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Saturated fat, vitamin C and smoking predict long-term population all-cause mortality rates in the Seven Countries Study

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Background	The Seven Countries Study has shown that population mortality rates for various chronic diseases are related to diet and smoking. This paper addresses the associations between diet, smoking and 25-year all-cause mortality.
Methods	Baseline surveys were carried out between 1958 and 1964 on 12 763 middle-aged men constituting 16 cohorts in seven countries. In 1987/88 equivalent food composites representing the average food intake of each cohort at baseline were collected and chemically analysed in one central laboratory. During 25 years of follow-up 5973 men died and age-adjusted population mortality rates were calculated for each cohort.
Results	Multivariate linear regression analyses showed that the population intake of saturated fat and the prevalence of smoking were positively associated with population all-cause mortality rates. Population vitamin C intake was inversely associated with all-cause mortality. It was calculated that a reduction in saturated fat intake of 5% of energy, a 20 mg/d increase in vitamin C and a 10% decrease in the prevalence of smokers may decrease the 25-year all-cause population mortality rate by 12.4% (95% CI : 5.6, 19.4%) at an average population all-cause mortality rate of 45%.
Conclusion	At the population level saturated fat, vitamin C and cigarette smoking are important determinants of all-cause mortality.

Keywords	Saturated fat, vitamin C, smoking, all-cause mortality, ecologic analysis, Seven Countries Study
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Introduction

Within Europe large difference exist in all-cause mortality with high rates in Eastern Europe and low rates in Western Europe.[1] In men aged 45–74 there is a more than twofold difference in all-cause mortality between men in Iceland and the Ukraine. From a public health point of view it is important to know what the determinants of these population differences in all-cause mortality are.

This question could be addressed by using data of the Seven Countries Study. In this study that started in 1958, 13 European cohorts were enrolled, one from the US and two from Japan. Associations between nutrient intake, cigarette smoking and alcohol intake were investigated at the population level because only nutrient and alcohol intake data representing the average intake of each cohort were available. Earlier reports on the results of the Seven Countries Study addressed the associations between nutrient intake and major diet-related chronic diseases e.g. coronary heart disease, colon cancer and stomach cancer. The population intake of saturated fat was positively associated with population coronary heart disease mortality rates.[2] Flavonoids, powerful dietary antioxidants, present in tea, onions, apples and red wine, were protective against coronary heart disease at the population level.[3] Population colorectal cancer rates were inversely related with dietary fibre[4] and population stomach cancer rates with vitamin C intake.[5]

These diet-related diseases are major causes of death in developed countries. Therefore it may be hypothesized that dietary determinants of these diseases are also major determinants of all-cause mortality. In addition the effect of other important lifestyle-related determinants of population all-cause

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mortality rates, cigarette smoking and alcohol intake[6] were taken into account. The objective of the present study was to investigate the associations between the population intake of different nutrients and alcohol, the prevalence of cigarette smoking and all-cause mortality rates in the Seven Countries Study.

Methods

Between 1958 and 1964, 12 763 men aged 40–59 were enrolled in the Seven Countries Study. In these countries 16 cohorts were established: 11 in rural areas in Finland, Italy, Greece, the former Yugoslavia and Japan, two cohorts of railroad employees in the US and Italy, one of workers in a large co-operative in Serbia, one of university professors in Belgrade and one of inhabitants of a small commercial market town in the Netherlands. The characteristics of these cohorts have been described in detail.[7–9]

Information on smoking was collected by questionnaire and the percentage of cigarette smokers per cohort was calculated. Between 1959 and 1964 dietary information was collected in small random samples of 14 of the 16 cohorts.[10] In the other two cohorts dietary information was gathered around 1970. These samples consisted of 8–49 men per cohort. The weighed record method was used in all dietary surveys. In 1985 and 1986 the original dietary data of all these cohorts were coded in a standardized way. The average intake of different foods consumed in the 16 cohorts was calculated and summarized in 16 food groups.[10]

In 1987, equivalent food composites representing the average food intake of each cohort at baseline were collected from local markets by two dieticians. These foods were transported in cooling boxes to the laboratory of the Department of Human Nutrition, Agricultural University, Wageningen, the Netherlands (Head: MB Katan). The foods were cleaned and equivalent food composites prepared according to the average consumption patterns of the cohorts. Oxalic acid was added to the equivalent food composites in order to preserve the vitamin C content. The foods were homogenized and frozen at –20°C until chemical analyses of the different nutrients took place.

