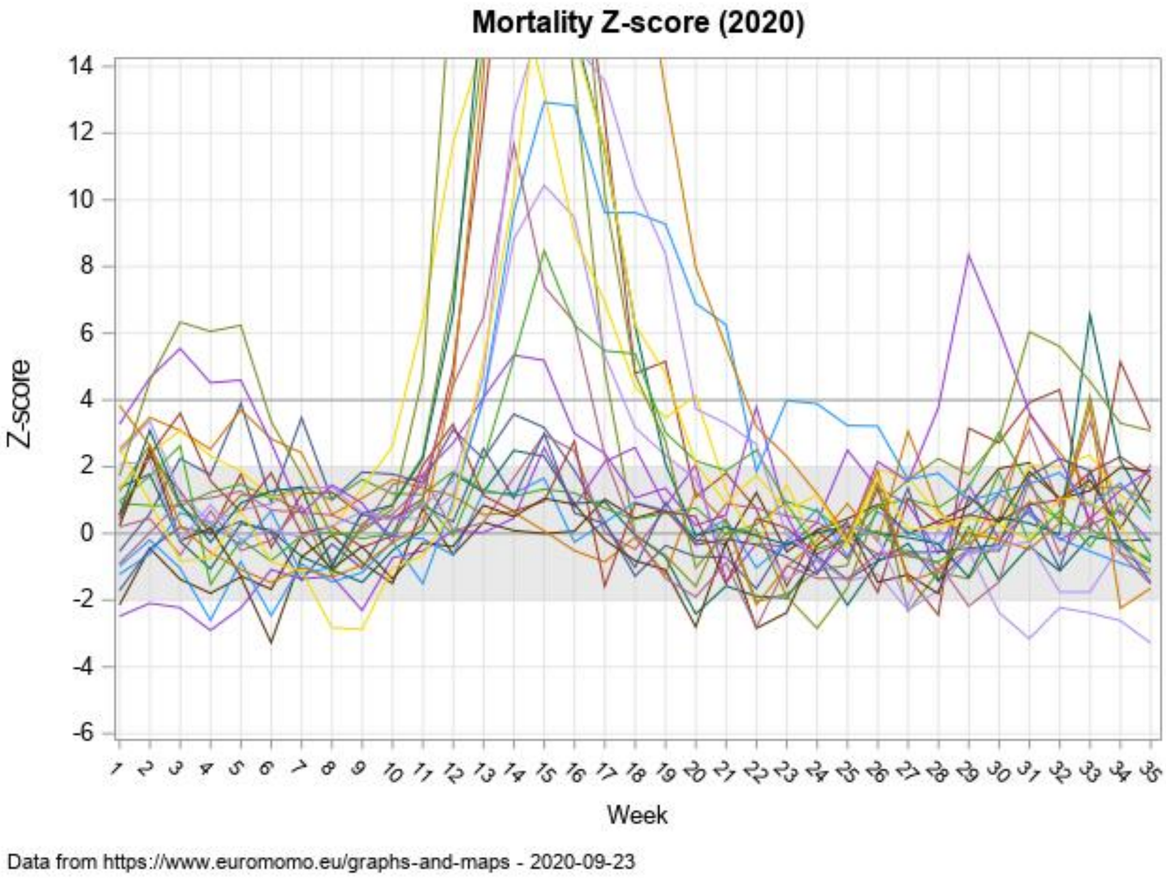

Figure 2

Figure 3 shows Z-score by year for each of the 24 EuroMOMO countries. Many countries recorded their maximum excess mortality in 2020. Identification of the thirteen countries with maximum 2020-H1 Z-score > 4 is relatively straightforward (Belgium, France, Ireland, Italy, Netherlands, Portugal, Spain, Sweden, Switzerland, and UK: England, Northern Ireland, Scotland, Wales).

