Excess mortality during the COVID-19 pandemic in countries across the globe: results from the C-MOR consortium study

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COVID-19 MORtality (C-MOR) Consortium

- An international consortium consisting of 58 institutions across six continents was established to investigate the mortality impact of COVID-19, https://www.unic.ac.cy/coronavirus/mortality/

- Recent publications:

1) Achilleos, S., Quattrocchi, A., Gabel, J., *et al*. Excess all-cause mortality and COVID-19- related mortality: a temporal analysis in 22 countries, from January until August 2020, *International Journal of Epidemiology*, 2021;,dyab123, https://doi.org/10.1093/ije/dyab123

2) Ugarte, M.P., Achilleos, S., Quattrocchi, A. *et al.* Premature mortality attributable to COVID- 19: potential years of life lost in 17 countries around the world, January–August 2020. *BMC Public Health* **22,** 54 (2022). https://doi.org/10.1186/s12889-021-12377-1

2) Demetriou, C.A., Achilleos, S., Quattrocchi, Al, et al, on Behalf of the C-MOR Consortium, Impact of the COVID-19 pandemic on total, sex- and age-specific all-cause mortality in 20 countries worldwide during 2020: results from the C-MOR project, *International Journal of Epidemiology*, 2022;, dyac170, https://doi.org/10.1093/ije/dyac170

Background

- Analysis of all-cause mortality is an important tool to investigate the impact of the COVID-19 pandemic
- Possibly a more informative metric of impact than COVID-19 specific mortality due to:
  - Differences in testing and reporting COVID-19 deaths in different countries
  - Reflects both direct and indirect COVID-19 mortality

Objective

To investigate the overall, sex and age-specific excess all-cause mortality in 2020, using national mortality databases from 20 countries part of the C-MOR consortium

Results published in:
Christiana A Demetriou, Souzana Achilleos, Annalisa Quattrocchi, et al, on Behalf of the C-MOR Consortium, Impact of the COVID-19 pandemic on total, sex- and age-specific all-cause mortality in 20 countries worldwide during 2020: results from the C-MOR project, *International Journal of Epidemiology*, 2022;, dyac170, https://doi.org/10.1093/ije/dyac170

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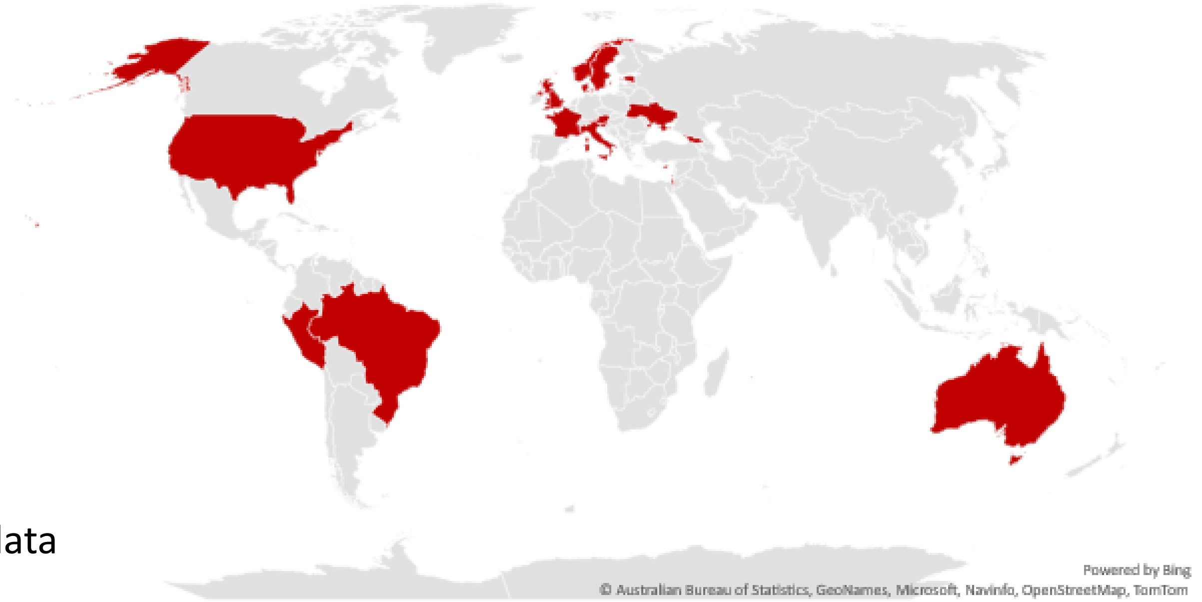
Methodology – Data Collection

- National all-cause mortality data was provided by C-MOR partners from national mortality databases:
  - Total, sex and age-specific weekly all-cause mortality
  - Time period: 2015–2020
  - 20 countries



- Week was defined as ISO, Epi or national counting week depending on the country
- Mortality data collected during June-July 2021
- Data provided was cross-checked against publicly available data for countries for which information was available
  - Minor inconsistencies observed; can be explained by retrospective addition of cases and/or delays in reporting of deaths.

Methodological challenges: reporting delays

- Delays in reporting of deaths
  - Ranging from a few days to a few weeks, depending on the country

- Data were collected during June-July 2021, several months after the end of the study period, to account for reporting delays and to allow enough time for data consolidation by reporting authorities toward better data quality

Methodological challenges: COVID-19 death definition

- COVID-19-death reporting differed between countries
  - Some countries reported as COVID-19 deaths any deaths among positive cases irrespective of where COVID-19 was listed on the death certificate
    - Thus, COVID-19 was either listed among the chain of causes leading to death or as a contributing condition on the death certificate
  - Other countries reported as COVID-19 deaths only the deaths for which COVID-19 was listed among the chain of causes leading to death
    - Of these latter countries, France reported only hospital and nursing-home COVID-19 deaths.

- This heterogeneity in COVID-19 death reporting precluded any comparisons of COVID-19 direct mortality or any calculations of the % of excess mortality that is attributable to COVID-19
  - Further supports the use of all-cause mortality as a valid and more homogeneous measure of the impact of the COVID-19 pandemic.

