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Seasonal variation in cause-specific mortality: Are there high-risk groups? 25-year follow-up of civil servants from the first Whitehall study

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Objectives	To determine the seasonal effect on all-cause and cause-specific mortality and to identify high-risk groups.
Methods	A 25-year follow-up of 19 019 male civil servants aged 40–69 years.
Results	All-cause mortality was seasonal (ratio of highest mortality rate during winter versus lowest rate during summer 1.22, 95% CI : 1.1–1.3), largely due to the seasonal nature of ischaemic heart disease. Participants at high risk based on age, employment grade, blood pressure, cholesterol, forced expiratory volume, smoking and diabetes did not have higher seasonal mortality, although participants with ischaemic heart disease at baseline did have a higher seasonality effect (1.38, 95% CI : 1.2–1.6) than those without (1.18, 95% CI : 1.1–1.3) (P = 0.03).
Conclusions	Seasonal mortality differences were greater among those with prevalent ischaemic heart disease and at older ages, but were not greater in individuals of lower socioeconomic status or with a high multivariate risk score. Since seasonal differences showed no evidence of declining over time, elucidating their causes and preventive strategies remains a public health challenge.

Mortality rates show strong seasonal effects, with all-cause mortality rates highest in the winter.[1–5] Over half of the excess is due to cardiovascular disease with much of the remainder due to respiratory diseases.[1,2,4] The mechanisms underlying seasonal variation in mortality are not yet completely elucidated, but may include outside and inside air temperature, wind chill factors, snowfall, sunlight exposure, air pollution, activity pattern, influenza incidence, psychological condition and/or food intake, and their effects on pathophysiological mechanisms related to disease.[6–9]

Identification of groups who are at high risk for a seasonal death offers the opportunity to both elucidate potential mechanisms and to design preventive strategies. Previous studies have suggested that the winter excess may be greater amongst people of lower social class[10] (who may for example be less able to afford housing insulation or central heating), older people and those with pre-existing health problems.[11] The seasonal variation in blood pressure may be greater among smokers compared to non-smokers,[12] but few studies have examined whether risk factors for premature morality identify groups with greater seasonal effects. Most previous analyses have examined routinely available mortality data and have therefore had little information characterizing individual risk.

We sought therefore to determine in the Whitehall cohort study of British civil servants the effect of season on all-cause and cause-specific mortality. Furthermore we determined whether seasonality effects were greater in high-risk groups defined on the basis of age, employment grade, pre-existing disease, or multivariate combinations of risk factors.

Subjects and Methods

A total of 19 019 male civil servants aged 40–69 years attended the screening examination of the Whitehall study between September 1967 and January 1970. More details regarding design and methods are provided elsewhere.[13] In short, each participant filled in a standard questionnaire that included age, self-reported smoking, civil servants' employment grade and symptoms of chest pain and chronic bronchitis. At the screening examination

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a single blood pressure reading was obtained with the participant seated, blood was drawn for plasma cholesterol estimation, a glucose tolerance test was conducted and a forced expiratory volume in one second (FEV_1) was measured.

High-risk groups were defined on the basis of age at death, employment grade, prevalent ischaemic heart disease, prevalent chronic bronchitis, or multivariate combinations of risk factors. Age was categorized as 40–64 years, 65–74 years and ⩾75 years. Employment grade, a measure of socioeconomic status, was categorized as high grades (administrative, professional and executive) and low grades (clerical and other grades, e.g. messengers and other unskilled workers). For the analyses using employment grade, 886 men from the Diplomatic Service and the British Council were excluded, as their employment status was not comparable with the employment grades above. Prevalent ischaemic heart disease was defined by self-reported angina, prolonged chest pain ('pain of possible myocardial infarction'), previous admission to hospital for ischaemic heart disease or an electrocardiogram suggesting ischaemia (any of Minnesota codes 1.1–3, 4.1–4, 5.1–3 or 7.1). Chronic bronchitis was defined as the presence of persistent phlegm (MRC questionnaire). Finally, the participants were classified into groups with differing degrees of risks. For each cause of death a multiple logistic regression model was fitted to our data using the following terms: age, employment grade, systolic blood pressure, plasma cholesterol concentration, FEV_1, (adjusted for age and height), smoking habits and the presence of diabetes or glucose intolerance. Four separate risk scores (for all-cause, ischaemic heart disease, cerebrovascular diseases, and respiratory diseases) were computed from the coefficients of these regressions. The participants were ranked according to each of these scores as either low risk (<60th percentile), moderate risk (60–80th percentile) or high risk (>80th percentile).

Records from 99.3% men were flagged at the National Health Service Central Registry, which notified us of all deaths up to the end of January 1995. Causes were classified according to the *International Classification of Disease*, Eighth Revision (ICD-8). The following codes were analyzed: ischaemic heart disease (410–414), cerebrovascular disease (430–438), other cardiovascular diseases (390–404, 420–429, 440–448), malignancy (140–239) and respiratory disease (460–519). For 28 people, cause of death was missing and these people were excluded from all analyses. In total 18 841 men were followed up for at least 25 years with 8347 having a known cause of death.

