

Summertime, and the livin' is easy: Winter and summer pseudoseasonal life expectancy in the United States

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Abstract

BACKGROUND: In temperate climates, mortality is seasonal with a winter-dominant pattern, due in part to specific causes of death, including pneumonia, influenza and cold-induced thrombosis. Cardiac causes, which are the leading cause of death in the United States, are winter-seasonal although the pathways are incompletely understood. Interactions between circulating respiratory viruses (f.e., influenza) and cardiac conditions have been suggested as a cause of winter-dominant mortality patterns.

OBJECTIVE: To quantify the total mortality burden of winter in the United States.

METHODS: We calculate “pseudo-seasonal” life expectancy, dividing the year into two six-month spans, one encompassing winter, and the other summer.

RESULTS: During the summer when cold weather is absent and the circulation of respiratory viruses is drastically reduced, life expectancy is about one year longer. We also quantify the seasonal mortality difference in terms of seasonal “equivalent ages” (defined herein) and proportional hazards.

CONTRIBUTION: We quantify the effects of winter mortality. The population-level mortality reduction of a perfect influenza vaccine (which can only reduce a portion of winter-attributable mortality) would be much more modest than is often recognized.

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*Summertime,
And the livin' is easy
Fish are jumpin'
And the cotton is high*
— George Gershwin
“Summertime”



Introduction

The primary goal of this paper is to quantify the mortality impact of winter in the United States, in terms of life expectancy. To accomplish this, we analyze life expectancy in the United States from a seasonal perspective. We calculate two life expectancies per 12-month period (“pseudowinter” and “pseudosummer”), using methods described below. The point is to estimate life expectancy in the absence of respiratory viruses (most notably, influenza) and the effects of cold, using pseudosummer as an approximation. Pseudowinter, on the other hand, estimates life expectancy in the presence of these viruses and cold-induced conditions. The difference between life expectancy in pseudowinter and pseudosummer gives the total mortality impact of winter. The pseudoseasonal approach also illuminates within-year mortality fluctuations.

Mortality in temperate climates is highly seasonal, with winter peaks and summer troughs (Rosenberg 1966, Land and Cantor 1983, Kalkstein and Davis 1989, Mackenbach et al. 1992, Rau 2006, Deschênes and Moretti 2009, Deschênes and Greenstone 2011). Respiratory and cardiovascular causes, including stroke (Sheth et al. 1999, Yang et al. 2016), dominate the seasonal effects, with cancer being negligibly cyclical (Crombie et al., 1995). Heat wave mortality peaks are ephemeral interruptions of this overall pattern (f.e. Basu and Samet 2002, Klinenberg 2002, Valleron and Boumendil 2004, Kaiser et al. 2007, Toulemon and Barbieri 2008, Rocklöv et al. 2011, Robine et al. 2012, Åström et al. 2013). Heat wave-associated deaths have a different composition by cause compared to summer mortality (Huynen et al. 2001, Basagaña et al. 2011), although Rey et al. (2007) report increases in most causes at older ages. Heat wave mortality interacts with air pollution (Rooney et al. 1998, Bhaskaran et al. 2009). Both severity and duration of heat waves are important for mortality (Anderson and Bell, 2009).

Temperature is thought to play a role in mortality seasonality (Mackenbach et al. 1993, Braga et al. 2001, 2002, Curriero et al. 2002, Mercer 2003). However, temperature-associated deaths in a literal sense (f.e., hypothermia or heat stroke) are relatively unimportant, with cold-related deaths slightly exceeding heat-related deaths, at least in the United States (Berko et al., 2014). Nonetheless, the expansion over time of adequate winter heating in the United States has been suggested as a possibly-overlooked factor in the long-term decline of heart disease (Seretakis et al., 1997). Congruently, Kunst et al. (1991) report declines in winter excess mortality in the Netherlands between the 1950s and the 1980s. On the other hand, van Rossum et al. (2001), do not find changes in seasonal mortality over 25 years in English civil servants. Insufficient winter heating among the poor may not play a significant role in mortality in Britain (Wilkinson et al., 2004) or Denmark (Rau, 2004). Healy (2003) demonstrates that the coefficient of seasonal variation in mortality (CSVM) is correlated with mean winter temperature (warmer temperature, higher CSVM) at the country level in Europe; see also Keatinge et al. (1997, 2000), Díaz et al. (2005), Gasparrini et al. (2015), and Carmona et al. (2016). Analitis et al. (2008) also find an association between cold weather and mortality in European cities, and similarly note greater cold effect in warmer climates. Yang et al. (2012) and Zhao et al. (2015) find similar results in subtropical Asia. Kysely et al. (2009) find increased cardiovascular mortality in all ages above 25 during cold spells in the Czech republic. Mortality in nursing homes appears to be sensitive to both hot and cold temperature extrema (Stafoggia et al. 2006, Hajat et al. 2007).

The role of temperature in mortality is an important topic in historical demography, too large to survey completely here. Much of this work focuses on summer mortality, especially diarrhea among infants and children (f.e. Galloway 1985, Breschi and Livi-Bacci 1986*a,b,c*, Woods et al. 1989). There is a smaller body of work on winter peaks in infant mortality before the twentieth century. In particular, the hypothermia hypothesis suggests that neonatal mortality increased in cold periods (Dalla-Zuanna and Rosina 2009, 2011; see also Derosas 2009, 2010 and Dalla-Zuanna and Rosina 2010). Analyzing historical data from a cold-winter climate, Åström et al. (2016) find that warmer spells are associated with lower mortality. Ekamper et al. (2009) find a strong social class influence on temperature-mortality relationships in historical data from the Netherlands, and review some of the literature on cold and mortality in the past.

Cold temperature affects susceptibility to viruses in mice (Foxman et al., 2015) and in human cells *in vitro* (Foxman et al., 2016), although the evi-

dence in humans is mixed (Dowling et al. 1958, Douglas et al. 1968, Graham 1990, Mourtzoukou and Falagas 2007, Footitt and Johnston 2009, Eccles and Wilkinson 2015, Ikäheimo et al. 2016). There may be synergistic effects of temperature and humidity (Lowen et al. 2007, Mäkinen et al. 2009, Shaman and Kohn 2009, te Beest et al. 2013). In the United States, mortality peaks coincide with the Christmas and New Year's holidays, which occur during the northern hemisphere winter (Phillips et al., 2004, 2010). However, Christmas effects on cardiovascular mortality also occur in New Zealand, where the holiday falls in the summertime (Knight et al., 2016). Hypovitaminosis D, which is seasonal with winter peaks (Kasahara et al., 2013), is also thought to play a role in fatal diseases (Holick, 2007).

Mortality seasonality at temperate latitudes is influenced by more than just viral circulation. Cold can affect thrombosis, with consequences for stroke and myocardial infarction (Keatinge et al. 1984, 1986). Pan et al. (1995) write: "poor thermoregulation in older people may precipitate cardiovascular disease events." Zöller et al. (2013) note winter peaks in venous thromboembolism in Sweden. The causal connection between winter cold and thromboembolism may be coagulation factors (Dentali et al., 2009). On the other hand, there is some evidence that extreme cold (below -30°C) may reduce mortality (Otrachshenko et al. 2017), although the mechanism may be as prosaic as people staying indoors when it is that cold outside.

Air pollution is another contributor to mortality seasonality in temperate climates. All else equal, air pollution is positively associated with increased mortality (Schwartz and Dockery 1992, Chay et al. 2003, Chay and Greenstone 2003, 2005, Currie et al. 2009). This relationship can affect mortality in winter and summer. In the summertime, daytime UV radiation plays a role in air pollution (Cleveland and Graedel, 1979). In the wintertime, solar UV incidence is lower, but some air pollution, including particulates, is often higher due to home heating emissions (Currie and Neidell 2005, Janhäll et al. 2006, Olofson et al. 2009, Johnston et al. 2013, Tang et al. 2017). Pollution is another example of multidimensionality of the seasonality of mortality.

The root causes of infectious disease mortality seasonality remain poorly understood (Dowell 2001, Cheng 2005). There seems to be a nexus between viral activity and adverse cardiovascular events (Bainton et al. 1978, Kunst et al. 1993, Madjid et al. 2004, Huy et al. 2012, Udell et al. 2013). However, the extent to which respiratory virus transmission during the winter (Glezen et al., 1987) causes increased mortality from other causes is debated (Reichert et al. 2004, Warren-Gash et al. 2012, Foster et al. 2013). The role of astronomical season (*viz.*, through associated weather changes) in the

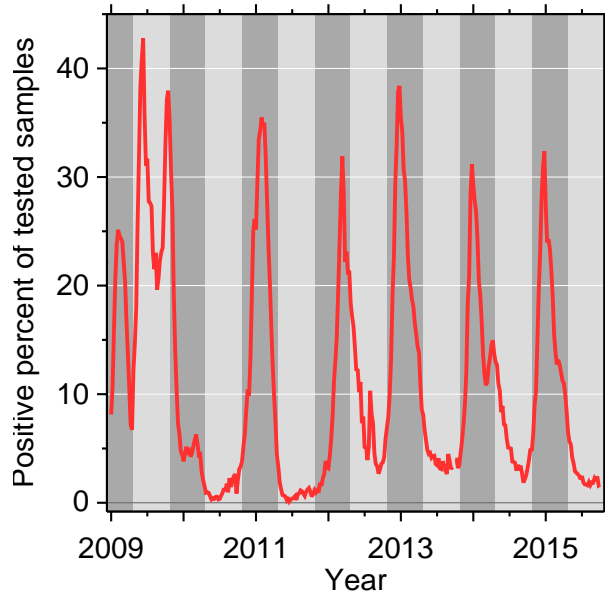


Figure 1: Percent of respiratory specimens testing positive for influenza virus, 2009–15. Weekly data from CDC (2015). Pseudowinters are shaded dark.

cyclicality of infectious disease is also debated (Fisman 2012, Treanor 2016), with the school calendar (Grenfell and Anderson, 1989), and dynamic resonance (Dushoff et al., 2004) among alternate hypotheses. The plurality of explanations suggests to us that “the mechanisms underlying seasonality [of viral transmission] still remain essentially unexplained” (Yorke et al., 1979, pp. 104–5); see also Lofgren et al. (2007). Determining the *causes* of seasonality of respiratory virus transmission is beyond our scope. Rather, we are concerned with estimating the mortality *consequences* of such seasonality.

