EPIDEMIOLOGY

Mortality in participants and non-participants of a multifactorial prevention study of cardiovascular diseases: a 28 year follow up of the Helsinki Businessmen Study

Timo E Strandberg, Veikko V Salomaa, Hannu T Vanhanen, Vesa A Naukkarinen, Seppo J Sarna, Tatu A Miettinen

Abstract

Objective—To investigate pretrial risk factors and long term mortality (1964–1992) in participants and non-participants of a multifactorial primary prevention trial.

Design—A prospective study among 3313 initially healthy businessmen. During the 1960s (1964 onwards), 3490 healthy male business executives born between 1919 and 1934 participated in voluntary health checks at the Institute of Occupational Health in Helsinki. From that period cardiovascular disease (CVD) risk factors were available in 3313 men. In the beginning of the 1970s these men were invited to join a multifactorial primary prevention trial of CVD. Six groups were formed: (I) healthy participants in a high risk intervention group (n = 612), and (II) their randomised control group (n = 610); (III) a non-participant low risk group (n = 593); (IV) an excluded group with signs of CVD (n = 563); (V) a refused group (n = 867); and (VI) dead (n = 68). Groups I and II participated in the five year prevention trial which started in 1974. Other groups were followed up through registers, with no personal contact.

Measurements—Cardiovascular risk factors during the 1960s. Mortality follow up using national registers up to 31 December, 1992.

Main results—Baseline risk factors were lowest in the low risk group, highest in the excluded group, intermediate and comparable in other groups. Eighteen-year (1974–1992) mortality (per 1000) was 79.3, 106.6, 155.2, 179.9, and 259.3 in the low risk, control, intervention, refused, and excluded groups, respectively ($P < 0.001$). In the whole population of 3313 men, the 28-year (1964–1992) total (n = 577) and coronary deaths (n = 199) were significantly predicted by smoking, blood pressure, and cholesterol; cancer deaths (n = 163) by smoking only; and violent deaths (n = 83) by none of the risk factors. One-hour postload glucose was significantly associated with total mortality in

the intervention group only. When the intervention and control groups were included in the same model, the effect of group on total mortality tended to be dependent on the 1 h blood glucose value ($P = 0.06$ for the group by 1 h glucose interaction term).

Conclusion—The traditional risk factors (smoking, blood pressure, and cholesterol) are significantly associated with 28-year mortality in this high social class population with previous health education. Conversely, a “clustering” of low risk factors predicted low total, coronary, and cancer mortality. The findings on 1 h blood glucose suggest that factors related to glucose tolerance explain in part the excess mortality in the intervention group compared with the control group.

(Br Heart J 1995;74:449–454)

Keywords: cardiovascular disease prevention; mortality; mortality in non-participants

Several multifactorial prevention studies aimed at reducing cardiovascular diseases were started during the 1970s.¹ One of these was the Helsinki Businessmen Study which employed a five year treatment period to modify risk factors.² Despite effective lowering of risk factor levels by the intervention methods, the 15 year follow up revealed a significantly higher total, cardiac, and violent mortality in the intervention group than in the control group.³ The reasons for the unexpected results were not readily explained by analyses of risk factors and drug treatments, and therefore explanations have been sought from play of chance or unsuccessful randomisation.^{4–6} Various interpretations of the study results, for example falsely linking increased coronary heart disease and violent deaths to the treatment of hypercholesterolaemia, may even have led to undue pessimism about reducing cardiovascular risk factors.⁷ Because of this discussion we became interested in analysing the results in their epidemiological context, that is, in the whole “background”

Department of Medicine, University of Helsinki, Helsinki, Finland

T E Strandberg
H T Vanhanen
T A Miettinen

National Public Health Institute, Helsinki, Finland
V V Salomaa

Department of Medicine, Jorvi Hospital, Espoo, Finland
V A Naukkarinen

Department of Public Health, University of Helsinki, Helsinki, Finland
S J Sarna

Correspondence to:
Dr Timo E Strandberg,
Department of Medicine,
University of Helsinki, FIN-
00290 Helsinki, Finland