Data analyses

We created an expanded dataset for these analyses in which, for each subject and each individual month of follow-up, a new record was created giving the total days of follow-up during that month. Deaths were allocated to the appropriate month, current age group, calendar year and risk group. This analysis allows for the fact that recruitment into the study took just over 2 years and also for the differing lengths of the months. This expanded dataset was then summarized by computing the total number of deaths from each specific cause and the total person time at risk in these separate categories. Creation of the summary dataset was done using the statistical package SAS.[14]

Seasonal variation in mortality was modelled assuming that the outcome of interest followed a sinusoidal curve with a period of one year. This curve can be described mathematically using just two parameters: a sine and cosine term. The test of seasonality was computed using a likelihood ratio test with two degrees of freedom by comparing two models, with and without the seasonality terms. The models with the seasonal components were also compared with models showing overall heterogeneity between the 12 months to assess whether the seasonal model described the month-to-month variation adequately. The sinusoidal variations in mortality rates can be summarized using two useful terms; one showing the month of peak incidence and the other showing the estimated ratio of the highest (winter) to lowest (summer) incidence rates. Both these terms can be derived using the coefficients of the sine and cosine parameters and have been used to describe the seasonal effects previously.[15]

For the analyses of the seasonal effect by age, employment grade, multivariate risk score group and prevalent disease status, the highest (winter) to lowest (summer) mortality rate ratios were assessed for all calendar years combined. Tests for differences in the magnitude of the seasonality effect between risk groups were computed using the more conservative test of heterogeneity, rather than test of trend. In cases where the seasonality effect actually changes monotonically across risk groups, a test for trend would have given a more extreme *P*-value.

All models for mortality were fitted using Poisson regression with the statistical package GLIM, which was also used to compute the mortality rate ratios and 95% CI.

Results

Figure 1 shows the seasonal variation in all-cause and cause-specific mortality rates. The number of deaths, test of seasonality, estimated month of the peak incidence and the highest: lowest ratio by cause of death are shown in Table 1. A strong seasonal variation was seen for all-cause mortality. The pattern was mainly due to seasonal variation in ischaemic heart diseases, cerebrovascular diseases and respiratory diseases with a slight effect due to 'other cardiovascular'. No seasonal fluctuation was seen for neoplasm and 'other' deaths. All models containing seasonality terms showed adequate fits to the observed month-by-month mortality rates. For most causes of death showing seasonal effects, the winter peak was in January. The largest relative fluctuation of the mortality rates with season was seen for respiratory diseases. During the winter peak the respiratory disease mortality rate was nearly twice that of the lowest rate (1.98, 95% CI : 1.64–2.40). However, ischaemic heart disease, the commonest cause of death, contributed the greatest part to the absolute difference between the lowest (summer) and the highest (winter) rates in all-cause mortality and, together with respiratory disease accounted for over three-quarters of this difference.

In Table 2 the amplitudes of the seasonal fluctuation are given for three different age-at-death groups. The seasonal fluctuation in all-cause mortality rates tended to increase with age (*P*-value for heterogeneity = 0.06). However, this increase in seasonal fluctuation with age was not so marked for the specific causes which show a seasonal pattern (test of heterogeneity: $P = 0.27$ for ischaemic heart disease and $P > 0.50$ for cerebrovascular diseases and respiratory diseases). The difference between the seasonal variation in all-cause mortality of the younger and

