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Summertime, and the livin’ is easy:
Winter and summer pseudoseasonal
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Abstract
In temperate climates, mortality is seasonal with a winter-dominant pattern, due in part to pneumonia and influenza. Cardiac causes, which are the leading cause of death in the United States, are also winter-seasonal although it is not clear why. Interactions between circulating respiratory viruses (e.g., influenza) and cardiac conditions have been suggested as a cause of winter-dominant mortality patterns. We propose and implement a way to estimate an upper bound on mortality attributable to winter-dominant viruses like influenza. We calculate ‘pseudo-seasonal’ life expectancy, dividing the year into two six-month spans, one encompassing winter the other summer. During the summer when 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. We suggest that even if viruses cause excess winter cardiac mortality, the population-level mortality reduction of a perfect influenza vaccine would be much more modest than is often recognized.

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Introduction

The primary goal of this paper is to forecast the best-case scenario of life expectancy improvements that would accrue from the widespread uptake of a perfect flu vaccine. 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), using pseudosummer as an approximation. Pseudowinter, on the other hand, estimates life expectancy in the presence of these viruses. The difference between life expectancy in pseudowinter and pseudosummer gives an upper bound on the potential mortality impact of a perfect flu vaccine. 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). Respiratory and cardiovascular causes, including stroke (Sheth et al. 1999), dominate the seasonal effects, with cancer being negligibly cyclical (Crombie et al. 1995). Heat wave mortality peaks are ephemeral interruptions of this overall pattern (e.g., 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 (Braga et al. 2001, 2002, Curriero et al. 2002, Mercer 2003). However, temperature-associated deaths in a literal sense (e.g., 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). Insufficient winter heating among the poor may not play a significant role in mortality in Britain (Wilkinson et al. 2004). Healy (2003) demonstrate that the coefficient of seasonal variation in mortality (CSVM) is correlated with mean winter temperature (warmer temperature, higher CVSM) at the country level in Europe; see also Keatinge et al. (1997) and Díaz et al. (2005). 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 (e.g., Galloway 1985, Breschi and Livi-Bacci 1986a, 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, Aström et al. (2016) find that warmer spells are associated with lower mortality. Ekmper et al. (2009) find strong 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 evidence in humans is mixed (Dowling et al. 1958, Douglas et al. 1968). 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.
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).

The root causes of 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 cyclicity 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). 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 and, to the best of our knowledge, novel, approach to estimate the overall impact of winter-circulating viruses, especially influenza, 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 or other approaches which rely on cause of death reporting (f.e., Stewart 2011). An influenza-deleted life expectancy is calculated with flu mortality statistically removed (Manton et al. 1986), while our approach studies all-cause mortality, but truly in the absence of the flu virus, 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. Among the problems this avoids are classification errors regarding what is an influenza death (cf. Noymer and Nguyen 2013).

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 2014. 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

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

virus circulation or lack thereof (Thompson et al. 2009). The data begin with pseudosummer 1959 and end with pseudosummer 2014 (56 pseudosummer). There are 54 pseudowinters (1960–61 to 2013–14). Data for January through April 1959 were discarded since using these data for pseudowinter 1959–60 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. We then calculated sex- and age-specific death rates for each pseudoseason, from which we calculated sex-specific life tables in the standard way (Keyfitz 1971, Preston et al. 2001).
Figure 3: Summer advantage over winter in pseudoseasonal life expectancy, females (upper series) and males (lower series).

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 \( e(0)+1 \), so 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 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 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). There are three important features. First, no secular time trend is evident. Second, the data are strongly negatively autocorrelated: declines are followed by increases,
Figure 4: Heatmap of winter:summer ratio, 1960–2014. At younger ages (above childhood), summer has higher mortality, although this has decreased over time. At older ages, winters have higher mortality.

and vice versa. Third, in addition to higher life expectancy, women have a higher summer−winter difference, 1.13±0.21 years, versus 0.82±0.21 years for males (mean±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 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 summer mortality for age $\geq 45$, separately by sex. Thus, we model $W = P^Y S$ where $W$ is the $N$-element (agewise) vector of winter death rates for
Figure 5: Proportional hazard analysis. The proportional hazard is winter death rates above age 45 as a multiple of summer death rates.

A given year, $P_Y$ is the year-specific proportional hazard (scalar), and $S$ is the vector of summer death rates. The proportional hazard is estimated as:

$$P_Y = \exp \left( \frac{\sum_{x=45}^{\infty} \left[ \log (M^W_x) - \log (M^S_x) \right]}{N} \right)$$

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). 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. There are no meaningful sex differences in the proportional hazard.\footnote{This is in contrast to Denmark, where Rau and Doblhammer (2003) find greater seasonal fluctuations for males.}

If we drop the $Y$ superscript and model a single proportional hazard for the entire data set, then $W$ and $S$ 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.

**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 (cf. Abdullatif and Novmer 2016, p. 207), the coefficients of which are given at the top of the table. Symbolically:

\[
M^S_x = \exp(\hat{\alpha}^S + \hat{\beta}^S \cdot x^S) \hspace{1cm} (2)
\]

\[
M^W_x = \exp(\hat{\alpha}^W + \hat{\beta}^W \cdot x^W) \hspace{1cm} (3)
\]

\[
w.e.a.(x^S) = (\hat{\alpha}^S - \hat{\alpha}^W + \hat{\beta}^S \cdot x^S)/\hat{\beta}^W \hspace{1cm} (4)
\]

where $S,W$ superscripts are for summer and winter, $x$ is age, and $\hat{\alpha}, \hat{\beta}$, are estimated coefficients. The solution for $w.e.a.(x^S)$ 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 $w.e.a.(x^S)$ is plugged into (3) for $x^W$, it will produce a death rate equivalent to the desired $M^S_x$. The same formula holds, *mutatis mutandis*, for 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 II 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
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: $M_x = \exp(\alpha + \beta x)$. 

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. 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 are less than the ceteris paribus analysis represented by the proportional hazards (and the summer-into-winter changes, more).

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, eradicating influenza, respiratory syntical virus, and other pathogens which circulate in the winter, and, what is more, making the winter pattern of cardiac mortality look like the summer pattern (regardless of the reason for its seasonality), 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 influenza, then it would be like living 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 $\ell_x$, 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 influenza.

The novelty of our approach lies not in the idea that elimination of a seemingly-major cause (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 $\ell_x$ 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 influenza deaths also won’t have a big effect. Vaupel’s study (1986) of the relation between $e(0)$ and $M_x$ is also relevant. 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 influenza (viz., including knock-on effects of flu 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 colinearity 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).

This study has a number of strengths and weaknesses. The principal strength is that it uses all-cause mortality and so automatically includes
any influenza-related deaths that would ordinarily be missed. 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 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).

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 a 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.

The question of mortality in a world with much more effective flu vaccines is not purely of theoretical importance. One of the chief reasons influenza vaccine is not optimally effective is the constant evolution of the virus (Treanor 2004). This leads directly to two related obstacles to good population-level immunity: the need to reformulate the flu vaccine each year, with not all years having equal vaccine efficacy (Keitel et al. 1997), and the need for people to be revaccinated each year. Progress is being made toward a vaccine that solves both of these problems (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.

In conclusion, the effect of influenza 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 knock-on effect of influenza on other causes, most notably heart disease. This must be regarded as an upper bound on the gains to life expectancy from a universal flu vaccine, which could — theoretically — eradicate influenza, but not other winter-circulating respiratory pathogens. The morality impact of such a vaccine would be neither negligible nor enormous.

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