National and regional seasonal dynamics of all-cause and cause-specific mortality in the USA from 1980 to 201~~3~~6

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Abstract

~~It has been hypothesized that a warmer world may lower winter mortality in~~ In temperate climates, ~~where~~ winter deaths exceed summer ones. However, there is limited information on how the timing and the relative magnitudes of minimum and maximum mortality, by local climate age group, sex and medical cause of death. We used geo-coded mortality data and ~~wavelet analytical techniques~~wavelets to analyse the seasonality of ~~all-cause and cause-specific~~ mortality by age group and sex from 1980 to 201~~3~~6 in ~~the~~ USA~~, nationally~~ and ~~in~~its subnational climatic regions. Death rates in men and women ≥45 years ~~exhibited statistically significant seasonality with peak in January/~~peaked in December to February and ~~minimum~~were lowest in June~~/July~~ to August, driven by ~~seasonality of~~ cardiorespiratory diseases and injuries. In these ages, percent difference in death rates between peak and minimum months did not vary across climate regions, ~~and was largely unchanged~~nor changed from 1980 to 201~~3~~6. Under five years ~~of age~~, seasonality of all-cause mortality largely disappeared after ~~the~~ 1990s. In adolescents and young adults, especially in males, death rates peaked in June/July and were lowest in December/January, driven by ~~seasonality of~~ injury deaths.

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Introduction

~~It is well-established that death rates vary throughout the year, and in temperate climates there tend to be more deaths in winter than in summer (Campbell, 2017; Fowler et al., 2015; Healy, 2003; McKee, 1989). Therefore, it has been hypothesized that a warmer world may lower winter mortality in temperate climates (Langford & Bentham, 1995; Martens, 1998). In a large country like the USA, which possesses distinct climate regions, the seasonality of mortality may vary geographically, due to geographical variations in mortality, localized weather patterns, and regional differences in adaptation measures such as heating, air conditioning and healthcare (Davis, Knappenberger, Michaels, & Novicoff, 2004; Ferreira Braga, Zanobetti, &~~

~~Schwartz, 2001; Kalkstein, 2013; Medina-Ramón & Schwartz, 2007). The presence and extent of seasonal variation in mortality may also itself change over time, due to shifts in weather regimes, lifestyle, adaptation technologies, and healthcare (Bobb, Peng, Bell, & Dominici, 2014; Carson, Hajat, Armstrong, & Wilkinson, 2006; Seretakis, 1997; Sheridan, Kalkstein, & Kalkstein, 2009).~~

It is well-established that death rates vary throughout the year, and in temperate climates there tend to be more deaths in winter than in summer (Campbell, 2017; Fowler et al., 2015; Healy, 2003; McKee, 1989). It has therefore been hypothesized that a warmer world may lower winter mortality in temperate climates (Langford & Bentham, 1995; Martens, 1998). In a large country like the USA, which possesses distinct climate regions, the seasonality of mortality may vary geographically, due to geographical variations in mortality, localized weather patterns, and regional differences in adaptation measures such as heating, air conditioning and healthcare (Davis, Knappenberger, Michaels, & Novicoff, 2004; Ferreira Braga, Zanobetti, & Schwartz, 2001; Kalkstein, 2013; Medina-Ramón & Schwartz, 2007). The presence and extent of seasonal variation in mortality may also itself change over time (Bobb, Peng, Bell, & Dominici, 2014; Carson, Hajat, Armstrong, & Wilkinson, 2006; Seretakis, 1997; Sheridan, Kalkstein, & Kalkstein, 2009).

A thorough understanding of the long-term dynamics of seasonality of mortality, and its geographical and demographic patterns, is needed to identify at-risk groups, plan responses at the present time as well as under changing climate conditions. Although mortality seasonality is well-established, there is limited information on how seasonality, including the timing of 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)~~(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.~~

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, to over three decades of national mortality data. Wavelets have been used to study the dynamics of weather phenomena (Moy, Seltzer, Rodbell, & Anderson, 2002) and infectious diseases (Grenfell, Bjørnstad, & Kappey, 2001). We also used centre of gravity analysis and circular statistics methods to understand the timing of mortality minimum and maximum. In addition, we identify how the percentage difference between death rates in maximum and minimum mortality months has changed over time.