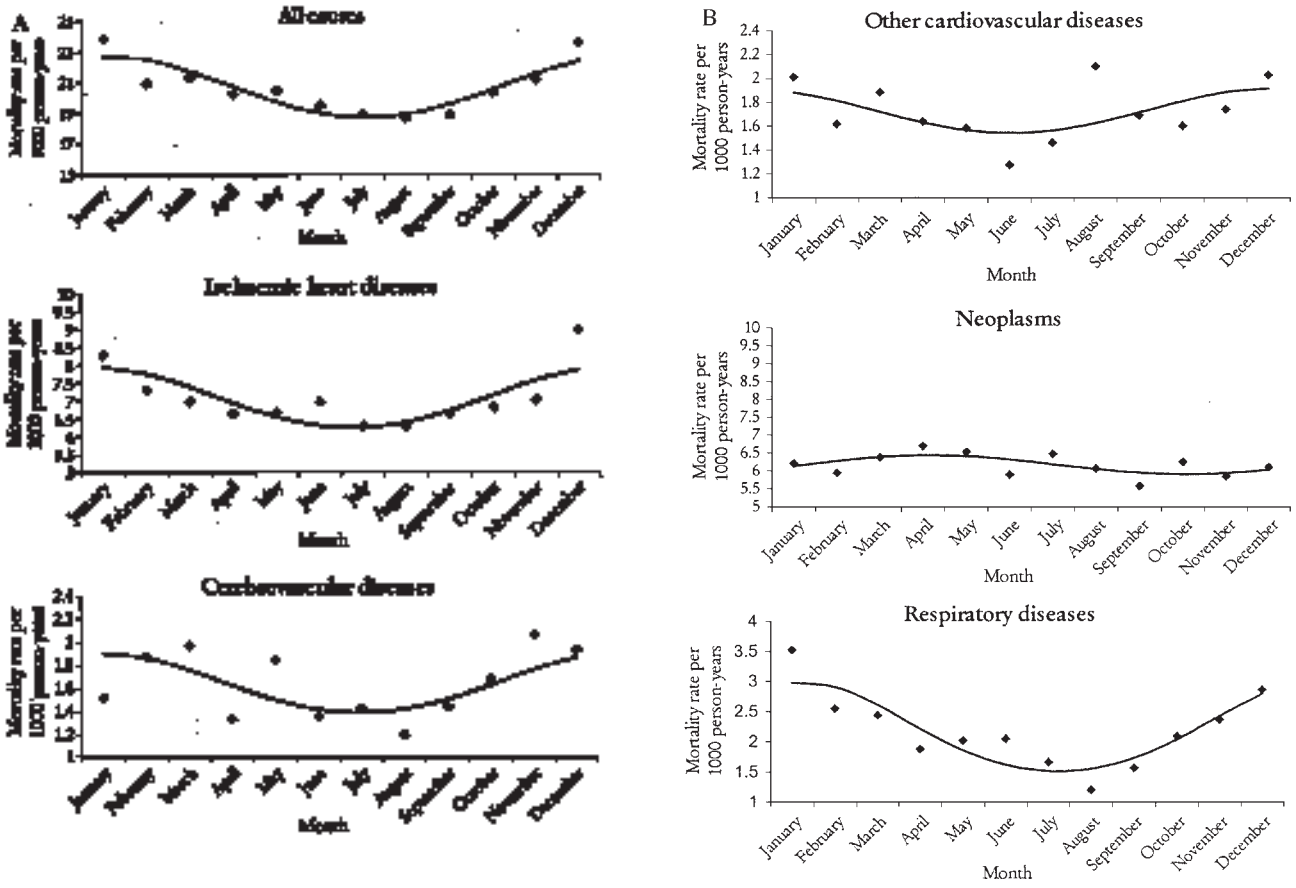

Figure 1 Seasonality in mortality rates by cause of death

Table 1 Number of deaths, heterogeneity of rates, test of seasonality, estimated date of the highest peak and rate ratio of the highest: lowest mortality rates by cause of death

Cause of death	No. of deaths	Overall heterogeneity of rates with 11 d.f.	Test of seasonality with 2 d.f.	Month of highest mortality rate	Rate ratio of highest:lowest[a] (95% CI)
All causes	8347	50.38***	39.61***	January	1.22 (1.14–1.29)
Ischaemic heart disease	2858	32.52***	20.45***	January	1.27 (1.14–1.41)
Cerebrovascular disease	661	19.55	8.17*	January	1.37 (1.10–1.70)
Other cardiovascular diseases	694	13.31	4.04	December	1.24 (1.01–1.53)
Neoplasms	2489	6.44	2.43	April	1.09 (0.98–1.22)
Respiratory diseases	882	65.74***	50.64***	January	1.98 (1.64–2.40)
Other deaths	763	8.55	0.78	November	1.09 (0.90–134)

[a] Ratio of highest mortality rate in 'winter':lowest mortality rate in 'summer', adjusted for age.

*** $P < 0.001$; ** $P < 0.01$; * $P < 0.05$.

Table 2 Ratio of highest:lowest mortality rates by cause of death and age at death

	Age at death						
	40–64 years		65–74 years		⩾75 years		
Causes of death	No. of deaths	Rate ratio of highest:lowest[a] (95% CI)	No. of deaths	Rate ratio of highest:lowest[a] (95% CI)	No. of deaths	Rate ratio of highest:lowest[a] (95% CI)	Test of heterogeneity *P*-value
All causes	1908	1.08 (1.0–1.2)	3422	1.23 (1.1–1.4)	3017	1.32 (1.2–1.5)	0.06
Ischaemic heart disease	794	1.11 (0.9–1.4)	1198	1.33 (1.1–1.6)	866	1.35 (1.1–1.6)	0.27
Cerebrovascular disease	85	1.78 (1.0–3.3)	261	1.68 (1.2–2.4)	315	1.37 (1.0–1.9)	>0.5
Respiratory diseases	106	1.76 (1.0–3.0)	307	2.27 (1.6–3.2)	469	1.98 (1.5–2.6)	>0.5

[a] Ratio of highest mortality rate in 'winter':lowest mortality rate in 'summer', adjusted for age.

older age groups was due to the different pattern of causes of death in these age groups. The proportion of deaths due to respiratory disease, which showed the largest seasonal variation, increased from 5.6% at ages 40–64 up to 15.5 at ages ⩾75.

There is some indication that the amplitude of seasonal fluctuation in mortality has decreased over recent decades.[10,16] To test whether this trend continues in the last two decades we calculated the amplitudes stratified both by age group and calendar period. No clear decreasing effect of seasonal variation in all-cause mortality was observed (results not shown).

However, this variation in all-cause mortality could be biased by the pattern of causes of death. For that reason, we assessed the amplitude of the seasonal fluctuation in those causes of death that showed a seasonal pattern, i.e. cardiovascular diseases and respiratory diseases. Table 3 shows that, after stratifying and controlling for age at death, in the last three decades no clear decreasing effect of season on causes with a seasonal pattern exists. However, the proportion of deaths due to seasonally-related causes decreased with calendar period and, within each calendar period the proportion of deaths that were from seasonally sensitive causes increased with age at death. The month of the peak mortality rates were confined to a 3-month period (December–February) for 17 of the 21 age-at-death and calendar-period cells.

Compared to higher grades, the lower grades had higher rates for mortality from most causes of death, but no significant differences were seen in the seasonal fluctuations between the two employment grades ($P > 0.50$ for all comparisons). The seasonality effect for all-cause mortality, ischaemic heart disease, stroke and respiratory mortality were 1.23, 1.34, 1.28 and 2.07 in the high grades and 1.22, 1.22 1.59 and 2.00 in the low grades respectively.

Table 4 shows the amplitudes of the seasonal effect by groups based on a multivariate cause-specific mortality risk score. For all-cause mortality, the seasonality effect did not differ by risk group. However for stroke mortality, the rate ratio was highest in the high-risk group (1.61, 95% CI : 1.2–2.2) and lowest in the low risk group (1.13, 95% CI : 0.7–1.7).

Table 5 shows the amplitudes of the seasonal effect by presence of ischaemic heart disease or chronic bronchitis at baseline. Men with prevalent ischaemic heart disease had a higher seasonality effect on all-cause mortality (rate ratio 1.38, 95% CI : 1.2–1.6) than those without (rate ratio 1.18, 95% CI : 1.1–1.3) (*P*-value for heterogeneity = 0.03). Furthermore, non-significant increases for the seasonally related causes of death were observed.