Accepted for publication
22 May 1995

Table 1 Pretrial risk factor levels in the groups defined in 1974

Risk factor*	Low risk group (n = 593)	Control (n = 610)	Intervention (n = 612)	Excluded (n = 563)	Refused (n = 867)	Dead in 1974 (n = 68)
Age in 1974 (years)	47 (4)	48 (4)	48 (4)	49 (4)	48 (4)	50 (4)
Body mass index (kg/m ²)	25(2)	26 (3)	26 (3)	26 (3)	26 (3)	26 (3)
Blood pressure (mm Hg)						
Systolic	130 (11)	135 (15)	135 (13)	144 (20)	136 (17)	147 (22)
Diastolic	83 (7)	86 (9)	86 (9)	92 (13)	86 (10)	93 (15)
Cholesterol (mmol/l)	6.6 (1.0)	7.4 (1.3)	7.4 (1.2)	7.4 (1.3)	7.2 (1.3)	7.6 (1.4)
Triglycerides (mmol/l)	1.2 (0.6) n = 211†	1.7 (1.0) n = 260	1.6 (0.7) n = 255	1.7 (1.0) n = 399	1.5 (0.8) n = 278	
1 h Glucose (mmol/l)	5.8 (1.5) n = 479†	6.4 (1.8) n = 493	6.3 (1.8) n = 498	6.7 (2.3) n = 524	6.3 (2.0) n = 701	6.4 (2.6) n = 67
Smokers (%)‡	24.8	43.1	44.5	45.7	46.9	52.1
Risk score§	12 (8)	22 (17)	21 (18)	29 (28)	21 (22)	43 (50)

*Data are mean (SD).

†n = number with measurement.

‡Includes also less than 10 cigarettes/day.

§Calculated according to Keys¹⁰ (risk of cardiac death or Q wave infarction per 5 years and 1000 men).

cancer mortality was lowest in the low risk group (fig 2, table 2). Total mortality was highest in the excluded group, even without the 53 men who had had a non-fatal infarction or stroke before 1974 (data not shown); the second highest mortality was observed in the refused group. Not only cardiac but also cancer mortality was highest in these two groups. Between the intervention and control groups significant differences were observed in the 18 year total (RR 1.46, 95% CI 1.08 to 1.96), coronary (RR 2.05, 95% CI 1.20 to 3.50), and violent deaths (RR 15.9, 95% CI 2.12 to 120.0, table 2). We should point out,

however, that the incidence of violent deaths is similar in the low risk and intervention groups, and there tended to be more deaths in the refused group than in the intervention group (RR 1.16, 95% CI 0.92 to 1.46; table 2, fig 2).

FACTORS ASSOCIATED WITH MORTALITY DURING FOLLOW UP

The associations between initial risk factors and mortality were examined in all 3313 men for the 28 year (1964–1992) follow up period. Total deaths were significantly predicted by age (RR 1.48, 95% CI 1.31 to 1.66), systolic blood pressure (RR 1.18, 95% CI 1.13 to 1.24), serum cholesterol (RR 1.11, 95% CI 1.04 to 1.19), and smoking (RR 1.87, 95% CI 1.55 to 2.25); coronary deaths by age (RR 1.44, 95% CI 1.19 to 1.75), systolic blood pressure (RR 1.24, 95% CI 1.15 to 1.34), and cholesterol (RR 1.26, 95% CI 1.13 to 1.41). Cancer deaths were significantly predicted by age (RR 2.20, 95% CI 1.76 to 2.76) and smoking (RR 3.45, 95% CI 2.38 to 4.99). No significant associations were observed between the measured risk factors (including cholesterol) and violent (non-illness) deaths. Since 1 h postload glucose was determined in only 2762 men in the 1960s, relative risks associated with this criterion were assessed separately (but using all the other risk factors

Figure 2 Kaplan-Meier survival curves up to 31 December, 1992, of the groups defined in 1974. 1. Low risk group; 2. Control group; 3. Intervention group; 4. Refused group; 5. Excluded group. Difference between groups: $P < 0.001$ (Wilcoxon).

Table 2 Deaths during the 18 year (1974–1992) follow up of the study groups

Death*	Low risk group (n = 593)	Control group (n = 610)	Intervention (n = 612)	Excluded (n = 563)	Refused (n = 867)
Coronary heart disease	15.2 (9)	31.1 (19)	63.7 (39)	119.0 (67)	50.7 (44)
Ischaemic stroke	1.7 (1)	3.2 (2)	0 (0)	12.4 (7)	12.7 (11)
Intracranial haemorrhage	1.7 (1)	6.6 (4)	3.3 (2)	0 (0)	0 (0)
Subarachnoid haemorrhage	1.7 (1)	0 (0)	0 (0)	7.1 (4)	5.8 (5)
Other cardiovascular disease	1.7 (1)	1.6 (1)	1.6 (1)	24.9 (14)	3.5 (3)
Neoplasms	28.7 (17)	47.5 (29)	44.1 (27)	53.3 (30)	55.4 (48)
Violent deaths	25.3 (15)	1.6 (1)	26.1 (16)	21.3 (12)	18.5 (16)
Accidents	16.9 (10)	1.6 (1)	21.2 (13)	16.0 (9)	11.5 (10)
Suicide	6.7 (4)	0 (0)	3.3 (2)	5.3 (3)	5.8 (5)
Homicide	1.7 (1)	0 (0)	1.6 (1)	0 (0)	1.2 (1)
Other	3.4 (2)	13.1 (8)	14.7 (9)	16.0 (9)	30.0 (26)
Unknown	(0)	(1)	(1)	(3)	(3)
All	79.3 (47)	106.6 (65)	155.2 (95)	259.3 (146)	179.9 (156)