Methodological challenges: differences in population denominators between countries and between years

- To account for differences in population denominators between years and between countries, **mortality rates** rather than deaths were used

- Mid-year population estimates
  - From the United Nations Population Division/World bank, except for:
    - The UK nations: sub-level data from the Office for National Statistics
    - Cyprus: Eurostat data including only the population in the Republic of Cyprus government-controlled area.

$$Crude\ mortality\ rate\ (CMR)_{y,w} = \frac{D_{y,w}}{P_y\ /\ N_w} \times 100{,}000 \qquad (1)$$

where $D_{y,w}$ = number of deaths in all age-groups in one week, P=mid-year population, and N_w = number of weeks in the year.

Methodological challenges: differences in age structure between countries and between years

- To account for differences in population age structure between years and between countries, **age-standardized mortality rates** were used for total and sex-specific all-cause mortality
  - Crude mortality rates were used for the age-specific comparisons

$$Age\ specific\ mortality\ rate\ (ASpDR)_{y,w,i} = \frac{D_{y,w,i}}{P_{y,i}\ /\ N_w} \times\ 100{,}000 \qquad (2)$$

where $D_{y,w,i}$ = number of deaths in the age-group i in one week, P=mid-year population in age group i , and N_w= number of weeks in the year.

$$Age - standardised\ mortality\ rate\ (ASMR) = \sum_{i=1}^{n} (p_i^s\ ASpDR_{y,w,i}) \qquad (3)$$

where, index i denotes the aggregate age groups (see Supplementary Table S2) and the standard population weights $p^i{}_s$ correspond to the respective broad age intervals in the WHO World Standard Population 2000-2025

Methodological challenges: differences in age groups provided by countries

- Several countries did not report weekly mortality by consistent 5-year or more granular age groups
  - For the age-standardisation, aggregate age groups were created for each country, based on the provided age-specific all-cause mortality data
    - Method proposed by Klimkin et al. (2021)

Age groups (a) (<15, 15-44, 45-64, 65+)	Age groups (b) (<19, 20-49, 50-69, 70+)	Age groups (c) (<19, 20-49, 50-64, 65+)	Age groups (d) (<15, 15--64, 65+)	Age groups (e) (<19, 20-54, 55-69, 70+)

  - This method is not as robust as standardisation using detailed 5-year age groups. However, its results have been shown to only slightly deviate in a downward shift from the ASMR obtained using 5-year age groups

Klimkin I, Shkolnikov VM, Jdanov DA. Calculation of week-specific age-standardised death rates from STMF data on mortality by broad age intervals [Internet]. 0 ed. Rostock: Max Planck Institute for Demographic Research; 2021 Mar p. WP-2021-004. Report No.: WP-2021-004. Available from: https://www.demogr.mpg.de/en/publications_databases_6118/publications_1904/mpidr_working_papers/calculation_of_week_specific_age_standardised_death_rates_from_stmf_data_on_mortality_by_broad_age_intervals_6967

Methodology – Time Series Analysis

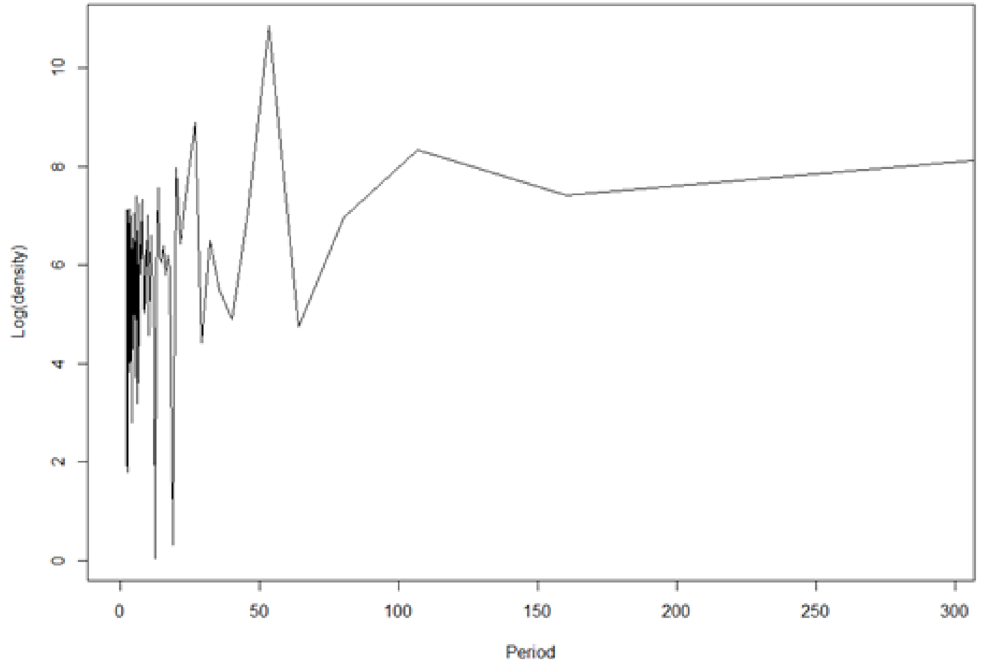
- Excess weekly mortality for 2020 was calculated by comparing observed against expected weekly crude (CMR) and age-standardized (ASMR) mortality rate (per 100,000 population) for 2020
  - Expected 2020 weekly mortality rate was estimated using a GLM (Generalized Linear Model) with Poisson regression, accounting for overdispersion, based on 2015-19 data
  - $Y_t = \alpha + \beta_1 (t) + \beta_2 [\sin(2\pi t/52)] + \beta_3 [\cos(2\pi t/52)] + \beta_3 [\sin(2\pi t/26)] + \beta_4 [\cos(2\pi t/26)]$

