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An Analysis of the Seasonal Variation of Coronary Heart Disease and Respiratory Disease Mortality in New Zealand

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Marshall R J (Department of Community Health and General Practice, School of Medicine, University of Auckland, Private Bag, Auckland, New Zealand), Scragg R and Bourke P. An analysis of the seasonal variation of coronary heart disease and respiratory disease mortality in New Zealand. *International Journal of Epidemiology* 1988, 117: 325–331. The seasonal variation of coronary heart disease mortality rates in New Zealand is analysed by age, sex and race using monthly national mortality data for the period 1970–83. A 35% variation from the winter peak to summer low is found in the crude mortality rate, but the size of the seasonal variation is age-dependent, being more pronounced in the elderly, and more so in males than in females. The hypothesis that respiratory infections are linked to coronary heart disease, and that their seasonal occurrence explains the seasonal variation in coronary rates, is examined by an analysis of the association between coronary disease and respiratory disease mortality rates. By partial correlation analysis and by examining the residual correlation after filtering the seasonal variation from both series, it is suggested that the season acts as a confounding factor to cause an apparent association between the two rates. After controlling for season there is a tenuous relationship, but it is apparent only in the elderly.

Many countries observe a seasonal variation in coronary heart disease mortality,[1–4] rates being higher in winter than in summer. The reasons are not fully understood. Some studies have suggested that low environmental temperatures are directly responsible,[5–9] the body cooling effect possibly placing increased stress on the heart or altering a body parameter such as blood coaguability, while others have implicated winter respiratory infections;[2,10] possibly viral infections increase the risk of thrombosis. A further hypothesis[11] is that summer ultra-violet radiation, by increasing body levels of vitamin D, protects against CHD since vitamin D has been observed to be lower in coronary patients.[12]

There are two objectives to the present study. First we analyse the seasonal variation of CHD mortality in New Zealand with respect to age, sex and race. As we demonstrate there is a substantial seasonal variation of about 35%, with age differences. In the search for the aetiology of the disease an annual variation of this magnitude seems as important a consideration as the more widely reported decline in CHD mortality rates. Second we examine the association between CHD mortality and mortality from respiratory disease, since both have similar seasonal patterns and there is evidence that respiratory infections are a stimulus for coronary heart disease.[13–17]

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METHODS AND DATA

Monthly CHD and respiratory disease mortality statistics were obtained from the National Health Statistics Centre for the period January 1970 to December 1982. CHD is defined, prior to 1979, by the 8th revision ICD codes 410–413 and post-1979 by the 9th revision codes 410–414. Disease of the respiratory tract covers pneumonia (ICD codes 480–486), influenza (ICD codes 470–472 8th revision, 487 9th revision) and bronchitis, emphysema and asthma (ICD codes 490–493 8th revision, 490–496 9th revision). Data were classified by age, in five groups 35–44, 45–54, 55–64, 65–74 and 75+ years, and by sex and race. Two racial groups were considered: Maori and non-Maori. The Maori community is about 10% of New Zealand's three million population. The formal definition of Maori requires that the deceased has at least 50% Maori blood. The monthly CHD and respiratory disease mortality statistics have been adjusted to a 30-day month by subtracting a 1/31 part from those of 31-day months and adding a 2/28 (or 1/29 in leap years) part to February statistics.

To compute mortality rates, population figures by

age, race and sex were obtained from published census data for March 1971, 1976 and 1981. (At the time of the analysis the 1986 census data were not available.) Population estimates for intercensus months in the 1970–1982 period were obtained by linear interpolation and extrapolation from the census statistics. Implicit in this estimation procedure is the reasonable assumption that population size is not seasonal.

Investigation of the seasonal phenomenon was done by elementary statistical summaries and by using the following seasonal regression model

$$\log (CHD_t) = m + a\text{Sin}(\pi t/6 + b) + ct + Z \quad (1)$$

where t indexes a particular month, running from 1 to 156 for the 13-year period and CHD_t is the monthly CHD mortality rate. The sinosoidal term describes the seasonality, a being its amplitude and b its phase, that is, b determines when in the year CHD attains a peak. The term ct describes a possible trend to account for the reported decline in CHD[18], m is a general mean and Z is residual random variation. When b is regarded as a parameter to be estimated the model is non-linear and it was fitted by the SAS procedure NLIN.[19] However, we also fixed to coincide with the peak mid-winter rate, thereby rendering the model linear, and used the SAS linear regression procedure GLM, which is computationally much faster and allows greater flexibility in testing effects. Tests for the significance of the parameters a and c amount to tests for a seasonal component and a time trend respectively.

