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

2   **USA from 1980 to 2013**

3   Robbie M Parks[1,2], James E Bennett[1,2,3], Kyle J Foreman[1,2,4], Ralf Toumi[5], Majid Ezzati[1,2,3*]

4   [1] MRC-PHE Centre for Environment and Health, Imperial College London, London, United

5   Kingdom, W2 1PG

6   [2] Department of Epidemiology and Biostatistics, School of Public Health, Imperial College

7   London, London, United Kingdom, W2 1PG

8   [3] WHO Collaborating Centre on NCD Surveillance and Epidemiology, Imperial College

9   London, London, United Kingdom, W2 1PG

10   [4] Institute for Health Metrics and Evaluation, University of Washington, Seattle, USA, WA

11   98121

12   [5] Space and Atmospheric Physics, Imperial College London, London, United Kingdom, W7

13   2AZ

14   Address correspondence to Majid Ezzati (majid.ezzati@imperial.ac.uk)

15

16   **Abstract**

17   It has been hypothesized that a warmer world may lower winter mortality in temperate

18   climates, where winter deaths exceed summer ones. We used geo-coded mortality data and

19   wavelet analytical techniques to analyse the seasonality of all-cause and cause-specific

20   mortality by age group and sex from 1980 to 2013 in the USA, nationally and in subnational

21   climatic regions. Death rates in men and women ≥45 years exhibited statistically significant

22   seasonality with peak in January/February and minimum in June/July, driven by seasonality of

23   cardiorespiratory diseases and injuries. In these ages, percent difference in death rates between

24   peak and minimum months did not vary across climate regions, and was largely unchanged

25   from 1980 to 2013. Under five years of age, seasonality of all-cause mortality largely

26 disappeared after the 1990s. In adolescents and young adults, especially in males, death rates

27 peaked in June/July and were lowest in December/January, driven by seasonality of injury

28 deaths.

29

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). Therefore, it has been hypothesized that a warmer world may lower

34 winter mortality in temperate climates (Langford & Bentham, 1995; Martens, 1998). In a large

35 country like the USA, which possesses distinct climate regions, the seasonality of mortality

36 may vary geographically, due to geographical variations in mortality, localized weather

37 patterns, and regional differences in adaptation measures such as heating, air conditioning and

38 healthcare (Davis, Knappenberger, Michaels, & Novicoff, 2004; Ferreira Braga, Zanobetti, &

39 Schwartz, 2001; Kalkstein, 2013; Medina-Ramón & Schwartz, 2007). The presence and extent

40 of seasonal variation in mortality may also itself change over time, due to shifts in weather

41 regimes, lifestyle, adaptation technologies, and healthcare (Bobb, Peng, Bell, & Dominici,

42 2014; Carson, Hajat, Armstrong, & Wilkinson, 2006; Seretakis, 1997; Sheridan, Kalkstein, &

43 Kalkstein, 2009).

44

45 A thorough understanding of the long-term dynamics of seasonality of mortality, and its

46 geographical and demographic patterns, is needed to identify at-risk groups, plan responses at

47 the present time as well as under changing climate conditions. Although mortality seasonality

48 is well-established, there is limited information on how seasonality, including the timing of

49 minimum and maximum mortality, varies by local climate and how these features have

changed over time, especially in relation to age group, sex and medical cause of death (Rau, 2004; Rau, Bohk-Ewald, Muszyńska, & Vaupel, 2018).

In this paper, we comprehensively characterize the spatial and temporal patterns of all-cause and cause-specific mortality seasonality in the USA by sex and age group, through the application of wavelet analytical techniques, which have been used to study the dynamics of weather phenomena (Moy CM, Seltzer GO, Rodbell DT, 2002) and infectious diseases (Grenfell, Bjørnstad, & Kappey, 2001), to over three decades of national mortality data. We also used centre of gravity analysis and circular statistics methods to understand the timing of mortality minimum and maximum where seasonality has been identified.

Results

All-cause mortality in males had a statistically significant 12-month seasonality in all age groups, except in those aged 35-44 years, for whom there was statistically significant periodicity at 6 months (Figure 2). In females, there was significant 12-month seasonality in all groups except 5-14 and 25-35 years (Figure 2). While seasonality persisted throughout the entire analysis period in older ages, it largely disappeared after late 1990s in children aged 0-4 years in both sexes and in women aged 15-24 years.

Mortality from all four cause groups was seasonal above 75 years of age (Figure 2). Seasonality in cancer deaths only appeared after 55 years of age, whereas deaths from cardiorespiratory causes exhibited statistically significant seasonality throughout the life-course. In addition to older ages, injuries were also seasonal from childhood through 44 years in women and 64 years in men.