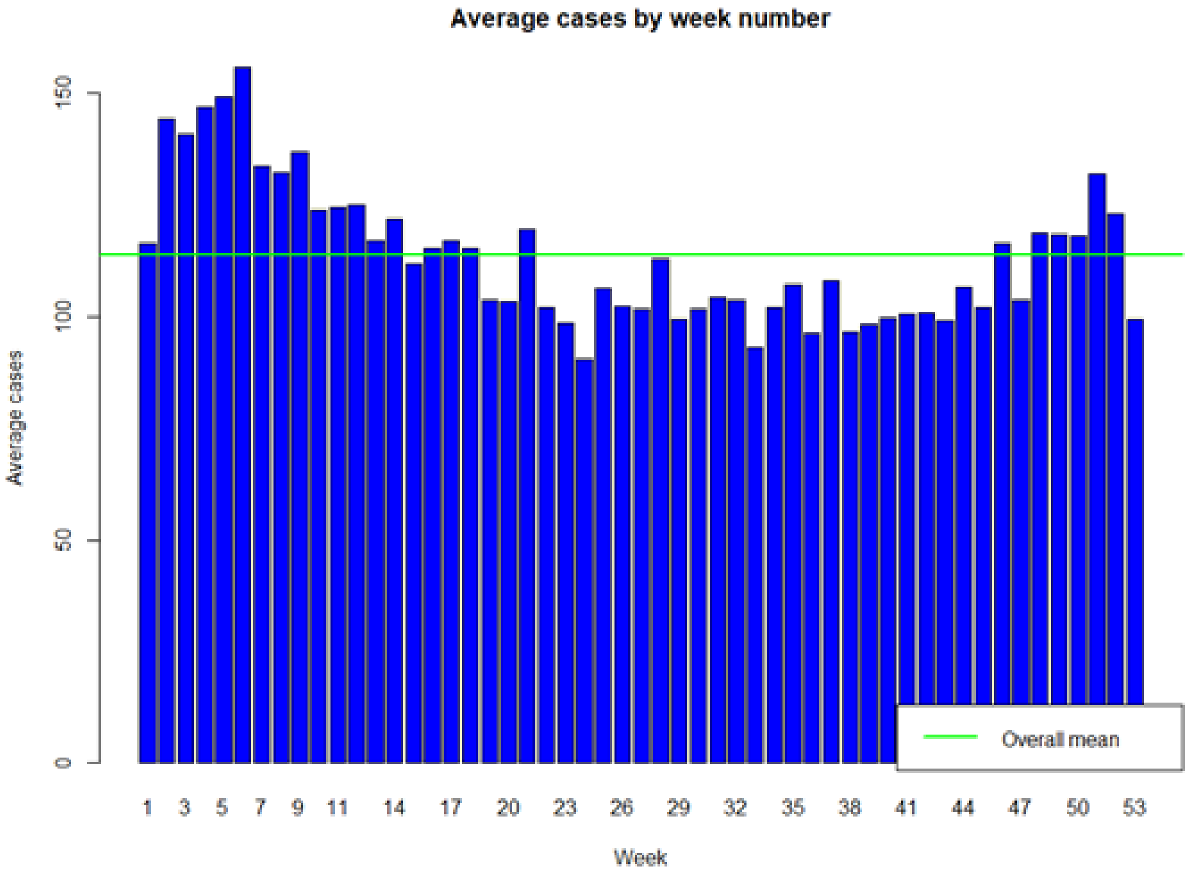
Linear time trend , t=1,…, n week

One year seasonality

Half year seasonality

Periodicity (example: Cyprus)





frequencies with the three highest peaks in the periodogram: 53,27,107

Methodology – Time Series Analysis

- Excess CMR (or ASMR) =

Observed CMR (or ASMR) – Expected CMR (or ASMR), estimated for each week of 2020

- *Z-score* = 2020 Excess CMR (or ASMR) / standard deviation of residuals

- Normal: -2< *Z-scores*< 2
- Substantial increase: *Z-scores* > 4

Cause specific mortality

- **Causes investigated:**
  - Respiratory disease (ICD-10: J00-J999)
  - Cardiovascular disease (ICD-10: I00-I09, I11, I20-151, I60-69, I70-78, I80-I99)
  - Cancer (ICD-10: C00-C97)

- Respiratory death numbers were collected and analysed using a similar methodology
  - Only CMR was analysed since age-group specific death numbers were not available for these causes for most countries to allow for age-standardization

- Changes in cause-specific mortality were calculated as % difference in weekly average mortality rates, p-values were estimated using the independent samples t-test.