Results

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

All-cause mortality in males had a ~~statistically significant~~ 12-month seasonality in all age groups, except ~~in those aged~~ages 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~~34 years (p-values=0.21 and 0.25, respectively) (Figure ~~2~~3). 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~~Deaths from all ~~four cause groups was~~ causes of death were seasonal in older adults (above 65 or 75 years ~~of age (Figure~~ depending on cause, p-values<0.06) (Figures 2~~).~~ ~~Seasonality in cancer deaths only appeared after 55 years of age, whereas deaths~~-11 and respective figure supplements), except for intentional injuries and substance use disorders. Deaths from cardiorespiratory ~~causes~~diseases, and within it respiratory infections, exhibited ~~statistically significant~~ seasonality throughout the life-course~~.~~ (p-values<0.06) except for males aged 5-24 years and females aged 15-24 years (p-values>0.11). In addition to older ages, ~~injuries~~injury deaths were ~~also~~ seasonal from childhood through 44 years in women and through 64 years in men~~.~~ (p-values<0.09). Unintentional injuries drove the seasonality of injury deaths for females, whereas both unintentional and intentional injuries were seasonal in males in most ages, with the exception of below 15 years and above 85 years when intentional injuries were not seasonal (Figure 8-figure supplement 1). Consistent seasonality in cancer deaths (Figures 3 and 4) only appeared after 55 years of age (p-values<0.05). No consistent seasonality was evident in substance use disorders (Figure 10-supplementary figure 5 and Figure 11-supplementary figure 5) or maternal conditions (Figure 11-supplementary figure 6).

~~Death~~

Centre of gravity analysis showed that death rates in men aged ≥45 years and women aged ≥35 years peaked in December, January ~~and~~or February and were lowest in June~~-~~ to August, for all-cause mortality as well as for all non-injury and non-maternal causes of death ~~with statistically significant seasonality~~(Figure 12 and respective figure supplements). Deaths from cardiorespiratory diseases, including ~~injuries (Figure 3).~~cardiovascular diseases, chronic respiratory diseases and respiratory infections, were also consistently highest in January and February and lowest in July and August across all ages, except for chronic respiratory diseases in ages 5-24 years where there are few deaths from this cause leading to unstable estimates (p-values for seasonality from wavelet analysis ranged from 0.35 to 0.48 for these ages). A similar temporal pattern was seen for all-cause and non-injury mortality in children younger than five years of age, whose all-cause death rate was highest in February and lowest in August. ~~These months also represented maximum and minimum~~In contrast, among males aged 5-34 years, all-cause mortality ~~of children for non-injury causes. In contrast injury deaths in children, adolescents and young and middle-aged adults~~ peaked in June~~/July and were lowest in December/January. Among older boys and young men, not only did injury mortality~~ or July, as did deaths from injuries, which generally had a summer peak in ~~in June/July, but all-cause mortality also.~~ males and females below 45 years of age.

From 1980 to 201~~3~~6, the proportional (percent) difference in all-cause death rates between peak and minimum months declined little for people older than 45 years of age (~~non-significantly and~~ by less than eight percentage points with p-values for declining trend>0.1) (Figure ~~4~~13). In contrast, the difference between peak (summer) and minimum (winter) death rates declined ~~significantly~~ in younger ages, by over 25 percentage points in males aged 5-14 years and 15-24 years~~,~~ (p-values<0.01), largely driven in the declining difference between summer and winter injury deaths. Under five years of age, percent seasonal difference in all-cause death rates declined by ~~a statistically-significant~~ 13 percentage points (~~95% CI 8 to 18~~p-value<0.01) for boys but only ~~a statistically-non-significant~~ 5 percentage points ~~(~~(p-value=0.12~~ to 2~~) for girls. These declines in seasonality of child deaths were a net effect of declining winter-summer difference in cardiorespiratory diseases deaths and increasing summer-winter difference in injury deaths~~.~~, itself driven by increasing difference in non-intentional injuries (Figure 13-figure supplement 2). Within specific cardiorespiratory diseases in under-five children, percent difference declined for cardiorespiratory diseases, cardiovascular diseases, and chronic respiratory diseases while increasing for respiratory infections.