Discussion

In a 25-year follow-up of over 18 000 men, the winter excesses in ischaemic heart disease and respiratory disease together explained more than three-quarters of the winter excess in all-cause mortality. The burden of winter mortality excess was greater among elderly people, since a larger proportion of deaths in the elderly is from seasonally sensitive causes. Men with prevalent ischaemic heart disease at baseline showed significantly greater seasonality for all-cause mortality than those without. Participants at high multivariate risk of all-cause, coronary, stroke or respiratory mortality did not have greater seasonality effects than those at lower risk. This suggests the importance of other, as yet unidentified, factors in characterizing groups in whom seasonal effects may be greater. Given that the magnitude of seasonal differences in mortality did not decline between 1967 and 1995, better understanding of the causes of seasonal differences in mortality in order to inform preventive intervention is urgent.[17]

An important strength in this study was the ability to test whether the seasonal variation in mortality was larger among high-risk groups, characterized by older age, low socioeconomic status, prior disease or multivariate disease risk. It has been hypothesized that elderly people are more sensitive to seasonal effects, as it is likely that among elderly people influenza epidemics are more frequent or that their body response to the outside temperature is less adequate. Furthermore, blood pressure may vary more among elderly people between winter and summer.[18,19] Our finding that the excess of deaths in winter is larger among elderly people is consistent with this hypothesis. However, in contrast to other studies which also reported age-gradients for specific causes of death,[2,4,10,20,21] in our study the ratio of the mortality rate for specific causes of death during winter and during summer did not increase significantly with age. Thus, the difference between the seasonal variation in all-cause mortality of the younger and older age groups was not caused by a larger amplitude of the seasonal variation among the elderly, but was due to the different pattern of causes of death in these age groups. In other words, elderly people are not more sensitive to seasonal effects, but they are more likely to die from causes with a seasonal pattern.

It has been proposed that lower socioeconomic status may be associated with a larger winter excess in mortality.[4] This may arise if lower grade employees were less able to protect themselves from the effects of temperature (for example because of poorer housing insulation or less central heating) or, independent of temperature, were more prone to other seasonal precipitants of mortality, such as infection. Indeed it has further been proposed that differences in domestic microclimate might contribute to socioeconomic status differences in coronary mortality.[22] However, we found no evidence for greater seasonal effects among those of lower social status, consistent with other recent studies.[23,24]

We found no evidence that conventional risk factors identified groups in whom the seasonality effect was greater. The seasonality effects were found consistently across disease-specific risk groups defined from a multiple logistic regression using age, employment grade, systolic blood pressure, cholesterol, FEV_1, smoking and diabetes. We further tested whether high-risk groups defined by the Framingham risk equation[25] for cardiovascular disease were associated with greater seasonality, but they were not (data not shown). This suggests the importance of additional, as yet unidentified, factors in characterizing groups in whom seasonality effects are greater. Possible factors, which were not included in our analyses, are genetic factors and/or environmental factors, such as food habits or climate factors.

The importance of identifying such factors is underscored by the lack of decline in seasonality effects between 1967–1995. The marked increases in availability of domestic measures to control ambient temperature as well as the increasing use of influenza vaccination had no discernible effect on the degree of

Table 3 Ratio of highest:lowest mortality rates for cardiovascular and respiratory diseases by age at death and calendar period

	Calendar period																			
	1967–1974					1975–1979					1980–1984					1985–1989					1990–1995				
Age at death	n[a]	(%)[b]	RR[c]	(95% CI)	Peak	n	(%)	RR[c]	(95% CI)	Peak	n	(%)	RR[c]	(95% CI)	Peak	n	(%)	RR[c]	(95% CI)	Peak	n	(%)	RR[c]	(95% CI)	Peak
40–54 years	105	(53)	1.48	(0.9–2.6)	Feb	51	(59)			[d]	15	(68)			[d]	[e]					[e]				
55–59 years	141	(61)	1.75	(1.1–2.8)	Mar	114	(64)	0.79	(0.5–1.3)	Aug	62	(57)			[d]	13	(52)			[d]	[e]				
60–64 years	168	(58)	1.57	(1.0–2.4)	Dec	178	(61)	0.77	(0.5–1.2)	Aug	161	(61)	1.41	(0.9–2.2)	Feb	88	(51)			[d]	20	(51)			[d]
65–69 years	124	(59)	1.24	(0.8–2.0)	Nov	203	(63)	2.03	(1.4–3.0)	Jan	219	(59)	1.60	(1.1–2.3)	Dec	218	(59)	1.47	(0.5–1.2)	Feb	126	(50)	1.74	(1.1–2.9)	Dec
70–74 years	36	(64)			[d]	186	(63)	1.50	(1.0–2.3)	Feb	306	(62)	1.42	(1.0–2.0)	Dec	316	(61)	1.41	(1.0–2.1)	Dec	303	(56)	1.53	(1.1–2.1)	Jan
75–79 years	0				[d]	45	(71)			[d]	200	(66)	1.29	(0.9–1.9)	Jan	356	(63)	1.44	(1.0–1.9)	Dec	431	(63)	1.34	(1.0–1.8)	Jan
80–84 years	[e]					0				[d]	52	(70)			[d]	202	(65)	1.38	(1.1–1.9)	Jan	402	(64)	1.90	(1.4–2.5)	Jan
⩾85 years	[e]					[e]					1	(100)			[d]	55	(81)			[d]	198	(63)	1.60	(1.1–2.4)	Dec

[a] No. of deaths due to cardiovascular and respiratory diseases.

[b] Proportion of cardiovascular and respiratory death of all causes of death.

[c] Ratio of highest mortality rate in 'winter':lowest mortality rate in 'summer'. 'Winter' defined as November–March; 'summer' defined as June–September.

[d] Rate ratio for highest:lowest is only computed when number of deaths >100.

