

1 **National and regional seasonal dynamics of all-cause and cause-specific mortality in the**

2 **USA from 1980 to 2016.**

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17 **Abstract**

18 In temperate climates, winter deaths exceed summer ones. However, there is limited
19 information on how the timing and the relative magnitudes of minimum and maximum
20 mortality, by local climate age group, sex and medical cause of death. We used geo-coded
21 mortality data and wavelets to analyse the seasonality of mortality by age group and sex from
22 1980 to 2016 in USA and its subnational climatic regions. Death rates in men and women ≥ 45
23 years peaked in December to February and were lowest in June to August, driven by
24 cardiorespiratory diseases and injuries. In these ages, percent difference in death rates between
25 peak and minimum months did not vary across climate regions, nor changed from 1980 to
26 2016. Under five years, seasonality of all-cause mortality largely disappeared after 1990s. In
27 adolescents and young adults, especially in males, death rates peaked in June/July and were
28 lowest in December/January, driven by injury deaths.

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30 **Introduction**

31 It is well-established that death rates vary throughout the year, and in temperate climates there
32 tend to be more deaths in winter than in summer (Campbell, 2017; Fowler et al., 2015; Healy,
33 2003; McKee, 1989). It has therefore been hypothesized that a warmer world may lower winter
34 mortality in temperate climates (Langford & Bentham, 1995; Martens, 1998). In a large country
35 like the USA, which possesses distinct climate regions, the seasonality of mortality may vary
36 geographically, due to geographical variations in mortality, localized weather patterns, and
37 regional differences in adaptation measures such as heating, air conditioning and healthcare
38 (Davis, Knappenberger, Michaels, & Novicoff, 2004; Ferreira Braga, Zanobetti, & Schwartz,
39 2001; Kalkstein, 2013; Medina-Ramón & Schwartz, 2007). The presence and extent of
40 seasonal variation in mortality may also itself change over time (Bobb, Peng, Bell, & Dominici,

61 2014; Carson, Hajat, Armstrong, & Wilkinson, 2006; Seretakis, 1997; Sheridan, Kalkstein, &
62 Kalkstein, 2009).

63

64 A thorough understanding of the long-term dynamics of seasonality of mortality, and its
65 geographical and demographic patterns, is needed to identify at-risk groups, plan responses at
66 the present time as well as under changing climate conditions. Although mortality seasonality
67 is well-established, there is limited information on how seasonality, including the timing of
68 minimum and maximum mortality, varies by local climate and how these features have
69 changed over time, especially in relation to age group, sex and medical cause of death (Rau,
70 Rau, Bohk-Ewald, Muszyńska, & Vaupel, 2018).

71

72 In this paper, we comprehensively characterize the spatial and temporal patterns of all-cause
73 and cause-specific mortality seasonality in the USA by sex and age group, through the
74 application of wavelet analytical techniques, to over three decades of national mortality data.
75 Wavelets have been used to study the dynamics of weather phenomena (Moy, Seltzer, Rodbell,
76 & Anderson, 2002) and infectious diseases (Grenfell, Bjørnstad, & Kappey, 2001). We also
77 used centre of gravity analysis and circular statistics methods to understand the timing of
78 mortality minimum and maximum. In addition, we identify how the percentage difference
79 between death rates in maximum and minimum mortality months has changed over time.

80

81 Results

82 Table 1 presents number of deaths by cause of death and sex. Deaths from cardiorespiratory
83 diseases make up nearly half of all deaths (48.1%), with most deaths from cardiovascular
84 diseases. Next highest during the study period were deaths from cancers (23.2%), followed by
85 injuries (6.8%), with two thirds of those being from unintentional injuries.

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Deleted: (Rau, 2004; Rau, Bohk-Ewald, Muszyńska, & Vaupel, 2018)

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116

117 All-cause mortality in males had a 12-month seasonality in all age groups, except ages 35-44
118 years, for whom there was periodicity at 6 months (Figure 2). In females, there was 12-month
119 seasonality in all groups except 5-14 and 25-35 years (*p*-values=0.20 and 0.24, respectively).

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120 While seasonality persisted throughout the entire analysis period in older ages, it largely
121 disappeared after late 1990s in children aged 0-4 years in both sexes and in women aged 15-
122 24 years.