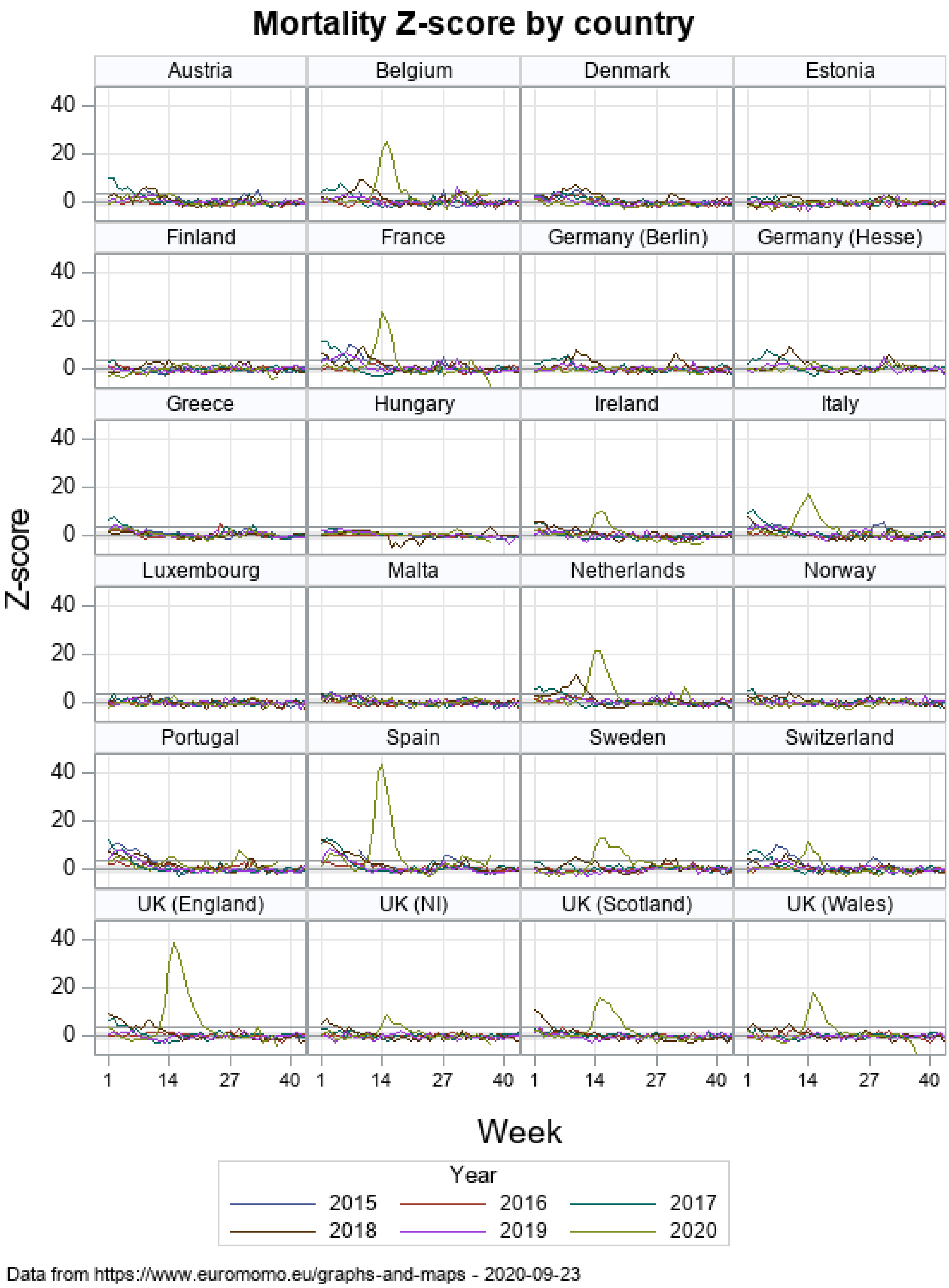

Figure 3

Median Z-score, IQR and IDR are shown in Figure 4 for the period 2015-1 to 2020-35, summarising all 24 countries. The peak of the median for 2020-15 is 6.30 (IDR 0.97, 25.08), which is one point higher than the previous peak of 2017-2 (Table 1). There is, however, a striking difference in distribution, with an 8-point rise in IQR (P75, 75th percentile) and a 14-point rise in IDR (P90, 90th percentile) indicating a substantial difference in all-cause mortality distribution pattern for 2020.

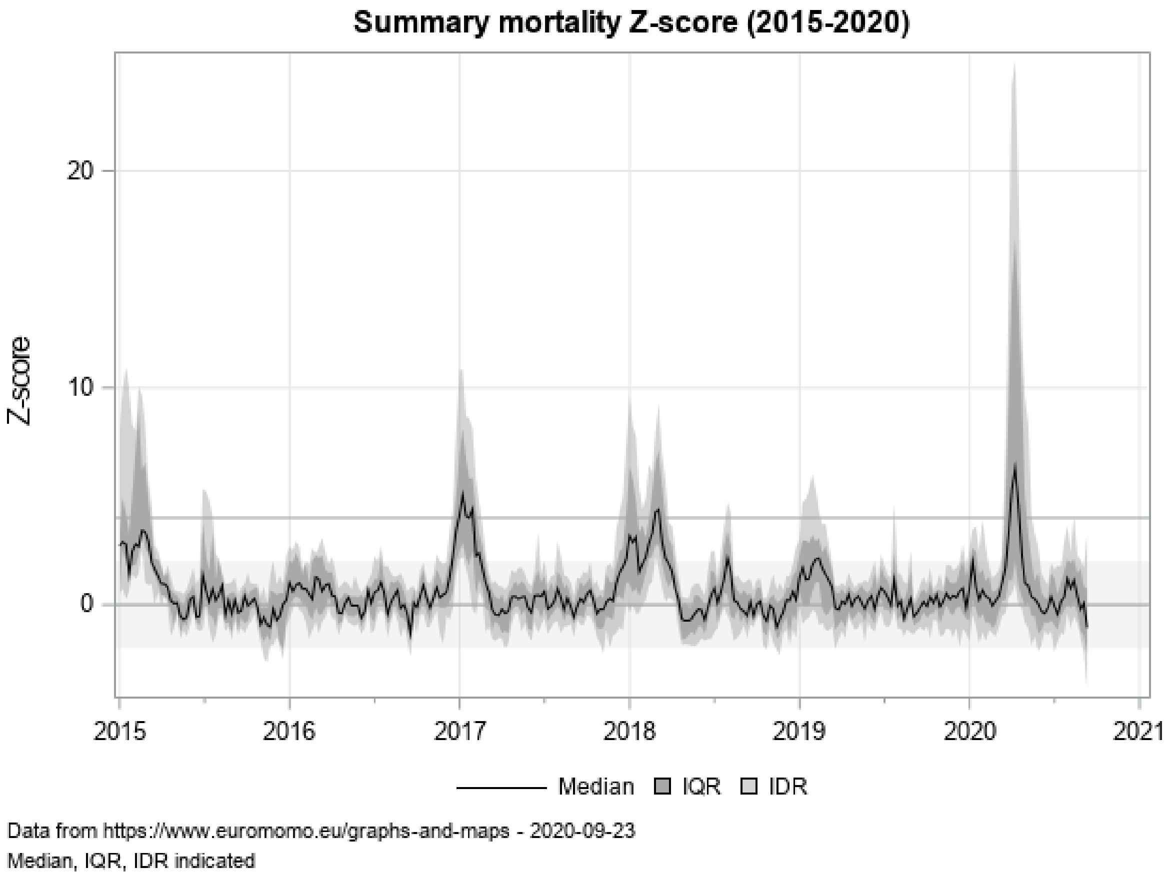

Figure 4

Week	Median	P10	P90	P25	P75
2015-8	3.42	2.53	9.64	3.26	6.22
2016-52	3.41	1.42	7.95	1.97	4.97
2017-2	5.06	2.21	10.87	2.85	8.11
2018-10	4.40	1.65	9.34	2.74	7.13
2019-7	2.15	-0.95	4.30	1.06	3.10
2020-15	6.30	0.97	25.08	1.99	16.87

Table 1 Peak median, IQR and IDR Z-scores for 2015-2020 from EuroMOMO all-cause mortality database (23/SEP/2020)

Classification by high excess 2020 COVID19 mortality (maximum 2020-H1 Z-score > 4) is shown in Figure 5. A Loess regression of both sets of data shows evidence of an epidemic peak in countries without high excess mortality, and limited evidence of rising mortality from 2020-30. No geographic classifiers were able to separate countries into high and low excess mortality (not shown).