Data and methods

We present a simple approach to estimate the overall impact of winter on mortality. We divide the year into two six-month “pseudoseasons”, and calculate life expectancy for these periods. The seasonal binning approach using *all-cause mortality* avoids potential classification pitfalls of counterfactual approaches such as cause-deleted life tables (in which winter-dominant causes such as respiratory viruses and thrombosis are deleted) or other approaches which rely on cause of death reporting (f.e., Stewart, 2011). Cause-deleted

life expectancy is calculated with specific causes statistically removed (Manton et al., 1986), while our approach studies all-cause mortality, but truly in the absence of winter-related mortality, i.e., in the summertime. The major strength of our approach is that our mortality estimates are not hypothetical “as if” constructs, but reflect observed conditions when no (or very little) flu virus circulates and in which there is no cold-related thrombosis mortality, and so on. Among the problems this avoids are classification errors regarding what is an influenza (or thrombosis or etc.) death (cf. Noymer and Nguyen, 2013).

Regarding the influenza component of winter mortality, the noncirculation of flu viruses in the summertime is not absolute, as figure 1 shows. This is a time series plot of respiratory specimens (f.e., nasal swabs) positive for any strain of the influenza virus (as a percentage, so peaks are not reflective of more samples during the winter). Note that even in the peaks, most samples test negative; there are many causes of upper respiratory illness other than influenza virus. Most peaks of influenza occur in the shaded pseudowinters, but the 2009 swine-origin influenza pandemic is a major exception. During influenza pandemics, which involve emergence of new strains, viral circulation in the summer is more likely (Webster et al., 1992).

From the mortality detail files of the National Center for Health Statistics (NCHS 2015), we extracted monthly data on every death in the United States, January 1959 to December 2014¹. The data were then aggregated by sex and 22 age groups (0,1–4,5–9,...,95–99,≥100), and binned into six-month pseudoseasons. Pseudowinter is November through April, and pseudosummer is May through October; pseudoseasons do not nest into calendar years. In long-run averages, these six-month periods best capture influenza virus circulation or lack thereof.² The data begin with pseudosummer 1959 and end with pseudosummer 2014 (56 pseudosummers). There are 55 pseudowinters (1960–61 to 2013–14). Data for January through April 1959 were

¹Prior to 1959, digitized mortality data are not available for the United States that are simultaneously disaggregatable by age, sex, and month.

²The exact onset and cessation of the flu season — by which we mean epidemiologically-significant influenza virus transmission — varies from year to year. Thompson et al. (2009) (p. 38) use October to April, but we prefer, for symmetry, to have six-month pseudoseasons. There is not much flu transmission in October in the United States (Simonsen et al. 2005, p. 268). Furthermore, Nunes et al. (2011) note: “In the absence of any reliable external source of information to define the E_a [i.e., transmission] periods one should definitely choose the fixed period approach” (p. 343) — since most of our data precede influenza viral monitoring, we are definitely in this boat, so our approach is best-practice. Moreover, evaluations have shown that fixed versus variable winter-season approaches produce very similar results for flu-specific disease burden estimates (Newall et al. 2010).

discarded since using these data for pseudowinter 1958–59 would be biased due to the omission of November and December 1958. Similarly, November and December 2014 were discarded. We constructed denominators using age- and sex-specific calendar-year exposure data from the Human Mortality Database (2016). We graduated these person-years-at-risk data to months, adjusting for days per month and leap years, and then re-aggregated to make pseudoseasonal exposures. The specifics of the denominator construction are described in the appendix. We then calculated sex- and age-specific death rates (deaths divided by person-years lived) for each pseudoseason, from which we calculated sex-specific period life tables in the standard way (Keyfitz 1970, Preston et al. 2001).

Using pseudoseasons, as defined, is the closest approximation to respiratory virus transmission patterns. Some early flu seasons start in November, and some late flu seasons can persist into April. An alternative would be to omit shoulder periods, by using December–March for pseudowinter and June–September for pseudosummer. This would provide greater winter–summer contrast, but has the disadvantage of leaving some data unused. More importantly, enhancing contrast is not our goal. We are trying to account for the overall influence of winter on mortality, whether there is contrast or not. What is more, cold weather occurs well before and after the winter astronomical season (i.e., between the winter solstice and vernal equinox), so for cold-related causes of death like thrombosis, a similar logic applies.

Results

Figure 2 presents four $e(0)$ (life expectancy) time series: pseudowinter (solid) and pseudosummer (dashed), for both males (lower series, blue) and females (upper series, red). The gray tubes enveloping each sex are 2-year-wide bands centered on calendar-year life expectancy from the Human Mortality Database (HMD); these are not uncertainty intervals. The top of the gray band represents the calendar-year $e(0)+1$; thus, in our data, the summer pseudoseasonal life expectancy is never greater than one year above the neighboring calendar-year life expectancy. Similarly, since the bottom of the gray band is the calendar-year $e(0)-1$, it shows that, in this data set, winter pseudoseasonal life expectancy is always within one year of the neighboring calendar-year $e(0)$. Using the HMD $e(0)$ data as the center of the band also provides an external check of our life expectancy calculations, since our pseudoseasonal data should fairly neatly sandwich the calendar-year series.

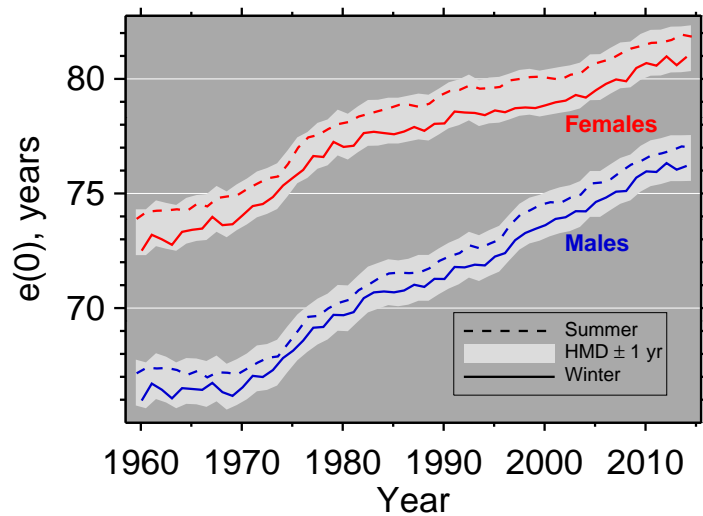


Figure 2: Life expectancy ($e(0)$) time series by sex and by pseudoseason. The band enveloping the series is two years in height, centered on the calendar-year $e(0)$ estimates from Human Mortality Database (2016); it is not an uncertainty interval.

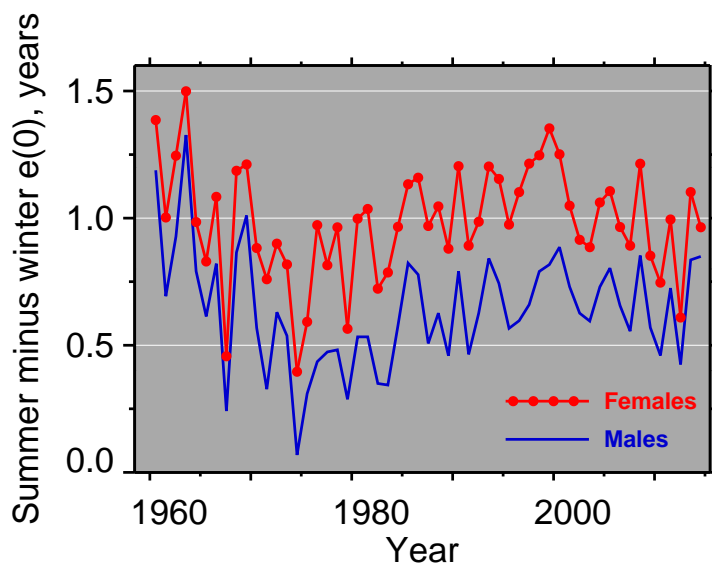


Figure 3: Summer advantage over winter in pseudoseasonal life expectancy, females (upper series) and males (lower series).