123

124 Deaths from all causes of death were seasonal in older adults (above 65 or 75 years depending
125 on cause, *p*-values<0.06) (Figure 2 and Supplementary Figure 1), except for intentional injuries
126 and substance use disorders. Deaths from cardiorespiratory diseases, and within it respiratory
127 infections, exhibited seasonality throughout the life-course (*p*-values<0.03) except for males
128 aged 5-24 years and females aged 15-24 years (*p*-values>0.11). In addition to older ages, injury
129 deaths were seasonal from childhood through 44 years in women and through 64 years in men
130 (*p*-values<0.08). Unintentional injuries drove the seasonality of injury deaths for females,
131 whereas both unintentional and intentional injuries were seasonal in males in most ages, with
132 the exception of below 15 years and above 85 years when intentional injuries were not seasonal
133 (Supplementary Figure 1). Consistent seasonality in cancer deaths only appeared after 55 years
134 of age (*p*-values<0.04). No consistent seasonality was evident in maternal conditions or
135 substance use disorders (Supplementary Figure 1).

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137 Centre of gravity analysis showed that death rates in men aged ≥45 years and women aged ≥35
138 years peaked in December, January or February and were lowest in June to August, for all-
139 cause mortality as well as for all non-injury and non-maternal causes of death (Figure 3 and
140 Supplementary Figure 2). Deaths from cardiorespiratory diseases, including cardiovascular

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163 diseases, chronic respiratory diseases and respiratory infections, were also consistently highest
164 in January and February and lowest in July and August across all ages, except for chronic
165 respiratory diseases in ages 5-24 years where there are few deaths from this cause leading to
166 unstable estimates (p-values for seasonality from wavelet analysis ranged from 0.35 to 0.49 for
167 these ages). A similar temporal pattern was seen for all-cause and non-injury mortality in

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168 children younger than five years of age, whose all-cause death rate was highest in February
169 and lowest in August. In contrast, among males aged 5-34 years, all-cause mortality peaked in
170 June or July, as did deaths from injuries, which generally had a summer peak in males and
171 females below 45 years of age.

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172 From 1980 to 2016, the proportional (percent) difference in all-cause death rates between peak
173 and minimum months declined little for people older than 45 years of age (by less than eight
174 percentage points with p-values for declining trend > 0.1) (Figure 4). In contrast, the difference
175 between peak (summer) and minimum (winter) death rates declined in younger ages, by over
176 25 percentage points in males aged 5-14 years and 15-24 years (p-values < 0.01), largely driven
177 in the declining difference between summer and winter injury deaths. Under five years of age,
178 percent seasonal difference in all-cause death rates declined by 13 percentage points (p-

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179 value < 0.01) for boys but only 5 percentage points (p-value = 0.12) for girls. These declines in
180 seasonality of child deaths were a net effect of declining winter-summer difference in
181 cardiorespiratory diseases deaths and increasing summer-winter difference in injury deaths,
182 itself driven by increasing difference in non-intentional injuries (Supplementary Figure 3).
183 Within the cardiorespiratory diseases cluster in under-five children, percent difference declined
184 for cardiorespiratory diseases, cardiovascular diseases, and chronic respiratory diseases while
185 increasing for respiratory infections.

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206 The subnational centre of gravity analysis showed that all-cause mortality peaks and minima
207 in different climate regions are consistent with the national ones (Figure 5), indicating the
208 seasonality is largely independent of geography. The relative homogeneity of the timing of
209 maximum and minimum mortality contrasts with the large variation in seasonal temperatures
210 among climate regions. For example, in men and women aged 65-74 years, all-cause mortality
211 peaked in February in the Northeast and Southeast, even though the average temperatures for
212 those regions were different by over 13 degrees Celsius (9.3 in the Southeast compared with -
213 3.8 in the Northeast). Furthermore, above 45 years of age, there was little inter-region variation
214 in the percent seasonal difference in all-cause mortality, despite the large variation in
215 temperature difference between the peak and minimum months (Figure 6).
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217 Strengths and limitations

218 The strengths of our study are its innovative methods of characterizing seasonality of mortality
219 dynamically over space and time, by age group and cause of death; using wavelet and centre
220 of gravity analyses; using ERA-Interim data output to compare the association between
221 seasonality of death rates and regional temperature. A limitation of our study is that we did not
222 investigate seasonality of mortality by socioeconomic characteristics which may help with
223 understanding its determinants and planning responses.