[e] No deaths since cell has no person-years of follow-up.

Table 4 Ratio of highest:lowest mortality rates by causes of death and multivariate risk score

	Disease-specific risk group[a]						
	Group with lowest risk (<60th percentile)		Group with moderate risk (60th–80th percentile)		Group with the highest risk (>80th percentile)		**Test for heterogeneity**
Causes of death	No. of deaths	Rate ratio of highest:lowest[b] (95% CI)	No. of deaths	Rate ratio of highest:lowest[b] (95% CI)	No. of deaths	Rate ratio of highest:lowest[b] (95% CI)	***P*-value**
All causes	2879	1.13 (1.0–1.3)	2120	1.29 (1.1–1.5)	2990	1.27 (1.1–1.4)	0.19
Ischaemic heart disease	966	1.27 (1.1–1.5)	740	1.39 (1.1–1.7)	1039	1.24 (1.0–1.5)	>0.5
Cerebrovascular disease	170	1.13 (0.7–1.7)	165	1.21 (0.8–1.9)	298	1.61 (1.2–2.2)	0.37
Respiratory diseases	156	2.11 (1.3–3.3)	178	1.97 (1.3–3.0)	500	1.98 (1.5–2.6)	>0.5

[a] Separate scores for coronary, stroke and respiratory mortality based on multiple logistic regression of age, employment grade, systolic blood pressure, plasma cholesterol concentration, FEV_1, smoking and diabetes.

[b] Ratio of highest mortality rate in 'winter':lowest mortality rate in 'summer', adjusted for age.

Table 5 Ratio of highest:lowest mortality rates[a] by cause of death and presence of prevalent ischaemic heart disease or chronic bronchitis

	Ischaemic heart disease at baseline				
	No (n = 15 554)		Yes (n = 3284)		
Causes of death	No. of Deaths	Rate ratio of highest:lowest[a] (95% CI)	No. of deaths	Rate ratio of highest:lowest[a] (95% CI)	*P*-value
All causes	6389	1.18 (1.1–1.3)	1972	1.38 (1.2–1.6)	0.03
Ischaemic heart disease	2006	1.26 (1.1–1.4)	847	1.31 (1.1–1.6)	>0.5
Cerebrovascular disease	510	1.35 (1.1–1.7)	150	1.48 (0.9–2.3)	>0.5
Respiratory diseases	670	1.91 (1.5–2.4)	211	2.33 (1.6–3.5)	0.39
	Chronic bronchitis at baseline				
	No (n = 14 458)		Yes (n = 4370)		
Causes of death	No. of Deaths	Rate ratio of highest:lowest[a] (95% CI)	No. of deaths	Rate ratio of highest:lowest[a] (95% CI)	*P*-value
All causes	5878	1.19 (1.1–1.3)	2471	1.28 (1.1–1.4)	0.30
Ischaemic heart diseases	2105	1.27 (1.1–1.4)	746	1.29 (1.1–1.6)	>0.5
Cerebrovascular diseases	489	1.25 (1.0–1.6)	170	1.96 (1.3–3.0)	0.08
Respiratory diseases	469	2.04 (1.6–2.7)	408	1.96 (1.5–2.6)	>0.5

[a] Ratio of highest mortality rate in 'winter':lowest mortality rate in 'summer', adjusted for age.

seasonal mortality. In absolute terms, the number of people dying from seasonally sensitive diseases is decreasing. Curwen *et al.*, McDowall *et al*. and Seretakis *et al*. in the US reported a decline in the seasonal variation by calendar period.[10,16,22] McDowall *et al.* suggested that the decline in the seasonal variation from the 1960s to the 1980s was due to increased use of a central heating system and an enormous fall in air pollution period.[10]

A winter excess in coronary, stroke and respiratory mortality is reported in several other studies.[1,20,26–33] The mechanisms explaining the seasonal variation in coronary, stroke and respiratory mortality are poorly understood. Climatic factors are clearly important, with both outdoor and indoor air temperature exerting biological effects on haemostasis, blood viscosity, lipids, the sympathetic nervous system and vasoconstriction.[18,34,35] Other climatic factors may also be important, such as sunlight, wind speed and air pollution. The rise in respiratory diseases during winter might be explained by influenza epidemics.[16,21] Kunst *et al*. have reported that influenza may explain 34% of the cold related mortality in The Netherlands.[36] The rise in influenza might also cause a rise in cardiovascular diseases during winter.[37] Coronary disease is an inflammatory process in which acute (or chronic) infections may stimulate inflammatory pathways. Variation in the severity of the influenza epidemics from year to year may have affected our results. During years with a more severe influenza epidemic, the seasonal variation in cardiovascular diseases might be expected to be larger.

Humans, like other organisms, display seasonal behaviour; food habits, activity patterns, smoking habits (more smoking indoors during winter) and psychosocial factors such as loneliness may all differ between winter and summer. Several psychosocial stressors show a larger effect on blood pressure during winter.[38] Mundal *et al*. showed that the seasonal fluctuation in physical fitness may provide an explanation for the seasonal variation in blood pressure.[39] Several other cardiovascular risk factors have been shown to exhibit seasonal variation; e.g. cholesterol,[35,40,41] haemostatic factors, fibrinogen,[15,35,37,42–44] and blood pressure.[12,34,45]

A further strength of the study is its population basis. In several studies the winter excess in mortality is examined in hospital-based studies.[34,38,46] Rothwell reported that the widely varying winter excess in mortality in hospital-based studies might be an artifact of a variation in the likelihood of

hospital admissions.[27] Our study is free from this possible bias since we studied seasonal variation in a non-hospitalized prospective cohort study.