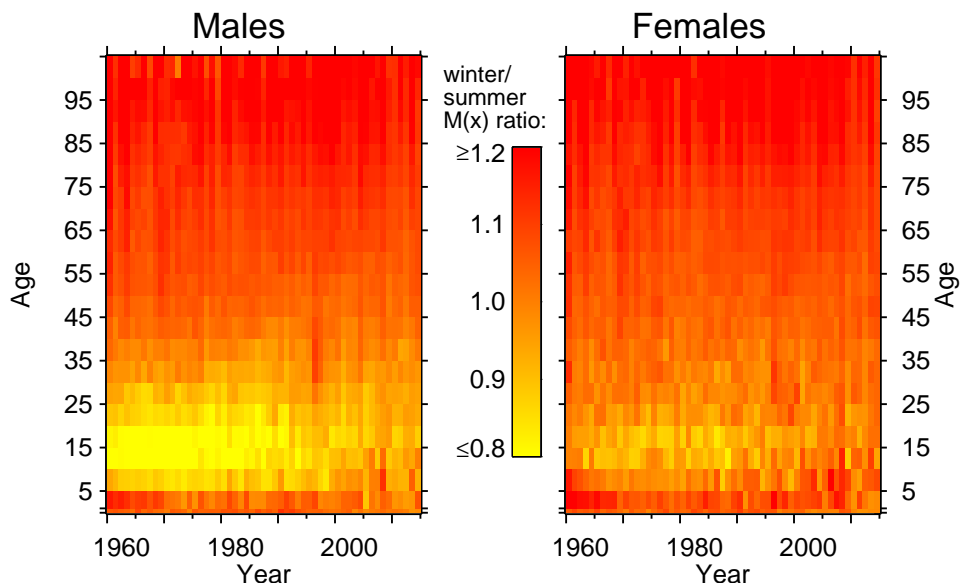


Figure 4: Heatmap of winter:summer ratio of M_x , 1960–2014. At younger ages (above childhood), summer has higher mortality, although this has decreased over time. At older ages, winters have higher mortality.

Figure 3 shows the difference between $e(0)$ in summers and their preceding winters (from the summer of 1960 minus the winter of 1959–60, to the summer of 2014 minus the winter of 2013–14); all comparisons are summer-to-previous-winter, although summer-to-following-winter analyses give similar results. There are three important features. First, no secular time trend is evident. Second, the data are strongly negatively autocorrelated: declines are followed by increases, and vice versa. Third, in addition to higher life expectancy, women have a higher summer–winter difference, 0.99 ± 0.22 years, versus 0.64 ± 0.23 years for males (mean \pm SD).

Figure 4 is a heat map of the winter:summer ratio of the mortality rate by age (M_x), over time. Several features of figure 4 are especially relevant to seasonal differences. First, summer advantage in mortality is an age-related phenomenon. At younger ages (approximately 5–35), summers are more deadly. The summer excess is more pronounced for males, and is declining over time. It is particularly noticeable in the so-called accident bump (Pampel, 2001). Indeed, summer mortality at younger ages is associated with motor vehicle fatalities (Farmer and Williams, 2005) and external causes

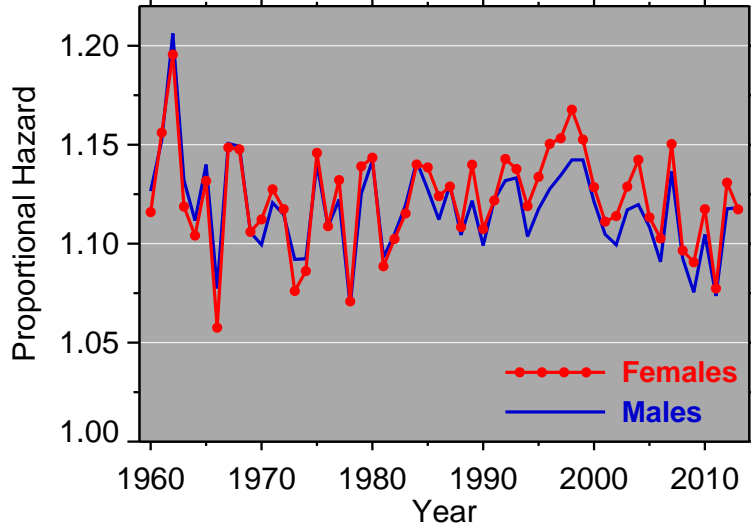


Figure 5: Proportional hazard analysis. The proportional hazard is winter death rates above age 45 as a multiple of summer death rates.

generally (Feinstein, 2002). Winter overtakes summer above age 45, where death rates are (much) higher in absolute terms.

Figure 5 helps quantify the pseudoseasonal differences seen in figure 4. Here we present, on a year-by-year basis, the proportional hazard (P^Y) of pseudoseasonal mortality for age ≥ 45 , separately by sex. Thus, we model $\mathbf{W} = P^Y \mathbf{S}$ where \mathbf{W} is the N -element (age-wise) vector of winter death rates for a given year, P^Y is the year-specific proportional hazard (scalar), and \mathbf{S} is the vector of summer death rates. The proportional hazard is estimated as:

$$P^Y = \exp \left(\frac{\sum_{x=45}^{\omega} [\log (M_x^W) - \log (M_x^S)]}{N} \right) \quad (1)$$

where the superscripts (W, S) refer to winter and summer and M_x is the age-specific death rate. The proportional hazard is the same as the winter to summer ratio of the geometric mean death rate (see Schoen 1970).³ Figure 6 gives an example of how P^Y works, showing winter and summer pseudoseasonal M_x as well as “simulated” winter: $M_{x,\text{simu}}^W = M_{x,\text{data}}^S P^Y$.

Figure 6 shows good agreement between simulated and true winter, especially between ages 60–90. These are the ages (among $x \geq 50$) at which

³Note that this is not a Cox proportional hazard model, nor is there any statistical modeling in the calculation of P^Y beyond that given in equation 1.

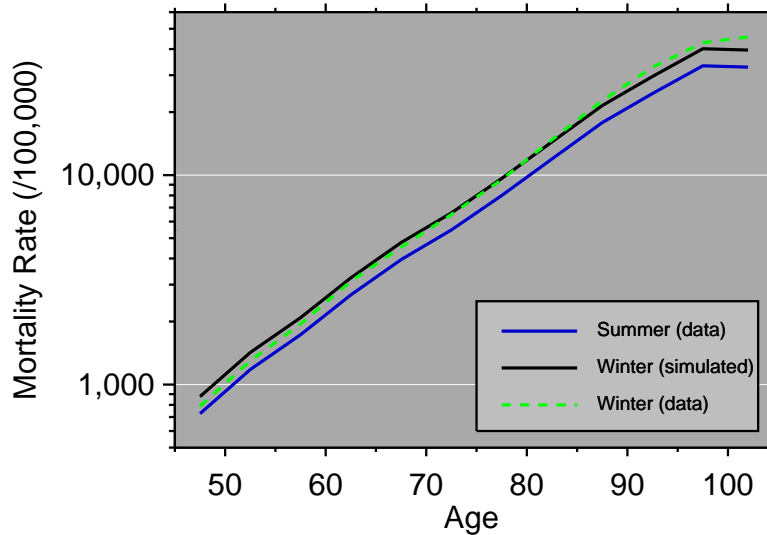


Figure 6: Proportional hazard analysis. Example graph showing M_x by age (males, ≥ 45), for summer 1962 and winter 1962–63, as well as “simulated” winter data, which is the summer data multiplied by the constant proportional hazard, P^Y . This year was chosen because it has the largest P^Y value (cf. figure 5).

most deaths occur (below age 60 there are fewer deaths because rates are lower and above age 90 because exposures are lower). Figure 5 shows that most winters have a mortality pattern that is between 110%–115% of the previous summer’s mortality. The proportional hazard model is an excellent fit, with all the year-specific $R^2 > 0.99$, which is not especially surprising, since it is based on pairwise comparisons of adjacent pseudoseasons. The year-by-year goodness of fit (R^2) statistics are given in figure 7. This shows that the proportional hazard approach is an excellent fit for both sexes and over time. Females are a better fit in almost every year. There are no meaningful sex differences in the proportional hazard.⁴ If we drop the Y superscript and model a single proportional hazard for the entire data set, then \mathbf{W} and \mathbf{S} become year \times age matrices, and P is 1.119 for males and 1.124 for females. Naturally, when modeling the whole time span with a single P , the goodness of fit declines, but it is still not poor: $R^2 = 0.89$ for males and $R^2 = 0.88$ for females.

⁴This is in contrast to Denmark, where Rau and Doblhammer (2003) find greater seasonal fluctuations for males.

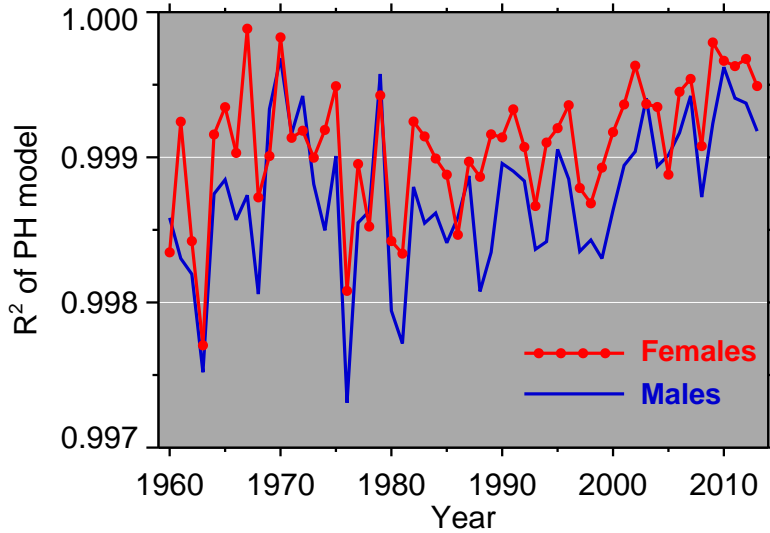


Figure 7: Proportional hazard analysis, goodness of fit. This gives R^2 of the comparison between real and simulated winter data, by year (see figure 6 for an example).