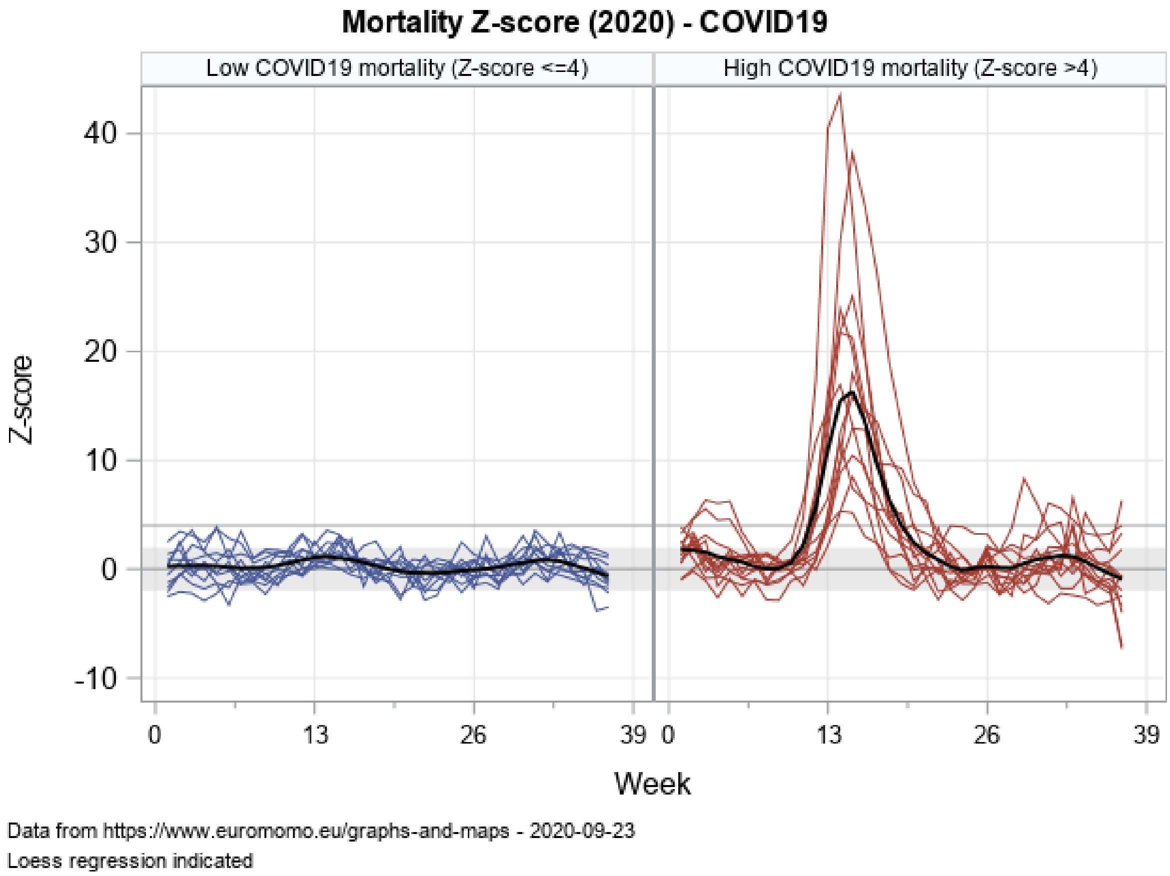

Figure 5

Rolling average all-cause mortality Z-scores

A rolling mortality score captures overall all-cause mortality over a period of interest. Summing deaths over the previous 26-week period (i.e., half-year) indicates whether excess mortality in the previous six-month rolling period has had any impact on current mortality. For example, a large seasonal influenza epidemic early in a year might manifest in lower mortality later in the year as people may have died earlier. Figure 6 shows the 26-week rolling average mortality for the period 2015-2020 subdivided by high excess 2020 COVID19 mortality (maximum 2020-H1 Z-score > 4). It is notable that many countries with high 2020 excess mortality show consistently high past excess mortality during the winters of 2016-2017 and 2017-2018.

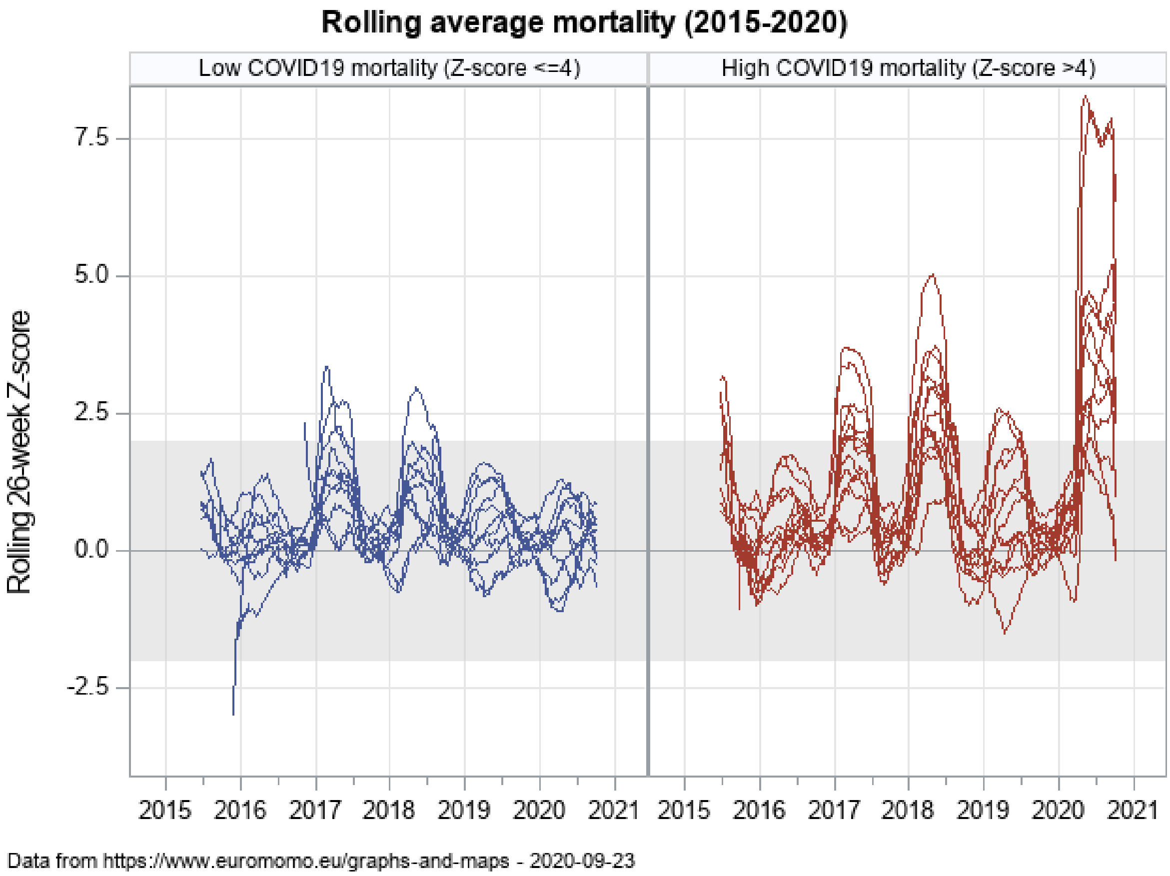

Figure 6

Comparing individual countries (N = 1) with summary distributions from all other countries (i.e., N = 23), Figure 7 presents examples of four possible combinations of epidemic profiles with individual country mortality above and below the median for 2018-2019 and above and below the median for 2019-2020. Figure 8 shows the same plot for the “BIG4” countries, Figure 9 the Scandinavian countries, Figure 10 the Germanic countries, and Figure 11 the United Kingdom by constituent country. It is notable that outside of Germanic countries, the plots show few consistent patterns for prediction of 2020 COVID19 mortality.