By using $\log (CHD_t)$ as the dependent variable the seasonal and trend effects are multiplicative. For example, since the amplitude of the sine term is a, the peak monthly CHD rate is e^a times the base monthly rate, other factors being held constant, and the seasonal percentage variation is $100 (e^a - 1)$ per cent of the base rate. Similarly the trend can be expressed as percentage changes to the coronary rate over a given time period. The variance of $\log (CHD_t)$ is approximately equal to the numerator in the computation of the CHD rate. The numerator was accordingly used as a weighting function in the regression procedures. The adequacy of a fitted model was examined by testing for serial correlation[20] in the residual series.

An interpretation of the association between monthly coronary and respiratory mortality rates raises some methodological issues. Since both series exhibit a similar seasonal pattern we require to distinguish a direct hypothesis, that the seasonal variation in CHD is a direct result of the seasonal pattern of respiratory disease, from an indirect hypothesis, that both series are inherently seasonal, due to extraneous and as yet unquantifiable mechanisms, and that the observed association is due to confounding with 'season'. To discriminate these hypotheses we examined the correlation between any two of the three variables—CHD mortality, respiratory disease mortality and season—while controlling for the third. If, for example, coronary and respiratory mortality are uncorrelated, after controlling for season, it gives support to the indirect hypothesis, but on the other hand, a weak correlation between season and CHD while controlling for respiratory rates supports the direct hypothesis since, under the direct hypothesis, there would be no seasonal variation in CHD rate were the respiratory rate held constant. Partial correlation analysis was used for these computations by introducing a season variable defined as a harmonic function with a fixed phase, b, to centre on a mid-July peak. We also carried out an analysis of the residual correlation between coronary and respiratory mortality rates after filtering the seasonal component. The filtering was achieved by fitting the seasonal model in equation (1) to both the coronary and respiratory rates (omitting the trend term for respiratory rates). This approach tests whether an excess, or deficit, in CHD mortality from its seasonal average coincides with an excess or deficit in respiratory mortality from its seasonal average.

RESULTS

A plot of crude monthly CHD mortality rates in over 35 year olds (Figure 1) demonstrates an obvious seasonal effect. The seasonal model, equation (1), fitted to this series, with the phase parameter b estimated, gave a peak winter to summer variation of 35.4% with the peak rate occurring at month 7.49, that is, mid-July. The trend term was also significant; the ten-year rate of decline being 9.2%.

We next examined the seasonal variation by age, sex and race. Non-Maori coronary mortality rates for each calendar month as a percentage of the monthly base rates, which are given for reference in Table 1, are shown in Figure 2. The seasonal variation is most marked in the elderly for whom it shows little sex differential. However, it seems to affect younger females to a greater degree than males and, in particular, for females aged 35–44 it is most striking, although the coronary mortality rate for this group is very low (1.2/100 000) and the approximate standard error of each monthly estimate is about 20%; the strong seasonality should thus be treated cautiously. The corresponding plots for Maoris were rather difficult to interpret, because their smaller numbers result in less stable rates, and are omitted. However, seasonal varia-