In 1987 and 1988 total lipids were isolated according to Osborne and Voogt[11] and fatty acids were determined by gas chromatography.[12] The total flavonoid content was quantified by high-performance liquid chromatography as the sum of quercetin, kaempferol, myricetin, luteolin and apigenin.[13] Alcohol was determined by the method of Boehringer-Mannheim.[14] Total dietary fibre was determined with an enzymatic gravimetric method.[15] Vitamin C was determined by a fluorimetric method.[16]

The vital status of all men was checked roughly every 5 years. Over 25 years 5973 men (47%) died. Only 56 men (0.4%) were lost to follow-up. The underlying cause of death of the men who died was established centrally by Blackburn and Menotti during the first 10 years of follow-up and after 10 years of follow-up by Menotti. The endpoint of primary interest in the present study is all-cause mortality. Also the population mortality rates for coronary heart disease (ICD-8 codes 410–414 plus cases of sudden death judged of coronary origin and cases of chronic heart disease of possible coronary origin classified as codes 402, 404 and 427), lung cancer (ICD-8 code 162), colorectal cancer(ICD-8 codes 152–154) and stomach cancer (ICD-8 codes 151) are reported. Age-adjusted all-cause mortality rates were calculated using the age distribution of all participants in the Seven Countries Study as a standard.

The dietary intake variables represent the average for each cohort. The log absolute alcohol intake was used in the analyses in order to normalize the alcohol distribution. Analyses concern only inter-cohort comparisons, using simple and multiple linear regression models. Because of the limited degrees of freedom, the multiple regression models never included more than four independent variables. We started the multivariate linear regression analyses with the model: All-cause mortality = saturated fat + smoking, because we observed earlier that this combination of independent variables is a strong predictor of coronary heart disease mortality.[3] Other variables e.g. vitamin C, dietary fibre, flavonoids, alcohol, were added one by one and the model explaining most of the variance in all-cause mortality rates was selected. Only two-sided *P*-values are reported.

Results

Large differences in saturated fat intake were observed between the different cohorts (Table 1). The average intake varied between 3.9% of energy in Tanushimaru (Japan) to 22.7% in East Finland. Fibre intake varied between 21 g/d in Ushibuka (Japan) and 50 g/d in East Finland. An eightfold difference in vitamin C intake was observed varying between 17 mg/d in Velika Krsna (Serbia) and 142 mg/d in the US railroad cohort. Flavonoid intake varied between 2.6 mg/d in West Finland and 68.2 mg/d in Ushibuka (Japan). The absolute alcohol intake varied between 1.8 g/d in East Finland and 91.2 g/d in Dalmatia (Croatia). A twofold range was observed in the prevalence of current smokers, varying between 44% in Belgrade (Serbia) and 78% in Ushibuka (Japan).

The lowest 25-year age-adjusted all-cause mortality rates were observed in Belgrade (Serbia, 29.5%) and Crete, Greece (31.4%) and the highest in Slavonia, Croatia (61.0%) and East Finland (59.7%) (Table 2). These results show that there is a twofold range in all-cause mortality rates in the Seven Countries Study comparing the cohorts with the highest mortality rates with those of the lowest mortality rates. Even larger ranges were observed for coronary heart disease (sixfold), lung cancer mortality (sevenfold), colorectal cancer (20-fold) and stomach cancer (26-fold) age-adjusted mortality rates.

Univariate analyses showed that the different dietary variables, alcohol intake and the prevalence of smokers were not significantly associated with 25-year age-adjusted all-cause mortality rates (Table 3). The strongest associations were obtained for saturated fat intake, prevalence of smoking and vitamin C intake. Earlier analyses showed that the non-significant association between the prevalence of smokers and the 25-year population mortality rates for coronary heart disease became statistically significant when both the prevalence of cigarette smokers and saturated fat intake were added to the model.[3] In the present study the prevalence of smokers and saturated fat intake were significantly associated with all-cause mortality in a multivariate model. The model improved further when vitamin C intake was added but not when flavonoid, dietary fibre intake or alcohol were added. In the final model, the prevalence of smokers, and the average

Table 1 Average population intake of different dietary variables and the prevalence of smoking in the Seven Countries Study

