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Season of cancer diagnosis exerts distinct effects upon short- and long-term survival

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Several epidemiological studies have shown an association between the season in which certain cancers are diagnosed and survival, with diagnosis in summer and autumn being associated with better survival. In this study, we have added resolution to the analysis of seasonality in cancer survival by considering mortality within several nonoverlapping time periods following diagnosis, thereby quantifying the separate contributions of mechanisms operating in the short term and in the longer term. We found evidence of seasonality acting on mortality within 2 distinct periods following diagnosis. Diagnosis in the summer was associated with substantially decreased mortality within the first month of diagnosis compared with winter in men with prostate cancer, those of both sexes with colorectal or lung cancer, and most strikingly, amongst women with breast cancer (hazard ratio 0.81 [95% confidence interval 0.75–0.86]). Adjusting for monthly variations in general mortality greatly attenuated the seasonal effects on short-term mortality. At long-term follow-up (>5 years), there was a consistent shift in the seasonality pattern, with autumn diagnosis alone being associated with decreased mortality, both in female breast cancer cases and in lung cancer cases of both sexes. We conclude that the higher survival observed amongst patients diagnosed in summer and autumn is predominantly a short-term phenomenon that is largely attributable to generally higher mortality in winter. However, the distinct mortality reduction observed in the long term amongst those diagnosed in the autumn, especially amongst breast cancer patients, may indicate the presence of a seasonally variable protective mechanism.

Key words: season; cancer; survival; infections; vitamin D

In recent years, several large epidemiological studies[1–6] have shown an association between the season in which certain cancers are diagnosed and subsequent survival, with diagnosis in the summer and autumn months being associated with better survival in most of these studies. However, none of these studies has isolated the contribution of mortality events occurring in the short term.

Robsahm *et al.*[1] analyzed cancers of the breast, colon and prostate amongst the entire Norwegian population, comparing the survival of patients diagnosed in the winter with those diagnosed in each of the other 3 seasons. The period of follow-up was truncated 3 years after diagnosis, and a separate analysis covered the complete available period with mean duration of follow-up of 7.2, 3.9 and 4.0 years for breast, colon and prostate cancer, respectively. Substantial and statistically significant dependence of survival on season of diagnosis was observed. This was most pronounced in the 3-year follow-up analysis, with relative risks of cancer death of 0.68 to 0.85 in the patients diagnosed in summer and autumn compared with those diagnosed in the winter.

In a previous study,[2] we showed a similar variation in cancer survival dependent on season of diagnosis in a large cohort of breast, colorectal, prostate and additionally lung cancer patients from South East England. This was evident in analyses of the 0–1 year and 0–5 year periods of follow-up after cancer diagnosis. Since then, further reports from Norway have restated the observation of seasonality in cancer survival.[3–6]

It has been suggested by the authors of these studies that exposure to sunlight and the associated higher levels of cutaneous vitamin D production at the time of diagnosis and/or treatment might be the underlying biological basis for the improved survival of patients diagnosed in the summer and autumn months. However, this inference relies on studies without individual information on vitamin D exposure, and it is plausible that other seasonally variable factors acting both in the short term and the longer term may influence the relationship between season of diagnosis and cancer survival.

Firstly, cancer incidence as recorded in a population-based cancer registry varies over the year due to health care system related and social factors, in a pattern that reflects seasons of holidays and religious events. In the South East of England, the incidence of cancer per day is 4–8% lower than expected in the months of August and December. This monthly variation in recorded incidence is associated with variations in case-fatality and survival. Patients diagnosed in months with low incidence have a less favorable case-mix and a poorer survival than patients diagnosed in months with high incidence (Thames Cancer Registry, unpublished data).

Secondly, there is a strong seasonal variation in all-cause mortality in the general population, which in the UK amounts to a 30% difference between summer and winter. Vascular and respiratory diseases (including coronary and cerebrovascular disease, pneumonia and influenza) make the greatest contribution to excess winter deaths.[7] These background variations can be expected to exert themselves on the study cohort, affecting short-term mortality patterns.

In this study, we have attempted to add resolution to the analysis of seasonality in cancer survival by considering mortality within several nonoverlapping time periods following the diagnosis of cancer, thereby quantifying the separate contributions of mechanisms operating in the short term and the longer term. In our analysis of short-term survival, we have also explored the influences of monthly variations in cancer incidence and in general population mortality.