**More recent analysis – including also 2021 death numbers

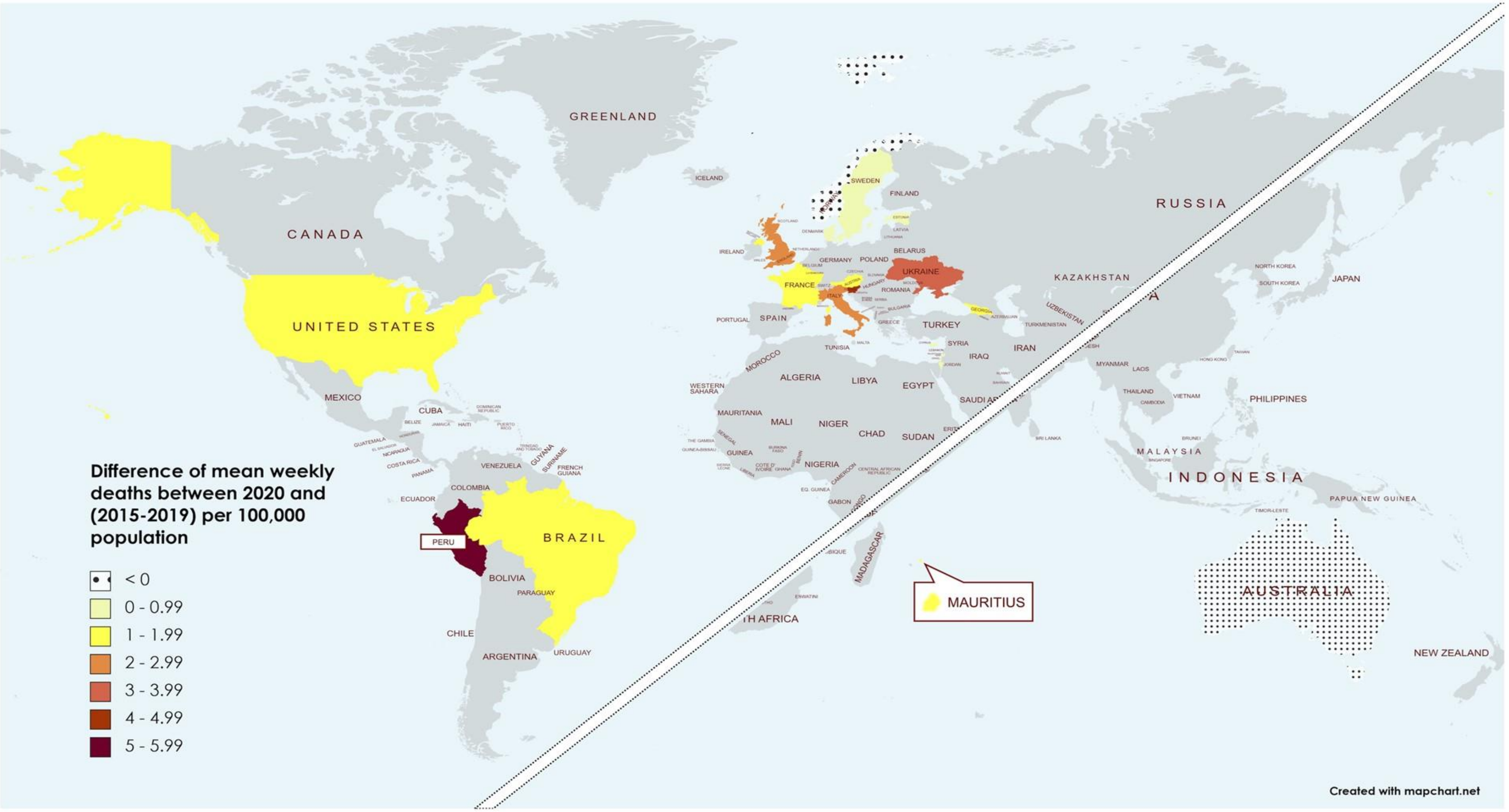
Results

Data Quality

- Quality of civil registration and vital statistics systems varied between countries
  - 17 countries (85.0%) had very high or high quality
  - One country (Peru) had medium quality
  - Two countries (Georgia and Ukraine) had low quality
    - Results from the latter countries need to be interpreted with caution

Mikkelsen L, Phillips DE, AbouZahr C, et al. A global assessment of civil registration and vital statistics systems: monitoring data quality and progress. *The Lancet*. Elsevier; 2015 Oct 3;**386**(10001):1395–1406.

Difference in weekly mean of observed mortality rates between 2020 and 2015-19 for each participating country, per 100,000 population