*Deaths per 1000 men until 31 December, 1992. Classified according to the Finnish version of the *International classification of diseases* (ICD-9). The numbers in parentheses indicate absolute events.

as covariates). In these analyses 1 h glucose was not significantly associated with the 28 year mortality. Exclusion of the intervention group did not change the results.

Additional age adjusted analyses showed that particularly coronary mortality but also total mortality rose by the cholesterol quintile of the 1960s. RRs for total mortality were 1.00, 1.03, 1.21, 1.18, and 1.51 (95% CI 1.17 to 1.95) from the lowest to the highest cholesterol quintile. No association was observed between cholesterol and cancer deaths or violent deaths. Examinations of suicides ($n = 23$) and other non-illness deaths ($n = 60$) separately gave similar results. Further division of the lowest cholesterol quintile with 92 deaths into tertiles (cut off points 5.2 and 5.9 mmol/l) showed that the lowest cholesterol level was associated with the lowest risk (RRs 1, 1.4, 1.3).

In stratified analyses examining the risk factors for total mortality in the different groups defined in 1974, smoking was consistently significant (RRs 1.5 to 2.8 compared with non-smokers; table 3). In addition, systolic blood pressure predicted mortality in the excluded and refused groups and marginally so in the control group. Interestingly, while age consistently predicted mortality in other groups (45–70% increase in RR per five years) the 19% increase in the intervention group was not statistically significant (table 3). One-hour glucose (logarithmically transformed value) was significantly associated with total mortality in the intervention group (RR 16.0, 95% CI 2.5 to 100.9), but not in the other groups. The result was seemingly different from that in the control group (RR 1.01, 95% CI 0.1 to 10.6), but as the confidence intervals overlapped we also explored the association using an interaction term in the Cox models. These analyses showed that in the combined intervention plus control groups total mortality was significantly associated with log 1 h glucose (RR 5.79, 95% CI 1.39 to 24.17), Keys' risk score (RR 1.09, 95% CI 1.01 to 1.17), and group (control group 0, intervention group 1: RR 1.53, 95% CI 1.07 to 2.18). When the interaction term (log 1 h glucose $\times$ group) was included in the model the relative risks of group and the glucose were no longer significant, whereas the interaction term

approached statistical significance with a P value of 0.06.

Discussion

The unexpected result of the Helsinki Businessmen Study seemed to give a pessimistic impression of multifactorial primary prevention,²³ and the 18 year results still show a higher mortality in the intervention than in the control group (table 2, fig 2). However, the present analysis of the background population of 3313 men gives an important new perspective on this outcome. The initial setting of the study and the data linkage with the national death register offered a unique chance of obtaining information on pretrial risk factors and survival follow up from men who refused to participate in or were excluded from the actual prevention trial. The present results show that the low risk group—as defined by the cardiovascular risk factor status in the 1960s and 1974—continues to have the best prognosis after 18 years. This concerns not only coronary, but cancer and total mortality as well. Furthermore, those who refused the intervention trial fare even worse than the intervention group. On the other hand, smoking, serum cholesterol, and blood pressure also significantly predicted total deaths in this population of high social class. Unexpectedly, baseline smoking (smoker/non-smoker) did not significantly predict coronary mortality (RR 1.22, 95% 0.89 to 1.67), but the effect is probably diluted by smoking cessation over the follow up years. As a whole, the Helsinki Businessmen Study results cannot be interpreted as refuting the current idea of cardiovascular risk factors.