Material and methods

The Thames Cancer Registry (TCR) is a population-based registry that collects cancer data on 12 million residents in London and the South East of England. The patients registered at the TCR represent a cohort of cancer patients followed up from the date of cancer diagnosis to death. All cases of cancer diagnosed in the period 1975–2004 were extracted from the registry database. Cases registered solely from death certificates and those diagnosed with nonmelanoma skin cancer (ICD-10 C44) were excluded from analysis.

Differences in all-cause mortality between patients diagnosed in different seasons were examined using Cox proportional hazards models. Seasons were defined as Winter (December-February); Spring (March-May); Summer (June-August) and Autumn

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TABLE I – ABSOLUTE NUMBERS OF CASES AND DEATHS BY SEASON OF DIAGNOSIS AND TIME SINCE DIAGNOSIS IN WOMEN

Cancer site	Season of diagnosis	Time since diagnosis				Total cases (deaths)
		0–1 month Total cases (deaths)	1 month–1 year Total cases (deaths)	1–5 years Total cases (deaths)	>5 years Total cases (deaths)	
Breast	Total	187,263 (6,540)	180,178 (13,860)	158,793 (39,269)	90,629 (30,744)	187,263 (90,413)
	Winter	43,929 (1,693)	41,691 (3,328)	37,022 (9,176)	20,965 (7,187)	43,929 (21,384)
	Spring	46,956 (1,625)	45,331 (3,533)	39,702 (10,093)	22,501 (7,703)	46,956 (22,954)
	Summer	48,828 (1,581)	47,247 (3,569)	41,644 (10,372)	23,890 (8,245)	48,828 (23,767)
	Autumn	47,550 (1,641)	45,909 (3,430)	40,425 (9,628)	23,273 (7,609)	47,550 (22,308)
Colorectum	Total	76,600 (11,357)	65,051 (18,514)	44,339 (18,277)	19,873 (8,378)	76,600 (56,526)
	Winter	18,324 (2,770)	15,362 (4,399)	10,605 (4,368)	4,723 (1,968)	18,324 (13,505)
	Spring	19,097 (2,904)	16,193 (4,613)	11,002 (4,550)	4,975 (2,117)	19,097 (14,184)
	Summer	19,759 (2,812)	16,947 (4,845)	11,507 (4,730)	5,134 (2,144)	19,759 (14,531)
	Autumn	19,420 (2,871)	16,549 (4,657)	11,225 (4,629)	5,041 (2,149)	19,420 (14,306)
Lung	Total	61,407 (14,821)	46,403 (31,139)	14,122 (9,635)	3,131 (1,210)	61,407 (56,805)
	Winter	14,501 (3,741)	10,577 (7,126)	3,301 (2,275)	713 (296)	14,501 (13,438)
	Spring	15,634 (3,826)	11,808 (7,968)	3,598 (2,470)	815 (326)	15,634 (14,590)
	Summer	15,826 (3,643)	12,183 (8,218)	3,624 (2,488)	803 (314)	15,826 (14,663)
	Autumn	15,446 (3,611)	11,835 (7,827)	3,599 (2,402)	800 (274)	15,446 (14,114)
All sites[1]	Total	606,501 (78,918)	525,932 (144,811)	362,883 (117,872)	187,327 (64,027)	606,501 (405,628)
	Winter	144,390 (19,994)	122,745 (34,119)	85,627 (28,025)	43,930 (15,125)	144,390 (97,263)
	Spring	151,924 (19,978)	131,946 (36,881)	90,213 (29,823)	46,365 (16,092)	151,924 (102,774)
	Summer	156,967 (19,444)	137,523 (37,743)	94,751 (30,778)	49,000 (16,923)	156,967 (104,888)
	Autumn	153,220 (19,502)	133,718 (36,068)	92,292 (29,246)	48,032 (15,887)	153,220 (100,703)

[1]Excluding nonmelanoma skin cancer.

(September-November). Hazard ratios for the different seasons were calculated after adjustment for age and period of diagnosis (each stratified into 5-year groups). Person-years at risk were calculated from the date of diagnosis to the census date (31st December 2004) or the date of death, whichever occurred first. Cases for which the date of diagnosis and date of death were recorded as identical ("zero-survival" cases) were included in the analysis by assigning them half a day of survival.