224

225 Discussion

226 We used wavelet and centre of gravity analyses, which allowed systematically identifying and
227 characterizing seasonality of total and cause-specific mortality in the USA, and examining how
228 seasonality has changed over time. We identified distinct seasonal patterns in relation to age
229 and sex, including higher all-cause summer mortality in young men (Feinstein, 2002; Rau et
230 al., 2018). Importantly, we also showed that all-cause and cause-specific mortality seasonality

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244 is largely similar in terms of both timing and magnitude across diverse climatic regions with
245 substantially different summer and winter temperatures. Insights of this kind would not have
246 been possible analysing data averaged over time or nationally, or fixed to pre-specified
247 frequencies.

248

249 Prior studies have noted seasonality of mortality for all-cause mortality and for specific causes
250 of death in the USA (Feinstein, 2002; Kalkstein, 2013; Rau, 2004; Rau et al., 2018;
251 Rosenwaike, 1966; Seretakis, 1997). Few of these studies have done consistent national and
252 subnational analyses, and none has done so over time, for a comprehensive set of age groups
253 and causes of death, and in relation to regional temperature differences. Our results on strong
254 seasonality of cardiorespiratory diseases deaths and weak seasonality of cancer deaths,
255 restricted to older ages, are broadly consistent with these studies (Feinstein, 2002; Rau et al.,
256 2018; Rosenwaike, 1966; Seretakis, 1997), which had limited analysis on how seasonality
257 changes over time and geography (Feinstein, 2002; Rau et al., 2018; Rosenwaike, 1966).
258 Similarly, our results on seasonality of injury deaths are supported by a few prior studies
259 (Feinstein, 2002; Rau et al., 2018; Rosenwaike, 1966), but our subnational analysis over three
260 decades revealed variations in when injury deaths peaked and in how seasonal differences in
261 these deaths have changed over time in relation to age group which had not been reported
262 before.

263

264 A study of 36 cities in the USA, aggregated across age groups and over time, also found that
265 excess mortality was not associated with seasonal temperature range (Kinney et al., 2015). In
266 contrast, a European study found that the difference between winter and summer mortality was
267 lower in the colder Nordic countries than in warmer southern European nations (Healy, 2003;
268 McKee, 1989)(the study's measure of temperature was mean annual temperature which

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270 differed from the temperature difference between maximum and minimum mortality used in
271 our analysis although the two measures are correlated). The absence of variation in the
272 magnitude of mortality seasonality indicates that different regions in the USA are similarly
273 adapted to temperature seasonality, whereas Nordic countries may have better environmental
274 (e.g., housing insulation and heating) and health system measures to counter the effects of cold
275 winters than those in southern Europe. If the observed absence of association between the
276 magnitude of mortality seasonality and seasonal temperature difference across the climate
277 regions also persists over time, the changes in temperature as a result of global climate change
278 are unlikely to affect the winter-summer mortality difference.

279

280 The cause-specific analysis showed that the substantial decline in seasonal mortality
281 differences in adolescents and young adults was related to the diminishing seasonality of
282 (unintentional) injuries, especially from road traffic crashes, which are more likely to occur in
283 the summer months (National Highway Traffic Safety Administration, 2005) and are more
284 common in men. The weakening of seasonality in boys under five years of age was related to
285 two phenomena: first, the seasonality of death from cardiorespiratory diseases declined, and
286 second, the proportion of deaths from perinatal conditions, which exhibit limited seasonality
287 (Supplementary Figure 1), increased (MacDorman & Gregory, 2015).

288

289 In contrast to young and middle ages, mortality in older ages, where death rates are highest,
290 maintained persistent seasonality over a period of three decades (we note that although the
291 percent seasonal difference in mortality has remained largely unchanged in these ages, the
292 absolute difference in death rates between the peak and minimum months has declined because
293 total mortality has a declining long-term trend). This finding demonstrates the need for
294 environmental and health service interventions targeted towards this group irrespective of

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314 geography and local climate. Examples of such interventions include enhancing the availability
315 of both environmental and medical protective factors, such as better insulation of homes, winter
316 heating provision and flu vaccinations, for the vulnerable older population (Public Health
317 England, 2017). Social interventions, including regular visits to the isolated elderly during peak
318 mortality periods to ensure that they are optimally prepared for adverse conditions, and
319 responsive and high-quality emergency care, are also important to protect this vulnerable group
320 (Healy, 2003; Lerchl, 1998; Public Health England, 2017). Emergent new technologies, such
321 as always-connected hands-free communications devices with the outside world, in-house
322 cameras, and personal sensors also provide an opportunity to enhance care for the older, more
323 vulnerable groups in the population, especially in winter when the elderly have fewer social
324 interactions (Morris, 2013). Such interventions are important today, and will remain so as the
325 population ages and climate change increases the within- and between-season weather
326 variability.