Discussion

Taking only mortality into account, how much happier should an adult be during the summer? Death rates will be, typically, 10% to 15% higher in the winter (figure 5). However, by the time summer arrives, up to half a year will have passed, and death rates will be higher due to aging, even half a year's worth. How does winter:summer mortality difference compare to age-related changes? We propose calculating “equivalent ages”, as follows. In table 1, the M_x columns give death rates by age, sex, and pseudoseason. The “w.e.a.” columns give the *winter equivalent age*, or the age at which one would have to be in the winter to experience the same (summer) death rate. Similarly, the “s.e.a.” columns give the *summer equivalent age*, or the summer age that experiences the same (winter) death rate. The M_x , w.e.a. and s.e.a. are calculated from a Gompertz mortality model estimated by Poisson regression, the coefficients of which are given at the top of the table.⁵ Sym-

⁵That is to say, we estimated a Poisson regression like: $\log(D_x) = \alpha + \beta x + \log(K_x)$ where D_x are deaths in the age group centered on x , K_x is the exposure (person-years) for that age group, and α, β are the coefficients to be estimated; cf. Abdullatif and Noymer (2016), p. 207. This is a Poisson rate regression, with exposure as an offset (see Agresti, 2002, p. 385).

bologically:

$$M_x^S = \exp(\hat{\alpha}^S + \hat{\beta}^S \cdot x^S) \quad (2)$$

$$M_x^W = \exp(\hat{\alpha}^W + \hat{\beta}^W \cdot x^W) \quad (3)$$

$$\text{w.e.a.}(x^S) = (\hat{\alpha}^S - \hat{\alpha}^W + \hat{\beta}^S \cdot x^S) / \hat{\beta}^W \quad (4)$$

where S, W superscripts are for summer and winter, x is age, and $\hat{\alpha}, \hat{\beta}$, are estimated coefficients. The solution for $\text{w.e.a.}(x^S)$ in (4) comes from setting mortality rates (i.e., [2] and [3]) equal, and solving for x^W in terms of x^S and the estimated coefficients. Thus, if $\text{w.e.a.}(x^S)$ is plugged into 3 for x^W , it will produce a death rate equivalent to the desired M_x^S . The same formula holds, *mutatis mutandis*, for $\text{s.e.a.}(x^W)$. The (winter/summer) equivalent age is a function of the estimated Gompertz coefficients for both pseudoseasons and of the age for which an equivalency is being calculated.

Table 1 gives specific examples, using 2010 data. An 80 year old woman in the winter experiences death rates of an 81 year old woman in the summer. Death rates are higher in the winter, so the equivalent age in the summer is older. The difference is one year of age. On the other hand, a 70 year old man living in the summer has death rates equivalent to a 69.1 year old man in the winter. Summer mortality is more lenient and therefore it's as if he is a younger man, compared to winter. The absolute value of the difference between biological age and w.e.a. or s.e.a. becomes larger as biological age increases, since M_x increases exponentially with age.

There is a micro-macro disconnect here: for populations, mortality is clearly lower in the summer, holding age constant, and holding the pair of pseudoseasonal life tables constant. From the point of view of an individual, holding age constant is meaningless; one cannot go from winter to summer without aging approximately half a year. Thus, the winter-into-summer mortality changes experienced by an individual in the above thought experiment are less than the *ceteris paribus* analysis represented by the proportional hazards (and the summer-into-winter changes, more). Moreover, this ignores long-term trends; it only considers seasonal and age-related changes.

In terms of life expectancy, the effect of the winter increase in mortality is similarly modest: on average, just over one year of life expectancy for women and just under one year for men. If we could wave a magic wand, making the winter pattern of mortality look like the summer pattern, this would be equivalent to about seven years' worth (in terms of time) of recent mortality progress (i.e., based on the slopes of figure 2).

The reason for this modest difference is easy to see, at least in retrospect. If we could eradicate winter-related mortality, then it would be like living

(x) Age	Women				Men			
	SUMMER		WINTER		SUMMER		WINTER	
	$\hat{\alpha} =$	-10.94	$\hat{\alpha} =$	-10.95	$\hat{\alpha} =$	-9.80	$\hat{\alpha} =$	-9.85
	$\hat{\beta} =$.0975	$\hat{\beta} =$.0989	$\hat{\beta} =$.0869	$\hat{\beta} =$.0888
	M_x	w.e.a.	M_x	s.e.a.	M_x	w.e.a.	M_x	s.e.a.
50	231.1	49.40	245.1	50.60	428.6	49.53	446.8	50.48
60	612.6	59.27	658.7	60.74	1,021.9	59.32	1,085.5	60.70
70	1,623.7	69.13	1,770.0	70.89	2,436.0	69.11	2,637.0	70.91
80	4,303.9	78.99	4,756.4	81.03	5,807.4	78.89	6,406.2	81.13
90	11,408.1	88.85	12,781.3	91.17	13,844.4	88.68	15,563.1	91.35

Table 1: Equivalent age analysis for 2010, as explained in the main text. M_x : modeled death rate per 100,000; w.e.a. is “winter equivalent age”, or the age at which an individual would experience the same death rate, living in the winter, and s.e.a. is the same, *mutatis mutandis*, for living in the summer. Coefficients from a Poisson regression; the prediction equation is: $M_x = \exp(\alpha + \beta x)$.

in the summer. To put it another way, people would experience their “summer equivalent age”, as in the example above. Although reducing death rates by about 12% seems like a great thing, it only makes a small difference in equivalent age, and, therefore, has a modest effect on $e(0)$. Mindel Sheps’s (1958) observation that changes in death rates usually are smaller when viewed through the lens of concomitant changes in survival rates, is highly relevant. The appreciable pseudoseasonal difference in M_x results in a rather modest difference in $e(0)$ because life expectancy is the integral of the life table ℓ_x , or survivor, column, not the M_x column. The Gompertzian relationship that holds above age 45, where by far the majority of deaths occur, guarantees that age-associated increases in mortality would swamp the hypothetical change generated by eradication of winter excess mortality.

The insight from our approach lies not in the idea that elimination of seemingly-major causes (in this case, approximated by pseudosummer) will have a small impact on $e(0)$. This is well understood; for example, Keyfitz (1985) (pp. 62–72) considers it in relation to the Shannon entropy, H , of the life table ℓ_x column. Because of competing risks of, say, heart disease, even eradicating cancer does not cause huge changes in $e(0)$ (*ibid.*), so it is clear that removing winter deaths also won’t have a big effect. Vaupel’s study (1986) of the relation between $e(0)$ and M_x is also relevant (see also Pollard, 1982). The greater mortality seasonality of women as measured by life expectancy differences (figure 3) than as measured by the winter:summer

proportional hazard (figure 5), is consistent with this; the effect of a constant multiple of M_x affects $e(0)$ differently at different levels of M_x . What the present study shows, however, is that the *total* mortality impact of winter (viz., including knock-on effects on heart disease) is not very large in the grand scheme of things.

Another approach to estimating the role of viruses in all-cause mortality would be to use direct measures of viral circulation (as in figure 1) instead of summer and winter as instrumental indicators. This would have the disadvantage of not being applicable to historical data (viral surveillance like that shown in figure 1 begins in the late 1990s). On the other hand, an advantage is that it could be applied to the tropics, where influenza circulation is more haphazard (see f.e. Aungkulanon et al., 2015), and therefore the collinearity of flu season and “winter” is neither an appropriate identification strategy nor a lurking problem. Using nominal influenza mortality as an instrument, instead of the seasons, is another possibility, but is not without its problems (Noymer and Nguyen, 2013). Our results are broadly consistent with other seasonal analyses of mortality in the United States, going back to Rosenwaike (1966), as well as more recent work (Feinstein, 2002).

This study has a number of strengths and weaknesses. The principal strength is that it uses all-cause mortality and so automatically includes any winter-related deaths that would be missed by studying an ensemble of winter-dominant causes like influenza and thrombosis. One limitation is that we can only observe summers that follow winters, and vice versa. The more lenient mortality of the summer leads to the accumulation of frail individuals who then become more likely to die in the winter. Similarly, the more severe mortality of the winter leaves a more robust residual population, less likely to die in the summer; here we use “robust” and “frail” in the usual demographic sense (Keyfitz and Littman 1979, Vaupel et al. 1979, Vaupel and Yashin 1985, Manton et al. 1986). Thus, diminution of winter mortality from (f.e.) the invention of a perfect influenza vaccine could precipitate small *increases* in summer mortality, as a result of perturbing the frail/robust cycle. Goldstein et al. (2012) (p. 833) likewise speculate that these effects are limited in magnitude. The negative autocorrelation seen in figures 3 and 5 may well be driven by similar effects. It is also possible that influenza and other respiratory pathogens are under-ascertained in the summertime, and thus that the roots of seasonal mortality are misunderstood, although this seems unlikely given figure 1 and other work (Hayward et al., 2014).

Using data from the entire United States is both a strength and limitation. If the intent is to draw conclusions regarding the whole United States, then using data from the entire country is clearly appropriate. Given the size

and climatic diversity of the United States, idiosyncratic factors such as summer heat waves tend to get averaged-out, which can be regarded as a positive given our focus on winter. However, the national approach also averages-out the potentially-interesting relation between winter temperature and the coefficient of seasonal variation in mortality that is seen in Europe (cf. the literature review).