Time after cancer diagnosis was divided into the following periods of follow-up: 0–1 month; 1 month-1 year; 1–5 years and >5 years. These periods were chosen to enable us to study separately the seasonal effects in the very short term, the short to medium term, the medium term and the long term, whilst including sufficient numbers of events for high statistical power. Separate analyses were performed for each follow-up period. Cancers of the breast (ICD-10 C50) in females, prostate (C61), colorectum (C18–C21), lung (C33–C34) and all cancers combined (but excluding nonmelanoma skin cancer, C44) were analyzed.

Additional adjustments were made to allow for monthly variations in recorded incidence and in overall mortality of the general population. This was done by calculating a monthly incidence index and a monthly mortality index. The monthly incidence index was sex and cancer site specific, and was derived by first calculating the average numbers of incident cases (over the whole time period) per day in each month. Each month was then characterized by its relative excess or deficit in numbers of registrations per day.

For the mortality index, the monthly all-cause mortality per day for England & Wales over the period 1975–1999 was obtained from the Office for National Statistics (ONS). Then, for each individual, the proportion of the first 30 days after diagnosis that fell into each month was calculated, and these proportions were used as weights to apply to the ONS monthly figures to give an estimate of the average daily mortality excess or deficit in the 30 days following diagnosis.

In the presentation of our results, we have emphasized estimated hazard ratios representing an excess or deficit of more than 5% in absolute terms which are also statistically significantly different from unity at the conventional p-value of < 0.05.

Results

After exclusions, a total of 1,187,447 incident cancers were available for analysis (606,501 in women and 580,946 in men) with a total follow-up of 4,518,459 person-years. Tables I and II provide an overview of cohort sizes and numbers of deaths in the analyses. There was substantial seasonal variation in incidence, with summer showing the highest incidence in all cancers investigated.

Tables III and IV show the all-cause mortality hazard ratios (HRs) and their associated 95% confidence intervals (CIs) by season of diagnosis and by time since diagnosis in women and men, respectively. Winter was used as the baseline season, against which the other seasons were compared. The hazard ratios were adjusted for age at diagnosis and period of diagnosis. For comparability with other studies, we have also included an analysis of seasonal variation in mortality in all periods of follow-up taken as a whole.

For both men and women, a marked seasonal pattern was evident in the first month after diagnosis. For women with breast cancer, men with prostate cancer and for colorectal and lung cancer in both sexes, there was a robust seasonal variation in survival in the period one month following diagnosis, with summer consistently bearing the lowest mortality. This effect persisted into the 1 month–1 year period in the case of breast cancer. The greatest mortality reduction in the first month after diagnosis was seen in women diagnosed with breast cancer in the summer compared with the winter (HR 0.81 [95% CI 0.75–0.86]). In the 1–5 year postdiagnosis interval, there was a smaller decrease in mortality in patients diagnosed with breast cancer in the autumn and in men diagnosed with lung cancer in the summer.

In long-term follow-up (>5 years after diagnosis), there was a notable shift in the seasonality pattern, with only autumn diagnosis being associated with reduced mortality, both in breast cancer in females (HR 0.93 [95% CI 0.90–0.96]) and in lung cancer in both sexes (HR 0.79 [95% CI 0.67–0.93] in females and HR 0.89 [95% CI 0.80–0.99] in males). There was also a less substantial but nevertheless statistically significant mortality reduction after more than 5 years in females with breast cancer diagnosed in the spring (HR 0.95 [95% CI 0.92–0.99]). No such tendency was seen in patients with colorectal cancer or prostate cancer.

Tables V and VI examine survival in the first month after cancer diagnosis in greater detail, looking at the effects of 2 adjustments on the observed mortality hazard ratios. The figures in the "unadjusted" column are those from the previous tables (*i.e.* adjusted only for age and period of diagnosis). In the following columns, the analysis is sequentially adjusted for monthly variation in