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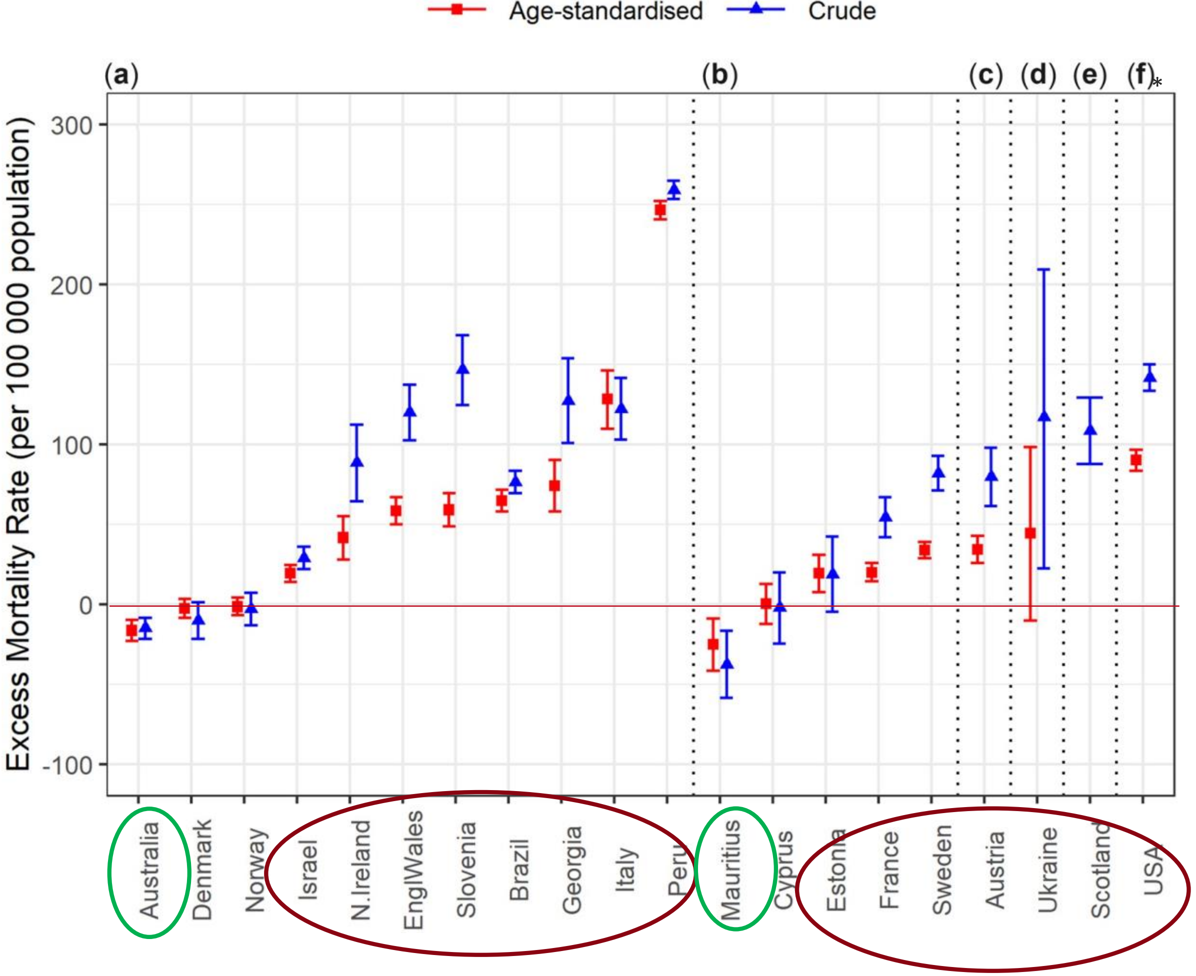
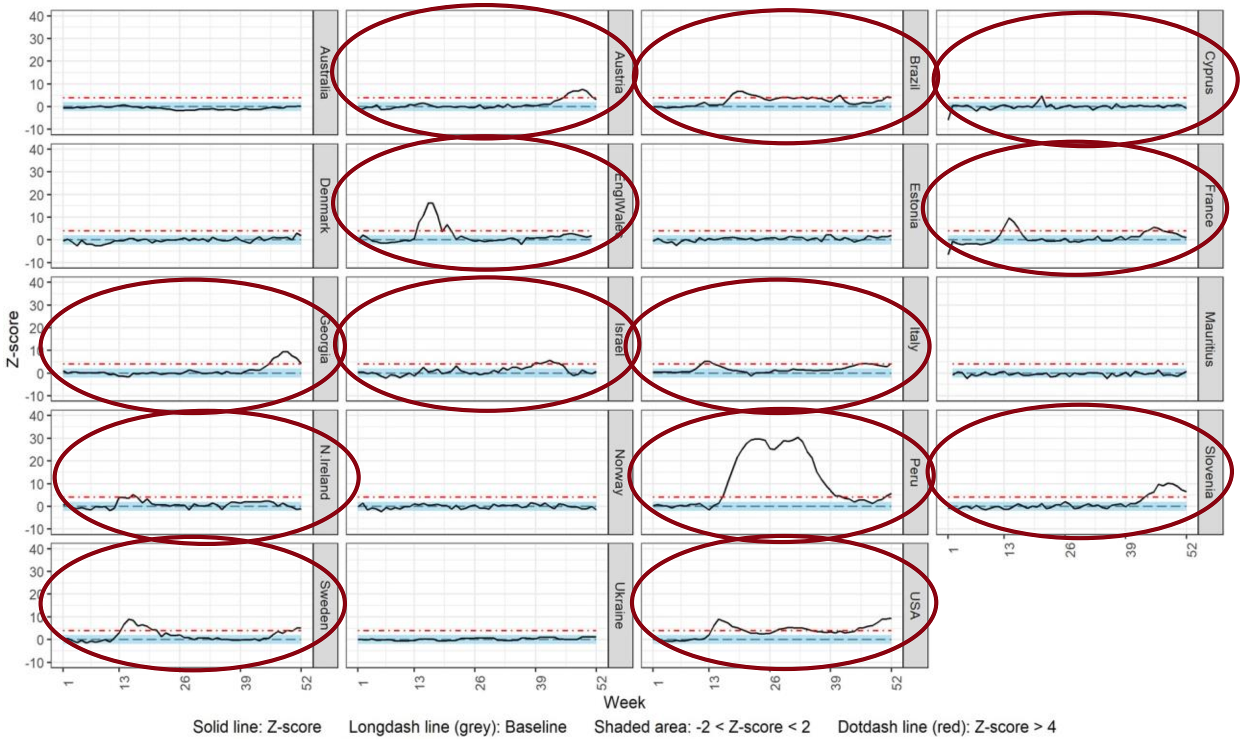
Excess Mortality in 2020

