Seasonal variation in coronary heart disease in Scotland

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Abstract

**Study objective** - Seasonality of coronary heart disease (CHD) was examined to determine whether fatal and non-fatal disease have the same annual rhythm.

**Design** - Time series analysis was carried out on retrospective data over a 10 year period and analysed by age groups (<45 to >75 years) and gender.

**Setting** - Data by month were obtained for the years 1962–71. The Registrar General provided information on deaths and the Research and Intelligence Unit of the Scottish Home and Health Department on hospital admissions.

**Subjects** - In Scotland, between 1962 and 1971, 123,000 patients were admitted to hospital for CHD, of whom 29,000 died. There were a further 97,000 CHD deaths outside hospital. These two groups were also examined as one (coronary incidence) - that is, all coronary deaths and coronary admissions discharged alive.

**Statistical analysis and main results** - Where there was a single annual peak, the sine curve was analysed by cosinor analysis. When there were two peaks the analysis was by normal approximation to Poisson distribution. In younger men (under 45 years) admitted to hospital there was a dominant spring peak and an autumn trough. A bimodal pattern of spring and winter peaks was evident for hospital admissions in older male age groups: with increasing age the spring peak diminished and the winter peak increased. In contrast, female hospital admissions showed a dominant winter/summer pattern of seasonal variation in male and female CHD deaths seasonal variation showed a dominant pattern of winter peaks and summer troughs, with the winter peak spreading into spring in the two youngest male age groups. CHD incidence in women showed a winter/summer rhythm, but in men the spring peak was dominant up to the age of 55.

**Conclusions** - The male, age related spring peak in CHD hospital admissions suggests there is an androgenic risk factor for myocardial infarction operating through an unknown effector mechanism. As age advances and reproduction becomes less important, the well defined winter/summer pattern of seasonal variation in CHD is superimposed, and shows a close relationship with the environment, especially temperature, or the autumn and early winter fall in temperature.

Studies of seasonal variation in coronary heart disease (CHD) are almost entirely based on data derived from national registers of deaths. Studies based on seasonal variation of CHD hospital admissions are few. Dunnigan et al found a bimodal pattern of seasonal variation with spring and winter peaks in a study of 47,281 admissions to all Scottish hospitals in 1962–66 in the diagnostic category ICD 420.1. The spring peak declined with age, while the winter peak became more prominent. Surprisingly, no further large studies of seasonal variation in CHD incidence have been published, but two small studies have similarly challenged the conventional belief that all seasonality of CHD follows a winter/summer rhythm. The present investigation extends the sample size of the original Scottish study to 10 years (1962–71), and examines the effects of age and sex in more detail.

**Methods**

Between 1962 and 1971 inclusive, the Scottish Home and Health Department recorded 123,000 CHD discharges/admissions to all Scottish hospitals, of whom 29,000 died. The General Register Office for Scotland recorded a further 97,000 deaths from CHD outside hospital over this period. Between 1962 and 1967, the ICD 7th Revision (420.1) was used, and thereafter the 8th Revision (410). Deaths and admissions were analysed by gender, age, and month of occurrence (corrected to 31 day months). Month correction causes an annual total greater than the true total (see tables). The General Register Office for Scotland also provided data on births between 1962 and 1971.

**STATISTICAL ANALYSIS**

Cosinor analysis was used to determine the significance of seasonal variation in CHD events. This technique forces a sine curve on the data, the peak being six months ahead of the trough. The amplitude of seasonal fluctuation is expressed as a percentage above the mean for the month of highest value (acrophase, zenith, or peak). Cosinor analysis is reliable only if the data fit a single sine curve and may be invalidated by two peaks, as in part of our data. Significance
data and sin (t) and cos (t). This analysis gives the multiple correlation coefficient (r), its statistical significance (p), and the angular position in the year (converted to the nearest month) where the fitted sinusoidal regression line has its highest value. The technique is exemplified in figure 1(B).

**Normal approximation to Poisson distribution (NAPD)**

This statistical method was applied to the whole data set but was of particular value in the examination of the two peaks in the annual rhythm of non-fatal coronary onsets in patients arriving alive at hospital. In using this, two assumptions are made, firstly, that the population at risk is large compared with the number of hospital coronary admissions and, secondly, that these appear "independently" in time.

The technique is exemplified (fig 1(A)) for 79,746 male hospital admissions. The expected monthly value was calculated allowing for different month-length.