TABLE II – ABSOLUTE NUMBERS OF CASES AND DEATHS BY SEASON OF DIAGNOSIS AND TIME SINCE DIAGNOSIS IN MEN

Cancer site	Season of diagnosis	Time since diagnosis				Total cases (deaths)
		0–1 month Total cases (deaths)	1 month–1 year Total cases (deaths)	1–5 years Total cases (deaths)	>5 years Total cases (deaths)	
Prostate	Total	101,083 (5,277)	95,412 (13,719)	76,218 (29,397)	28,456 (13,250)	101,083 (61,643)
	Winter	24,612 (1,395)	22,823 (3,248)	18,543 (7,173)	7,012 (3,301)	24,612 (15,117)
	Spring	24,719 (1,269)	23,450 (3,412)	18,557 (7,242)	6,909 (3,245)	24,719 (15,168)
	Summer	25,374 (1,273)	24,101 (3,519)	19,083 (7,384)	7,085 (3,320)	25,374 (15,496)
	Autumn	26,378 (1,340)	25,038 (3,540)	20,035 (7,598)	7,459 (3,384)	26,378 (15,862)
Colorectum	Total	73,860 (9,227)	64,401 (17,343)	44,591 (19,848)	17,927 (7,841)	73,860 (54,259)
	Winter	17,800 (2,280)	15,288 (4,014)	10,890 (4,840)	4,382 (1,977)	17,800 (13,111)
	Spring	18,553 (2,301)	16,252 (4,401)	11,210 (5,049)	4,446 (1,974)	18,553 (13,725)
	Summer	18,943 (2,348)	16,595 (4,527)	11,392 (5,151)	4,549 (1,979)	18,943 (14,005)
	Autumn	18,564 (2,298)	16,266 (4,401)	11,099 (4,808)	4,550 (1,911)	18,564 (13,418)
Lung	Total	124,859 (30,678)	93,976 (64,533)	27,871 (20,150)	6,054 (2,805)	124,859 (118,166)
	Winter	29,673 (7,735)	21,733 (14,982)	6,544 (4,784)	1,377 (675)	29,673 (28,176)
	Spring	31,671 (7,887)	23,784 (16,425)	7,014 (5,180)	1,453 (673)	31,671 (30,165)
	Summer	32,229 (7,509)	24,720 (16,888)	7,391 (5,292)	1,643 (755)	32,229 (30,444)
	Autumn	31,286 (7,547)	23,739 (16,238)	6,922 (4,894)	1,581 (702)	31,286 (29,381)
All sites[1]	Total	580,946 (90,474)	488,845 (182,777)	288,886 (122,568)	119,081 (48,365)	580,946 (444,184)
	Winter	140,049 (22,826)	115,596 (42,957)	69,846 (29,765)	28,842 (12,078)	140,049 (107,626)
	Spring	145,405 (22,949)	122,456 (46,340)	71,647 (30,878)	29,352 (12,053)	145,405 (112,220)
	Summer	148,101 (22,280)	125,821 (47,404)	73,742 (31,493)	30,217 (12,230)	148,101 (113,407)
	Autumn	147,391 (22,419)	124,972 (46,076)	73,651 (30,432)	30,670 (12,004)	147,391 (110,931)

[1]Excluding nonmelanoma skin cancer.

TABLE III – MORTALITY HAZARD RATIOS BY SEASON OF DIAGNOSIS AND TIME SINCE DIAGNOSIS IN WOMEN

Cancer site	Season of diagnosis	Time since diagnosis				Total hazard ratio[2]
		0–1 month hazard ratio[2]	1 month–1 year hazard ratio[2]	1–5 years hazard ratio[2]	>5 years hazard ratio[2]	
Breast	Winter	1.00	1.00	1.00	1.00	1.00
	Spring	**0.89 (0.83–0.95)**	0.97 (0.92–1.01)	1.01 (0.98–1.04)	**0.95 (0.92–0.99)**	**0.97 (0.96–0.99)**
	Summer	**0.81 (0.75–0.86)**	**0.92 (0.88–0.97)**	0.98 (0.95–1.00)	0.97 (0.94–1.00)	**0.95 (0.94–0.97)**
	Autumn	**0.87 (0.81–0.93)**	**0.94 (0.89–0.98)**	**0.95 (0.93–0.98)**	**0.93 (0.90–0.96)**	**0.94 (0.92–0.95)**
Colorectum	Winter	1.00	1.00	1.00	1.00	1.00
	Spring	1.00 (0.95–1.05)	1.00 (0.96–1.04)	0.99 (0.95–1.03)	1.00 (0.94–1.06)	0.99 (0.97–1.02)
	Summer	**0.93 (0.88–0.98)**	1.00 (0.96–1.04)	0.99 (0.95–1.03)	1.01 (0.95–1.07)	0.98 (0.96–1.00)
	Autumn	0.96 (0.91–1.01)	1.00 (0.96–1.04)	1.01 (0.96–1.05)	1.04 (0.97–1.10)	1.00 (0.97–1.02)
Lung	Winter	1.00	1.00	1.00	1.00	1.00
	Spring	**0.93 (0.89–0.97)**	1.00 (0.97–1.03)	0.98 (0.93–1.03)	0.98 (0.84–1.15)	**0.97 (0.95–1.00)**
	Summer	**0.86 (0.82–0.90)**	1.02 (0.99–1.05)	0.99 (0.93–1.04)	0.96 (0.82–1.13)	**0.97 (0.94–0.99)**
	Autumn	**0.88 (0.84–0.92)**	1.01 (0.98–1.04)	0.96 (0.91–1.02)	**0.79 (0.67–0.93)**	**0.96 (0.94–0.98)**
All sites[1]	Winter	1.00	1.00	1.00	1.00	1.00
	Spring	**0.93 (0.92–0.95)**	1.01 (0.99–1.02)	0.99 (0.98–1.01)	0.98 (0.96–1.00)	**0.98 (0.98–0.99)**
	Summer	**0.87 (0.85–0.89)**	**0.98 (0.97–1.00)**	**0.98 (0.96–0.99)**	0.99 (0.97–1.01)	**0.96 (0.95–0.97)**
	Autumn	**0.90 (0.88–0.91)**	**0.98 (0.97–1.00)**	**0.97 (0.95–0.98)**	**0.94 (0.92–0.96)**	**0.95 (0.94–0.96)**