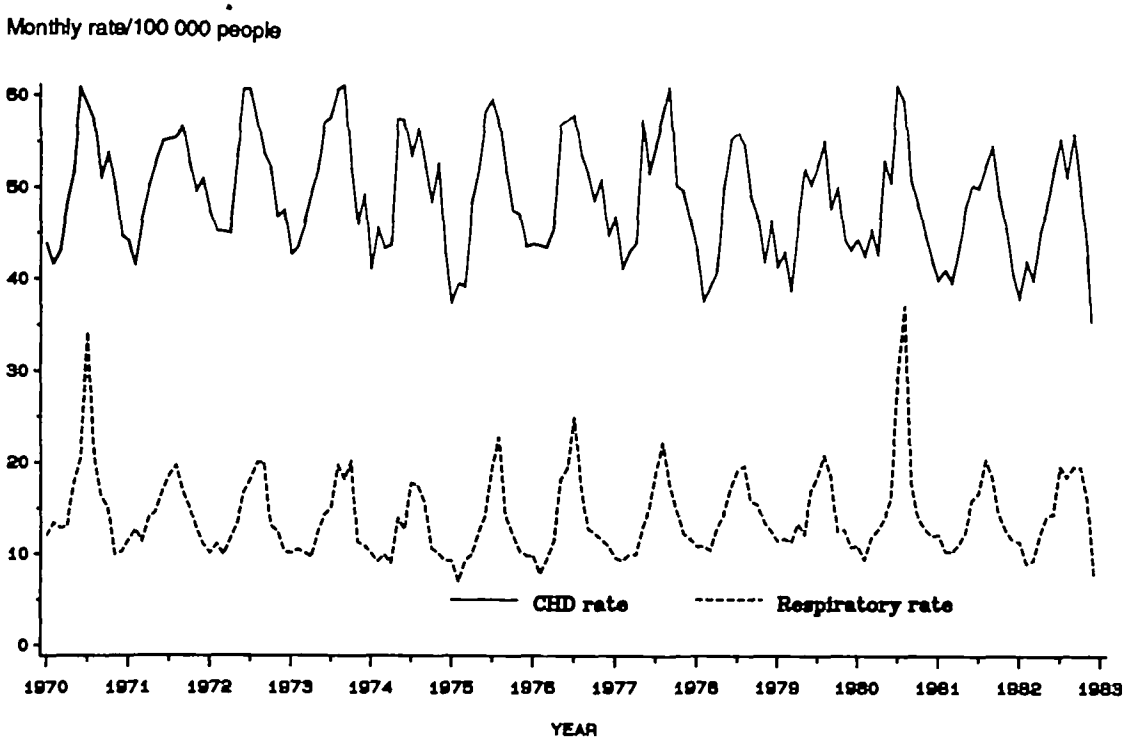

FIGURE 1 *Monthly coronary (CHD) and respiratory mortality rates. Crude rates for over 35 year olds.*

tion was apparent for all ages combined and was more noticeable in Maori males.

To supplement this descriptive analysis the seasonal model in equation (1) was fitted to age-sex-race specific rates. Estimates of the seasonal components are given in Table 2. For non-Maoris seasonal variation is significant only for the over 55s, with the exception of the curious seasonality for females aged 35–44 mentioned above. For Maoris the seasonal component is only significant for the over 65s. The suggestion that seasonal variations are age dependent was examined by fitting the seasonal model to sex-race specific rates and including age as a covariate together with an age-by-season interaction term. The interaction between season and age (Table 3) is significant in all cases except Maori males and it is more pronounced in non-Maori males than it is in females.

The trend term in the regression analysis was significant, in non-Maoris, for all ages and both sexes. The effect is about equal between the sexes but is age dependent; the expected 10-year decline being 33% in the 35–44 age group for both sexes but only 12% in the 75+ group. The pattern for Maoris differs in that the decline is only significant in the middle 45–64 age range.

For each fitted model we plotted the estimated autocorrelations of the residuals for lags 1 to 24. A few autocorrelations attained statistical significance, but

TABLE 1 *Average monthly age-sex-race specific CHD mortality figures. (1) monthly rate per 100 000 people; (2) average number of CHD deaths per month in New Zealand*

	Non-Maori				Maori			
	Male		Female		Male		Female	
Age (years)	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)
35–44	4.4	6.9	1.2	1.8	1.9	0.9	1.9	0.6
45–54	21.1	31.3	5.1	7.3	28.9	2.3	15.4	1.2
55–64	62.7	77.6	19.0	25.0	79.1	3.6	45.8	2.1
65–74	143.1	115.9	63.8	62.0	174.1	3.7	118.0	2.4
75+	308.9	110.8	198.7	124.0	274.4	1.9	186.3	1.4