Cohort	Saturated fat %E	Fibre g/d	Vitamin C mg/d	Flavanoid mg/d	Alcohol g/d	Smoking %
US railroad	21.7	22.5	142	12.9	4.7	59
East Finland	22.7	50.0	80	9.6	1.8	69
West Finland	19.2	43.0	65	2.6	1.9	57
Zutphen, Neth.	20.3	25.2	110	33.1	2.6	75
Crevalcore, Italy	13.4	25.3	50	23.3	46.5	63
Montegiorgio, Italy	9.8	27.6	44	33.9	37.4	59
Rome, Italy	9.8	26.5	53	23.1	37.8	65
Dalmatia, Croatia	9.5	30.1	60	40.2	91.1	58
Slavonia, Croatia	16.8	36.7	41	58.2	12.3	60
Velika Krsna, Serbia	13.8	38.8	17	9.0	8.7	49
Zrenjanin, Serbia	15.5	34.8	112	13.1	9.5	63
Belgrade, Serbia	18.9	25.6	71	13.3	3.9	44
Crete, Greece	8.9	43.1	36	15.7	10.8	57
Corfu, Greece	7.3	57.2	125	15.6	16.2	64
Tanushimaru, Japan	3.9	24.3	39	60.8	11.9	71
Ushibuka, Japan	5.2	21.0	45	68.2	14.0	78

Table 2 Age-adjusted population mortality rates (%) after 25 years of follow-up in the Seven Countries Study

Cohort	No.	CHD[a]	Lung cancer	Colorectal cancer	Stomach cancer	All causes
US railroad	2571	20.2	3.3	2.0	0.5	45.1
East Finland	817	28.8	7.3	0.1	2.9	59.7
West Finland	860	19.2	4.4	0.9	2.3	50.3
Zutphen, Netherl.	878	19.7	7.2	2.0	1.7	48.0
Crevalcore, Italy	993	13.4	3.0	1.6	3.2	49.8
Montegiorgio, It.	719	11.5	1.0	1.1	4.0	46.2
Rome, Italy	768	13.2	3.3	1.4	1.6	39.7
Dalmatia, Croatia	671	8.1	3.6	0.5	1.1	43.3
Slavonia, Croatia	696	14.2	1.9	1.2	3.8	61.0
Velika Krsna, Serbia	511	12.2	1.6	1.7	2.6	50.0
Zrenjanin,Serbia	516	17.7	2.1	1.4	1.8	57.9
Belgrade, Serbia	538	11.8	2.1	0.6	0.2	29.5
Crete, Greece	686	4.6	2.0	0.9	0.5	31.4
Corfu, Greece	529	9.5	2.8	0.4	1.3	40.4
Tanushimaru, Japan	508	4.5	1.0	1.6	5.1	39.4
Ushibuka, Japan	502	6.3	2.6	1.0	5.1	51.5

[a] Coronary heart disease.

Table 3 Regression coefficients for population averages of different dietary variables, smoking and alcohol and 25-year age-adjusted all cause mortality in the Seven Countries Study

	All-cause mortality				
Exposure variable	Univariate	95%CI	Multivariate[a]	95%CI	*P*
Saturated fat (%E/d)	0.55	–0.36, 1.29	0.94	0.29, 1.59	0.015
Fibre (g/d)	0.13	–0.22, 0.58			
Vitamin C (mg/d)	–0.05	–0.17, 0.07	–0.10	–0.20, 0.00.	0.062
Flavonoids (mg/d)	0.06	–0.18, 0.30			
Smoking (%)	0.37	–0.25, 0.88	0.57	0.14, 0.90	0.024
Alcohol (log g/d)	–1.34	–5.40, 2.07			
			$R^2 = 0.52$		

[a] Multivariate model: All cause mortality = saturated fat + vitamin C + smoking.

R = Multiple correlation coefficient.

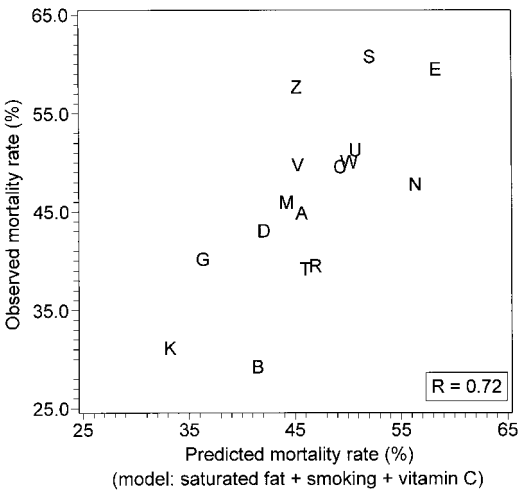

Figure 1 Association between the observed and the predicted age-adjusted 25-year mortality rate