327

328 Materials and methods

329 Data

330 We used data on all 85,854,176 deaths in the USA from 1980 to 2016 from the National Center
331 for Health Statistics (NCHS). Age, sex, state of residence, month of death, and underlying
332 cause of death were available for each record. The underlying cause of death was coded
333 according to the international classification of diseases (ICD) system (9th revision of ICD from
334 1980 to 1998 and 10th revision of ICD thereafter). Yearly population counts were available
335 from NCHS for 1990 to 2016 and from the US Census Bureau prior to 1990 (Ingram et al.,
336 2003). We calculated monthly population counts through linear interpolation, assigning each
337 yearly count to July.

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343 We also subdivided the national data geographically into nine climate regions used by the
344 National Oceanic and Atmospheric Administration (Figure 1 and Table 2) (Karl & Koss, 1984).
345 On average, the Southeast and South are the hottest climate regions with average annual
346 temperatures of 18.4°C and 18°C respectively; the South also possesses the highest average
347 maximum monthly temperature (27.9°C in July). The lowest variation in temperature
348 throughout the year is that of the Southeast (an average range of 17.5°C). The three coldest
349 climate regions are West North Central, East North Central and the Northwest (7.8°C, 8.0°C,
350 8.1°C respectively). Mirroring the characteristics of the hottest climate regions, the largest
351 variation in temperature throughout the year is that of the coldest region, West North Central
352 (an average range of 30.5°C), which also has the lowest average minimum monthly
353 temperature (-6.5°C in January). The other climate regions, Northeast, Southwest, and Central,
354 possess similar average temperatures (11 to 13°C) and variation within the year of (23 to 26°C),
355 with the Northeast being the most populous region in the United States (with 19.8% total
356 population in 2016).

357
358 Data were divided by sex and age in the following 10 age groups: 0-4, 5-14, 25-34, 35-44, 45-
359 54, 55-64, 65-74, 75-84, 85+ years. We calculated monthly death rates for each age and sex
360 group, both nationally and for sub-national climate regions. Death rate calculations accounted
361 for varying length of months, by multiplying each month's death count by a factor that would
362 make it equivalent to a 31-day month.

363
364 For analysis of seasonality by cause of death, we mapped each ICD-9 and ICD-10 codes to
365 four main disease categories (Table 1) and to a number of subcategories which are presented
366 in the Supplementary Note. Cardiorespiratory diseases and cancers accounted for 56.4% and
367 21.2% of all deaths in the USA, respectively, in 1980, and 40.3% and 22.4%, respectively, in

Deleted: We used data on all 77,771,264 deaths in the USA from 1980 to 2013 from the National Center for Health Statistics (NCHS). Age, sex, state of residence, month of death, and underlying cause of death were available for each record. Yearly population counts were available from NCHS for 1990 to 2013 and from the US Census Bureau prior to 1990 (Ingram et al., 2003). We calculated monthly population counts through linear interpolation, assigning each yearly count to July. We also subdivided the national data geographically by climate regions used by the National Oceanic and Atmospheric Administration (Figure 1) (Karl & Koss, 1984). The underlying cause of death was coded according to the international classification of diseases (ICD) system (9th revision of ICD from 1980 to 1998 and 10th revision of ICD thereafter). .

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384 2016. Deaths from cardiorespiratory diseases have been associated with cold and warm
385 temperatures (Basu, 2009; Basu & Samet, 2002; Bennett, Blangiardo, Fecht, Elliott, & Ezzati,
386 2014; Braga, Zanobetti, & Schwartz, 2002; Gasparrini et al., 2015). Injuries, which accounted
387 for 8% of all deaths in the USA in 1980 and 7.3% in 2016, may have seasonality that is distinct
388 from so-called natural causes. We did not further divide other causes because the number of
389 deaths could become too small to allow stable estimates when divided by age group, sex and
390 climate region.

391

392 We obtained data on temperature from ERA-Interim, which combines predictions from a
393 physical model with ground-based and satellite measurements (Dee et al., 2011). We used
394 gridded four-times-daily estimates at a resolution of 80km to generate monthly population-
395 weighted temperature by climate region throughout the analysis period.