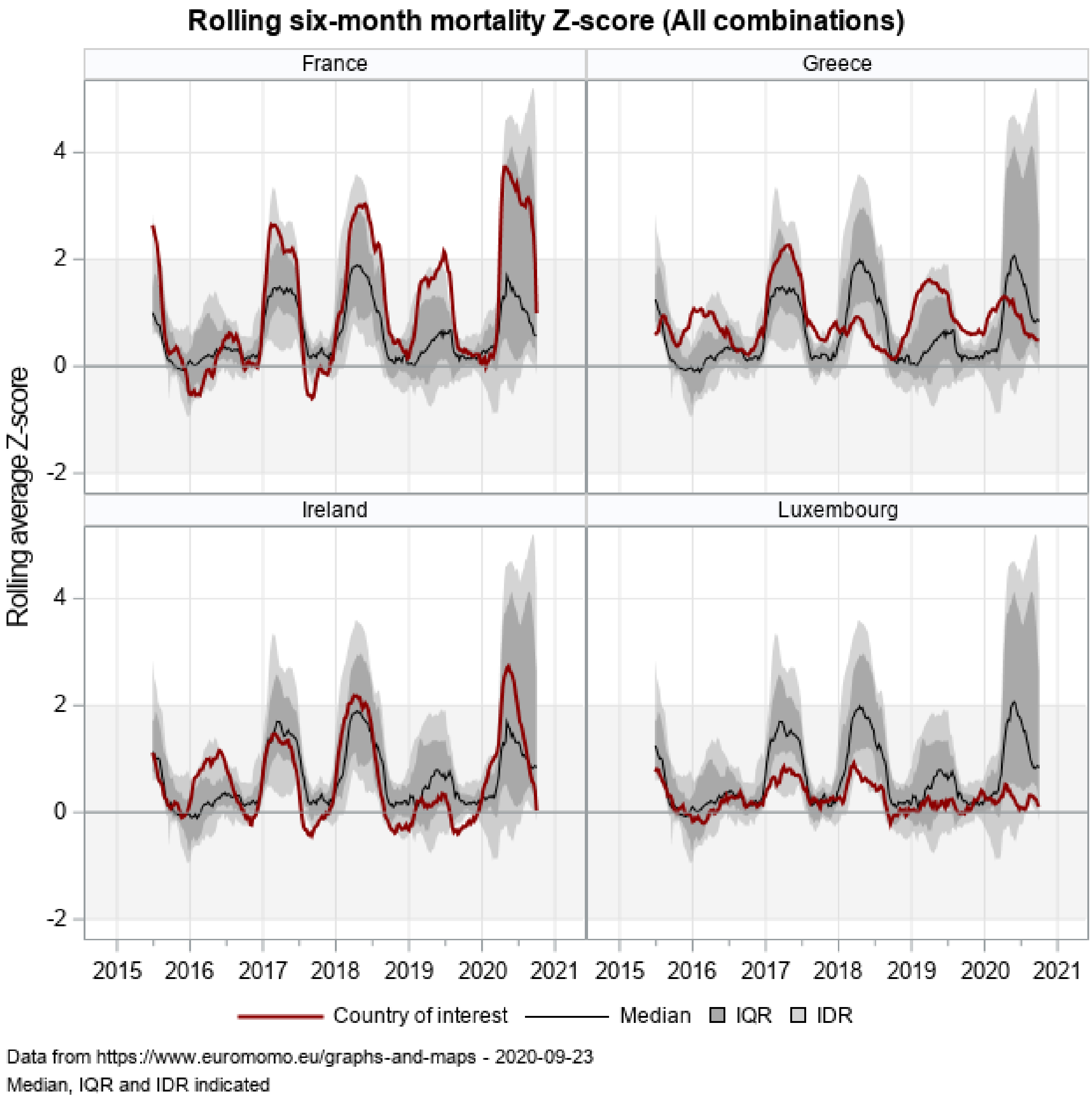
Rolling six-month mortality Z-score (All combinations)
France
Greece
Ireland
Luxembourg
Rolling average Z-score
4
2
0
-2
2015 2016 2017 2018 2019 2020 2021
Country of interest
Median
IQR
IDR
Data from https://www.euromomo.eu/graphs-and-maps - 2020-09-23
Median, IQR and IDR indicated

Figure 7

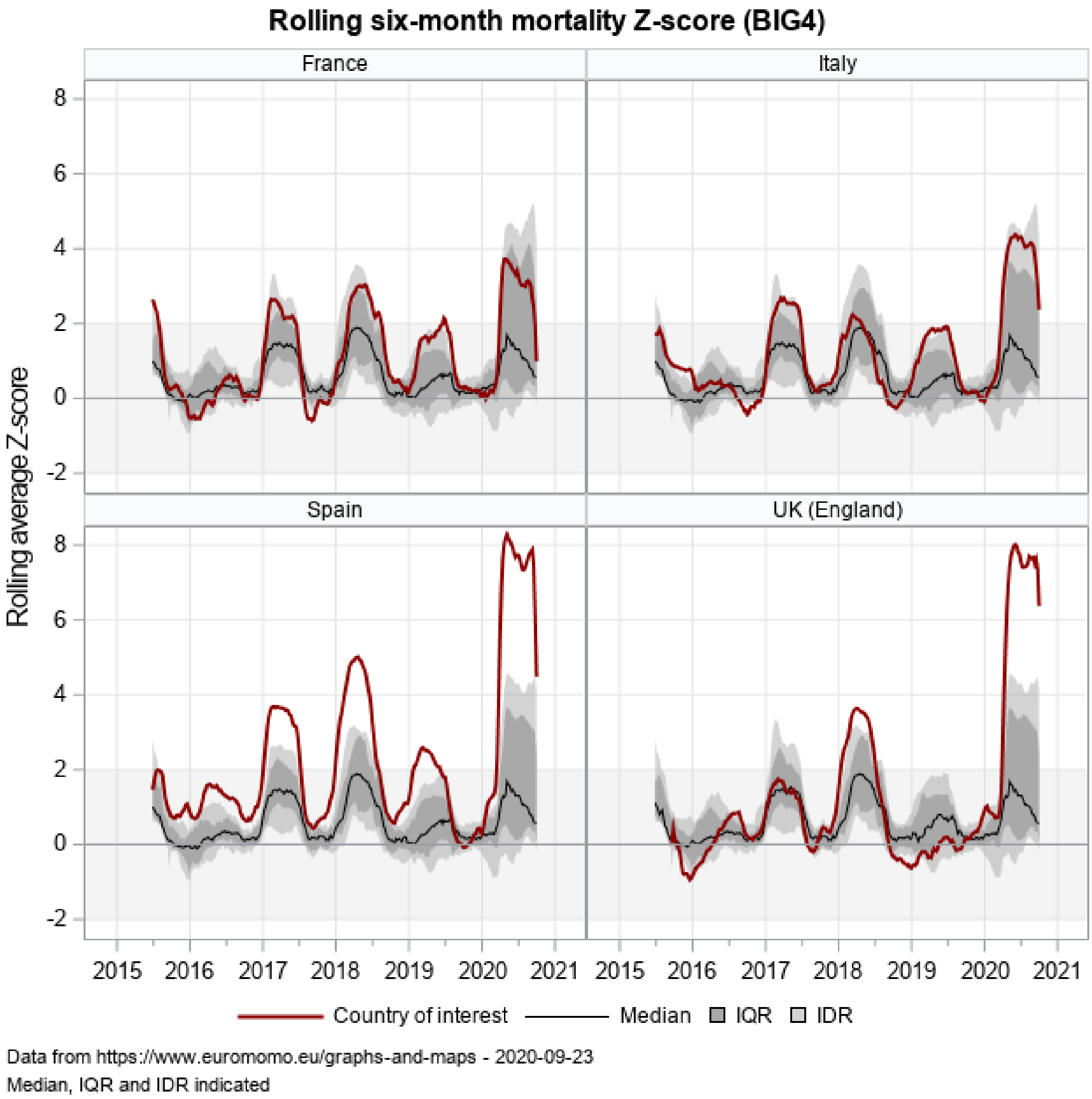
Rolling six-month mortality Z-score (BIG4)
France
Italy
Spain
UK (England)
Rolling average Z-score
8
6
4
2
0
-2
2015
2016
2017
2018
2019
2020
2021
Country of interest
Median
IQR
IDR
Data from https://www.euromomo.eu/graphs-and-maps - 2020-09-23
Median, IQR and IDR indicated