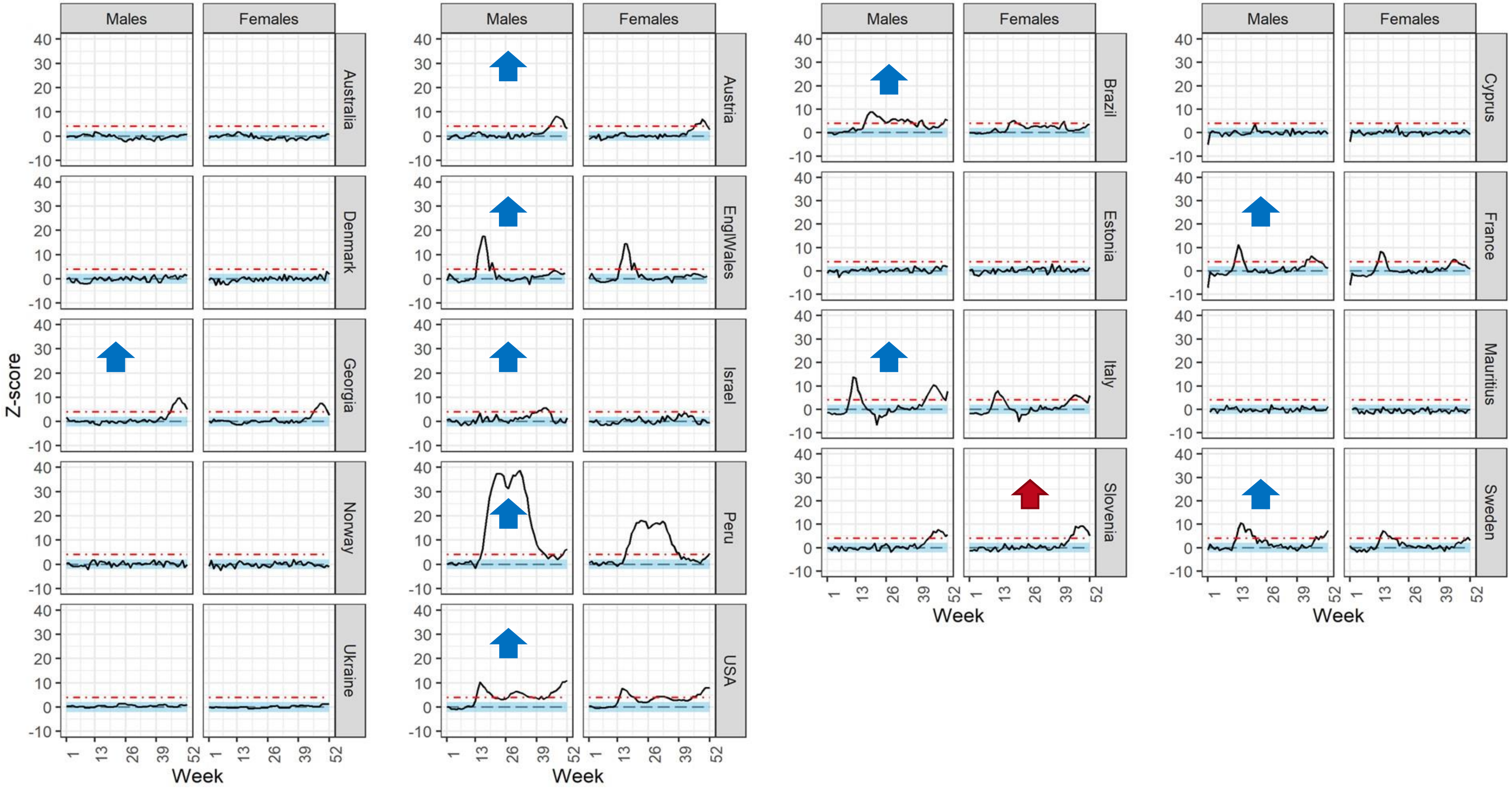




*Plot letters correspond to the age groups in which countries have provided data and therefore the age groups used for age standardization: (a) age groups <15, 15–44, 45–64, 65+; (b) age groups <19, 20–49, 50–69, 70+; (c) age groups <19, 20–49, 50–64, 65+; (d) age groups <15, 15–64, 65+; (e) age groups <19, 20–54, 55–69, 70+

Note: Z-score = (observed – expected mortality rate) / standard deviation of residuals

Sex-specific weekly ASMR z-scores over 2020



Solid line: Z-score Longdash line (grey): Baseline Shaded area: -2 < Z-score < 2 Dotdash line (red): Z-score > 4

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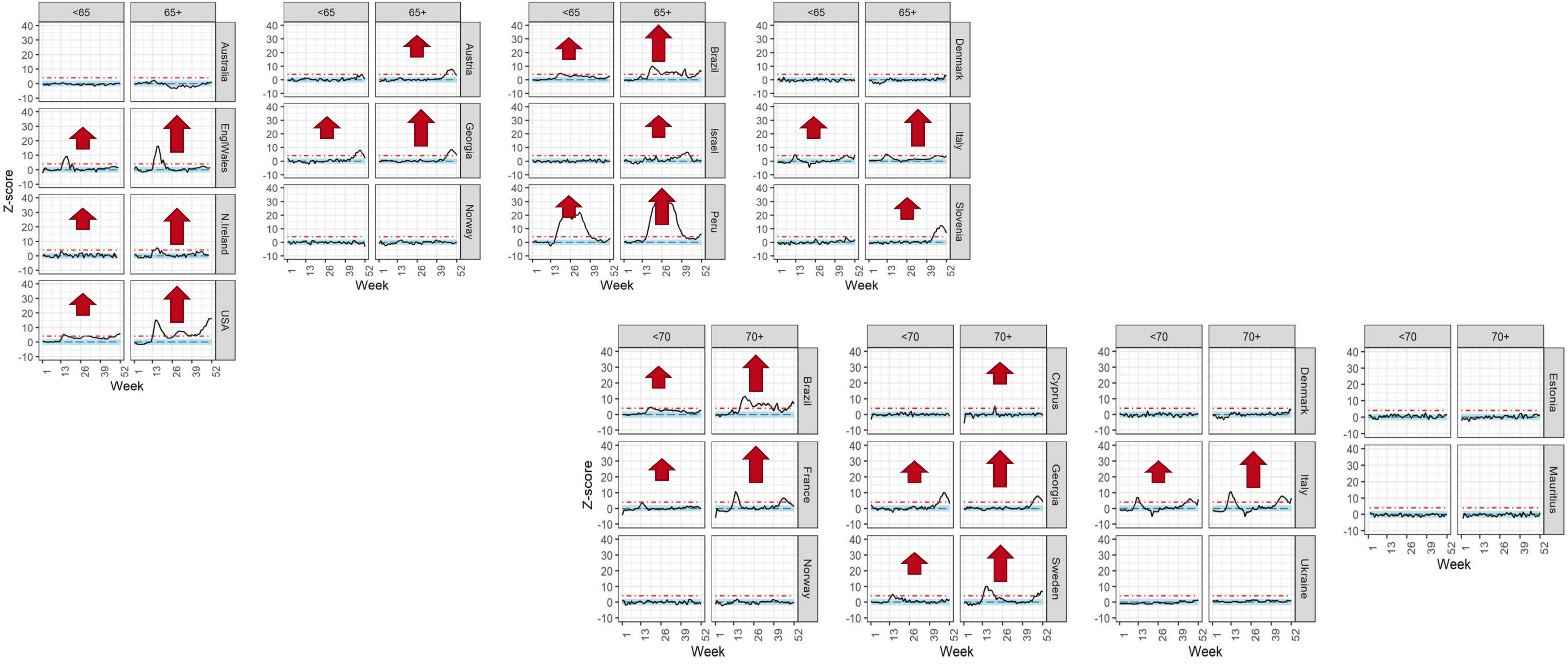
Age-specific weekly CMR z-scores over 2020