The subnational centre of gravity analysis showsed that all-cause mortality peaks and minima in different climate regions are consistent with the national ones (~~Figure 5~~Figures 14-17), indicating the seasonality is largely independent of geography. The relative homogeneity of the timing of maximum and minimum mortality contrasts with the large variation in seasonal temperatures among climate regions. For example, in men and women aged 65-74 years, all-cause mortality peaked in February in the Northeast and Southeast, even though the average temperatures for those regions were different by over 13 degrees Celsius (9.3 in the Southeast compared with -3.8 in the Northeast). Furthermore, above 45 years of age, there was little inter-region variation in the percent seasonal difference in all-cause mortality, despite the large variation in temperature difference between the peak and minimum months (Figure ~~6). The only cause of death with regional differences in seasonality was injuries in men aged 55-64 years and women aged 65-74 years. Injury death rates in these age-sex groups seemed to peak in January in the Northeast peak and in August in the (Supplementary Figure 1).~~18).

~~**Strengths and limitations**~~

~~The strengths of our study are its innovative methods of characterizing seasonality of mortality dynamically over space and time, by age group and cause of death; using wavelet and centre of gravity analyses; using ERA-Interim data output to compare the association between seasonality of death rates and regional temperature. A limitation of our study is that we used broad causes of death so that we have sufficient number of deaths by age group, sex, year, climate region and cause of death. Different diseases and injuries may be differentially affected by environmental, behavioural and healthcare factors associated with season and hence differ in their seasonal behaviour. For example, suicides have been found to peak in early spring (Feinstein, 2002), and cardiovascular disease mortality may peak earlier in the winter than that from respiratory conditions (Mackenbach, Kunst, & Looman, 1992). Similarly, the seasonality of influenza, and how it has changed over time, may be different than that of other respiratory diseases due to disease-specific interventions (Simonsen et al., 2005). Further, we did not investigate seasonality of mortality by socioeconomic characteristics which may help with understanding its determinants and planning responses.~~

~~Discussion~~

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Discussion

We used wavelet and centre of gravity analyses, which allowed ~~not only~~ systematically identifying and characterizing seasonality of total and cause-specific mortality in the USA, ~~but also examining how seasonality has changed over time. We identified distinct seasonal behaviours in relation to age and sex, including the higher summer mortality in young men (Feinstein, 2002; Rau et al., 2018).~~and examining how seasonality has changed over time. We identified distinct seasonal patterns in relation to age and sex, including higher all-cause summer mortality in young men (Feinstein, 2002; Rau et al., 2018). Importantly, we also showed that all-cause and cause-specific mortality seasonality is largely similar in terms of both timing and magnitude across diverse climatic regions with substantially different summer and winter temperatures~~, with a notable exception of injuries in older ages.~~. Insights of this kind would not have been possible analysing data averaged over time or nationally, or fixed to pre-specified frequencies.

~~Prior studies have noted seasonality of mortality for all-cause mortality and for specific causes of death in the USA (Feinstein, 2002; Kalkstein, 2013; Rau, 2004; Rau et al., 2018; Rosenwaike, 1966; Seretakis, 1997). Few of these studies have done consistent national and subnational analyses, and none has done so over time, for a comprehensive set of age groups and causes of death, and in relation to regional temperature differences. Our results on strong seasonality of cardiorespiratory deaths and weak seasonality of cancer deaths, restricted to older ages, are broadly consistent with these studies (Feinstein, 2002; Rau et al., 2018; Rosenwaike, 1966; Seretakis, 1997), which had limited analysis on how seasonality changes over time and/or geography (Feinstein, 2002; Rau et al., 2018; Rosenwaike, 1966). Similarly, our results on seasonality of injury deaths are supported by a few prior studies (Feinstein, 2002; Rau et al., 2018; Rosenwaike, 1966), but our subnational analysis over three decades revealed~~

~~variations in when injury deaths peaked and in how seasonal differences in these deaths have changed over time which had not been reported before.~~

~~The observed geographical similarity in seasonal mortality variation in the USA, also seen in a study of 36 cities using deaths aggregated across age groups and over time (Kinney et al., 2015), contrasts from the pattern observed across Europe, where the difference between winter and summer mortality tends to be lower in the colder Nordic countries than in warmer southern European nations (Fowler et al., 2015; Healy, 2003; McKee, 1989). The absence of association between the magnitude of mortality seasonality and seasonal temperature difference indicates that different regions in the USA are similarly adapted to temperature seasonality, whereas Nordic countries may have better environmental (e.g., housing insulation and heating) and health system measures to counter the effects of cold winters than those in southern Europe.~~