The estimated standard error of a Poisson distribution is the square root of the actual value. Ninety nine per cent confidence intervals are used (see fig 1(A)). Significance refers to the 1% level.

**Results**

"Hospital admissions" refer to patients who arrived alive at the hospital, whether they subsequently died or survived. "Deaths" refers to total deaths, including those at home plus those in hospital. "Coronary incidence" refers to all coronary deaths plus all coronary admissions discharged alive examined as one group.

**MALE HOSPITAL ADMISSIONS (FIGS 1(A), 2, AND 4, TABLES 1 AND 2)**

Total male CHD hospital admissions show a spring peak with a late summer/early autumn trough and an early winter peak. Using NAPD, the numbers for May and December are significantly higher, and those for August and September significantly lower, than the annual average (see figs 1(A) and 4). The spring peak is dominant in males under 45 years; this is significant on cosinor analysis. The bimodal pattern of spring and winter peaks is evident in older decades, with the spring peak waxing and the winter peak waning with age. This bimodal pattern of seasonal variation invalidates cosinor analysis except for the youngest age group <45 years. The amplitude of the spring peak exceeds that of the winter peak in all but the oldest age group (>75 years). In patients aged between 55–74 (60% of the total series) May, but not December, is significantly higher on NAPD (see fig 4).

**FEMALE HOSPITAL ADMISSIONS (FIGS 1(B), 2, 3, AND 4, TABLES 1 AND 2)**

Total female CHD hospital admissions show a winter peak and a summer trough, demonstrated by cosinor analysis (fig 1(B)) and
confirmed by NAPD (fig 4). Using the latter, December and January are significantly higher than the annual average at the 99% confidence interval and July, August, and September are significantly lower. The numbers in the two youngest age groups do not allow the expression of a clear pattern of seasonal variation. The three oldest age groups showed a dominant and significant pattern of winter peaks in admissions (NAPD fig 4).

MALE DEATHS (FIGS 3 AND 4, TABLES 1 AND 2)
Overall, the rhythm is winter/summer, with the three older age groups having a peak in January. The peak is in February for the 45–54 years age group, and in March for the under 45 group. In all age groups the rise in deaths in the autumn is precipitous. In the oldest age group the rises and falls to and from the winter peak are almost symmetrical. The younger the age group the slower the fall from the peak, because of a spring "shoulder". The older the age group, the greater the winter excess.

Of the 79,000 male admissions, 17,000 died in hospital. The latter deaths had a single, February peak, with an otherwise similar pattern of seasonal variation to that of male deaths as a whole. The amplitude of the seasonal variation, however, was smaller (8.7%) inside hospital than outside (12%). The proportions in each age group that died inside and outside hospital were almost identical. The amplitude difference is not related to any age difference.

FEMALE DEATHS (FIGS 3 AND 4, TABLES 1 AND 2)
A significant pattern of winter/summer variation in deaths is evident in the four oldest age
groups. No clear pattern of seasonal variation is evident in the youngest age group, because of the small sample size. As with males, the seasonal excess increases with age. The amplitude of the winter/summer seasonal variation in female deaths is substantially greater than that for female hospital admissions, as is that for male deaths.

CORONARY INCIDENCE: MEN AND WOMEN (TABLE 3, FIGS 4 AND 5)
Total coronary incidence shows on cosinor analysis in men that the spring peak is present in the <45 years age group and in the group age <55 years (table 3). The addition of the deaths to admissions has given statistical significance on cosinor analysis in men under 55 years. Also, in males under 55 years on the NAPD (1% level) both May and December peaks are significant (table 3, figs 4 and 5). The May peak seen in hospital admissions of men 55–75+ was "drowned out" by the increasing deaths in these age groups when examined as coronary incidence, leaving only the winter peak (fig 5). The number of women under the age of 55 years is relatively small and no significant peaks are found. A non-significant trend is to a winter peak style. Other female groupings show a winter peak (fig 4).
## Table 1  Deaths (outside and inside hospital) and hospital admissions (survived or died) due to myocardial infarction in Scotland 1962-71 in relation to gender, age group, and month of occurrence