75 Death rates in men aged ≥45 years and women aged ≥35 years peaked in January and February

76 and were lowest in June-August, for all-cause mortality as well as for causes of death with

77 statistically significant seasonality, including injuries (Figure 3). A similar temporal pattern

78 was seen for all-cause mortality in children younger than five years of age, whose all-cause

79 death rate was highest in February and lowest in August. These months also represented

80 maximum and minimum mortality of children for non-injury causes. In contrast injury deaths

81 in children, adolescents and young and middle-aged adults peaked in June/July and were lowest

82 in December/January. Among older boys and young men, not only did injury mortality peak in

83 in June/July, but all-cause mortality also.

84

85 From 1980 to 2013, the proportional (percent) difference in all-cause death rates between peak

86 and minimum months declined little for people older than 45 years of age (non-significantly

87 and by less than eight percentage points) (Figure 4). In contrast, the difference between peak

88 (summer) and minimum (winter) death rates declined significantly in younger ages, by over 25

89 percentage points in males aged 5-14 years and 15-24 years, largely driven in the declining

90 difference between summer and winter injury deaths. Under five years of age, percent seasonal

91 difference in all-cause death rates declined by a statistically-significant 13 percentage points

92 (95% CI 8 to 18) for boys but only a statistically-non-significant 5 percentage points (-12 to 2)

93 for girls. These declines in seasonality of child deaths were a net effect of declining winter-

94 summer difference in cardiorespiratory deaths and increasing summer-winter difference in

95 injury deaths.

96

97 The subnational centre of gravity analysis shows that all-cause mortality peaks and minima in

98 different climate regions are consistent with the national ones (Figure 5), indicating the

99 seasonality is largely independent of geography. The relative homogeneity of the timing of

100 maximum and minimum mortality contrasts with the large variation in seasonal temperatures

101 among climate regions. For example, in men and women aged 65-74 years, all-cause mortality

102 peaked in February in the Northeast and Southeast, even though the average temperatures for

103 those regions were different by over 13 degrees Celsius (9.3 in the Southeast compared with -

104 3.8 in the Northeast). Furthermore, above 45 years of age, there was little inter-region variation

105 in the percent seasonal difference in all-cause mortality, despite the large variation in

106 temperature difference between the peak and minimum months (Figure 6). The only cause of

107 death with regional differences in seasonality was injuries in men aged 55-64 years and women

108 aged 65-74 years. Injury death rates in these age-sex groups seemed to peak in January in the

109 Northeast peak and in August in the (Supplementary Figure 1).

110

111 **Strengths and limitations**

112 The strengths of our study are its innovative methods of characterizing seasonality of mortality

113 dynamically over space and time, by age group and cause of death; using wavelet and centre

114 of gravity analyses; using ERA-Interim data output to compare the association between

115 seasonality of death rates and regional temperature. A limitation of our study is that we used

116 broad causes of death so that we have sufficient number of deaths by age group, sex, year,

117 climate region and cause of death. Different diseases and injuries may be differentially affected

118 by environmental, behavioural and healthcare factors associated with season and hence differ

119 in their seasonal behaviour. For example, suicides have been found to peak in early spring

120 (Feinstein, 2002), and cardiovascular disease mortality may peak earlier in the winter than that

121 from respiratory conditions (Mackenbach, Kunst, & Looman, 1992). Similarly, the seasonality

122 of influenza, and how it has changed over time, may be different than that of other respiratory

123 diseases due to disease-specific interventions (Simonsen et al., 2005). Further, we did not

124 investigate seasonality of mortality by socioeconomic characteristics which may help with

125 understanding its determinants and planning responses.

126

127 **Discussion**

128 We used wavelet and centre of gravity analyses, which allowed not only systematically

129 identifying and characterizing seasonality of total and cause-specific mortality in the USA, but

130 also examining how seasonality has changed over time. We identified distinct seasonal

131 behaviours in relation to age and sex, including the higher summer mortality in young men

132 (Feinstein, 2002; Rau et al., 2018). Importantly, we also showed that all-cause and cause-

133 specific mortality seasonality is largely similar in terms of both timing and magnitude across

134 diverse climatic regions with substantially different summer and winter temperatures, with a

135 notable exception of injuries in older ages. Insights of this kind would not have been possible

136 analysing data averaged over time or nationally, or fixed to pre-specified frequencies.