Conclusion

It is reasonably well established that at least part of the reduction in cardiovascular mortality during the summer is due to the absence of influenza virus (Warren-Gash et al., 2009, 2011). The connection between influenza vaccine use and reduction of wintertime heart mortality is less clear, but has been studied (Seo et al., 2014). Influenza vaccine use is correlated with general health-seeking behavior, and so confounding is a problem in direct empirical approaches to this question. In this study, we took an indirect approach, using whole-population data, and summers as a sort of natural experiment. This quantifies the mortality impact of winter, not of influenza per se, which is smaller.

Progress is being made toward a much better flu vaccine (Keitel et al. 1997, Treanor 2004, Pica and Palese 2013). A universal flu vaccine (as such shots are called) is a clearly-expressed public health desideratum (Fineberg, 2014), but remains on the drawing board. Realistic expectations for mortality changes should be part of the policy analysis in this area. The mortality burden of winter, quantified herein, includes a number of factors of which influenza is only one; universal flu vaccines, even if successful, will have a modest impact on life expectancy.

In conclusion, the effect of winter on life expectancy in the United States is less than 1.25 years for women and less than 1.0 year for men. This estimate is based on summer-winter differences and so implicitly includes the synergies among causes that can be hard to measure using a bundle of cause-specific approaches. The insalubrious effects of winter include not only respiratory viruses but also air pollution as well as the linkage between cold and thrombosis, affecting, in turn, heart attack and stroke. The mortality impact of winter, quantified in terms of life expectancy, is neither negligible nor enormous.

Appendix: Denominator construction

The numerators (i.e., the death counts) are recorded monthly, so aggregation of these into pseudoseasons is completely straightforward. Our denominator, or exposure, values (i.e., person-years at risk) come from the Human Mortality Database (HMD), and are for calendar years. To re-cast these into pseudoseasons, we followed the following graduation/aggregation procedure.

The HMD exposure values for each year are centered at mid-year (i.e., July 1st), and are one year (of time) wide. We interpolated these values between consecutive Julys by fitting an exponential function using the two July 1st values, K_0 and K_1 . That is to say, we estimate the function $K_t = K_0 \exp(rt)$ where K_t is the calendar-year-wide exposure, centered at an arbitrary time, K_0 is the earlier of the two July 1st exposures, t is time since July 1st, and r is the growth rate, which works out to $\log(K_1/K_0)$. We did this repeatedly, always estimating r from the two July 1st values that sandwich the months being interpolated. While it is possible to fit r from three or more Julys, doing it pairwise ensures that the fitted curve passes through both K_0 and K_1 . The goal here is interpolation, not smoothing, so by repeatedly fitting off two points we stick as close as possible to the data. As described so far, the procedure produces K_t values centered on any month desired, but these are still one year wide, each. These values were then adjusted to months by multiplying by 31/365 for January, 28/365 for February, and so on. In leap years, 31/366, 29/366, . . . , were used.

In practice, these values are not far off simply averaging consecutive K values and dividing by 12 (especially post-aggregation into pseudoseasons), but nonetheless, doing the interpolation and using days per month gives more accuracy. The months were then aggregated into November through April for pseudowinter and May through October for pseudosummer. All these calculations were performed with HMD “1×1” exposures, that is to say, values for one year of age and one year of time. Therefore, these were aggregated by age (into 5-year age groups) as well as by pseudoseason.

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References

- Åström, Daniel Oudin, Sören Edvinsson, Daniel Hondula, Joacim Rocklöv, and Barbara Schumann. 2016. "On the association between weather variability and total and cause-specific mortality before and during industrialization in Sweden." *Demographic Research* 35(33):991–1010.
- Åström, Daniel Oudin, Bertil Forsberg, Sören Edvinsson, and Joacim Rocklöv. 2013. "Acute fatal effects of short-lasting extreme temperatures in Stockholm, Sweden: Evidence across a century of change." *Epidemiology* 24(6):820–829.
- Abdullatif, Viytta N. and Andrew Noymer. 2016. "*Clostridium difficile* infection: An emerging cause of death in the twenty-first century." *Biodemography and Social Biology* 62(2):198–207.
- Agresti, Alan. 2002. *Categorical data analysis*. Wiley, Hoboken, New Jersey, second ed.
- Analitis, A., K. Katsouyanni, A. Biggeri, M. Baccini, B. Forsberg, L. Bisanti, U. Kirchmayer, F. Ballester, E. Cadum, P. G. Goodman, A. Hojs, J. Sunyer, P. Tiittanen, and P. Michelozzi. 2008. "Effects of cold weather on mortality: Results from 15 European cities within the PHEWE project." *American Journal of Epidemiology* 168(12):1397–1408.
- Anderson, Brooke G. and Michelle L. Bell. 2009. "Weather-related mortality: How heat, cold, and heat waves affect mortality in the United States." *Epidemiology* 20(2):205–213.
- Aungkulanon, Suchunya, Po-Yung Cheng, Khanitta Kusreesakul, Kanitta Bundhamcharoen, Malinee Chittaganpitch, McCarron Margaret, and Sonja Olsen. 2015. "Influenza-associated mortality in Thailand, 2006–2011." *Influenza and Other Respiratory Viruses* 9(6):298–304.
- Bainton, David, Glynne R Jones, and David Hole. 1978. "Influenza and ischaemic heart disease – A possible trigger for acute myocardial infarction?" *International Journal of Epidemiology* 7(3):231–239.
- Basagaña, Xavier, Claudio Sartini, Jose Barrera-Gómez, Payam Dadvand, Jordi Cunillera, Bart Ostro, Jordi Sunyer, and Mercedes Medina-Ramon. 2011. "Heat waves and cause-specific mortality at all ages." *Epidemiology* 22(6):765–772.
- Basu, Rupa and Jonathan M. Samet. 2002. "Relation between elevated ambient temperature and mortality: A review of the epidemiologic evidence." *Epidemiologic Reviews* 24(2):190–202.
- Berko, Jeffrey, Deborah D. Ingram, Shubhayu Saha, and Jennifer D. Parker. 2014. "Deaths attributed to heat, cold, and other weather events in the United States, 2006–2010." *National Health Statistics Reports* 76.
- Bhaskaran, K., S. Hajat, A. Haines, E. Herrett, P. Wilkinson, and L. Smeeth. 2009. "Effects of ambient temperature on the incidence of myocardial infarction." *Heart* 95(21):1760–1769.
- Braga, Alféio L. F., Antonella Zanobetti, and Joel Schwartz. 2002. "The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities." *Environmental Health Perspectives* 110(9):859–863.

- Braga, Alfésio Luís Ferreira, Antonella Zanobetti, and Joel Schwartz. 2001. "The time course of weather-related deaths." *Epidemiology* 12(6):662–667.
- Breschi, Marco and Massimo Livi-Bacci. 1986a. "Saison et climat comme contraintes de la survie des enfants: L'expérience italienne au XIXe siècle." *Population* 41(1):9–35.
- . 1986b. "Stagione di nascita e clima come determinanti della mortalità infantile negli stati sardi di terraferma." *Genus* 42(1/2):87–101.
- . 1986c. "Effect du climat sur la mortalité infantile: Résultats pour la Savoie, le Piémont et la Ligurie en 1828–1837." *Population* 41(6):1072–1074.
- Carmona, R., J. Díaz, I. J. Mirón, C. Ortiz, M. Y. Luna, and C. Linares. 2016. "Mortality attributable to extreme temperatures in Spain: A comparative analysis by city." *Environment International* 91:22–28.
- CDC. 2015. *Weekly U.S. Influenza Surveillance Report*. <http://www.cdc.gov/flu/weekly/>. Accessed 9 June 2016.
- Chay, Kenneth, Carlos Dobkin, and Michael Greenstone. 2003. "The Clean Air Act of 1970 and adult mortality." *Journal of Risk and Uncertainty* 27(3):279–300.
- Chay, Kenneth Y. and Michael Greenstone. 2003. "The impact of air pollution on infant mortality: Evidence from geographic variation in pollution shocks induced by a recession." *Quarterly Journal of Economics* 118(3):1121–1167.
- . 2005. "Does air quality matter? Evidence from the housing market." *Journal of Political Economy* 113(2):376–424.
- Cheng, Tsung O. 2005. "Mechanism of seasonal variation in acute myocardial infarction." *International Journal of Cardiology* 100(1):163–164.
- Cleveland, William S. and T. E. Graedel. 1979. "Photochemical air pollution in the northeast United States." *Science* 204(4399):1273–1278.
- Crombie, D. L., D. M. Fleming, K. W. Cross, and R. J. Lancashire. 1995. "Concurrence of monthly variations of mortality related to underlying cause in Europe." *Journal of Epidemiology and Community Health* 49(4):373–378.
- Currie, Janet and Matthew Neidell. 2005. "Air pollution and infant health: What can we learn from California's recent experience?" *Quarterly Journal of Economics* 120(3):1003–1030.
- Currie, Janet, Matthew Neidell, and Johannes F. Schmieder. 2009. "Air pollution and infant health: Lessons from New Jersey." *Journal of Health Economics* 28(3):688–703.
- Curriero, Frank C., Karlyn S. Heiner, Jonathan M. Samet, Scott L. Zeger, Lisa Strug, and Jonathan A. Patz. 2002. "Temperature and mortality in 11 cities of the eastern United States." *American Journal of Epidemiology* 155(1):80–87.
- Dalla-Zuanna, Gianpiero and Alessandro Rosina. 2009. "The fatal season: An analysis of extremely high winter neonatal mortality." *Transylvanian Review* 18(1):245–276.
- . 2010. "A note on: The joint effect of maternal malnutrition and cold weather on neonatal mortality in -century Venice: An assessment of the hypothermia hypothesis, *Population Studies* 63(3):233–251 by Renzo Derosas." *Population Studies* 64(2):193–195.
- . 2011. "An analysis of extremely high nineteenth-century winter neonatal mortality in a local context of northeastern Italy." *European Journal of Population* 27(1):33–55.