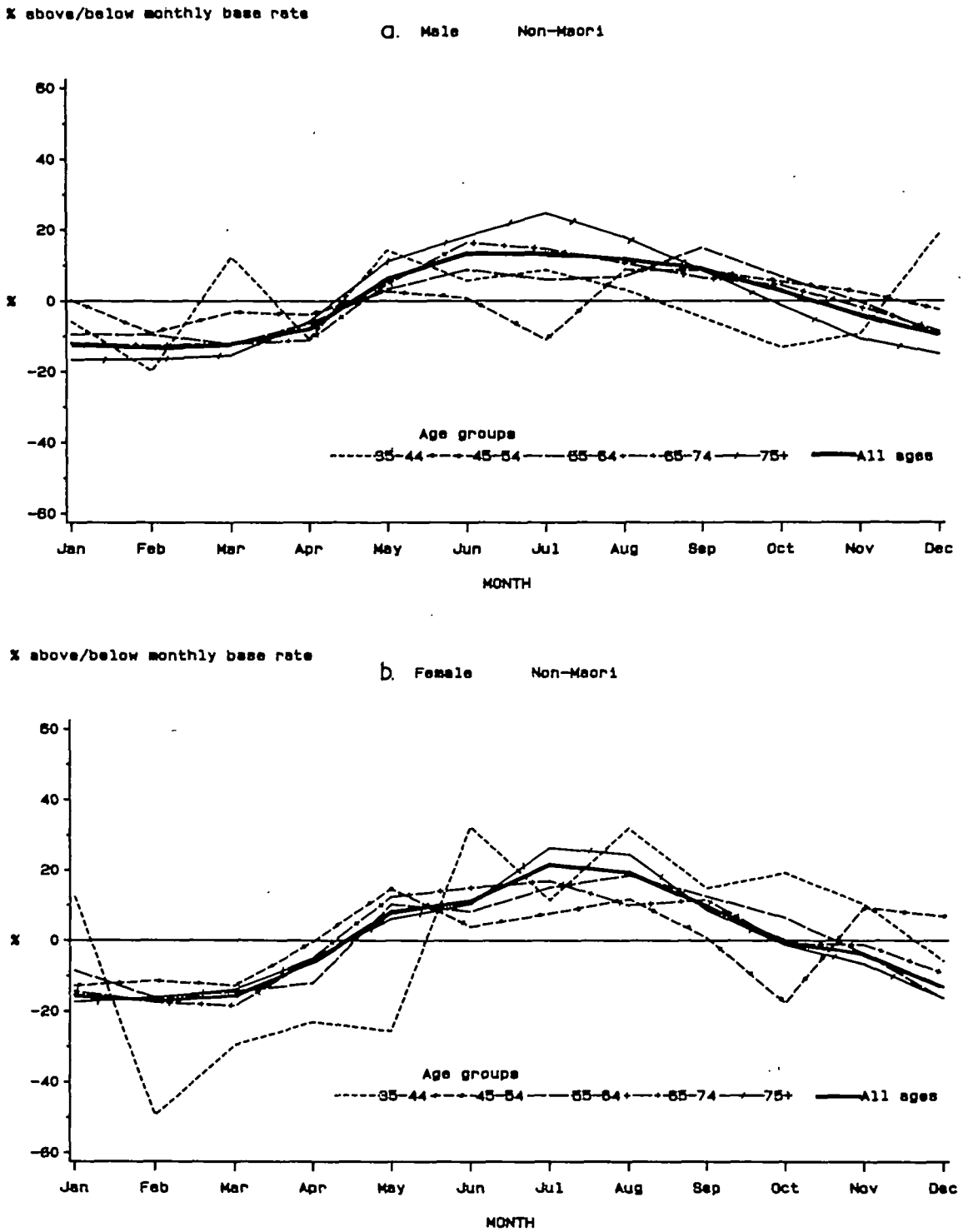

FIGURE 2 *Seasonal variation of CHD mortality by age and sex for non-Maoris, expressed as the percentage monthly excess (or deficit) of the mean monthly rates (Table 1). (a) Males; (b) Females.*

TABLE 2 *Seasonal variation of CHD, as a percentage of the monthly base-rate, ie 100 ($e^{a}-1$) %, derived from regression models fitted to each age-race-sex stratum. Approximate 95% confidence is determined by ±x. Underscored values are significant at 0.05 level*

	Non-Maori		Maori	
Age (years)	Male	Female	Male	Female
35–44	2.5 ± 8.1	19.8 ± 13.0	8.8 ± 13.4	2.1 ± 14.8
45–54	3.0 ± 4.4	7.3 ± 8.1	9.9 ± 11.6	1.5 ± 15.0
55–64	12.0 ± 2.4	17.5 ± 4.1	3.6 ± 10.5	0.2 ± 12.3
65–74	15.0 ± 2.4	17.7 ± 3.0	14.8 ± 10.7	17.7 ± 11.2
75+	22.3 ± 3.0	22.5 ± 2.4	21.4 ± 12.7	16.1 ± 13.4
All ages	15.1 ± 1.9	20.0 ± 1.6	10.8 ± 5.1	8.1 ± 5.7

none were larger than 0.25 in absolute value (0.16 being the critical level for significance), and there was no obvious pattern to suggest a dependence structure to the residuals. In particular, none of the autocorrelations for lag 12 were significant, suggesting that the seasonal component had been satisfactorily explained by the trigonometric function.