137

138 Prior studies have noted seasonality of mortality for all-cause mortality and for specific causes

139 of death in the USA (Feinstein, 2002; Kalkstein, 2013; Rau, 2004; Rau et al., 2018;

140 Rosenwaike, 1966; Seretakis, 1997). Few of these studies have done consistent national and

141 subnational analyses, and none has done so over time, for a comprehensive set of age groups

142 and causes of death, and in relation to regional temperature differences. Our results on strong

143 seasonality of cardiorespiratory deaths and weak seasonality of cancer deaths, restricted to

144 older ages, are broadly consistent with these studies (Feinstein, 2002; Rau et al., 2018;

145 Rosenwaike, 1966; Seretakis, 1997), which had limited analysis on how seasonality changes

146 over time and/or geography (Feinstein, 2002; Rau et al., 2018; Rosenwaike, 1966). Similarly,

147 our results on seasonality of injury deaths are supported by a few prior studies (Feinstein, 2002;

148 Rau et al., 2018; Rosenwaike, 1966), but our subnational analysis over three decades revealed

149   variations in when injury deaths peaked and in how seasonal differences in these deaths have

150   changed over time which had not been reported before.

151

152   The observed geographical similarity in seasonal mortality variation in the USA, also seen in

153   a study of 36 cities using deaths aggregated across age groups and over time (Kinney et al.,

154   2015), contrasts from the pattern observed across Europe, where the difference between winter

155   and summer mortality tends to be lower in the colder Nordic countries than in warmer southern

156   European nations (Fowler et al., 2015; Healy, 2003; McKee, 1989). The absence of association

157   between the magnitude of mortality seasonality and seasonal temperature difference indicates

158   that different regions in the USA are similarly adapted to temperature seasonality, whereas

159   Nordic countries may have better environmental (e.g., housing insulation and heating) and

160   health system measures to counter the effects of cold winters than those in southern Europe.

161

162   The cause-specific analysis showed that the substantial decline in seasonal mortality

163   differences in adolescents and young adults was related to the diminishing seasonality of

164   injuries, especially from road traffic crashes, which are more likely to occur in the summer

165   months (National Highway Traffic Safety Administration, 2005) and are more common in men.

166   The weakening of seasonality in boys under five years of age was related to two phenomena:

167   first, the seasonality of death from cardiorespiratory diseases declines, and second, the

168   proportion of deaths during the perinatal period, which have limited seasonality, increased

169   (MacDorman & Gregory, 2015).

170

171   In contrast to young and middle ages, mortality in older ages, where death rates are highest,

172   maintained persistent seasonality over a period of three decades (we note that although the

173   percent seasonal difference in mortality has remained largely unchanged in these ages, the

174 absolute difference in death rates between the peak and minimum months has declined because

175 total mortality has a declining long-term trend). This finding demonstrates the need for

176 environmental and health service interventions targeted towards this group irrespective of

177 geography and local climate. Examples of such interventions include enhancing the availability

178 of both environmental and medical protective factors, such as better insulation of homes, winter

179 heating provision and flu vaccinations, for the vulnerable older population (Public Health

180 England, 2017). Social interventions, including regular visits to the isolated elderly during peak

181 mortality periods to ensure that they are optimally prepared for adverse conditions, and

182 responsive and high-quality emergency care, are also important to protect this vulnerable group

183 (Healy, 2003; Lerchl, 1998; Public Health England, 2017). Emergent new technologies, such

184 as always-connected hands-free communications devices with the outside world, in-house

185 cameras, and personal sensors also provide an opportunity to enhance care for the older, more

186 vulnerable groups in the population, especially in winter when the elderly have fewer social

187 interactions (Kimberly Miller, 2013). Such interventions are important today, and will remain

188 so as the population ages and climate change increases the within- and between-season weather

189 variability.

190

191 **Materials and methods**

192 *Data*

193 We used data on all 77,771,264 deaths in the USA from 1980 to 2013 from the National Center

194 for Health Statistics (NCHS). Age, sex, state of residence, month of death, and underlying

195 cause of death were available for each record. Yearly population counts were available from

196 NCHS for 1990 to 2013 and from the US Census Bureau prior to 1990 (Ingram et al., 2003).

197 We calculated monthly population counts through linear interpolation, assigning each yearly

198 count to July. We also subdivided the national data geographically by climate regions used by

199 the National Oceanic and Atmospheric Administration (Figure 1) (Karl & Koss, 1984). The

200 underlying cause of death was coded according to the international classification of diseases

201 (ICD) system (9th revision of ICD from 1980 to 1998 and 10th revision of ICD thereafter).