Solid line: Z-score Longdash line (grey): Baseline Shaded area: -2 < Z-score < 2 Dotdash line (red): Z-score > 4

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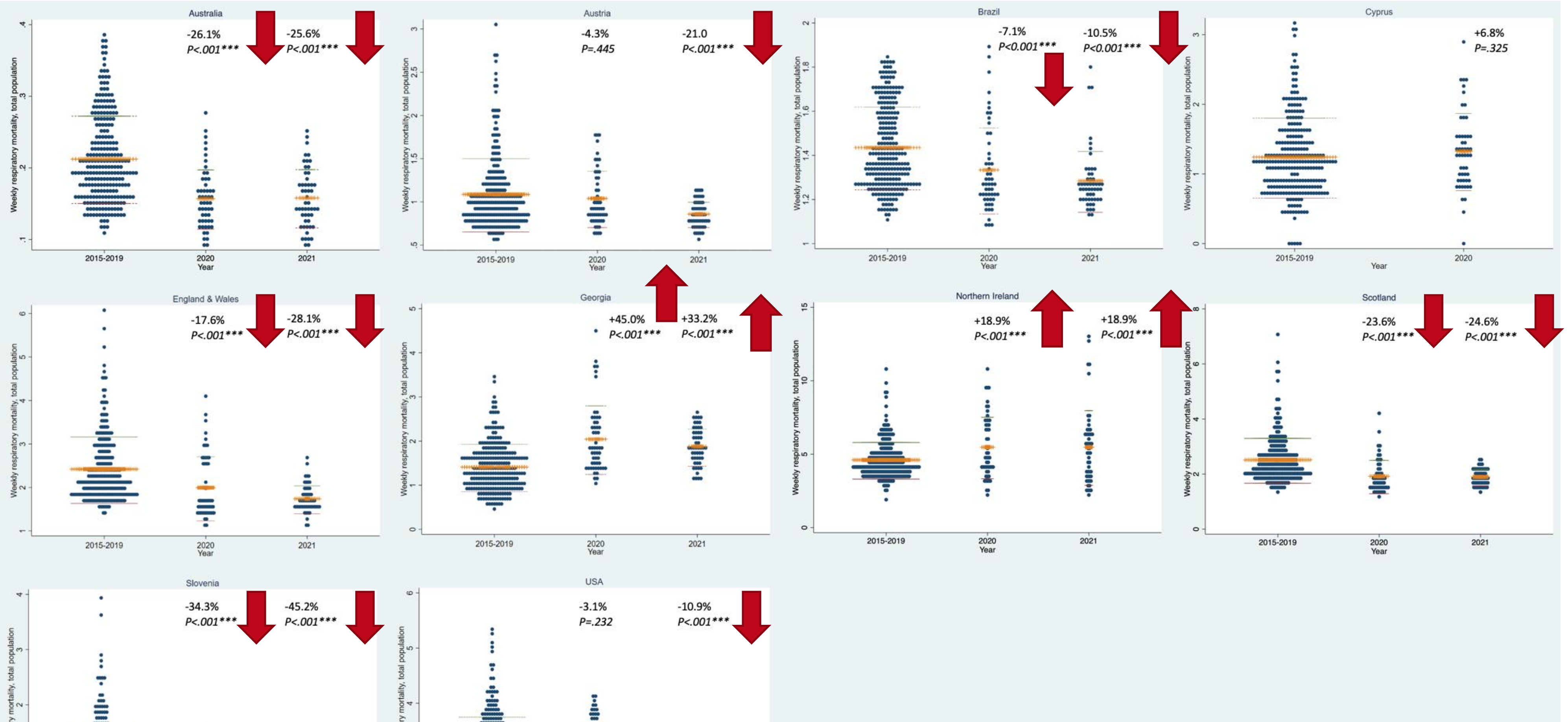
Average change in respiratory mortality for 2020 and 2021