Our method to assess the amplitude of the seasonal variation (rate ratio of the highest versus the lowest) provides a simple, statistically powerful model for the true variation in mortality rate during the season. There was no evidence, in our data, for any departure from this model. However, it has been found that besides a winter excess, there may also be a heat-related excess in deaths during summer.[11] Our data would need to be augmented with climate data for the whole of the follow-up period and require more deaths to be able to investigate this possibility.

Understanding and tackling seasonality in mortality is a public health challenge which has not been met. In relative terms, the seasonal effects showed no evidence of decline between 1967 and 1995; older age, low socioeconomic status or high multivariate risk did no identify a group more prone to seasonal, cause-specific mortality effects. However, seasonal effects were greater among those with prevalent ischaemic heart disease, suggesting, in this group at least, the potential for preventive strategies.

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References

[1] Mackenbach JP, Kunst AE, Looman CW. Seasonal variation in mortality in The Netherlands. *J Epidemiol Community Health* 1992; **46:**261–65.

[2] Crombie DL, Fleming DM, Cross KW, Lancashire RJ. Concurrence of monthly variations of mortality related to underlying cause in Europe. *J Epidemiol Community Health* 1995;**49:**373–78.

[3] Sakamoto-Momiyama M. Changes in the seasonality of human mortality: a medico-geographical study. *Soc Sci Med* 1978;**12:**29–42.

[4] Curwen M. Excess winter mortality: a British phenomenon. *Health Trends* 1990/91;**4:**169–75.

[5] McKee CM. Deaths in winter: can British learn from Europe? *Eur J Epidemiol* 1989;**5:**178–82.

[6] Kunst AE, Groenhof F, Mackenbach JP. The association between two windchill indices and daily morality variation in the Netherlands. *Am J Public Health* 1994;**84:**1738–42.

[7] Gorjanc ML, Flanders WD, VanDerslice J, Hersch J, Malilay J. Effects of temperature and snowfall on mortality in Pennsylvania. *Am J Epidemiol* 1999;**149:**1152–60.

[8] Eurowinter Group. Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. *Lancet* 1997; **349:**1341–46.

[9] Kloner RA, Poole WK, Perritt RL. When throughout the year is coronary death most likely to occur? A 12-year population-based analysis of more than 220 000 cases. *Circulation* 1999;**100:**1630–34.

[10] McDowall M. Long term trends in seasonal mortality. *Popul Trends* 1981;**26:**16–9.

[11] Mackenbach JP, Borst V, Schols JMGA. Heat-related mortality among nursing-home patients. *Lancet* 1997;**349:**1297–98.

[12] Kristal Boneh E, Harari G, Green MS. Seasonal change in 24-hour blood pressure and heart rate is greater among smokers than non-smokers. *Hypertension* 1997;**30:**436–41.

[13] Reid DD, Brett GZ, Hamilton PJ, Jarrett RJ, Keen H, Rose G. Cardiorespiratory disease and diabetes among middle-aged male Civil Servants. A study of screening and intervention. *Lancet* 1974; **i:**469–73.

[14] SAS Institute. *SAS User's Guide*: Carry NC, SAS Institute Inc; 1985.

[15] van der Bom JG, de Maat MP, Bots ML, Hofman A, Kluft C, Grobbee DE. Seasonal variation in fibrinogen in the Rotterdam Study. *Thromb Haemost* 1997;**78:**1059–62.

[16] Curwen M, Devis T. Winter mortality, temperature and influenza: has the relationship changed in recent years? *Popul Trends* 1988;**53:**17–20.

[17] Ross G. *The Strategy of Preventive Medicine.* Oxford: Oxford University Press, 1992.

[18] Ballester F, Corella D, Perez-Hoyos S, Saez M, Hervas A. Mortality as a function of temperature. A study in Valencia, Spain, 1991–1993. *Int J Epidemiol* 1997;**26:**551–61.

[19] Woodhouse PR, Khaw KT, Plummer M. Seasonal variation of blood pressure and its relationship to ambient temperature in an elderly population. *J Hypertens* 1993;**11:**1267–74.

[20] Bainton D, Moore F, Sweetnam P. Temperature and deaths from ischaemic heart disease. *Br J Prev Soc Med* 1977;**31:**49–53.

[21] Marshall RJ, Scragg R, Bourke P. An analysis of the seasonal variation of coronary heart disease and respiratory disease mortality in New Zealand. *Int J Epidemiol* 1988;**17:**325–31.

[22] Seretakis D, Lagiou P, Lipworth L, Signorello LB, Rothman KJ, Trichopoulos D. Changing seasonality of mortality from coronary heart disease. *JAMA* 1997;**278:**1012–14.

[23] Gemmell I, McLoone P, Boddy FA, Dickinson GJ, Watt GCM. Seasonal variation in mortality in Scotland. *Int J Epidemiol* 2000;**29:**274–79.

[24] Shah S, Peacock J. Deprivation and excess winter mortality. *J Epidemiol Community Health* 1999;**53:**499–502.

[25] Anderson KM, Wilson PW, Odell PM, Kannel WB. An updated coronary risk profile. A statement for health professionals. *Circulation* 1991;**83:**356–62.

[26] Ballaro A, Cortina-Borja M, Collin J. A seasonal variation in the incidence of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 1998;**15:**429–31.

[27] Rothwell PM, Wroe SJ, Slattery J, Warlow CP. Is stroke incidence related to season or temperature? The Oxfordshire Community Stroke Project. *Lancet* 1996;**347:**934–36.

[28] Anonymous. Cold at heart. *Lancet* 1989;**ii:**254.

29Anderson TW, Le Riche WH. Cold weather and myocardial infarction. *Lancet* 1970;**i:**291–96.