~~The cause-specific analysis showed that the substantial decline in seasonal mortality differences in adolescents and young adults was related to the diminishing seasonality of injuries, especially from road traffic crashes, which are more likely to occur in the summer months (National Highway Traffic Safety Administration, 2005) and are more common in men. The weakening of seasonality in boys under five years of age was related to two phenomena: first, the seasonality of death from cardiorespiratory diseases declines, and second, the proportion of deaths during the perinatal period, which have limited seasonality, increased (MacDorman & Gregory, 2015).~~

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

A study of 36 cities in the USA, aggregated across age groups and over time, also found that excess mortality was not associated with seasonal temperature range (Kinney et al., 2015). In contrast, a European study found that the difference between winter and summer mortality was lower in the colder Nordic countries than in warmer southern European nations (Healy, 2003; McKee, 1989)(the study's measure of temperature was mean annual temperature which differed from the temperature difference between maximum and minimum mortality used in our analysis although the two measures are correlated). The absence of variation in the magnitude of mortality seasonality indicates that different regions in the USA are similarly adapted to temperature seasonality, whereas Nordic countries may have better environmental (e.g., housing insulation and heating) and health system measures to counter the effects of cold winters than those in southern Europe. If the observed absence of association between the magnitude of mortality seasonality and seasonal temperature difference across the climate regions also persists over time, the changes in temperature as a result of global climate change are unlikely to affect the winter-summer mortality difference.

The cause-specific analysis showed that the substantial decline in seasonal mortality differences in adolescents and young adults was related to the diminishing seasonality of (unintentional) injuries, especially from road traffic crashes, which are more likely to occur in the summer months (National Highway Traffic Safety Administration, 2005) and are more common in men. The weakening of seasonality in boys under five years of age was related to two phenomena: first, the seasonality of death from cardiorespiratory diseases declined, and second, the proportion of deaths from perinatal conditions, which exhibit limited seasonality (Figure 10-figure supplement 4 and Figure 11-figure supplement 4), increased (MacDorman & Gregory, 2015).

In contrast to young and middle ages, mortality in older ages, where death rates are highest, maintained persistent seasonality over a period of three decades (we note that although the percent seasonal difference in mortality has remained largely unchanged in these ages, the absolute difference in death rates between the peak and minimum months has declined because total mortality has a declining long-term trend). This finding demonstrates the need for environmental and health service interventions targeted towards this group irrespective of geography and local climate. Examples of such interventions include enhancing the availability of both environmental and medical protective factors, such as better insulation of homes, winter heating provision and flu vaccinations, for the vulnerable older population ~~(Public Health England, 2017).~~(Public Health England, 2017). Social interventions, including regular visits to the isolated elderly during peak mortality periods to ensure that they are optimally prepared for adverse conditions, and responsive and high-quality emergency care, are also important to protect this vulnerable group ~~(Healy, 2003; Lerchl, 1998; Public Health England, 2017).~~(Healy, 2003; Lerchl, 1998; Public Health England, 2017). Emergent new technologies, such as always-connected hands-free communications devices with the outside world, in-house cameras, and personal sensors also provide an opportunity to enhance care for the older, more vulnerable groups in the population, especially in winter when the elderly have fewer social interactions ~~(Kimberly Miller, 2013).~~(Morris, 2013). Such interventions are important today, and will remain so as the population ages and climate change increases the within- and between-season weather variability.

Materials and methods

Data

~~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).~~

We used data on all 85,854,176 deaths in the USA from 1980 to 2016 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. 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). Yearly population counts were available from NCHS for 1990 to 2016 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 into nine climate regions used by the National Oceanic and Atmospheric Administration (Figure 1 and Table 2) (Karl & Koss, 1984). On average, the Southeast and South are the hottest climate regions with average annual temperatures of 18.4°C and 18°C respectively; the South also possesses the highest average maximum monthly temperature (27.9°C in July). The lowest variation in temperature throughout the year is that of the Southeast (an average range of 17.5°C). The three coldest climate regions are West North Central, East North Central and the Northwest (7.8°C, 8.0°C, 8.1°C respectively). Mirroring the characteristics of the hottest climate regions, the largest variation in temperature throughout the year is that of the coldest region, West North Central (an average range of 30.5°C), which also has the lowest average minimum monthly temperature (-6.5°C in January). The other climate regions, Northeast, Southwest, and Central, possess similar average temperatures (11 to 13°C) and variation within the year of (23 to 26°C), with the Northeast being the most populous region in the United States (with 19.8% total population in 2016).