- Dentali, Francesco, Roberto Manfredini, and Walter Ageno. 2009. "Seasonal variability of venous thromboembolism." *Current Opinion in Pulmonary Medicine* 15(5):403–407.
- Derosas, Renzo. 2009. "The joint effect of maternal malnutrition and cold weather on neonatal mortality in nineteenth-century Venice: An assessment of the hypothermia hypothesis." *Population Studies* 63(3):233–251.
- . 2010. "Reply to the note by Dalla-Zuanna and Rosina." *Population Studies* 64(2):197–198.
- Deschênes, Olivier and Michael Greenstone. 2011. "Climate change, mortality, and adaptation: Evidence from annual fluctuations in weather in the US." *American Economic Journal: Applied Economics* 3(4):152–85.
- Deschênes, Olivier and Enrico Moretti. 2009. "Extreme weather events, mortality, and migration." *Review of Economics and Statistics* 91(4):659–681.
- Díaz, Julio, Ricardo García, César López, Cristina Linares, Aurelio Tobías, and Luis Prieto. 2005. "Mortality impact of extreme winter temperatures." *International Journal of Biometeorology* 49(3):179–183.
- Douglas, R. Gordon, Jr., Keith M. Lindgren, and Robert B. Couch. 1968. "Exposure to cold environment and rhinovirus common cold." *New England Journal of Medicine* 279(14):742–747.
- Dowell, Scott F. 2001. "Seasonal variation in host susceptibility and cycles of certain infectious diseases." *Emerging Infectious Diseases* 7(3):369–374.
- Dowling, Harry F., George Gee Jackson, Irwin G. Spiesman, and Tohru Inouye. 1958. "Transmission of the common cold to volunteers under controlled conditions. III. The effect of chilling of the subjects upon susceptibility." *American Journal of Hygiene* 68(1):59–65.
- Dushoff, Jonathan, Joshua B. Plotkin, Simon A. Levin, and David J. D. Earn. 2004. "Dynamical resonance can account for seasonality of influenza epidemics." *Proceedings of the National Academy of Sciences of the United States of America* 101(48):16,915–16,916.
- Eccles, R. and J. E. Wilkinson. 2015. "Exposure to cold and acute upper respiratory tract infection." *Rhinology* 53(2):99–106.
- Ekamper, Peter, Frans van Poppel, Coen van Duin, and Joop Garssen. 2009. "150 Years of temperature-related excess mortality in the Netherlands." *Demographic Research* 21(14):385–426.
- Farmer, C. M. and A. F. Williams. 2005. "Temporal factors in motor vehicle crash deaths." *Injury Prevention* 11(1):18–23.
- Feinstein, Craig A. 2002. "Seasonality of deaths in the U.S. by age and cause." *Demographic Research* 6(17):469–486.
- Fineberg, Harvey V. 2014. "Pandemic preparedness and response: Lessons from the H1N1 influenza of 2009." *New England Journal of Medicine* 370(14):1335–1342.
- Fisman, D. 2012. "Seasonality of viral infections: Mechanisms and unknowns." *Clinical Microbiology and Infection* 18(10):946–954.
- Footitt, Joseph and Sebastian L. Johnston. 2009. "Cough and viruses in airways disease: Mechanisms." *Pulmonary Pharmacology & Therapeutics* 22(2):108–113.
- Foster, E. D., J. E. Cavanaugh, W. G. Haynes, M. Yang, A. K. Gerke, F. Tang, and P. M. Polgreen. 2013. "Acute myocardial infarctions, strokes and influenza: Seasonal and pandemic effects." *Epidemiology and Infection* 141(4):735–744.

- Foxman, Ellen F., James A. Storer, Megan E. Fitzgerald, Bethany R. Wasik, Lin Hou, Hongyu Zhao, Paul E. Turner, Anna Marie Pyle, and Akiko Iwasaki. 2015. "Temperature-dependent innate defense against the common cold virus limits viral replication at warm temperature in mouse airway cells." *Proceedings of the National Academy of Sciences of the United States of America* 112(3):827–832.
- Foxman, Ellen F., James A. Storer, Kiran Vanaja, Andre Levchenko, and Akiko Iwasaki. 2016. "Two interferon-independent double-stranded RNA-induced host defense strategies suppress the common cold virus at warm temperature." *Proceedings of the National Academy of Sciences of the United States of America* 113(30):8496–8501.
- Galloway, P. R. 1985. "Annual variations in deaths by age, deaths by cause, prices, and weather in London 1670 to 1830." *Population Studies* 39(3):487–505.
- Gasparrini, Antonio, Yuming Guo, Masahiro Hashizume, Eric Lavigne, Antonella Zanobetti, Joel Schwartz, Aurelio Tobias, Shilu Tong, Joacim Rocklöv, Bertil Forsberg, Michela Leone, Manuela De Sario, Michelle L Bell, Yue-Liang Leon Guo, Chang-fu Wu, Haidong Kan, Seung-Muk Yi, Micheline de Sousa Zanotti Stagliorio Coelho, Paulo Hilario Nascimento Saldiva, Yasushi Honda, Ho Kim, and Ben Armstrong. 2015. "Mortality risk attributable to high and low ambient temperature: A multicountry observational study." *Lancet* 386(9991):369–375.
- Glezen, W. Paul, Michael Decker, Sheldon W. Joseph, and Raymond G. Mercready Jr. 1987. "Acute respiratory disease associated with influenza epidemics in Houston, 1981–1983." *Journal of Infectious Diseases* 155(6):1119–1126.
- Goldstein, Edward, Cecile Viboud, Vivek Charu, and Marc Lipsitch. 2012. "Improving the estimation of influenza-related mortality over a seasonal baseline." *Epidemiology* 23(6):829–838.
- Graham, Neil M. H. 1990. "The epidemiology of acute respiratory infections in children and adults: A global perspective." *Epidemiologic Reviews* 12:149–178.
- Grenfell, B. T. and R. M. Anderson. 1989. "Pertussis in England and Wales: An investigation of transmission dynamics and control by mass vaccination." *Proceedings of the Royal Society of London, Series B: Biological Sciences* 236(1284):pp. 213–252.
- Hajat, S., R. S. Kovats, and K. Lachowycz. 2007. "Heat-related and cold-related deaths in England and Wales: Who is at risk?" *Occupational and Environmental Medicine* 64(2):93–100.
- Hayward, Andrew C., Ellen B. Fragaszy, Alison Bermingham, Lili Wang, Andrew Copas, W. John Edmunds, Neil Ferguson, Nilu Goonetilleke, Gabrielle Harvey, Jana Kovar, Megan S. C. Lim, Andrew McMichael, Elizabeth R. C. Millett, Jonathan S. Nguyen-Van-Tam, Irwin Nazareth, Richard Pebody, Faiza Tabasum, John M Watson, Fatima B. Wurie, Anne M. Johnson, and Maria Zambon. 2014. "Comparative community burden and severity of seasonal and pandemic influenza: Results of the Flu Watch cohort study." *Lancet Respiratory Medicine* 2(6):445–454.
- Healy, J. D. 2003. "Excess winter mortality in Europe: A cross country analysis identifying key risk factors." *Journal of Epidemiology and Community Health* 57(10):784–789.
- Holick, Michael F. 2007. "Vitamin D deficiency." *New England Journal of Medicine* 357(3):266–281.
- Human Mortality Database. 2016. <http://www.mortality.org/>. Accessed 15 August 2016.