Hazard ratios which differ significantly from unity ($p < 0.05$) are shown in bold, and values that are also outside the range 0.95–1.05 are highlighted.
[1]Excluding nonmelanoma skin cancer.–[2]Adjusted for age and period of diagnosis.

cancer incidence, monthly variation in all-cause mortality amongst the general population, and (in the final column) for both together.

For colorectal cancer in both sexes and for prostate cancer in males and breast cancer in females, adjusting for monthly differences in both cancer incidence and general population mortality completely eliminated any statistically significant seasonal variation in mortality hazard ratios. For example, in women with breast cancer, adjustment for the monthly incidence index increased the mortality hazard ratio for summer from 0.81 [(95% CI 0.75–0.86]) to 0.85 [95% CI (0.79–0.92]). Adjusting for the monthly mortality index resulted in a hazard ratio of 0.89 [95% CI (0.77–1.03]), and adjusting for both indices gave a hazard ratio of 0.97 [95% CI (0.83–1.14]). Adjusting for these 2 factors attenuated, but did not entirely eliminate, the seasonal variation in mortality hazard ratios in men and women with lung cancer.

Tables III–VI also include the analyses of all cancers combined. In these analyses, the substantial mortality reduction in summer/autumn in the first month of follow-up is evident in both females and males. Additionally, a long-term effect was observed, with reduced mortality in patients diagnosed in the autumn, in part contributed to by reductions in breast cancer and lung cancer mortality. The short-term seasonal variation in hazard ratios in the first month after diagnosis was more robust to statistical adjustment in the analysis of all cancers than in the analysis of breast, colorectal and prostate cancers individually.

Discussion

Short-term mortality patterns

Our unadjusted analyses show a substantial variation in mortality within the first month of diagnosis, with those diagnosed in the summer having a consistently better chance of surviving the first month than those diagnosed in the winter, most strikingly in the case of breast cancer. These early deaths would significantly affect the analysis of cancer survival at the longer-term follow-up periods used in earlier studies.

Winter is associated with a greatly increased incidence of upper and lower respiratory tract infections.[8,9] It may be that individuals have a lower expectation of well-being in the winter such that early, especially constitutional, symptoms of cancer do not attract such concern as in the summer. Similarly, healthcare workers may exhibit a seasonal bias in their threshold for concern, with those