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Data were divided by sex and age in the following 10 age groups: 0-4, 5-14, 25- 34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+ years. We calculated monthly death rates for each age and sex group, both nationally and for sub-national climate regions. Death rate calculations accounted for varying length of months, by multiplying each month's death count by a factor that would make it equivalent to a 31-day month. ~~For analysis of seasonality by cause of death, we mapped each ICD-9 and ICD-10 codes to the following four disease categories:~~

- ~~Cancers: ICD-9 140.0 – 239.9 and ICD-10 C00 – D48~~
- ~~Cardiorespiratory diseases: ICD-9 390.0 – 519.9 and ICD-10 I00 – J99~~
- ~~Injuries (external causes): ICD-9 800.0 – 999.9 and ICD-10 S00 – Z99~~
- ~~Other causes: ICD-9 and ICD-10 codes not in the above three categories~~

~~Cardiorespiratory diseases and cancers accounted for 56.4% and 21.2% of all deaths in the USA, respectively, in 1980, and 40.9% and 23.5%, respectively, in 2013. Deaths from cardiorespiratory diseases have been associated with cold and warm temperatures (Basu, 2009; Basu & Samet, 2002; Bennett, Blangiardo, Fecht, Elliott, & Ezzati, 2014; Braga, Zanobetti, & Schwartz, 2002; Gasparrini et al., 2015). Injuries, which accounted for 8% of all deaths in the USA in 1980 and 7.5% in 2013, may have seasonality that is distinct from so-called natural causes. We did not further divide other causes because the number of deaths could become too small to allow stable estimates when divided by age group, sex and climate region.~~

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

~~*Statistical methods*~~

~~We used wavelet analysis to investigate seasonality, both nationally and sub-nationally, for each age-sex group. Wavelet analysis uncovers the presence, and frequency, of repeated maxima and minima in each age-sex-specific death rate time series. In brief, a Morlet wavelet, described in detail elsewhere (Cazelles et al., 2008), is equivalent to using a moving window on the death rate time series and analysing periodicity in each window using a short-form~~

~~Fourier transform, hence generating a dynamic spectral analysis, which allows measuring dynamic seasonal behaviour, in which the periodicity of death rates may disappear, emerge, or change over time. In addition to coefficients that measure the frequency of periodicity, wavelet analysis gives an indication of statistical significance of results compared with random fluctuations that can be represented with white (an independent random process) or red (autoregressive of order 1 process) noise. We used the R package WaveletComp (version 1.0) for the wavelet analysis. Before analysis, we logarithmically transformed death rates, de-trended using a polynomial regression, and rescaled each all-cause mortality death rate time series so as to range between 1 and -1.~~

~~We identified age-sex groups whose wavelet power spectra differed from that of a white noise spectrum, which represents random fluctuations, at 5% significance level, for the entire study period (1980-2013). For age-sex groups which had statistically significant power spectra for 1980-2013~~For analysis of seasonality by cause of death, we mapped each ICD-9 and ICD-10 codes to four main disease categories (Table 1) and to a number of subcategories which are presented in the Supplementary Note. Cardiorespiratory diseases and cancers accounted for 56.4% and 21.2% of all deaths in the USA, respectively, in 1980, and 40.3% and 22.4%, respectively, in 2016. Deaths from cardiorespiratory diseases have been associated with cold and warm temperatures (Basu, 2009; Basu & Samet, 2002; Bennett, Blangiardo, Fecht, Elliott, & Ezzati, 2014; Braga, Zanobetti, & Schwartz, 2002; Gasparrini et al., 2015). Injuries, which accounted for 8% of all deaths in the USA in 1980 and 7.3% in 2016, may have seasonality that is distinct from so-called natural causes. We did not further divide other causes because the number of deaths could become too small to allow stable estimates when divided by age group, sex and climate region.