Figure 8

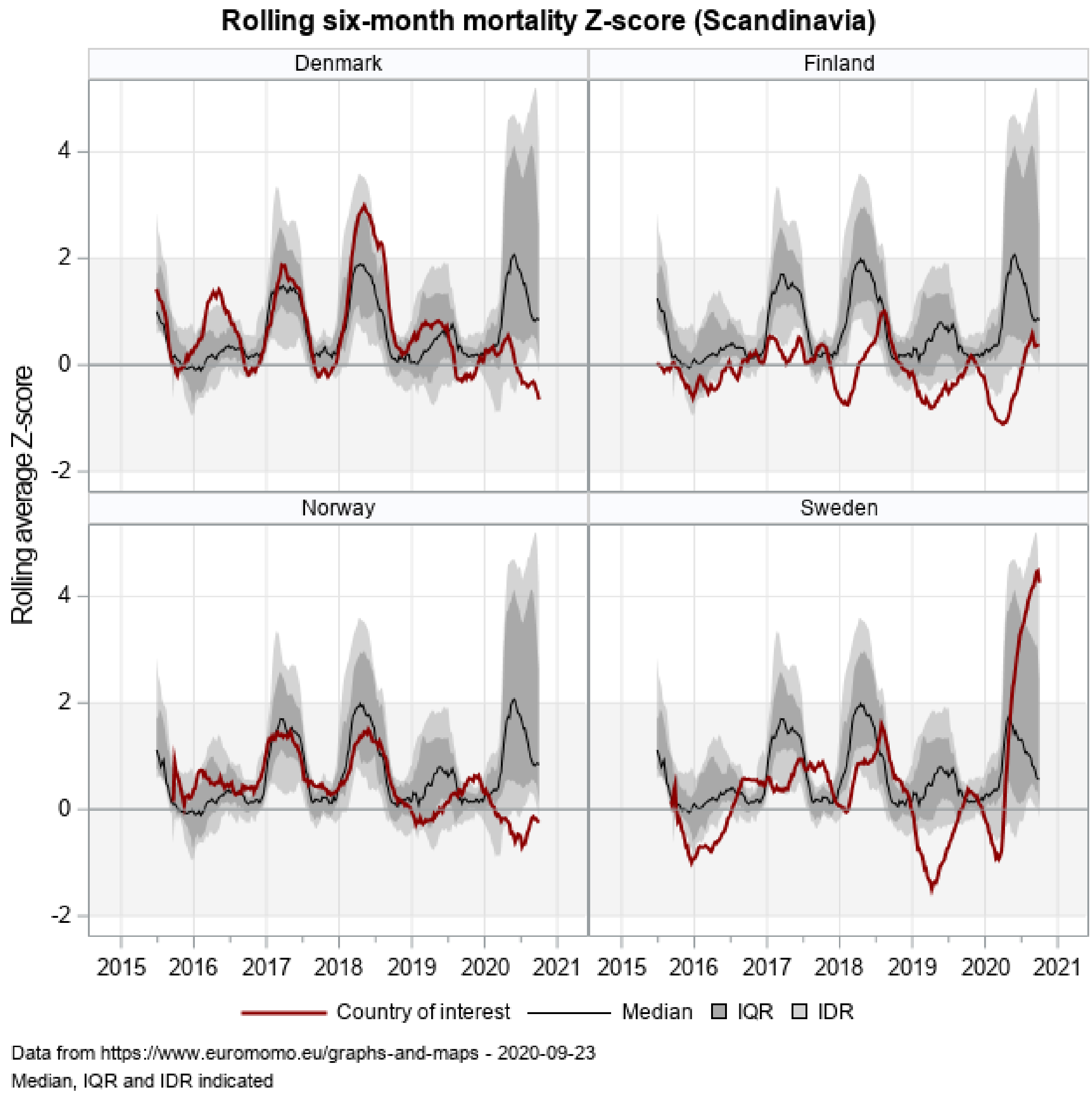
Rolling six-month mortality Z-score (Scandinavia)
Denmark
Finland
Norway
Sweden
Rolling average Z-score
4
2
0
-2
2015
2016
2017
2018
2019
2020
2021
Country of interest
Median
IQR
IDR
Data from https://www.euromomo.eu/graphs-and-maps - 2020-09-23
Median, IQR and IDR indicated

Figure 9

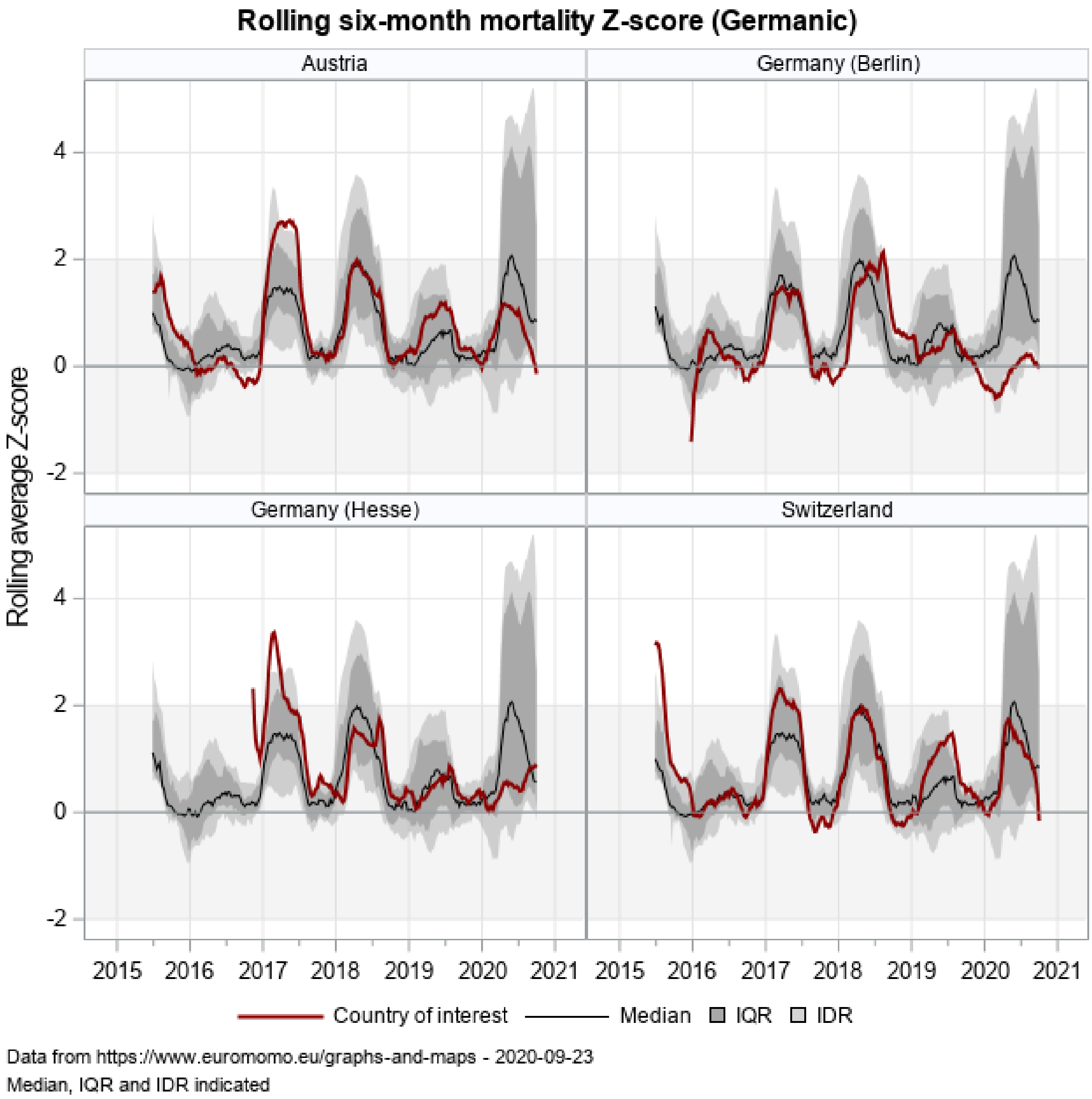
Rolling six-month mortality Z-score (Germanic)
Austria
Germany (Berlin)
Germany (Hesse)
Switzerland
Rolling average Z-score
4
2
0
-2
2015
2016
2017
2018
2019
2020
2021
Country of interest
Median
IQR
IDR
Data from https://www.euromomo.eu/graphs-and-maps - 2020-09-23
Median, IQR and IDR indicated