TABLE IV – MORTALITY HAZARD RATIOS BY SEASON OF DIAGNOSIS AND TIME SINCE DIAGNOSIS IN MEN

Cancer site	Season of diagnosis	Time since diagnosis				Total hazard ratio[2]
		0–1 month hazard ratio[2]	1 month–1 year hazard ratio[2]	1–5 years hazard ratio[2]	>5 years hazard ratio[2]	
Prostate	Winter	1.00	1.00	1.00	1.00	1.00
	Spring	**0.90 (0.84–0.97)**	1.03 (0.99–1.09)	1.02 (0.98–1.05)	0.97 (0.92–1.02)	1.00 (0.98–1.02)
	Summer	**0.87 (0.80–0.93)**	1.05 (1.00–1.10)	1.01 (0.98–1.05)	0.98 (0.93–1.02)	1.00 (0.98–1.02)
	Autumn	**0.88 (0.81–0.94)**	1.02 (0.97–1.07)	1.01 (0.98–1.04)	0.98 (0.93–1.03)	0.99 (0.97–1.01)
Colorectum	Winter	1.00	1.00	1.00	1.00	1.00
	Spring	0.98 (0.92–1.04)	1.04 (1.00–1.09)	1.01 (0.97–1.05)	0.98 (0.92–1.04)	1.01 (0.98–1.03)
	Summer	**0.94 (0.89–1.00)**	**1.04 (1.00–1.09)**	1.02 (0.98–1.06)	0.96 (0.90–1.02)	1.00 (0.98–1.03)
	Autumn	0.95 (0.89–1.00)	**1.06 (1.02–1.11)**	1.00 (0.96–1.04)	0.95 (0.89–1.01)	1.00 (0.98–1.02)
Lung	Winter	1.00	1.00	1.00	1.00	1.00
	Spring	**0.94 (0.91–0.97)**	0.99 (0.97–1.02)	1.01 (0.97–1.05)	0.92 (0.83–1.03)	**0.98 (0.96–1.00)**
	Summer	**0.87 (0.84–0.90)**	0.99 (0.97–1.01)	**0.96 (0.92–1.00)**	0.94 (0.85–1.04)	**0.95 (0.93–0.96)**
	Autumn	**0.90 (0.87–0.93)**	1.02 (0.99–1.04)	0.96 (0.93–1.00)	**0.89 (0.80–0.99)**	**0.97 (0.96–0.99)**
All sites[1]	Winter	1.00	1.00	1.00	1.00	1.00
	Spring	**0.96 (0.94–0.98)**	**1.03 (1.01–1.04)**	1.01 (1.00–1.03)	**0.96 (0.94–0.99)**	1.00 (0.99–1.01)
	Summer	**0.90 (0.89–0.92)**	**1.03 (1.01–1.04)**	1.01 (0.99–1.02)	**0.95 (0.93–0.97)**	**0.99 (0.98–0.99)**
	Autumn	**0.92 (0.90–0.93)**	**1.02 (1.00–1.03)**	**0.98 (0.97–1.00)**	**0.91 (0.88–0.93)**	**0.97 (0.96–0.98)**

Hazard ratios which differ significantly from unity ($p < 0.05$) are shown in bold, and values that are also outside the range 0.95–1.05 are highlighted.
[1]Excluding nonmelanoma skin cancer.–[2]Adjusted for age and period of diagnosis.

TABLE V – MORTALITY HAZARD RATIOS BY SEASON OF DIAGNOSIS IN THE PERIOD 0–1 MONTH AFTER DIAGNOSIS IN WOMEN

Cancer site	Season of diagnosis	Adjustment			
		Unadjusted hazard ratio[1]	Adjustment 1 hazard ratio[2]	Adjustment 2 hazard ratio[3]	Adjustment 3 hazard ratio[4]
Breast	Winter	1.00	1.00	1.00	1.00
	Spring	**0.89 (0.83–0.95)**	**0.91 (0.85–0.98)**	0.94 (0.85–1.05)	0.99 (0.89–1.10)
	Summer	**0.81 (0.75–0.86)**	**0.85 (0.79–0.92)**	0.89 (0.77–1.03)	0.97 (0.83–1.14)
	Autumn	**0.87 (0.81–0.93)**	**0.91 (0.84–0.98)**	0.93 (0.84–1.03)	0.98 (0.88–1.10)
Colorectum	Winter	1.00	1.00	1.00	1.00
	Spring	1.00 (0.95–1.05)	0.99 (0.94–1.05)	1.03 (0.95–1.11)	1.02 (0.94–1.11)
	Summer	**0.93 (0.88–0.98)**	**0.91 (0.86–0.97)**	0.97 (0.87–1.09)	0.96 (0.85–1.08)
	Autumn	0.96 (0.91–1.01)	0.95 (0.89–1.01)	0.99 (0.91–1.07)	0.98 (0.90–1.07)
Lung	Winter	1.00	1.00	1.00	1.00
	Spring	**0.93 (0.89–0.97)**	**0.92 (0.87–0.97)**	0.95 (0.89–1.02)	0.94 (0.88–1.01)
	Summer	**0.86 (0.82–0.90)**	**0.85 (0.81–0.90)**	**0.90 (0.81–0.99)**	**0.89 (0.81–0.98)**
	Autumn	**0.88 (0.84–0.92)**	**0.87 (0.83–0.92)**	**0.90 (0.84–0.97)**	**0.89 (0.83–0.96)**
All sites[5]	Winter	1.00	1.00	1.00	1.00
	Spring	**0.93 (0.92–0.95)**	**0.94 (0.92–0.96)**	**0.95 (0.92–0.98)**	**0.96 (0.93–0.99)**
	Summer	**0.87 (0.85–0.89)**	**0.89 (0.87–0.91)**	**0.89 (0.86–0.93)**	**0.91 (0.87–0.95)**
	Autumn	**0.90 (0.88–0.91)**	**0.91 (0.89–0.93)**	**0.91 (0.88–0.94)**	**0.92 (0.90–0.95)**