<table>
<thead>
<tr>
<th>Month</th>
<th>Deaths in age groups</th>
<th>Admissions in age groups</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;45</td>
<td>45-54</td>
<td>55-64</td>
</tr>
<tr>
<td>Men (%)</td>
<td>(9)</td>
<td>(22)</td>
<td>(37)</td>
</tr>
<tr>
<td>Aug</td>
<td>186</td>
<td>746</td>
<td>176</td>
</tr>
<tr>
<td>Sep</td>
<td>242</td>
<td>718</td>
<td>1765</td>
</tr>
<tr>
<td>Oct</td>
<td>215</td>
<td>758</td>
<td>1723</td>
</tr>
<tr>
<td>Nov</td>
<td>199</td>
<td>718</td>
<td>1981</td>
</tr>
<tr>
<td>Dec</td>
<td>237</td>
<td>902</td>
<td>2173</td>
</tr>
<tr>
<td>Jan</td>
<td>265</td>
<td>916</td>
<td>2085</td>
</tr>
<tr>
<td>Feb</td>
<td>235</td>
<td>816</td>
<td>2015</td>
</tr>
<tr>
<td>Mar</td>
<td>261</td>
<td>855</td>
<td>2013</td>
</tr>
<tr>
<td>Apr</td>
<td>238</td>
<td>833</td>
<td>1940</td>
</tr>
<tr>
<td>May</td>
<td>245</td>
<td>810</td>
<td>1754</td>
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<tr>
<td>Jun</td>
<td>247</td>
<td>783</td>
<td>1915</td>
</tr>
<tr>
<td>Jul</td>
<td>218</td>
<td>749</td>
<td>1749</td>
</tr>
</tbody>
</table>

**Significance**
- NS: Not significant
- *p* < 0.05
- **p** < 0.01

Cosinor analysis using 12 monthly variables. NS = not significant: *p* < 0.05, **p** < 0.01. The three highest monthly totals for each combination of gender, age group, and outcome are underlined. The data have been month corrected.

## Table 2  Cosinor analysis

<table>
<thead>
<tr>
<th>Month</th>
<th>Deaths</th>
<th>Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan</td>
<td>97</td>
<td>90</td>
</tr>
<tr>
<td>Dec</td>
<td>45</td>
<td>75</td>
</tr>
<tr>
<td>Feb</td>
<td>193</td>
<td>710</td>
</tr>
<tr>
<td>May</td>
<td>3893</td>
<td>3893</td>
</tr>
<tr>
<td>Jun</td>
<td>3716</td>
<td>3716</td>
</tr>
<tr>
<td>Jul</td>
<td>3185</td>
<td>3185</td>
</tr>
</tbody>
</table>

## Table 3  Coronary incidence in relation to month, sex, and age group

<table>
<thead>
<tr>
<th>Month</th>
<th>&lt;45y</th>
<th>45-54y</th>
<th>55-64y</th>
<th>65-74y</th>
<th>75+y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan</td>
<td>62</td>
<td>676</td>
<td>3745</td>
<td>6757</td>
<td></td>
</tr>
<tr>
<td>Feb</td>
<td>64</td>
<td>687</td>
<td>3745</td>
<td>6757</td>
<td></td>
</tr>
<tr>
<td>Mar</td>
<td>66</td>
<td>698</td>
<td>3745</td>
<td>6757</td>
<td></td>
</tr>
<tr>
<td>Apr</td>
<td>68</td>
<td>709</td>
<td>3745</td>
<td>6757</td>
<td></td>
</tr>
<tr>
<td>May</td>
<td>70</td>
<td>720</td>
<td>3745</td>
<td>6757</td>
<td></td>
</tr>
<tr>
<td>Jun</td>
<td>72</td>
<td>731</td>
<td>3745</td>
<td>6757</td>
<td></td>
</tr>
<tr>
<td>Jul</td>
<td>74</td>
<td>742</td>
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</tr>
<tr>
<td>Aug</td>
<td>76</td>
<td>753</td>
<td>3745</td>
<td>6757</td>
<td></td>
</tr>
<tr>
<td>Sep</td>
<td>78</td>
<td>764</td>
<td>3745</td>
<td>6757</td>
<td></td>
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<tr>
<td>Oct</td>
<td>80</td>
<td>775</td>
<td>3745</td>
<td>6757</td>
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<tr>
<td>Nov</td>
<td>82</td>
<td>786</td>
<td>3745</td>
<td>6757</td>
<td></td>
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<tr>
<td>Dec</td>
<td>84</td>
<td>797</td>
<td>3745</td>
<td>6757</td>
<td></td>
</tr>
</tbody>
</table>

**Significance**
- NS: Not significant
- *p* < 0.05
- **p** < 0.01

The three highest month totals for each combination of gender and age group are underlined.