Figure 10

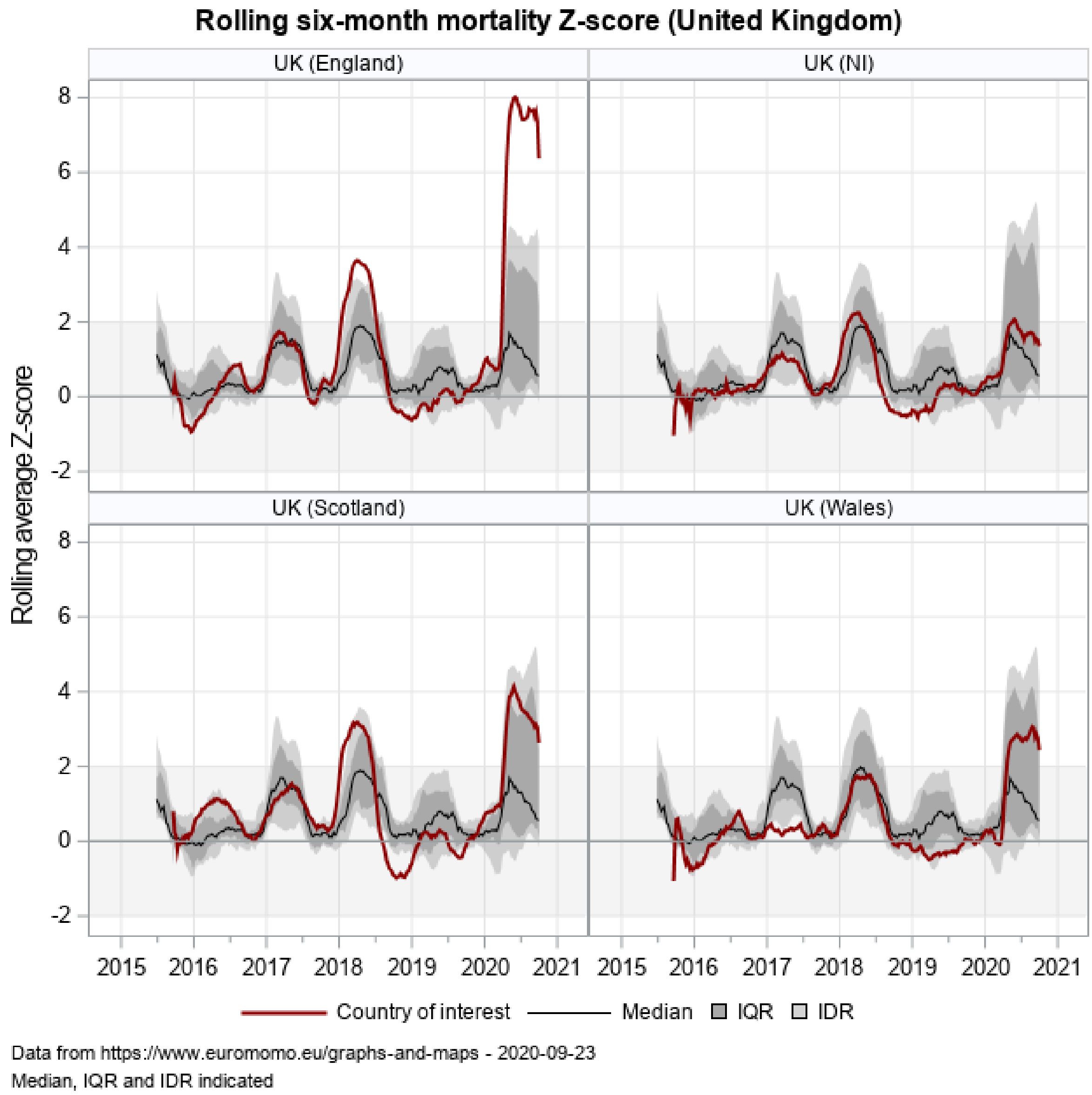

Figure 11

Regression analysis of previous epidemics with 2020

It is not unreasonable to presume that the magnitude of past epidemics may predict future epidemics. A period of excess mortality of susceptibles (who have survived or been missed by a previous influenza season) may follow a period of low excess mortality, and vice-versa. Regression analysis of maximum 2020-H1 Z-score vs. previous maximum Z-scores for 2018 and 2019 showed little correlation, with the exception of 2018-H1, and no correlation whatsoever for countries with maximum 2020-H1 Z-score $\leq$ 4 (Figure 12).