[30] McDowall M. The mortality of agricultural workers: using the thirteenth decennial occupational mortality. *Popul Trends* 1986;**45:**14–17.

[31] Rose G. Cold weather and ischaemic heart disease. *Br J Prev Soc Med* 1966;**20:**97–100.

[32] West R. Seasonal variation in CHD mortality. *Int J Epidemiol* 1989; **18:**463–65.

[33] Rogot E, Padgett SJ. Associations of coronary and stroke mortality with temperature and snowfall in selected areas of the United States, 1962–1966. *Am J Epidemiol* 1976;**103:**565–75.

[34] Kunes J, Tremblay J, Bellavance F, Hamet P. Influence of environmental temperature on the blood pressure of hypertensive patients in Montreal. *Am J Hypertens* 1991;**4:**422–26.

[35] Stout RW, Crawford V. Seasonal variations in fibrinogen concentrations among elderly people. *Lancet* 1991;**338:**9–13.

[36] Kunst AE, Looman CW, Mackenbach JP. Outdoor air temperature and mortality in The Netherlands: a time-series analysis. *Am J Epidemiol* 1993;**137:**331–41.

[37] Woodhouse PR, Khaw KT, Plummer M, Foley A, Meade TW. Seasonal variations of plasma fibrinogen and factor VII activity in the elderly: winter infections and death from cardiovascular disease. *Lancet* 1994;**343:**435–39.

[38] James GD, Yee LS, Pickering TG. Winter-summer differences in the effects of emotion, posture and place of measurement on blood pressure. *Soc Sci Med* 1990;**31:**1213–17.

[39] Mundal R, Kjeldsen SE, Sandvik L, Erikssen G, Thaulow E, Erikssen J. Seasonal covariation in physical fitness and blood pressure at rest and during exercise in healthy middle-aged men. *Blood Press* 1997;**6:**269–73.

[40] Woodhouse PR, Khaw KT, Plummer M. Seasonal variation of serum lipids in an elderly population. *Age Ageing* 1993;**22:**273–78.

[41] Gordon DJ, Hyde J, Trost DC *et al*. Cyclic seasonal variation in plasma lipid and lipoprotein levels: the Lipid Research Clinics Coronary Primary Prevention Trial Placebo Group. *J Clin Epidemiol* 1988; **41:**679–89.

[42] Keatinge WR, Coleshaw SR, Cotter F, Mattock M, Murphy M, Chelliah R. 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. *Br Med J* 1984;**289:** 1405–08.

[43] Stout RW, Crawford VL, McDermott MJ, Rocks MJ, Morris TC. Seasonal changes in haemostatic factors in young and elderly subjects. *Age Ageing* 1996;**25:**256–58.

[44] Brennan PJ, Greenberg G, Miall WE, Thompson SG. Seasonal variation in arterial blood pressure. *Br Med J* 1982;**285:**919–23.

[45] Rose G. Seasonal variation in blood pressure in man. *Nature* 1961; **189:**235.

[46] Douglas AS, Dunnigan MG, Allan TM, Rawles JM. Seasonal variation in coronary heart disease in Scotland. *J Epidemiol Community Health* 1995;**49:**575–82.

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Commentary: Short days—shorter lives: studying winter mortality to get solutions

Richard Mitchell

'*People who are getting up in years … die in the winter when the days are short, and in the hours after midnight. Life is at a low ebb after midnight and in the short days. Did you know that?*' Ira Solenberger, quoted by Roy Redd '*An Ozark gardener, 86, awaits coming of the greening season*'. NY Times 12 April 1976

'*Clearly, if disease is manmade, it can also be man-prevented. It should be the function of medicine to help people die young as late in life as possible.*' Dr Ernst Wunder, President, American Health Foundation: NY Times 30 September 1975

The papers by Aylin and colleagues and by van Rossum and colleagues in this volume of the *International Journal of Epidemiology* explore the seasonality of mortality.[1,2] These are two papers with different approaches and differing specific aims, but both are broadly focused on the same issues: what is the nature of the higher mortality rate Britain experiences in winter, what are its correlates and what are the implications?

The agreement and disagreement in the results of these two interesting, innovative and valuable studies is typical of British literature from this field. Despite Britain's relatively benign climate (the average January minimum temperature for Greenwich, London is 1.9°C, with July's minimum at 13.0°C), higher rates of mortality in winter have been noted for over 150 years. Such 'seasonality' was noted in the Registrar General's 2nd report in 1839 with several pages devoted to London's winter mortality rates in the 3rd report.[3] Since then, empirical studies have tried to determine which population groups experience greatest increases in the risk of mortality during winter, what they die from and whether this seasonal effect is increasing. These two papers do not entirely agree in their answers to these questions but do confirm the existence of a seasonal pattern to mortality rates—Ira Solenberger was at least right about life being at a low ebb during the shorter days.

The two papers concur with each other and with the wider literature (especially contemporary work) in finding weak or absent relationships between deprivation or poor socioeconomic circumstances and the risk of winter mortality.[4] Such a result seems counter-intuitive to me, and I suspect that it will to others. I would expect poverty to be strongly related to an elevated risk of winter death through its associated consequences of poor quality housing, fuel poverty, inadequate clothing and elevated risk factors for illness which winter is known to exacerbate (respiratory and cardiovascular disease). It is my supposition that

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elements of winter mortality are manmade, through material inequalities. This is not to suggest error in the two studies presented here, but rather highlights my own concerns about how we approach this whole topic.