* Two peaks but the earlier is much the larger and its cosinor analysis is significant.
events, but no reports of seasonality of CHD focussing on non-fatal onsets. We recognise the limitations of death certification, hospital discharge documentation, and record linkage. In the earlier survey, the records of 1000 admissions under rubric ICD 420.1 showed that 87% were due to acute myocardial infarction or acute ischaemia. The term admissions has been used loosely; these are recorded as hospital discharges – that is, those who were admitted and then died or were discharged.

The familiar association between low environmental temperature and CHD mortality has been discussed in detail previously. Our evidence suggests that this may result from the fall in temperature in autumn and early winter, rather than the absolute low temperature reached in later winter. Other meteorological and environmental influences may also be involved. The effector mechanism, however, is unclear. In addition to changes in cholesterol and blood pressure there are winter increases in haematocrit, white cell count, and fibrinogen concentration, all of which raise blood viscosity; while fibrinolysis is most active in the summer. Factor VII clotting activity, C-reactive protein, and α antitrypsin values are also raised in winter.

The age related spring increase in CHD non-fatal onsets is a predominantly male phenomenon. The dominant pattern of spring/autumn variation in the youngest male age group is replaced in older male age groups by a bimodal pattern in which a gradually declining spring peak exceeds the winter peak until old age (>75 years). In contrast, women aged 55 and over show a dominant pattern of winter/summer variation in CHD non-fatal onsets. The numbers in the younger female age groups are small, and a firm conclusion must await an even larger series. Seasonal variation in deaths shows a dominant winter/summer pattern in both sexes, with subsidiary spring “shoulders” on the winter peak in the two youngest male age groups. The results of examination of coronary incidence in men under 55 years of age strengthen these conclusions. The cause of the age related spring peak in non-fatal onsets is uncertain, but a risk factor which is dominant in younger men, reduces with age, and is inconspicuous in women suggests an androgenically driven effector mechanism. There is a similarity between seasonal variation of conceptions and non-fatal coronary onsets in young men. Moreover, seasonal variation in beard growth, rape and attempted rape (A S Douglas, personal communication, 1971) spermatogenesis, and levels of oestriol and luteinizing hormone all show spring-summer peaks.

The effector mechanism through which a putative spring increase in androgenic activity might operate is also speculative. Two studies of seasonal variation in serum cholesterol in Scotland and Israel found the highest values in the spring, but a larger study of two-monthly seasonal variation in the United States showed a high winter, low summer pattern, as have most other studies. Seasonal variation in blood pressure in most reports shows a dom-

**Discussion**

The original study covered 1962–66; we have added to it corresponding data for 1967–71. This has made possible clarification of the earlier results, with emphasis on hospital admissions. In recent times there has been an interest in the circadian rhythm of CHD

![Figure 4](http://jech.bmj.com/)

**Figure 4** Incidence, deaths, and hospital admissions for coronary heart disease in relation to age and sex in Scotland (1962–71). The dark areas are months which are significantly higher than the mean and the lightly stippled areas are significantly lower than the mean. Where there is no entry these points were not significantly different from the mean. The level of significance is p<0.01.
inhabit high winter, low summer pattern with a few showing a spring peak, for example. Eastham and Avis found adhesive platelet counts to be highest and non-adhesive counts lowest in the spring. Lacoste and Wirz-Justice found a spring/autumn pattern of platelet serotonin uptake strikingly similar to the spring/autumn pattern of CHD variation in the youngest group of Scottish men in the present study. Unfortunately, however, none of the foregoing studies were grouped according to age and sex. The seasonality of several parameters has been discussed, quoting only a small number of the available published papers. This paper is not a review: a recent bibliography provides a fuller reference source.

It is possible that the male, age related spring rise in CHD prevalence results from the emotional and physical effects of increased sexual activity in spring in men with pre-existing cardiovascular disease. It may also be relevant that the incidence of suicide peaks in May, and that its amplitude is greater in men than in women (A S Douglas personal communication).

Confirmatory studies of the pattern of seasonal variation in CHD non-fatal onsets shown in the present study are desirable, utilising comparably large data sets. Further elucidation of the mechanism of the spring rise in CHD incidence in men would require larger studies of seasonal variation in major cardiovascular risk factors and reproductive hormones divided by age and sex.

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