Figure 1 also shows the crude respiratory mortality rate among the over 35s. This is also clearly seasonal and the correlation with the crude CHD mortality rate is 0.74. Table 4 gives the direct and partial correlations coefficients of both these rates and a 'season' variable. After controlling for season there remains only a small, albeit significant, correlation (0.259) between CHD and respiratory rates, suggesting that season may be only acting as a confounding factor. Furthermore the much larger partial correlation (0.543) between coronary mortality rate and season, while controlling for the respiratory rate, reinforces this view, for, had there been a direct association of the CHD and respiratory rate, this partial correlation would have been close to zero, that is, with a hypothetical constant respiratory rate any seasonal variation in CHD should vanish. The alternative method of controlling for the season, by filtering out the seasonal variation, gave a residual correlation of 0.261. The same method of analysis applied to age-sex-race specific CHD rates and the crude respiratory mortality rate gave correlations of the seasonally filtered series that were only significant ($p<0.05$) in the age 75+ non-Maori group and direct correlations that increased with age (Table 5).

DISCUSSION

It is established that in New Zealand there is a marked seasonal variation in CHD mortality, with peak rates occurring in winter around mid-July. This phenomenon, in New Zealand, has not been previously reported but is well known in other countries. The seasonal variation increases with increasing age but there is a suggestion that it is more pronounced in younger non-Maori females than it is for young males. There is, however, no plausible biological reason why this should be so. Among Maoris of both sexes seasonal variation also exists, but it is not clear whether the pattern is as for non-Maoris. For Maori males the seasonal effect does not appear to be age-dependent, though again, there is no plausible explanation for why this group should differ in this respect. These observations offer no explanation as to why CHD mortality is seasonal.

Our analysis suggests that the seasonal variation is not a direct result of the seasonal variation of respiratory disease. After controlling for inherent seasonal variation, the association between CHD and respiratory mortality rates is significant only in the 75+ age group. Therefore, if the prevalence of respiratory infection does augment the coronary rate, the effect may not be substantial and is confined to the very elderly. In this group in particular there are uncertain-

TABLE 3 *Results of tests for age-dependent seasonal effects, by fitting a regression model to each sex-race stratum and including an age-season interaction term*

	Non-Maori		Maori	
	Male	Female	Male	Female
Interaction*	4.5 ± 1.8	2.7 ± 1.7	2.8 ± 4.2	5.2 ± 4.7
Associated p value	<0.0001	0.002	0.18	0.03

* Expressed as % increase in seasonality per ten-year age interval. ±x determines a 95% confidence interval.

TABLE 4 *Correlations, and partial correlations, between crude CHD and respiratory mortality rates and season*

	Coronary	Respiratory	Season†
Coronary	1.0	0.744*	0.841
Respiratory	0.259	1.0	0.778
Season	0.543	0.409	1.0

* Figures above the diagonal are direct correlations. Figures below the diagonal are the partial correlations between a variable pair controlling for the third variable.

† Described by a sinosoidal function peaking at mid-July.

TABLE 5 *Correlations between monthly age-sex-race specific mortality CHD rate and the crude respiratory mortality rate: (1) direct correlation; (2) after controlling for seasonality by regression modelling*

	Non-Maori				Maori			
	Male		Female		Male		Female	
Age (years)	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)
35–44	•	•	•	−0.19	0.20	•	•	•
45–54	•	•	0.20	•	•	•	•	•
55–64	0.37	•	0.42	•	•	•	•	•
65–74	0.58	0.17	0.54	•	0.27	•	0.22	•
75+	0.63	0.28	0.70	0.25	•	•	0.22	•

• All values less, in absolute value, than 0.16 the critical value for significance at the 0.05 level.

ties of death certification and it may not be clear whether respiratory infection or heart failure was the primary cause of death. There may well be, therefore, an excess due to respiratory disease.[2,10] However, it is not possible to conclude from a study of this sort, with data on groups, that respiratory disease increases the risk of CHD in an individual.

The seasonal phenomenon is likely to be a manifestation of a number of different factors. Our study gives only limited support to a direct link with respiratory disease. It is possible that climatic factors, such as temperature and sunlight, might directly induce a winter excess (or summer deficit) but the seasonal variation of other likely coronary risk factors—hypertension, fatty diet, smoking and lack of exercise, for instance—may offer alternative explanations. There is, for example, evidence for seasonal variation in total cholesterol levels.[21–23] An increased winter intake of fat[24] might explain these variations. Blood pressure levels have also been observed to be seasonal.[22,25,26] An increased incidence of deep vein thrombosis has been observed during winter months[27] and males with pre-clinical CHD have been reported to have a spring increase in fibrinogen.[28] Finally, patterns of exercise have been noted to be seasonal.[24,29]

Whether these, and other risk factors, as yet unknown, are responsible for the seasonal pattern of CHD will require more investigation. An understanding of the seasonal phenomenon would be an important step to establishing the aetiology of the disease.

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