- Huy, Christina, Dorothee Kuhn, Sven Schneider, and Iris Zöllner. 2012. "Seasonal waves of influenza and cause-specific mortality in Germany." *Central European Journal of Medicine* 7(4):450–456.
- Huynen, Maud M. T. E., Pim Martens, Dienneke Schram, Matty P. Weijenberg, and Anton E. Kunst. 2001. "The impact of heat waves and cold spells on mortality rates in the Dutch population." *Environmental Health Perspectives* 109(5):463–470.
- Ikäheimo, Tiina M., Kari Jaakkola, Jari Jokelainen, Annika Saukkoriipi, Merja Roivainen, Raija Juvonen, Olli Vainio, and Jouni J. K. Jaakkola. 2016. "A decrease in temperature and humidity precedes human rhinovirus infections in a cold climate." *Viruses* 8(244):1–10.
- Janhäll, Sara, K. Frans G. Olofson, Patrik U. Andersson, Jan B. C. Pettersson, and Mattias Hallquist. 2006. "Evolution of the urban aerosol during winter temperature inversion episodes." *Atmospheric Environment* 40(28):5355–5366.
- Johnston, Fay H., Ivan C. Hanigan, Sarah B. Henderson, and Geoffrey G. Morgan. 2013. "Evaluation of interventions to reduce air pollution from biomass smoke on mortality in Launceston, Australia: Retrospective analysis of daily mortality, 1994–2007." *British Medical Journal* 346:e8446.
- Kaiser, Reinhard, Alain Le Tertre, Joel Schwartz, Carol A. Gotway, W. Randolph Daley, and Carol H. Rubin. 2007. "The effect of the 1995 heat wave in Chicago on all-cause and cause-specific mortality." *American Journal of Public Health* 97(S1):S158–S162.
- Kalkstein, Laurence S. and Robert E. Davis. 1989. "Weather and human mortality: An evaluation of demographic and inter-regional responses in the United States." *Annals of the Association of American Geographers* 79(1):44–64.
- Kasahara, Amy K., Ravinder J. Singh, and Andrew Noymer. 2013. "Vitamin D (25OHD) serum seasonality in the United States." *PLoS One* 8(6):e65,785.
- Keatinge, W. R., S. R. K. Coleshaw, F. Cotter, M. Mattock, M. Murphy, and R. Chelliah. 1984. "Increases in platelet and red cell counts, blood viscosity, and arterial pressure during mild surface cooling: Factors in mortality from coronary and cerebral thrombosis in winter." *British Medical Journal* 289(6456):1405–1408.
- Keatinge, W. R., G. C. Donaldson, K. Bucher, G. Jendritsky, E. Cordioli, M. Martinelli, L. Dardanoni, K. Katsouyanni, A. E. Kunst, J. P. Mackenbach, C. McDonald, S. Nayha, and I. Vuori. 1997. "Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe." *Lancet* 349(9062):1341–1346.
- Keatinge, W. R., G. C. Donaldson, Elvira Cordioli, M. Martinelli, A. E. Kunst, J. P. Mackenbach, S. Nayha, and I. Vuori. 2000. "Heat related mortality in warm and cold regions of Europe: Observational study." *British Medical Journal* 321(7262):670–673.
- Keatinge, William R., Susan R. K. Coleshaw, John C. Easton, Finbar Cotter, Martin B. Mattock, and Ramani Chelliah. 1986. "Increased platelet and red cell counts, blood viscosity, and plasma cholesterol levels during heat stress, and mortality from coronary and cerebral thrombosis." *American Journal of Medicine* 81(5):795–800.
- Keitel, Wendy A., Thomas R. Cate, Robert B. Couch, Linda L. Huggins, and Kenneth R. Hesst. 1997. "Efficacy of repeated annual immunization with inactivated influenza virus vaccines over a five year period." *Vaccine* 15(10):1114–1122.
- Keyfitz, N. and G. Littman. 1979. "Mortality in a heterogeneous population." *Population Studies* 33(2):333–342.

- Keyfitz, Nathan. 1970. "Finding probabilities from observed rates, or how to make a life table." *American Statistician* 24(1):28–33.
- . 1985. *Applied mathematical demography*. Springer, New York, second ed.
- Klinenberg, Eric. 2002. *Heat wave: A social autopsy of disaster in Chicago*. University of Chicago Press.
- Knight, Josh, Chris Schilling, Adrian Barnett, Rod Jackson, and Phillip Clarke. 2016. "Revisiting the 'Christmas holiday effect' in the southern hemisphere." *Journal of the American Heart Association* 5(12):e005,098.
- Kunst, A. E., C. W. N. Looman, and J. P. Mackenbach. 1991. "The decline in winter excess mortality in the Netherlands." *International Journal of Epidemiology* 20(4):971–977.
- Kunst, Anton E., Casper W. N. Looman, and Johan P. Mackenbach. 1993. "Outdoor air temperature and mortality in the Netherlands: A time-series analysis." *American Journal of Epidemiology* 137(3):331–341.
- Kysely, Jan, Lucie Pokorna, Jan Kyncl, and Bohumir Kriz. 2009. "Excess cardiovascular mortality associated with cold spells in the Czech Republic." *BMC Public Health* 9(1):19.
- Land, Kenneth C. and David Cantor. 1983. "ARIMA models of seasonal variation in U.S. birth and death rates." *Demography* 20(4):541–568.
- Lofgren, Eric, N. H. Fefferman, Y. N. Naumov, J. Gorski, and E. N. Naumova. 2007. "Influenza seasonality: Underlying causes and modeling theories." *Journal of Virology* 81(11):5429–5436.
- Lowen, Anice C, Samira Mubareka, John Steel, and Peter Palese. 2007. "Influenza virus transmission is dependent on relative humidity and temperature." *PLoS Pathogens* 3(10):e151.
- Mackenbach, J. P., A. E. Kunst, and C. W. Looman. 1992. "Seasonal variation in mortality in The Netherlands." *Journal of Epidemiology and Community Health* 46(3):261–265.
- Mackenbach, J. P., C. W. Looman, and A. E. Kunst. 1993. "Air pollution, lagged effects of temperature, and mortality: The Netherlands 1979–87." *Journal of Epidemiology and Community Health* 47(2):121–126.
- Madjid, Mohammad, Ibrahim Aboshady, Imran Awan, Silvio Litovsky, and S. Ward Casscells. 2004. "Influenza and cardiovascular disease: Is there a causal relationship?" *Texas Heart Institute Journal* 31(1):4–13.
- Mäkinen, Tiina M., Raija Juvonen, Jari Jokelainen, Terttu H. Harju, Ari Peitso, Aini Bloigu, Sylvi Silvennoinen-Kassinen, Maija Leinonen, and Juhani Hassi. 2009. "Cold temperature and low humidity are associated with increased occurrence of respiratory tract infections." *Respiratory Medicine* 103(3):456–462.
- Manton, Kenneth G., Eric Stallard, and James W. Vaupel. 1986. "Alternative models for the heterogeneity of mortality risks among the aged." *Journal of the American Statistical Association* 81(395):635–644.
- Mercer, James B. 2003. "Cold—An underrated risk factor for health." *Environmental Research* 92(1):8–13.
- Mourtzoukou, E. G. and M. E. Falagas. 2007. "Exposure to cold and respiratory tract infections." *International Journal of Tuberculosis and Lung Disease* 11(9):938–943.
- National Center for Health Statistics. 2015. *Mortality multiple cause-of-death data files*, http://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm. National Center for Health Statistics. Accessed 12 December 2015.

- Newall, A. T., C. Viboud, and J. G. Wood. 2010. "Influenza-attributable mortality in Australians aged more than 50 years: A comparison of different modelling approaches." *Epidemiology and Infection* 138(6):836–842.
- Noymer, Andrew and Ann M. Nguyen. 2013. "Influenza as a proportion of pneumonia mortality: United States, 1959–2009." *Biodemography and Social Biology* 59(2):178–190.
- Nunes, Baltazar, Isabel Natário, and M. Lucília Carvalho. 2011. "Time series methods for obtaining excess mortality attributable to influenza epidemics." *Statistical Methods in Medical Research* 20(4):331–345.
- Olofson, K. Frans G., Patrik U. Andersson, Mattias Hallquist, Evert Ljungström, Lin Tang, Deliang Chen, and Jan B. C. Pettersson. 2009. "Urban aerosol evolution and particle formation during wintertime temperature inversions." *Atmospheric Environment* 43(2):340–346.
- Otrachshenko, Vladimir, Olga Popova, and Pavel Solomin. 2017. "Health consequences of the Russian weather." *Ecological Economics* 132:290–306.
- Pampel, Fred C. 2001. "Gender equality and the sex differential in mortality from accidents in high income nations." *Population Research and Policy Review* 20(5):397–421.
- Pan, Wen-Harn, Lung-An Li, and Ming-Jan Tsai. 1995. "Temperature extremes and mortality from coronary heart disease and cerebral infarction in elderly Chinese." *Lancet* 345(8946):353–355.
- Phillips, David, Gwendolyn E. Barker, and Kimberly M. Brewer. 2010. "Christmas and New Year as risk factors for death." *Social Science & Medicine* 71(8):1463–1471.
- Phillips, David P., Jason R. Jarvinen, Ian S. Abramson, and Rosalie R. Phillips. 2004. "Cardiac mortality is higher around Christmas and New Year's than at any other time: The holidays as a risk factor for death." *Circulation* 110(25):3781–3788.
- Pica, Natalie and Peter Palese. 2013. "Toward a universal influenza virus vaccine: Prospects and challenges." *Annual Review of Medicine* 64(1):189–202.
- Pollard, J. H. 1982. "The expectation of life and its relationship to mortality." *Journal of the Institute of Actuaries* 109(2):225–240.
- Preston, Samuel H., Patrick Heuveline, and Michel Guillot. 2001. *Demography: Measuring and modeling population processes*. Blackwell, Oxford.
- Rau, Roland. 2004. "Winter mortality in elderly people in Britain: Lack of social gradient in winter excess mortality is obvious in Denmark." *British Medical Journal* 329(7472):976–977.
- . 2006. *Seasonality in human mortality: A demographic approach*. No. 3 in Demographic Research Monographs, Springer, Berlin.
- Rau, Roland and Gabriele Doblhammer. 2003. "Seasonal mortality in Denmark: The role of sex and age." *Demographic Research* 9(9):197–222.
- Reichert, Thomas A., Lone Simonsen, Ashutosh Sharma, Scott A. Pardo, David S. Fedson, and Mark A. Miller. 2004. "Influenza and the winter increase in mortality in the United States, 1959–1999." *American Journal of Epidemiology* 160(5):492–502.
- Rey, Grégoire, Anne Fouillet, Éric Jouglu, and Denis Hémon. 2007. "Heat waves, ordinary temperature fluctuations and mortality in France since 1971." *Population-E* 62(3):457–485.