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We used wavelet analysis to investigate seasonality for each age-sex group. Wavelet analysis uncovers the presence, and frequency, of repeated maxima and minima in each age-sex-specific death rate time series (Hubbard, 1998; Torrence & Compo, 1998). In brief, a Morlet wavelet, described in detail elsewhere (Cazelles et al., 2008), is equivalent to using a moving window on the death rate time series and analysing periodicity in each window using a short-form Fourier transform, hence generating a dynamic spectral analysis, which allows measuring dynamic seasonal patterns, in which the periodicity of death rates may disappear, emerge, or change over time. In addition to coefficients that measure the frequency of periodicity, wavelet analysis estimates the probability of whether the data are different from the null situation of random fluctuations that can be represented with white (an independent random process) or red (autoregressive of order 1 process) noise. For each age-sex group, we calculated the p-values of the presence of 12-month seasonality for the comparison of wavelet power spectra of the entire study period (1980-2016) with 100 simulations against a white noise spectrum, which represents random fluctuations. We used the R package WaveletComp (version 1.0) for the wavelet analysis. Before analysis, we de-trended death rates using a polynomial regression, and rescaled each death rate time series so as to range between 1 and -1.

To identify the months of maximum and minimum death rates, we calculated the centre of gravity and the negative centre of gravity of monthly death rates. ~~These parameters show when~~

~~in the year, on average, maximum and minimum death rates occur, respectively. For calculating centre~~Centre of gravity~~, each month~~ was calculated as a weighted average of months of deaths, with each month weighted by its death rate; ~~for~~ negative centre of gravity~~,~~ was also calculated as a weighted average of months of deaths, but with each month was weighted by the difference between its death rate and the year's maximum death rate. In taking the weighted average, we allowed ~~January (month 1) to neighbour December (month 12), a technique called circular statistics.~~December (month 12) to neighbour January (month 1), representing each month by an angle subtended from 12 equally-spaced points around a unit circle. Using a technique called circular statistics, a mean ($\bar{\theta}$)of the angles ($\theta_1, \theta_2, \theta_3 \ldots, \theta_{n,}$) representing the deaths (with n the total number of deaths in an age-sex group for a particular cause of death) is found using the relation below:

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

where *arg* denotes the complex number argument and θ_j denotes the month of death in angular form for a particular death *j*. The outcome of this calculation is then converted back into a month value (Fisher, 1995). Along with each circular mean, a 95% confidence interval (CI) was calculated by using 1000 bootstrap samples. The R package CircStats (version 0.2.4) was used for this ~~purpose~~analysis.

For each age-sex group and cause of death, and for each year, we calculated the percent difference in death rates between the maximum and minimum mortality months. We fitted a linear regression to the time series of seasonal differences from 1980 to 2016, and used ~~a Poisson model~~the fitted trend line to estimate how much the percentage difference in death rates between the maximum and minimum mortality months ~~for each year, and its standard error which accounts for population size. We then fitted a linear regression to the time series~~

~~of seasonal differences for each age and sex group, weighting each~~had changed from 1980 to 2016. We weighted seasonal difference by the inverse of the square of its standard error~~. We calculated~~ , which was calculated using a Poisson model to take population size of each age-sex group through time into account. This method gives us a p-value for the change in ~~the fitted values from 1980 to 2013, reported as percentage point difference, as a quantitative~~seasonal difference per year, which we used to calculate the seasonal difference at the start (1980) and end (2016) of the period of study. Our method of analysing seasonal differences avoids assuming that any specific month or group of months represent highest and lowest number of deaths for a particular cause of death, which is the approach taken by the traditional measure of ~~how the seasonality of death rates has changed over time.~~ Excess Winter Deaths. It also allows the maximum and minimum mortality months to vary by age group, sex and cause of death.

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~~**Author contributions**~~

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

Competing financial interests

The authors declare no competing financial interests.

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Figure 1: Climate regions of the USA.

Figure 2: Wavelet power spectra for national time series of all-cause ~~and cause-specific~~ death rates for 1980-201~~3~~6, by age group ~~and cause of death~~ for ~~(A)~~ males ~~and (B) females~~. Wavelet power values increase from blue to red~~, with white contour lines indicating~~. The shaded regions at the ~~5% significance level against a white noise spectrum (~~left and right edge of each box indicate the ~~same~~cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 3: Wavelet power spectra for national time series of all-cause death rates for 1980-2016, by age ~~groups would remain significant if significance had been measured against a~~group for females. Wavelet power values increase from blue to red~~ noise spectrum).~~. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust.