A = US Railroad, B = Belgrade, C = Crevalcore, D = Dalmatia, E = East Finland, G = Corfu, K = Crete, M = Montegiorgio, N = Zutphen, R = Rome Railroad, S = Slavonia, T = Tanushimaru, U = Ushibuka, V = Velika Krsna, W = West Finland, Z = Zrenjanin

population saturated fat and vitamin C intake explained 52% of the variance in population all-cause mortality rates. Figure 1 shows the association between the observed 25-year age-adjusted all-cause mortality rates of the 16 cohorts and the predicted all-cause mortality rates based on average population intakes of saturated fat and vitamin C and the prevalence of smokers.

Discussion

The major finding of the present study is that the average population intake of saturated fat and vitamin C and the prevalence of smokers are major determinants of all-cause mortality rates. Saturated fat and smoking are detrimental, but vitamin C seems to be protective in relation to the health of populations.

The strength of the present study is the standardized methodology for data collection and the prospective design. Another advantage is the chemical analyses of the food consumption data, although the chemical analyses were carried out 25 years later in equivalent food composites representing the average food consumption pattern of each cohort in the 1960s. This delay could have biased the estimate of average population intake of the different nutrients. However, strong correlations were observed between fatty acids determined 25 years apart,[2] likely being good surrogates for other correlations.

The present study has several weaknesses. Only average nutrient and alcohol intake data were available for each cohort and no individual data. Eleven of the 16 cohorts were rural and consisted mostly of farmers. This made analyses on the effect of socioeconomic status and occupation on all-cause mortality rates impossible. The population data of only 16 cohorts provided limited possibilities for multivariate analyses. The representativeness of the dietary data of the small samples for the whole cohorts can be questioned. The average nutrient and alcohol intake of the samples provided probably a reasonable estimate for the average intake of each cohort. The *a priori* hypothesized regional differences in dietary patterns between different cohorts within one country were actually observed.[8] The 16 cohorts should be viewed as independent populations with different dietary habits. Because of the large differences in dietary habits these cohorts could be used to investigate associations between population nutrient intakes and all-cause mortality rates.

The results of the present analyses show that saturated fat, vitamin C and smoking are the major determinants of all-cause mortality at the population level. It has earlier been shown that at the population level smoking and saturated fat are major determinants of coronary heart disease and that vitamin C is protective in relation to stomach cancer.[2,5] The effect of these lifestyle-related variables is not only of importance in relation to specific diseases but also in relation to all-cause mortality. This does not mean that other nutrients and foods are unimportant. At the population level saturated fat intake is inversely related with alcohol intake and fish consumption.[17] Cohort studies have shown that a moderate alcohol intake and the consumption of fish at least once a week may protect against coronary heart disease mortality.[18,19] Populations with a low saturated fat intake may also be characterized by a moderate alcohol and fish intake and a high intake of vegetables and fruits as in the Greek cohorts of the Seven Countries Study. This means that a balanced diet low in saturated fat and high in vitamin C and with an adequate supply of other nutrients is compatible with a low all-cause mortality rate. This does not only hold at the population level but also at the individual level.[20]

One of the cohorts with the lowest all-cause mortality rate was that of farmers on Crete. They consumed a typical Mediterranean diet, low in saturated fat but high in mono-unsaturated fat because of a high olive oil consumption. Their alcohol and fish intake was moderate and they had a high intake of fruits and vegetables. A small cohort study in the elderly from Greece showed that the traditional Mediterranean diet was associated with lower all-cause mortality than a less traditional Mediterranean diet.[21] In an intervention trial in cardiac patients an alpha linolenic acid enriched Mediterranean diet was associated with a 70% reduction of all-cause mortality during 5 years of follow-up.[22] These results provide evidence that the Mediterranean diet is associated with a low level of all-cause mortality both at the population and at the individual level.

In 1960 57% of the Cretan farmers were smokers. In another analysis using individual data of the Seven Countries Study it was shown that the 25-year all-cause mortality rate for Greek farmers who smoked at least 10 cigarettes per day was 12% higher (39.8 versus 27.8%) compared with never smokers.[23] For the other cohorts the difference in all-cause mortality between smokers and never smokers varied between 9 and 24%. These results show that even in the Cretan situation there is room for improvement. A Cretan diet in combination with not smoking seems to be associated with the lowest all-cause mortality rates.