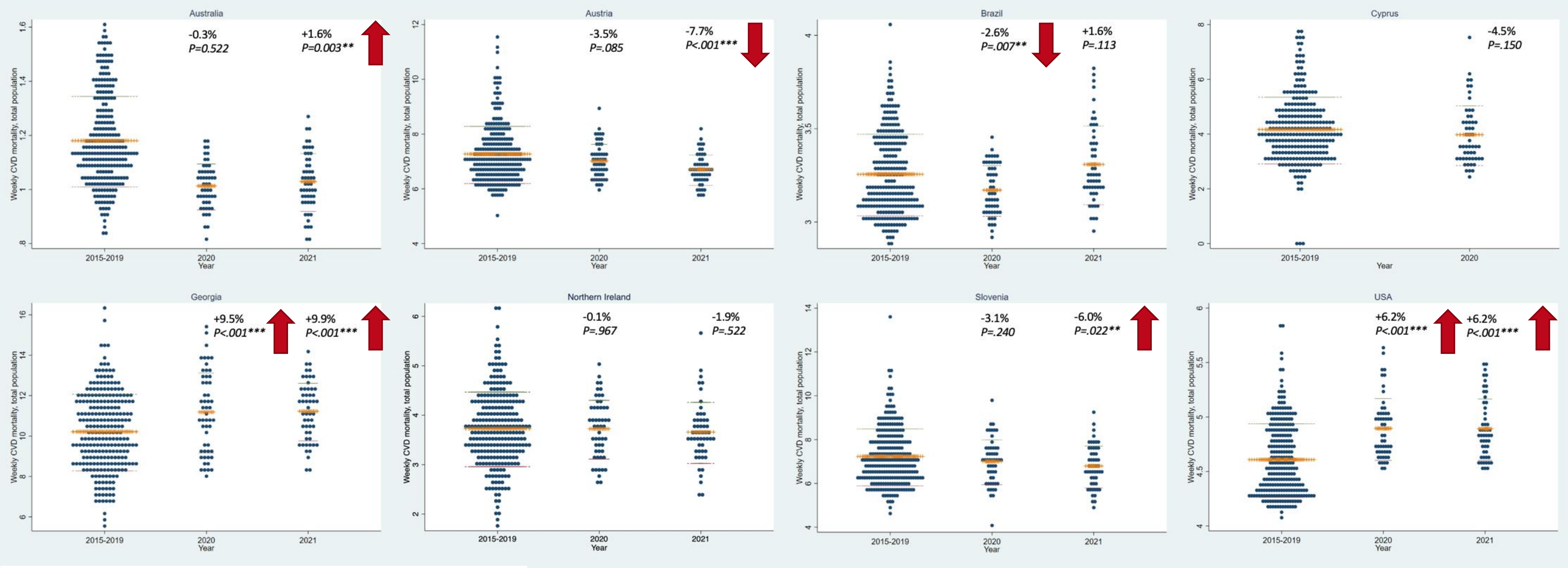


•=number of deaths per 100,000 population for a particular week

++++= weekly average for each time-period

---/---=mean +/- SD

Average change in CVD mortality for 2020 and 2021



•=number of deaths per 100,000 population for a particular week

++++= weekly average for each time-period

---/---=mean +/- SD

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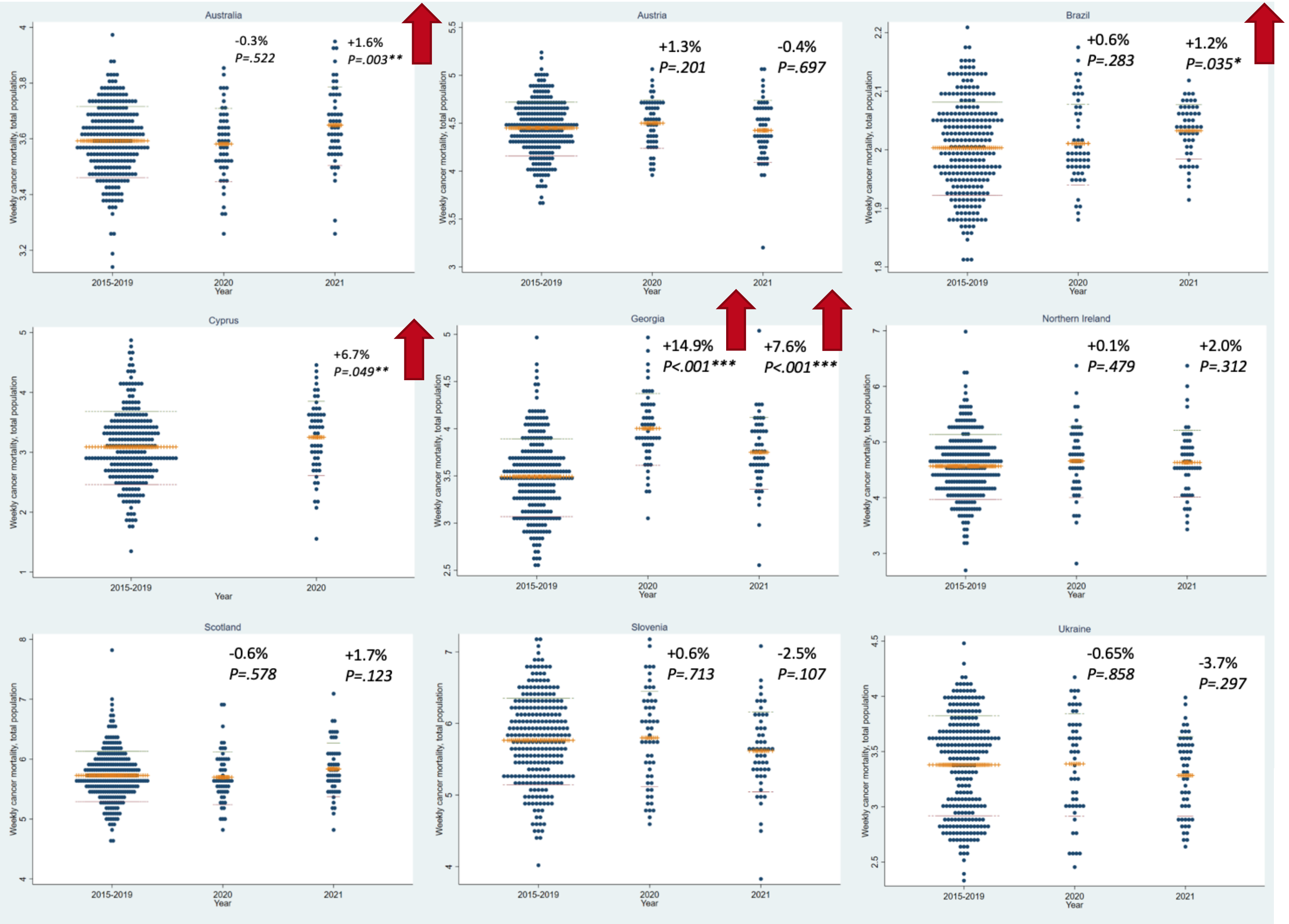
Average change in cancer mortality for 2020 and 2021



•=number of deaths per 100,000 population for a particular week

++++= weekly average for each time-period

---/---=mean +/- SD

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Conclusions

- The majority of investigated countries displayed significant excess mortality, for at least one week (1-37 weeks), during 2020
- The timing of the excess mortality differed across countries
- Differences could be explained by the variation in timing, strictness and duration of control measures; test-and-trace capacity, health expenditure, and other health indicators
- On average, males and oldest group (60+ or 70+) carried a heavier burden
- Respiratory mortality significantly decreased in the majority of included countries, but increased significantly in N. Ireland
- CVD mortality increased significantly in Australia, Georgia and the USA and decreased significantly in Austria and Brazil, while cancer mortality increased significantly in Georgia, Cyprus, Australia and Brazil
- As the pandemic continues, the lessons learned from the first months of the pandemic can prove useful to minimize increases in all-cause mortality
- There is still a need to juxtapose the all-cause and cause-specific mortality changes against COVID-19 direct and indirect mortality

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Thank you!

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