I would like research of this kind to pay more attention to the complexities of the individual/accommodation/climate relationship through a consideration of the aetiology and physiology of cold-related respiratory and cardiovascular disease. Cold temperatures induce changes in the respiratory tract as the mucosal surfaces cool and dry, and induce bronchoconstriction.[5] That non-ideal hygrothermal conditions within a home can damage the respiratory health of occupants is well known, and these internal conditions are known to reflect outside climate, mediated by the building's structure, heating and ventilation properties, and of course the occupants and their actions. Recent surveys suggest that more than 2 million households live in properties where the warmest room is below 16°C (the British legal minimum temperature to which sedentary workers can be exposed, for fear of adverse respiratory effects). Colder homes tend also to be damp, especially when the winter climate is wet with moderate, rather than extreme, cold. Damp air breeds mould which causes problems through allergy and infection. Cold outdoor and indoor temperatures may thus damage the natural defences of the respiratory system, with cold housing providing a fertile environment for micro-organisms.[5]

Goodwin's analysis of the relationship between cold, circulatory stress and the elderly population demonstrates the further complex relationships between physical activity and residence in a cold house.[6] Haematological and haemodynamic responses to cold air may be less effective in the elderly than in the younger population (see ref. 7 for example), leading to a potentially greater adverse reaction to temperature change (e.g. moving from a warm room to a cold room) and/or physical activity (e.g. going out to the shops on a cold day). All this tells us that housing quality varies (almost always in relation to poverty), that good quality housing protects against cold more effectively than poor quality housing, and that the combination of poor quality housing and cold is a potent recipe for adverse respiratory and cardiovascular effects.[8]

So, we know much about how cold might influence or hasten particular causes of death, even if the identity of the most vulnerable groups remains disputed (van Rossum *et al*. argue that elderly people are not more sensitive to seasonal effects, for example). Current understanding of possible mechanisms for winter deaths suggests a complex relationship between climate and the health of an individual, mediated by housing and the nature of day-to-day life. Perhaps such complexity shields the relationships between health, wealth and environment from conventional empirical investigation? These two papers make an excellent pairing because they tackle the issues from complementary perspectives. Van Rossum *et al*. have worked at the individual level of analysis but have not attempted to include housing as a mediating factor influencing a seasonal effect on mortality. Aylin *et al*. worked at an aggregate level, attempting to include housing as a mediating factor (though found difficulty in doing so due to data constraints). However, neither approach pays much attention to what is known about the possible mechanisms behind winter deaths. One works at the aggregate level, when we suspect the relationships of interest are complex at the individual level, and the other takes no account of housing—the crucial mediator.

I suggest these papers are best read as catalysts for methodological developments in the field. One such development might be to embrace work focusing on 'area effects' in other health outcomes (and in other disciplines). The area-effect is that portion of the between-area variation in a health outcome which cannot be ascribed to the (measured) individual characteristics of the study population, i.e. that which is attributable to a feature of the area of residence, not the residents themselves. Climate, as a spatial variable, is obviously a potential explanatory factor for between-area differences in health. The area effects field has its own methodologies and techniques that might shed further light on the winter mortality conundrum. One approach might be to treat the severity of winter as an area-level variable, and explore its impact having controlled for housing quality and other individual-level circumstances.[9] Even within Britain we have significant spatial variation in the duration and severity of the winter season and in the quality of housing. I wonder whether this variation can be used to create a natural experimental design to contrast differing climatic regimes, housing provision and mortality rates, or other health outcomes?

Such an approach would require data which describe individual circumstances in relation to housing and heating, activity, socioeconomic circumstances and medical histories, but which have sufficient spatial coverage to allow comparison between winter regimes. Aylin *et al*. have the spatial coverage, van Rossum *et al*. the individual detail, but these are currently (artificially) separated. The papers are important markers on the path towards more effective study of winter mortality in Britain and I very much welcome their contribution to the field and the new findings they present. I suspect that as new techniques and data are applied to the problem, we will discover that excess winter mortality is indeed partly a manmade problem—made through a combination of behaviour,[10] poor quality housing and adverse individual circumstances.

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References

[1] Aylin P, Morris S, Wakefield J, Grossinho A, Jarup L, Elliot P. Temperature, housing, deprivation and relationship to excess winter mortality in Great Britain, 1986–1996. *Int J Epidemiol* 2001;**30:** 1114–22.

[2] van Rossum C, Shipley M, Hemingway H, Grobbee D, Mackenbach J, Marmot M. Seasonal variation in cause-specific mortality: are there high-risk groups? *Int J Epidemiol* 2001;**30:**1123–30.

[3] General Register Office, *The Third Annual Report of Births, Marriages and Deaths.* London: HMSO, 1841, pp.102–09.

[4] Gemmell I, McLoone P, Boddy FA, Dickinson GJ, Watt GC. Seasonal variation in mortality in Scotland. *Int J Epidemiol* 2000;**29:**274–79.

[5] Collins K. Cold, cold housing and respiratory illnesses. In: Rudge J, Nicol F (eds). *Cutting the Cost of Cold; Affordable Warmth for Healthier Homes.* London: E&FN Spon, 2000.

[6] Goodwin J. Cold stress, circulatory illness and the elderly. In: Rudge J, Nicol F (eds). *Cutting the Cost of Cold; Affordable Warmth for Healthier Homes.* London: E&FN Spon, 2000.

[7] Collins KJ, Abdel-Rahman TA, Easton JC, Sacco P, Ison J, Dore CJ. Effects of facial cooling on elderly and young subjects: interactions with breath-holding and lower body negative pressure. *Clin Sci* 1996;**90:**485–92.

[8] Mitchell R, Blane D, Bartley D. Elevated risk of high diastolic blood pressure: climate and the inverse housing law. In press, 2001.

[9] Blane D, Mitchell R, Bartley M. The 'inverse housing law' and respiratory health. *J Epidemiol Community Health* 2000;**54:** 745–49.

[10] The Eurowinter Group. Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. *Lancet* 1997;**349:** 1341–46.