Another cohort with a low all-cause mortality rate was that of members of the faculty of Belgrade University. The diet of the Belgrade professors was high in saturated fat and they smoked moderately. During 25 years of follow-up the prevalence of smoking decreased from 44 to 15%.[24] There is no information available about changes in the diet of the Belgrade professors. The predicted all-cause mortality rate of the Belgrade professors

was 12.3% (41.8 versus 29.5%) higher than the observed mortality rate. This may be due to the substantial decrease in the prevalence of smokers during 25 years of follow-up. An alternative explanation could be that besides smoking and diet other factors such as socioeconomic status are also important determinants of all-cause mortality.[25]

The potential effect of changes in saturated fat, vitamin C and the prevalence of smokers can be illustrated as follows. A change in saturated fat of 5% of energy is associated with a 4.7% change in age-adjusted all-cause mortality rate (Table 3). A change in 20 mg vitamin C intake is associated with a 2.0% change in all-cause mortality rate. A 10% change in the prevalence of smokers is associated with a 5.7% change in all-cause mortality. If for instance the population saturated fat intake decreases from 15 to10% of energy, the vitamin C intake increases from 50 to 70 mg/day and the prevalence of smokers decreases from 40 to 30% it can be predicted that the age-adjusted all-cause mortality rate will decrease by 12.4% (95% CI : 5.6–19.4%). The average 25-year age-adjusted all-cause mortality rate in the Seven Countries Study was about 45%. This means that the best estimate for these changes in diet and smoking predicts a decrease in the 25-year population all-cause mortality rate from 45 to 33%. This predicted effect of changes in diet and smoking is probably an overestimate because as we discussed before saturated fat intake is associated with other risk factors.

That these type of changes may occur in reality can be illustrated with recently published results from Poland.[26] After two decades of rising rates a decrease of about 25% in coronary heart disease mortality rates was observed in men and women aged 45–64 between 1991 and 1994. The decrease in all-cause mortality rates amounted to about 10%. The most likely explanation for these changes was a 23% decrease in the intake of animal fats, a 48% increase in vegetable fats and a doubling in the import of exotic fruits (citrus fruits and bananas) between 1991 and 1994. The prevalence of smokers was stable between 1991 and 1994 and amounted to about 50% in men and 25% in women. These results show that important changes in fatty acid composition and vitamin C intake in populations may lead almost immediately to drastic changes in coronary heart disease and all-cause mortality rates.

It can be concluded that saturated fat, vitamin C and smoking are important predictors of all-cause mortality at the population level. The lowest all-cause mortality rates were observed among Cretan farmers and Belgrade professors, suggesting that besides diet and smoking socioeconomic status is also an important determinant of all-cause mortality rates. We did not collect information on other possible determinants of all-cause mortality e.g. access to and use of medical care. It is therefore not possible to present a complete picture on the determinants of population all-cause mortality rates. However, a balanced diet low in saturated fat in combination with not smoking is an important component of a long and probably healthy life expectancy.

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References

[1] Sans S, Kesteloot H, Kromhout D on behalf of the Task Force. The burden of cardiovascular diseases mortality in Europe. Task force of the European Society of Cardiology on Cardiovascular Mortality and Morbidity Statistics in Europe. *Eur Heart J* 1997;**18:**1231–48.

[2] Kromhout D, Menotti A, Bloemberg B *et al.* Dietary saturated and trans fatty acids, cholesterol and 25-year mortality form coronary heart disease. The Seven Countries Study. *Prev Med* 1995;**24:**308–15.

[3] Hertog MGL, Kromhout D, Aravanis C *et al.* Flavonoid intake and long-term risk of coronary heart disease and cancer in the Seven Countries Study. *Arch Intern Med* 1995;**155:**381–86.

[4] Jansen MCJF, Bueno de Mesquita HB, Buzina R *et al.* for the Seven Countries Study Research Group. Dietary fiber and plant foods in relation to colorectal cancer mortality: The seven countries study. *Int J Cancer* 1999;**81:**174–79.

[5] Ocké MC, Kromhout D, Menotti A *et al.* Average intake of antioxidant (pro)vitamins and subsequent cancer mortality in the 16 cohorts of the Seven Countries Study. *Int J Cancer* 1995;**61:**480–84.