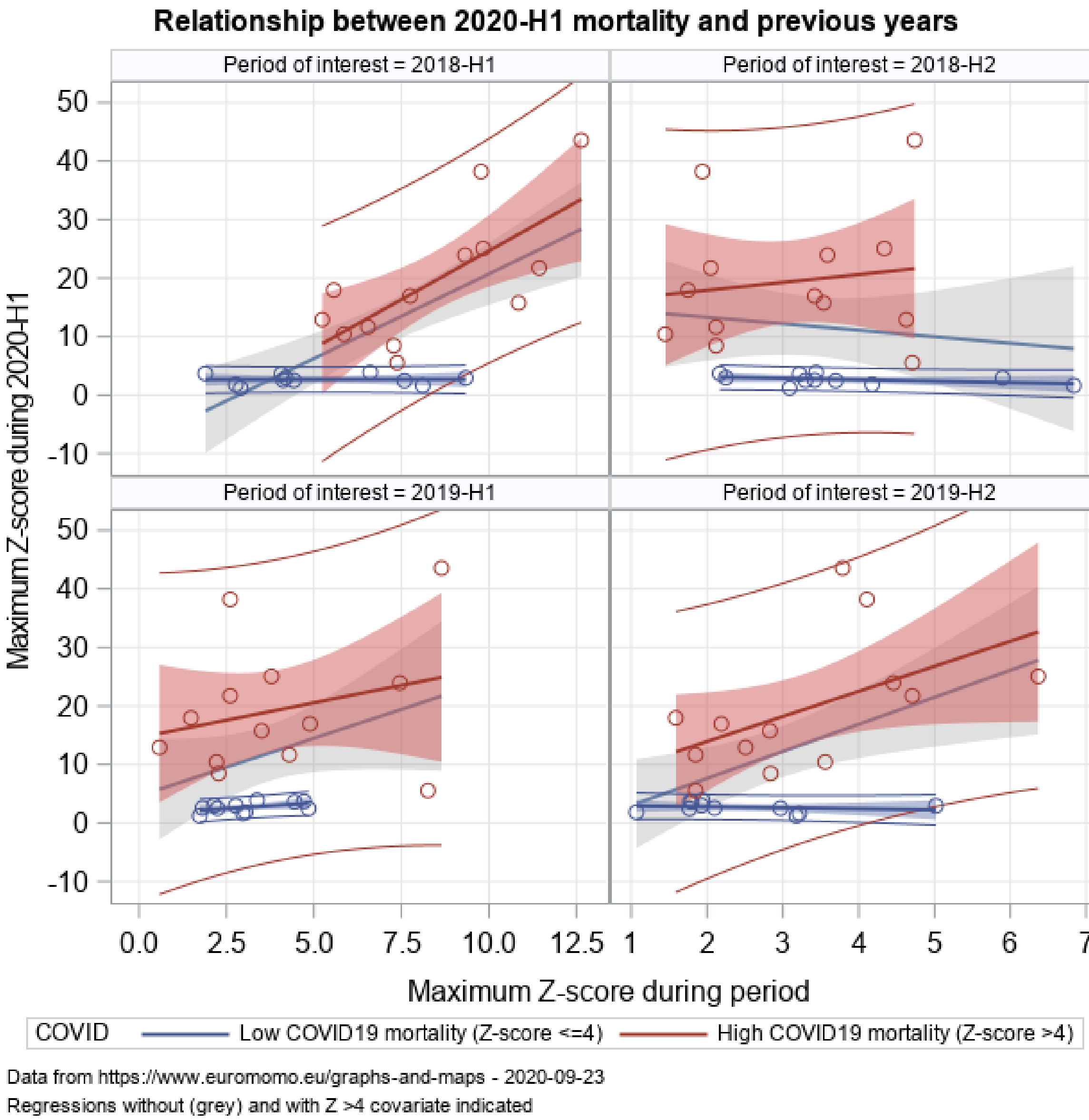

Figure 12

Selecting 2018-H1 as the best predictor of 2020-H1, there is a highly significant positive (rather than negative) correlation between 2018-H1 Z-score and 2020-H1 Z-score ($P < 0.001$, $R = 0.713$, Figure 13). This finding implies that countries that have previously suffered high excess mortality are more likely to have high 2020-H1 excess mortality.

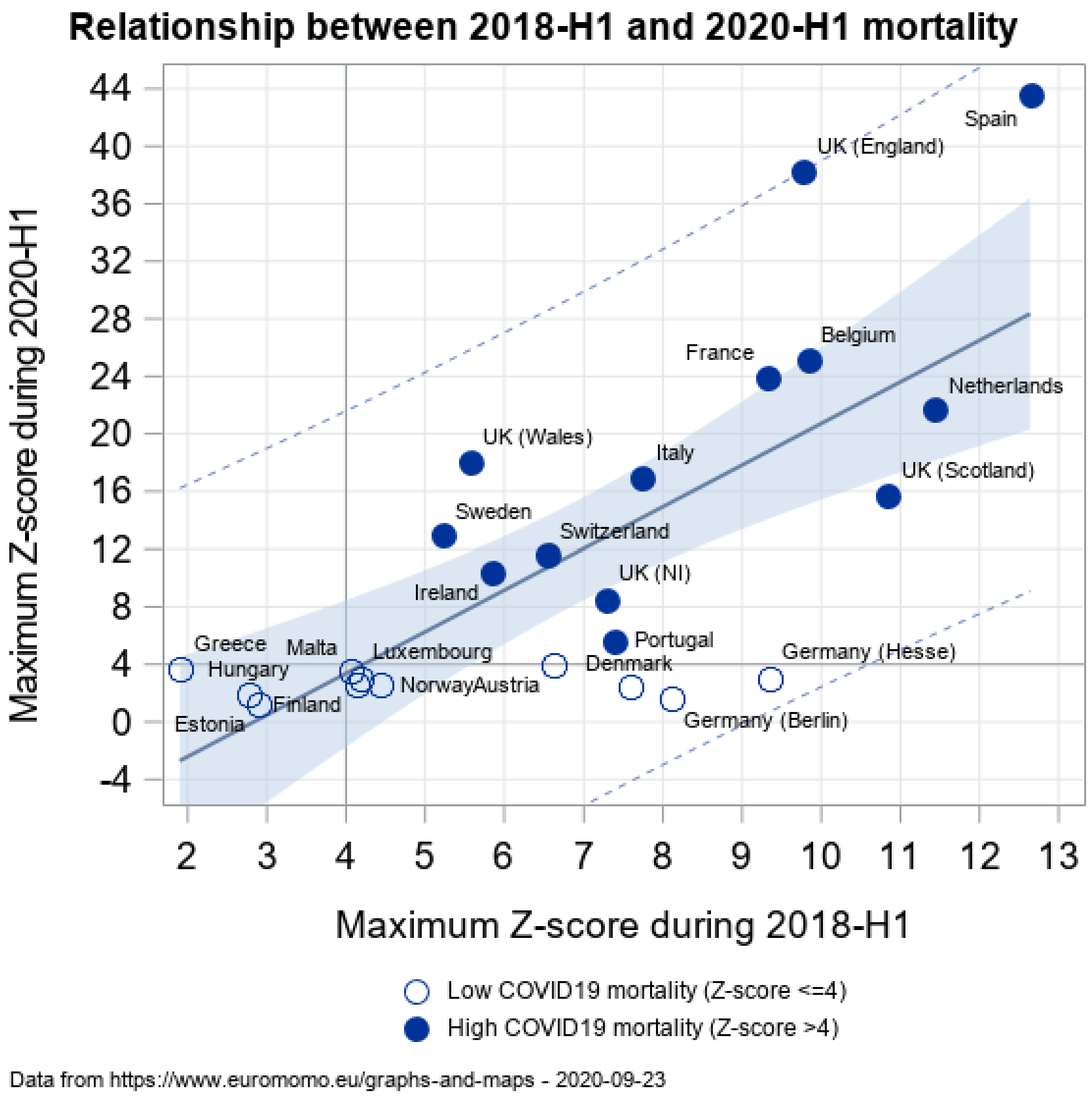

Figure 13

Predictors of COVID19 epidemic

A logistic regression was used to predict whether a country was likely to have high excess 2020 COVID19 mortality (maximum 2020-H1 Z-score > 4). Covariates included in the analysis were; OECD per capita healthcare spending; percentage spending on residential care (as a proxy for nursing home utility); mean COVID19 Government Response Tracker (OxCGRT) stringency; and previous maximum recorded Z-scores by half-year for 2019-H1 and 2018-H1.