202

203 Data were divided by sex and age in the following 10 age groups: 0-4, 5-14, 25- 34, 35-44, 45-

204 54, 55-64, 65-74, 75-84, 85+ years. We calculated monthly death rates for each age and sex

205 group, both nationally and for sub-national climate regions. Death rate calculations accounted

206 for varying length of months, by multiplying each month's death count by a factor that would

207 make it equivalent to a 31-day month. For analysis of seasonality by cause of death, we mapped

208 each ICD-9 and ICD-10 codes to the following four disease categories:

209

210 • Cancers: ICD-9 140.0 – 239.9 and ICD-10 C00 – D48

211 • Cardiorespiratory diseases: ICD-9 390.0 – 519.9 and ICD-10 I00 – J99

212 • Injuries (external causes): ICD-9 800.0 – 999.9 and ICD-10 S00 – Z99

213 • Other causes: ICD-9 and ICD-10 codes not in the above three categories

214

215 Cardiorespiratory diseases and cancers accounted for 56.4% and 21.2% of all deaths in the

216 USA, respectively, in 1980, and 40.9% and 23.5%, respectively, in 2013. Deaths from

217 cardiorespiratory diseases have been associated with cold and warm temperatures (Basu, 2009;

218 Basu & Samet, 2002; Bennett, Blangiardo, Fecht, Elliott, & Ezzati, 2014; Braga, Zanobetti, &

219 Schwartz, 2002; Gasparrini et al., 2015). Injuries, which accounted for 8% of all deaths in the

220 USA in 1980 and 7.5% in 2013, may have seasonality that is distinct from so-called natural

221 causes. We did not further divide other causes because the number of deaths could become too

222 small to allow stable estimates when divided by age group, sex and climate region.

223

224   We obtained data on temperature from ERA-Interim, which combines predictions from a

225   physical model with ground-based and satellite measurements (Dee et al., 2011). We used

226   gridded four-times-daily estimates at a resolution of 80km to generate monthly population-

227   weighted temperature by climate region throughout the analysis period.

228

229   *Statistical methods*

230   We used wavelet analysis to investigate seasonality, both nationally and sub-nationally, for

231   each age-sex group. Wavelet analysis uncovers the presence, and frequency, of repeated

232   maxima and minima in each age-sex-specific death rate time series. In brief, a Morlet wavelet,

233   described in detail elsewhere (Cazelles et al., 2008), is equivalent to using a moving window

234   on the death rate time series and analysing periodicity in each window using a short-form

235   Fourier transform, hence generating a dynamic spectral analysis, which allows measuring

236   dynamic seasonal behaviour, in which the periodicity of death rates may disappear, emerge, or

237   change over time. In addition to coefficients that measure the frequency of periodicity, wavelet

238   analysis gives an indication of statistical significance of results compared with random

239   fluctuations that can be represented with white (an independent random process) or red

240   (autoregressive of order 1 process) noise. We used the R package WaveletComp (version 1.0)

241   for the wavelet analysis. Before analysis, we logarithmically transformed death rates, de-

242   trended using a polynomial regression, and rescaled each all-cause mortality death rate time

243   series so as to range between 1 and -1.

244

245   We identified age-sex groups whose wavelet power spectra differed from that of a white noise

246   spectrum, which represents random fluctuations, at 5% significance level, for the entire study

247   period (1980-2013). For age-sex groups which had statistically significant power spectra for

248   1980-2013, we calculated the centre of gravity and the negative centre of gravity of monthly

249 death rates. These parameters show when in the year, on average, maximum and minimum

250 death rates occur, respectively. For calculating centre of gravity, each month was weighted by

251 its death rate; for negative centre of gravity, each month was weighted by the difference

252 between its death rate and the year's maximum death rate. In taking the weighted average, we

253 allowed January (month 1) to neighbour December (month 12), a technique called circular

254 statistics. Along with each circular mean, a 95% confidence interval (CI) was calculated by

255 using 1000 bootstrap samples. The R package CircStats (version 0.2.4) was used for this

256 purpose.

257

258 For each age-sex group and year, we used a Poisson model to estimate the percentage

259 difference in death rates between the maximum and minimum mortality months for each year,

260 and its standard error which accounts for population size. We then fitted a linear regression to

261 the time series of seasonal differences for each age and sex group, weighting each by the

262 inverse of the square of its standard error. We calculated change in the fitted values from 1980

263 to 2013, reported as percentage point difference, as a quantitative measure of how the

264 seasonality of death rates has changed over time.

265

269

270 **Author contributions**

271 All authors contributed to study concept, analytical approach, and interpretation of results. RP,

272 KF and ME collated and organised mortality files. RP performed the analysis, with input from

273 JB. RP and ME wrote the first draft of the paper; other authors contributed to revising and

274 finalising the paper.

275

276 **Competing financial interests**

277 The authors declare no competing financial interests.

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