P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 4: Wavelet power spectra for national time series of cancer death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 5: Wavelet power spectra for national time series of cancer death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 6: Wavelet power spectra for national time series of cardiorespiratory disease death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 6-figure supplement 1: Wavelet power spectra for national time series of cardiovascular disease death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 6-figure supplement 2: Wavelet power spectra for national time series of chronic respiratory disease death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 6-figure supplement 3: Wavelet power spectra for national time series of respiratory infection death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 7: Wavelet power spectra for national time series of cardiorespiratory disease death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 7-figure supplement 1: Wavelet power spectra for national time series of cardiovascular disease death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 7-figure supplement 2: Wavelet power spectra for national time series of chronic respiratory disease death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 7-figure supplement 3: Wavelet power spectra for national time series of respiratory infection death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 8: Wavelet power spectra for national time series of injury death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 8-figure supplement 1: Wavelet power spectra for national time series of intentional injury death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 8-figure supplement 2: Wavelet power spectra for national time series of unintentional injury death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 9: Wavelet power spectra for national time series of injury death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 9-figure supplement 1: Wavelet power spectra for national time series of intentional injury death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 9-figure supplement 2: Wavelet power spectra for national time series of unintentional injury death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 10: Wavelet power spectra for national time series of death rates from causes other than cancers, cardiorespiratory diseases and injuries for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 10-figure supplement 1: Wavelet power spectra for national time series of endocrine disorder death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 10-figure supplement 2: Wavelet power spectra for national time series of genitourinary disease death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 10-figure supplement 3: Wavelet power spectra for national time series of neuropsychiatric disorder death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 10-figure supplement 4: Wavelet power spectra for national time series of perinatal condition death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 10-figure supplement 5: Wavelet power spectra for national time series of substance use disorder death rates for 1980-2016, by age group for males. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 11: Wavelet power spectra for national time series of death rates from causes other than cancers, cardiorespiratory diseases and injuries for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 11-figure supplement 1: Wavelet power spectra for national time series of endocrine disorder death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 11-figure supplement 2: Wavelet power spectra for national time series of genitourinary disease death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 11-figure supplement 3: Wavelet power spectra for national time series of neuropsychiatric disorder death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 11-figure supplement 4: Wavelet power spectra for national time series of perinatal condition death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 11-figure supplement 5: Wavelet power spectra for national time series of substance use disorder death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 11-figure supplement 6: Wavelet power spectra for national time series of maternal condition death rates for 1980-2016, by age group for females. Wavelet power values increase from blue to red. The shaded regions at the left and right edge of each box indicate the cone of influence, where spectral analysis is less robust. P-values for the presence of 12-month seasonality are to the right of each figure at the 12-month line.

Figure 12: Mean timing of ~~national~~ maximum and minimum all-cause and cause-specific mortality at the national level, by sex and age group for 1980-201~~3~~6. Red arrows indicate the month of maximum mortality, and green arrows that of minimum mortality. The size of the arrow is inversely proportional to its respective ~~95% confidence interval. Only age-sex groups with statistically significant 12-month seasonality are included.~~

variance.

Figure 412-figure supplement 1: Mean timing of maximum and minimum mortality for specific cardiorespiratory diseases at the national level, by sex and age group for 1980-2016. Red arrows indicate the month of maximum mortality, and green arrows that of minimum mortality. The size of the arrow is inversely proportional to its respective variance.

Figure 12-figure supplement 2: Mean timing of maximum and minimum mortality for specific injuries at the national level, by sex and age group for 1980-2016. Red arrows indicate the month of maximum mortality, and green arrows that of minimum mortality. The size of the arrow is inversely proportional to its respective variance.

Figure 12-figure supplement 3: Mean timing of maximum and minimum mortality for the cluster of causes other than cancers, cardiorespiratory diseases and injuries at the national level, by sex and age group for 1980-2016. Red arrows indicate the month of maximum mortality, and green arrows that of minimum mortality. The size of the arrow is inversely proportional to its respective variance.