Automated selection criteria (SAS 9.4 proc hplogistic, forward selection based on Bayes Information Criteria, stopping when no suitable add or drop parameters could be found) identified OECD healthcare spending, percent residential care, and maximum 2018-H1 Z-score as significant predictors (all P < 0.05).

The final model had a ROC-AUC of 0.931, implying that more than 22/24 countries in the European dataset are correctly identified with these three covariates, the high sensitivity perhaps driven by the almost even split (13 – 11) for high and low 2020-H1 Z-scores (despite limited sample size). The final model identified significant odds ratios for excess mortality (albeit with relatively wide intervals) as follows: the odds ratios for a country having high excess 2020 COVID19 mortality (maximum 2020-H1 Z-score > 4) increase 1.68-fold (95% CI 1.05-2.69) for every 1% increase in residential care as a percentage of total healthcare spending, 2.84-fold (95% CI 1.07-7.50) fold for every 1-point increase in 2018-H1 Z-score, and reduce by 0.78-fold (95% CI 0.62-0.99) for every per capita £100-equivalent increase in OECD spending. Of note, average stringency of Government response was not a significant predictor (although only a summary measure was included).

Conclusions

Analysis of European all-age all-cause mortality data can provide a "gold standard" for investigation of the population effects of the ongoing global COVID19 epidemic. Standard measures of excess mortality are provided by the EuroMOMO group in the form of Z-scores – the number of standard deviations weekly observations are from historic Poisson regression predicted mean – and allow country-to-country comparisons. Z-score values of ±2 are within normal range for variability. Values greater than four signal cause for concern.

We analyse EuroMOMO weekly all-age all-cause mortality Z-scores for the period 2015-1 to 2020-35 for 24 European countries. Z-scores identify both seasonal winter influenza epidemics and summer heat-wave mortality. Values of greater than 10 are unusual. The highest recorded median Z-score across all 24 countries for the period 2015-2019 was 5.06 (IDR 2.2 – 10.9). From the 24 countries contained in the dataset, we identified thirteen countries with high excess 2020 COVID19 mortality (maximum 2020-H1 Z-score > 4), signalling grounds for concern. Geographic location was unable to account for this finding.

One explanation proposed for the high excess mortality observed in some countries in 2020, is that earlier influenza seasons were mild (with lower than expected mortality), leading to an increase in the population susceptible to COVID19. These people might have been expected to die when the SARS-COV2 epidemic hit, having avoided previous infectious peril. We find no evidence in all-age mortality data that this has happened on a European scale. In fact, we find examples of all possible counterfactuals. Six-month rolling average Z-scores for all countries were compared with the statistical distribution from the remaining 23 countries. We identified countries that had low 2018-2019 excess mortality (i.e., below the median of other countries), followed by high 2019-2020 excess mortality (i.e., above the median of other countries). However, we also find all other possible combinations (i.e., high/high, high/low and low/low), refuting the notion that high 2019-2020 excess mortality must have followed from a mild previous influenza epidemic.

To further test this hypothesis, correlations between past maximum half-year Z-scores were correlated with maximum 2020-H1 Z-score for the 24 EuroMOMO countries. Previous excess all-cause mortality might imply a negative correlation for 2018-H2, 2019-H1 and 2019-H2 Z-scores. No such negative correlation is found. In fact, we observed the opposite – countries that recorded high 2018-H1 excess mortality also recorded high 2020-H1 mortality, implicating other factors above and beyond past epidemic history.

In order to explain why some countries experienced high 2020-H1 excess mortality (defined as a maximum Z-score greater than 4), whilst others did not, we collated possible explanatory covariates relating to healthcare expenditure, healthcare provision, government intervention (Oxford COVID19 Government Response Tracker (OxCGRT), and past maximum excess mortality Z-scores. Using logistic regression, we find that whether a country experienced high excess mortality in 2020-H1 is well-predicted by OECD healthcare spending, percentage of healthcare spent on residential care (as a proxy for nursing home utility) and maximum recorded 2018-H1 Z-score. After adjusting for these covariates, average stringency of government response was not a predictor of high excess mortality (date of onset rather than an average measure was not tested). We find that reducing per capita OECD healthcare spending, increasing the proportion spent on residential care and the magnitude of previous excess mortality in 2018-H1 all increase the likelihood of high 2020-H1 excess mortality. As noted from the simple correlation analysis, countries that have a history of being affected by high excess seasonal mortality are more likely to have been affected by COVID19 in 2020.

In summary, we find no evidence from EuroMOMO European all-age all-cause mortality data to support the hypothesis that high excess mortality recorded in 2020 during the COVID19 epidemic has resulted from lower historic mortality. We do, however, find that reduced healthcare spending, increased residential care and a history of past epidemics are significant predictors of whether a country experienced excessive mortality in 2020.

Data sources

EuroMOMO all-age Z-score mortality data was sourced my manual input from https://www.euromomo.eu/graphs-and-maps/ on 23/SEP/2020. Note the Z-score is dependent on model inference, and very small deviations in Z-score are to be expected when the country model is periodically updated with new data. Data was subject to sparse QC for the period 2015-2019, with full QC for 2020.

Covariates for healthcare expenditure and utility were downloaded in csv format from the ONS website, input and merged.

https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthcaresystem/articles/howdoesukhealthcarespendingcomparewithothercountries/2019-08-29

The most up to date Oxford COVID-19 Government Response Tracker (OxCGRT) metric was downloaded from https://www.bsg.ox.ac.uk/research/research-projects/coronavirus-government-response-tracker. Summary measures for each EuroMOMO country were calculated and merged with other healthcare covariates. Date of onset of government action was not included as a covariate, nor mortality at date of onset.

Acknowledgements

We acknowledge the EuroMOMO organisation and the dedicated teams who collate official country-wide mortality statistics.

Further ongoing work

The work presented here relies on derived Z-scores from the 24-countries that form EuroMOMO for the period 2015-2020. Further work is ongoing using raw published mortality data from *The Human Mortality Database* collated at https://www.mortality.org/. This dataset features source mortality data for 41 countries including the United States and Japan. Historic data for the period 2000-2010 will be used to derive country-specific per capita mortality rate distributions by age group and week of year. Data-derived Z-scores for per capita mortality for a longer period in more countries can then be calculated.