Hazard ratios which differ significantly from unity ($p < 0.05$) are shown in bold, and values that are also outside the range 0.95–1.05 are highlighted.
[1]Adjusted only for age and period of diagnosis.–[2]Adjusted for age and period of diagnosis, plus monthly incidence index.–[3]Adjusted for age and period of diagnosis, plus monthly mortality index.–[4]Adjusted for age and period of diagnosis, plus both monthly incidence index and monthly mortality index.–[5]Excluding nonmelanoma skin cancer.

feeling generally unwell in the summer being investigated earlier compared to those with similar complaints in the winter. As a result, it is possible that the summer excess in incidence is largely composed of cancers of an earlier stage with less severe symptomatology than is average for the winter. Conversely, those patients presenting with acute severe cancer-related illness (for example pneumonia in lung cancer patients) would comprise a larger proportion of those diagnosed in the winter, with subsequent effects on short-term mortality.

Many of the deaths occurring within the first month postdiagnosis are likely to be attributable to the effects of treatment related complications, which may be subject to seasonal variation. It may be that patients are more susceptible to deaths such as those due to cardiorespiratory complications following anesthesia and surgery during the winter. Indeed, the incidence of hospital acquired pneumonia, a complication that commonly arises postoperatively, has been shown to vary substantially with season.[9] Additionally, mortality from cardiovascular and cerebrovascular events in the general population exhibits seasonal variation,[10] though to our knowledge this has not been definitively demonstrated in an inpatient population.

Given these considerations, we adjusted the first-month mortality hazard ratios for variations in cancer incidence and in background mortality in the general population. These adjustments appeared to attenuate the seasonality in first-month mortality hazard ratios independently, with adjustment for the general population mortality index having the greater effect. When performed together, they resulted in hazard ratios approaching unity amongst females with breast cancer, males with prostate cancer and those of both sexes with colorectal cancer.

However, the adjustments failed to eliminate seasonality in lung cancer mortality hazard ratios within the first month postdiagnosis or in those from cancers at all sites taken together. Lung cancer patients are at high risk of respiratory tract infection not only because tumor and surrounding changes form a focus for infection to develop but also because of the high prevalence of smoking-related comorbidities such as chronic obstructive pulmonary disease, resulting in higher rates of bronchial colonization in patients with lung cancer.[11] Such an increased susceptibility might serve to amplify the well-established seasonality in the prevalence of respiratory tract infections in the community. Immunocompromise resulting from chemotherapy may result in further increased

TABLE VI – MORTALITY HAZARD RATIOS BY SEASON OF DIAGNOSIS IN THE PERIOD 0–1 MONTH AFTER DIAGNOSIS IN MEN

Cancer site	Season of diagnosis	Adjustment			
		Unadjusted hazard ratio[1]	Adjustment 1 hazard ratio[2]	Adjustment 2 hazard ratio[3]	Adjustment 3 hazard ratio[4]
Prostate	Winter	1.00	1.00	1.00	1.00
	Spring	**0.90 (0.84–0.97)**	**0.89 (0.83–0.96)**	0.92 (0.82–1.03)	0.93 (0.83–1.04)
	Summer	**0.87 (0.80–0.93)**	**0.87 (0.81–0.94)**	0.90 (0.76–1.05)	0.92 (0.78–1.09)
	Autumn	**0.88 (0.81–0.94)**	**0.90 (0.83–0.98)**	0.89 (0.80–1.00)	0.94 (0.83–1.06)
Colorectum	Winter	1.00	1.00	1.00	1.00
	Spring	0.98 (0.92–1.04)	0.99 (0.93–1.04)	0.99 (0.91–1.08)	1.02 (0.93–1.13)
	Summer	**0.94 (0.89–1.00)**	0.96 (0.90–1.02)	0.97 (0.86–1.09)	1.02 (0.89–1.17)
	Autumn	0.95 (0.89–1.00)	0.96 (0.91–1.02)	0.96 (0.88–1.05)	1.00 (0.91–1.10)
Lung	Winter	1.00	1.00	1.00	1.00
	Spring	**0.94 (0.91–0.97)**	**0.95 (0.92–0.98)**	0.97 (0.93–1.02)	0.98 (0.93–1.02)
	Summer	**0.87 (0.84–0.90)**	**0.88 (0.85–0.91)**	**0.92 (0.86–0.98)**	**0.92 (0.86–0.99)**
	Autumn	**0.90 (0.87–0.93)**	**0.91 (0.88–0.94)**	**0.93 (0.89–0.98)**	**0.94 (0.89–0.98)**
All sites[5]	Winter	1.00	1.00	1.00	1.00
	Spring	**0.96 (0.94–0.98)**	**0.97 (0.95–0.98)**	0.97 (0.95–1.00)	0.98 (0.96–1.01)
	Summer	**0.90 (0.89–0.92)**	**0.92 (0.90–0.93)**	**0.92 (0.89–0.96)**	**0.94 (0.90–0.98)**
	Autumn	**0.92 (0.90–0.93)**	**0.93 (0.91–0.95)**	**0.93 (0.90–0.95)**	**0.94 (0.92–0.97)**