396

397 *Statistical methods*

398 We used wavelet analysis to investigate seasonality for each age-sex group. Wavelet analysis
399 uncovers the presence, and frequency, of repeated maxima and minima in each age-sex-specific
400 death rate time series (Hubbard, 1998; Torrence & Compo, 1998). In brief, a Morlet wavelet,
401 described in detail elsewhere (Cazelles et al., 2008), is equivalent to using a moving window
402 on the death rate time series and analysing periodicity in each window using a short-form
403 Fourier transform, hence generating a dynamic spectral analysis, which allows measuring
404 dynamic seasonal patterns, in which the periodicity of death rates may disappear, emerge, or
405 change over time. In addition to coefficients that measure the frequency of periodicity, wavelet
406 analysis estimates the probability of whether the data are different from the null situation of
407 random fluctuations that can be represented with white (an independent random process) or
408 red (autoregressive of order 1 process) noise. For each age-sex group, we calculated the p-

409 values of the presence of 12-month seasonality for the comparison of wavelet power spectra of
410 the entire study period (1980-2016) with 100 simulations against a white noise spectrum, which
411 represents random fluctuations. We used the R package WaveletComp (version 1.0) for the
412 wavelet analysis. Before analysis, we de-trended death rates using a polynomial regression,
413 and rescaled each death rate time series so as to range between 1 and -1.

414

415 To identify the months of maximum and minimum death rates, we calculated the centre of Deleted: Cancers: ICD-9 140.0 – 239.9 and ICD-10 C00 – ... [4]
416 gravity and the negative centre of gravity of monthly death rates. Centre of gravity was
417 calculated as a weighted average of months of deaths, with each month weighted by its death
418 rate; negative centre of gravity was also calculated as a weighted average of months of deaths,
419 but with each month was weighted by the difference between its death rate and the year's
420 maximum death rate. In taking the weighted average, we allowed December (month 12) to
421 neighbour January (month 1), representing each month by an angle subtended from 12 equally-
422 spaced points around a unit circle. Using a technique called circular statistics, a mean ($\bar{\theta}$) of
423 the angles ($\theta_1, \theta_2, \theta_3 \dots, \theta_n$) representing the deaths (with n the total number of deaths in an
424 age-sex group for a particular cause of death) is found using the relation below:

$$425 \bar{\theta} = \arg \left\{ \sum_{j=1}^n \exp(i\theta_j) \right\},$$

426 where \arg denotes the complex number argument and θ_j denotes the month of death in angular
427 form for a particular death j . The outcome of this calculation is then converted back into a
428 month value (Fisher, 1995). Along with each circular mean, a 95% confidence interval (CI) Deleted: January (month 1) to neighbour December (month 12), a
429 was calculated by using 1000 bootstrap samples. The R package CircStats (version 0.2.4) was
430 used for this analysis. Deleted: purpose

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444 For each age-sex group and cause of death, and for each year, we calculated the percent
445 difference in death rates between the maximum and minimum mortality months. We fitted a
446 linear regression to the time series of seasonal differences from 1980 to 2016, and used the
447 fitted trend line, to estimate how much the percentage difference in death rates between the
448 maximum and minimum mortality months had changed from 1980 to 2016. We weighted
449 seasonal difference by the inverse of the square of its standard error, which was calculated
450 using a Poisson model to take population size of each age-sex group through time into account.
451 This method gives us a p-value for the change in seasonal difference per year, which we used
452 to calculate the seasonal difference at the start (1980) and end (2016) of the period of study.
453 Our method of analysing seasonal differences avoids assuming that any specific month or
454 group of months represent highest and lowest number of deaths for a particular cause of death,
455 which is the approach taken by the traditional measure of Excess Winter Deaths. It also allows
456 the maximum and minimum mortality months to vary by age group, sex and cause of death.

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Deleted: . We calculated

Deleted: the fitted values from 1980 to 2013, reported as percentage point difference, as a quantitative

Deleted: how the seasonality of death rates has changed over time.

457

458 Acknowledgments

459 Robbie Parks is supported by a Wellcome Trust ISSF Studentship. Work on the US mortality
460 data is supported by a grant from US Environmental Protection Agency.

461

462 Author contributions

463 All authors contributed to study concept, analytical approach, and interpretation of results. RP,
464 KF and ME collated and organised mortality files. RP performed the analysis, with input from
465 JB. RP and ME wrote the first draft of the paper; other authors contributed to revising and
466 finalising the paper.

467

468 Competing financial interests

477 The authors declare no competing financial interests.

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