[6] Leon DA, Chenet L, Shkolnikov VM *et al.* Huge variation in Russian mortality rates 1984–1994: artefact, alcohol, or what? *Lancet* 1997; **350:**383–88.

[7] Keys A, Aravanis C, Blackburn HW *et al.* Epidemiological studies related to coronary heart disease: characteristics of men aged 40–59 in seven countries. *Acta Med Scand* 1967;**460(Suppl.):**1–392.

[8] Keys A (ed.). Coronary heart disease in seven countries. *Circulation* 1970;**41(Suppl.):**1–211.

[9] Keys A. *Seven Countries: A Multivariate Analysis of Death and Coronary Heart Disease*. Cambridge, MA: Harvard University Press, 1980.

[10] Kromhout D, Keys A, Aravanis C *et al.* Food consumption patterns in the 1960s in seven countries. *Am J Clin Nutr* 1989;**49:**889–94.

[11] Osborne DR, Voogt P. Soxhlet method. In: *Analysis of Nutrients and Foods. First Edn*. London, New York: Academic Press, 1978, pp.155–56.

[12] Metcalfe LD, Schmitz A, Pekka JR. Rapid preparation of fatty acid esters from lipids of gaschromatographic analyses. *Anal Chem* 1966; **18:**514–15.

[13] Hertog MGL, Hollman PCH, Venema DP. Optimization of a quantitative HPLC determination of potentially anticarcinogenic flavonoids in vegetables and fruits. *J Agric Food Chem* 1992;**40:**1591–98.

[14] *Methoden der Biochemischen Analytik und Lebensmittelanalytik.* Mannheim: Boehringer-Mannheim 1987:10–12.

[15] Williams S (ed.). Total dietary fiber in foods; enzymatic gravimetric method. Changes in methods. *J Ass Off Anal Chem* 1985;**68:**399.

[16] Roy RB, Conetta A, Salpeter J. Automated fluorimetric method for the determination of total vitamin C in food products. *J Ass Off Anal Chem* 1976;**59:**1244–50.

[17] Kromhout D, Bloemberg BPM, Feskens EJM, Hertog MGL, Menotti A, Blackburn H, for the Seven Countries Study Group. Alcohol, fish,

fiber and antioxidant vitamins do not explain population differences in coronary heart disease mortality. *Int J Epidemiol* 1996;**25:**753–59.

[18] Kromhout D. Fish consumption and sudden cardiac death (Editorial). *JAMA* 1998;**279:**65–66.

[19] Thun MJ, Peto R, Lopez AD *et al*. Alcohol consumption and mortality among middle-aged and elderly US adults. *N Engl J Med* 1997;**337:** 1705–14.

[20] Huijbregts P, Feskens E, Räsänen L *et al*. Dietary pattern and 20-year mortality in elderly men in Finland, Italy, and the Netherlands: Longitudinal cohort study. *Br Med J* 1997;**315:**13–17.

[21] Trichopoulou A, Kouris-Blazos A, Wahlqvist ML *et al*. Diet and overall survival in elderly people. *Br Med J* 1995;**311:**1457–60.

[22] De Logeril M, Renaud S, Mamelle N *et al*. Mediterranean alpha-linolenic acid-enriched diet in secondary prevention of coronary heart disease. *Lancet* 1994;**343:**1454–59.

[23] Jacobs D, Adachi H, Mulder I *et al*. for the Seven Countries Study Group. Cigarette smoking and mortality risk. 25-year follow-up of the Seven Countries Study. *Arch Intern Med* 1999;**159:**733–40.

[24] Kromhout D, Nedeljkovic SI, Grujic MZ *et al*. Changes in major risk factors for cardiovascular diseases during 25 years in the Serbian cohorts of the Seven Countries Study. *Int J Epidemiol* 1994; **23:**5–11.

[25] Mackenbach JP, Kunst AE, Cavelaars AEJM, Groenhof F, Geurts JJM and the EU working group on socioeconomic inequalities in health. Socioeconomic inequalities in morbidity and mortality in western Europe. *Lancet* 1997;**349:**1655–59.

[26] Zatonski WA, McMichael AJ, Powles JW. Ecological study of reasons for sharp decline in mortality from ischaemic heart disease in Poland since 1991. *Br Med J* 1998;**316:**1047–51.