Figure 13: National percent difference in death rates between the maximum and minimum mortality months ~~in 2013~~for all-cause and cause-specific mortality in 2016 versus 1980~~ by sex and age group. Only age-sex groups with statistically significant 12-month seasonality are included. Age-sex groups with a statistically significant change at the 5% level are highlighted with a bold pink outline.~~

, by sex and age group.

Figure ~~5~~13-figure supplement 1: National percent difference in death rates between the maximum and minimum mortality months for specific cardiorespiratory diseases in 2016 versus 1980, by sex and age group.

Figure 13-figure supplement 2: National percent difference in death rates between the maximum and minimum mortality months for specific injuries in 2016 versus 1980, by sex and age group.

Figure 13-figure supplement 3: National percent difference in death rates between the maximum and minimum mortality months for the cluster of causes other than cancers, cardiorespiratory diseases and injuries in 2016 versus 1980, by sex and age group.

Figure 14: Mean timing of ~~(A)~~ maximum ~~and (B) minimum~~ all-cause mortality for 1980-2016, by climate region~~, sex~~ and age group for ~~1980-2013. Only age-sex groups with significant 12-month seasonality~~ males. Average temperatures (in ~~the national analysis~~degrees Celsius) are included in white for the corresponding month of maximum and minimum mortality for each climate region.

Figure 15: Mean timing of minimum all-cause mortality for 1980-2016, by climate region and age group for males. Average temperatures (in degrees Celsius) are included in white for the corresponding month of maximum and minimum mortality for each climate region.

Figure 16: Mean timing of maximum all-cause mortality for 1980-2016, by climate region and age group for females. Average temperatures (in degrees Celsius) are included in white for the corresponding month of maximum and minimum mortality for each climate region.

Figure 17: Mean timing of minimum all-cause mortality for 1980-2016, by climate region and age group for females. Average temperatures (in degrees Celsius) are included in white for the corresponding month of maximum and minimum mortality for each climate region. ~~See Supplementary Figure 1 for results by cause of death.~~

Figure ~~6~~18: The relationship between percent difference in all-cause death rates and temperature difference between months with maximum and minimum mortality across climate regions, by sex and age group in ~~2013. Only age-sex groups with significant 12-month seasonality in the national analysis are included.~~2016.

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~~**Supplementary Figure 1:** Mean timing of (A) maximum and (B) minimum cause-specific mortality, by climate region, sex and age group for 1980-2013. Only age-sex groups with significant 12-month seasonality in the national analysis are included. Average temperatures (in degrees Celsius) are included in white for the corresponding month of maximum and mortality for each climate region.~~**Table 1:** Number of deaths, by cause of death and sex from 1980 to 2016.

Cause	**Male**	**Female**	**Total**
All cause	43,558,203	42,295,973	**85,854,176**
Cancers	10,481,582	9,476,530	19,958,112
Cardiorespiratory diseases	20,168,049	21,109,525	41,277,574
Cardiovascular diseases	16,238,344	17,210,556	33,448,900
Chronic respiratory diseases	2,791,652	2,595,950	5,387,602
Respiratory infections	1,138,053	1,303,019	2,441,072
Injuries	4,034,876	1,768,170	5,803,046
Unintentional	2,489,142	1,348,187	3,837,329
Intentional	1,545,734	419,983	1,965,717
Other causes	8,873,696	9,941,748	18,815,444

Table 2: Characteristics of climate regions of the USA.

Climate region	**Constituent states**	**Population (2016)**	**Mean annual temperature (1980-2016) (°C)**
Central	Illinois, Indiana, Kentucky, Missouri, Ohio, Tennessee, West Virginia	50,191,326	11.6
East North Central	Iowa, Michigan, Minnesota, Wisconsin	24,418,738	8
Northeast	Connecticut, Delaware, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont	64,046,741	10.6
Northwest	Alaska, Idaho, Oregon, Washington	13,811,810	8.2
South	Arkansas, Kansas, Louisiana, Mississippi, Oklahoma, Texas	45,388,414	18
Southeast	Alabama, Florida, Georgia, North Carolina, South Carolina, Virginia	59,356,072	18.4
Southwest	Arizona, Colorado, New Mexico, Utah	17,613,981	13.6
West	California, Hawaii, Nevada	43,708,574	16.6
West North Central	Montana, Nebraska, North Dakota, South Dakota, Wyoming	5,168,753	7.6