Hazard ratios which differ significantly from unity ($p < 0.05$) are shown in bold, and values that are also outside the range 0.95–1.05 are highlighted.

[1]Adjusted only for age and period of diagnosis.–[2]Adjusted for age and period of diagnosis, plus monthly incidence index.–[3]Adjusted for age and period of diagnosis, plus monthly mortality index.–[4]Adjusted for age and period of diagnosis, plus both monthly incidence index and monthly mortality index.–[5]Excluding nonmelanoma skin cancer.

susceptibility to infection both in the hospital and community, once again amplifying seasonality. Furthermore, in lung cancer, the room for improvement in prognosis by prompt diagnosis and expert treatment is considerably less than in breast or colorectal cancer.

Long-term mortality patterns

In addition to the short-term effect, we found evidence of a long-term effect at greater than 5 years postdiagnosis. However, there was a consistent shift in the seasonality pattern, with diagnosis in the autumn as opposed to the summer being associated with reduced mortality in the long term, most strikingly in the case of lung cancer in both sexes and breast cancer in females. This is of little practical significance in the case of lung cancer, where only 5% of patients survive to 5 years, but the reduction in mortality amongst breast cancer patients diagnosed in the autumn (and to a lesser degree the spring) is interesting and could indicate a beneficial long-term mechanism.

A seasonality in mortality that is present at greater than 5 years but largely absent at 1–5 years postdiagnosis raises important questions. Although five-year recurrence-free survival amongst cancer patients is classically considered equivalent to cure, Rosen *et al*.[12] have shown that the risk of breast cancer recurrence, while it peaks within the first 5 years of diagnosis, remains elevated within the 5–12 year postdiagnosis period. Cancer recurrence does occur at greater than 5 years following diagnosis, most likely as a result of micrometastasis. It is possible that the cells responsible are more amenable to the early differentiating effects of vitamin D, resulting in the observation of increased survival in the >5 year postdiagnosis period amongst those diagnosed in the spring or autumn. However, it should be noted that, despite the fact that colorectal cancer has been most strongly linked to serum Vitamin D,[13] no mortality reduction was found in colorectal cancer patients diagnosed in summer and autumn beyond the first month after diagnosis in our study.

Conclusions

We conclude that the previously observed higher survival in cancer patients diagnosed in the summer and autumn is predominantly a short-term phenomenon, and to a large extent caused by generally higher mortality in the winter months. It is unlikely that this effect involves the seasonal variation in serum vitamin D concentration. However, there exists an additional long-term effect that requires further detailed investigation.

Our findings raise a number of important issues relevant to the study of seasonality in cancer survival. Firstly, it is important to divide the follow-up into separate time windows to resolve distinct mechanisms acting simultaneously in the short and longer term. Secondly, the observation of seasonality in cancer survival is likely to be dependent on a number of different factors in addition to those with a biological basis, such as seasonal variations in expectations of health, in health care provision and access and in background fluctuations in general mortality. This implies that not all findings from one country or health care system may be fully generalizable to other countries and sociological settings. It is thus apparent that the analysis of the role of seasonality in cancer incidence and prognosis is a complex field of study, requiring a range of study designs and the incorporation of more detailed sociodemographic, clinical and biological parameters for reliable biological inferences to be made.

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