- Robine, J.-M., J.-P. Michel, and F. R. Herermann. 2012. "Excess male mortality and age-specific mortality trajectories under different mortality conditions: A lesson from the heat wave of summer 2003." *Mechanisms of Ageing and Development* 133(6):378–386.
- Rocklöv, Joacim, Kristie Ebi, and Bertil Forsberg. 2011. "Mortality related to temperature and persistent extreme temperatures: A study of cause-specific and age-stratified mortality." *Occupational and Environmental Medicine* 68(7):531–536.
- Rooney, Cleone, Anthony J. McMichael, R. Sari Kovats, and Michel P. Coleman. 1998. "Excess mortality in England and Wales, and in Greater London, during the 1995 heatwave." *Journal of Epidemiology and Community Health* 52(8):482–486.
- Rosenberg, Harry M. 1966. "Recent developments in seasonally adjusting vital statistics." *Demography* 3(2):305–318.
- Rosenwaike, Ira. 1966. "Seasonal variation of deaths in the United States, 1951–1960." *Journal of the American Statistical Association* 61(315):706–719.
- Schoen, Robert. 1970. "The geometric mean of the age-specific death rates as a summary index of mortality." *Demography* 7(3):317–324.
- Schwartz, Joel and Douglas W. Dockery. 1992. "Increased mortality in Philadelphia associated with daily air pollution concentrations." *American Review of Respiratory Disease* 145(3):600–604.
- Seo, Yu Bin, Won Suk Choi, Ji Hyeon Baek, Jacob Lee, Joon Young Song, Jin Soo Lee, Hee Jin Cheong, and Woo Joo Kim. 2014. "Effectiveness of the influenza vaccine at preventing hospitalization due to acute exacerbation of cardiopulmonary disease in Korea from 2011 to 2012." *Human Vaccines & Immunotherapeutics* 10(2):423–427.
- Seretakis, Dimitrios, Pagona Lagiou, Loren Lipworth, Lisa B. Signorello, Kenneth J. Rothman, and Dimitrios Trichopoulos. 1997. "Changing seasonality of mortality from coronary heart disease." *Journal of the American Medical Association* 278(12):1012–1014.
- Shaman, Jeffrey and Melvin Kohn. 2009. "Absolute humidity modulates influenza survival, transmission, and seasonality." *Proceedings of the National Academy of Sciences of the United States of America* 106(9):3243–3248.
- Sheps, Mindel C. 1958. "Shall we count the living or the dead?" *New England Journal of Medicine* 259(25):1210–1214.
- Sheth, Tej, Cyril Nair, James Muller, and Salim Yusuf. 1999. "Increased winter mortality from acute myocardial infarction and stroke: The effect of age." *Journal of the American College of Cardiology* 33(7):1916–1919.
- Simonsen, Lone, Thomas A. Reichert, Cecile Viboud, William C. Blackwelder, Robert J. Taylor, and Mark A. Miller. 2005. "Impact of influenza vaccination on seasonal mortality in the US elderly population." *Archives of Internal Medicine* 165(3):265–272.
- Stafoggia, Massimo, Francesco Forastiere, Daniele Agostini, Annibale Biggeri, Luigi Bisanti, Ennio Cadum, Nicola Caranci, Francesca de' Donato, Sara De Lisio, Moreno De Maria, Paola Michelozzi, Rossella Miglio, Paolo Pandolfi, Sally Picciotto, Magda Rognoni, Antonio Russo, Corrado Scarnato, and Carlo A. Perucci. 2006. "Vulnerability to heat-related mortality: A multicity, population-based, case-crossover analysis." *Epidemiology* 17(3):315–323.
- Stewart, Quincy Thomas. 2011. "The cause-deleted index: Estimating cause of death contributions to mortality." *Mathematical Population Studies* 18(4):234–257.

- Tang, Chia-Hsi, Brent A. Coull, Joel Schwartz, Qian Di, and Petros Koutrakis. 2017. "Trends and spatial patterns of fine-resolution aerosol optical depth-derived PM_{2.5} emissions in the Northeast United States from 2002 to 2013." *Journal of the Air & Waste Management Association* 67(1):64–74.
- te Beest, Dennis E., Michiel van Boven, Mariëtte Hooiveld, Carline van den Dool, and Jacco Wallinga. 2013. "Driving factors of influenza transmission in the Netherlands." *American Journal of Epidemiology* 178(9):1469–1477.
- Thompson, William W., Eric Weintraub, Praveen Dhankhar, Po-Yung Cheng, Lynnette Brammer, Martin I. Meltzer, Joseph S. Bresee, and David K. Shay. 2009. "Estimates of US influenza-associated deaths made using four different methods." *Influenza and Other Respiratory Viruses* 3(1):37–49.
- Toulemon, Laurent and Magali Barbieri. 2008. "The mortality impact of the August 2003 heat wave in France: Investigating the 'harvesting' effect and other long-term consequences." *Population Studies* 62(1):39–53.
- Treanor, John. 2004. "Influenza vaccine: Outmaneuvering antigenic shift and drift." *New England Journal of Medicine* 350(3):218–220.
- Treanor, John J. 2016. "Influenza vaccination." *New England Journal of Medicine* 375(13):1261–1268.
- Udell, Jacob A., Rami Zawi, Deepak L. Bhatt, Maryam Keshtkar-Jahromi, Fiona Gaughran, Arintaya Phrommintikul, Andrzej Ciszewski, Hossein Vakili, Elaine B. Hoffman, Michael E. Farkouh, and Christopher P. Cannon. 2013. "Association between influenza vaccination and cardiovascular outcomes in high-risk patients: A meta-analysis." *Journal of the American Medical Association* 310(16):1711–1720.
- Valleron, Alain-Jacques and Ariane Boumendil. 2004. "Épidémiologie et canicules: Analyses de la vague de chaleur 2003 en France." *Comptes Rendus Biologies* 327(12):1125–1141.
- van Rossum, Caroline T. M., Martin J. Shipley, Harry Hemingway, Diederick E. Grobbee, Johan P. Mackenbach, and Michael G. Marmot. 2001. "Seasonal variation in cause-specific mortality: Are there high-risk groups? 25-year follow-up of civil servants from the first Whitehall study." *International Journal of Epidemiology* 30(5):1109–1116.
- Vaupel, J. W. 1986. "How change in age-specific mortality affects life expectancy." *Population Studies* 40(1):147–157.
- Vaupel, James W., Kenneth G. Manton, and Eric Stallard. 1979. "The impact of heterogeneity in individual frailty on the dynamics of mortality." *Demography* 16(3):439–454.
- Vaupel, James W. and Anatoli I. Yashin. 1985. "The deviant dynamics of death in heterogeneous populations." *Sociological Methodology* 15:179–211.
- Warren-Gash, Charlotte, Krishnan Bhaskaran, Andrew Hayward, Gabriel M. Leung, Su-Vui Lo, Chit-Ming Wong, Joanna Ellis, Richard Pebody, Liam Smeeth, and Benjamin J. Cowling. 2011. "Circulating influenza virus, climatic factors, and acute myocardial infarction: A time series study in England and Wales and Hong Kong." *Journal of Infectious Diseases* 203(12):1710–1718.
- Warren-Gash, Charlotte, Andrew C. Hayward, Harry Hemingway, Spiros Denaxas, Sara L. Thomas, Adam D. Timmis, Heather Whitaker, and Liam Smeeth. 2012. "Influenza infection and risk of acute myocardial infarction in England and Wales: A CALIBER self-controlled case series study." *Journal of Infectious Diseases* 206(11):1652–1659.

- Warren-Gash, Charlotte, Liam Smeeth, and Andrew C. Hayward. 2009. "Influenza as a trigger for acute myocardial infarction or death from cardiovascular disease: A systematic review." *Lancet Infectious Diseases* 9(10):601–610.
- Webster, Robert G., William J. Bean, Owen T. Gorman, Thomas M. Chambers, and Yoshihiro Kawaoka. 1992. "Evolution and ecology of influenza A viruses." *Microbiological Reviews* 56(1):152–179.
- Wilkinson, Paul, Sam Pattenden, Ben Armstrong, Astrid Fletcher, R. Sari Kovats, Punam Mangtani, and Anthony J. McMichael. 2004. "Vulnerability to winter mortality in elderly people in Britain: Population based study." *British Medical Journal* 329(7467):647.
- Woods, R. I., P. A. Watterson, and J. H. Woodward. 1989. "The causes of rapid infant mortality decline in England and Wales, 1861–1921. Part II." *Population Studies* 43(1):113–132.
- Yang, Jun, Chun-Quan Ou, Yan Ding, Ying-Xue Zhou, and Ping-Yan Chen. 2012. "Daily temperature and mortality: A study of distributed lag non-linear effect and effect modification in Guangzhou." *Environmental Health* 11(1):art. no. 63.
- Yang, Jun, Peng Yin, Maigeng Zhou, Chun-Quan Ou, Mengmeng Li, Jing Li, Xiaobo Liu, Jinghong Gao, Yunning Liu, Rennie Qin, Lei Xu, Cunrui Huang, and Qiyong Liu. 2016. "The burden of stroke mortality attributable to cold and hot ambient temperatures: Epidemiological evidence from China." *Environment International* 92–93:232–238.
- Yorke, James A., Neal Nathanson, Giulio Pianigiani, and John Martin. 1979. "Seasonality and the requirements for perpetuation and eradication of viruses in populations." *American Journal of Epidemiology* 109(2):103–123.
- Zhao, Zhongwei, Yuan Zhu, and Edward Jow-Ching Tu. 2015. "Daily mortality changes in Taiwan in the 1970s: An examination of the relationship between temperature and mortality." *Vienna Yearbook of Population Research* 13:71–90.
- Zöller, Bengt, Xinjun Li, Henrik Ohlsson, Jan Sundquist, and Kristina Sundquist. 2013. "Age- and sex-specific seasonal variation of venous thromboembolism in patients with and without family history: a nationwide family study in Sweden." *Thrombosis and Haemostasis* 110(6):1164–1171.