The "cholesterol debate" has particularly involved the issue of associations between low cholesterol and non-cardiovascular mortality.^{11–13} These concerns have been opposed^{14–16}—most recently by the results of the 4S (Scandinavian Simvastatin Survival Study¹⁷)—and they were not supported by the present study which showed increasing total mortality with increasing serum cholesterol. Multivariate analyses suggested that a 1 mmol/litre rise in total cholesterol implies an 11% increase in mortality. The result is in accordance with earlier experience in Finland from

Table 3 Relative risks of total deaths (1974–1992) for initial risk factors in different groups

Risk factor	Group (number of deaths with complete risk factor data)					
	Low risk group (47)	Control (60)	Intervention (95)	Excluded (142)	Refused (95)	All (439)
Age, 5 year*	1.55† (1.08 to 2.23)	1.70 (1.21 to 2.37)	1.19 (0.92 to 1.53)	1.45 (1.07 to 1.74)	1.49 (1.18 to 2.20)	1.47 (1.30 to 1.65)
Body mass index, 5 kg/m ²	1.37 (0.65 to 2.77)	0.82 (0.49 to 1.37)	1.24 (0.85 to 1.18)	1.06 (0.80 to 1.40)	1.08 (0.78 to 1.50)	1.12 (0.94 to 1.32)
Systolic blood pressure, 10 mm Hg	1.18 (0.92 to 1.50)	1.18 (1.00 to 1.40)	1.02 (0.88 to 1.19)	1.14 (1.05 to 1.25)	1.17 (1.05 to 1.31)	1.18 (1.12 to 1.24)
Cholesterol, 1 mmol/l	0.83 (0.62 to 1.11)	0.97 (0.79 to 1.18)	1.08 (0.92 to 1.27)	1.16 (0.97 to 1.28)	1.11 (0.85 to 1.25)	1.10 (1.02 to 1.18)
Smoking, yes/no	2.27 (1.26 to 4.09)	2.78 (1.62 to 4.77)	1.53 (1.02 to 2.30)	1.69 (1.11 to 2.37)	1.56 (0.99 to 2.46)	1.90 (1.57 to 2.30)
1 h Glucose 1 mmol/l‡	0.30 (0.02 to 5.37)	1.01 (0.10 to 10.6)	16.0 (2.53 to 100.9)	3.27 (0.87 to 12.4)	0.55 (0.09 to 3.43)	2.53 (1.10 to 5.81)

*Interval used in the calculation of the relative risk.

†Relative risks were calculated using the Cox proportional hazards model (95% confidence interval in parentheses).

‡Separate model because of missing data on one-hour glucose (measured in 2695 men of these groups). Logarithmic transformed value adjusted for age, body mass index, systolic blood pressure, serum cholesterol and smoking.

the North Karelia Project¹⁸ and the Seven Countries Study.¹⁹ The impact of serum cholesterol on mortality depends on the proportion of coronary deaths in the population. When this proportion is low, the effect of serum cholesterol is weak as well.²⁰ This is demonstrated in table 3, showing the best association in the excluded group which also had the greatest coronary mortality. Several recent studies²¹⁻²³ but not all,²⁴ have failed to show an association between low cholesterol and cancer. In our study cancer deaths were not significantly associated with initial cholesterol in different analyses and the group with low risk for cardiovascular disease also had the lowest cancer mortality.

The rate of non-illness deaths (including accidents, suicide, and homicide) was significantly higher in the intervention than in the control group.³ On the other hand, a high rate of such deaths was observed in the low risk group. The rates of non-fatal violent events were also similar in these three groups.²⁵ The difference between intervention and control groups may thus be due to a chance, that is, an exceptionally low incidence in the control group. It has been suggested that low serum cholesterol or cholesterol lowering is associated with violent death^{11-13, 26} but the mechanisms are speculative, and, for example, a recent study from North Karelia did not find this association.²⁷ In the Helsinki Businessmen Study population, violent events were not associated with initial serum cholesterol, and in the intervention group fatal and non-fatal violent events were not predicted by in-trial hypolipidaemic drug use.²⁵ On the other hand, these events were independently associated with use of alcohol, which is an important possible confounding variable.

It has been suggested that the associations observed in some studies between low cholesterol and total or non-cardiovascular deaths are due to confounding factors.^{28, 29} In the recent analysis by Law *et al*¹⁶ low cholesterol was associated with excess deaths in community based studies, but not in employed cohorts. In accordance with this, no J curve was observed between cholesterol and total mortality of the whole cohort in the present study of businessmen.

Two findings in the present analyses do not support obvious doubts⁴ that the randomisation of the intervention and control groups could have been unsuccessful. First, as presented in table 1, the risk factor levels between these two groups were similar before and after randomisation. Second, unlike in the other groups, age was not a significant predictor of deaths in the intervention group (table 3), implying that there were modifying factors (intervention methods) on mortality. Taking into account that both blood pressure and cholesterol predicted mortality in the background population, the significant decrease of these risk factors during the intervention² should have improved prognosis in the intervention group. As this was not the case, a chance finding—such as the low mortality caused by violence in the control group

—or more likely something in the intervention methods needs to be considered as a possible explanation for the unexpected result.¹ The present findings may offer an additional potential clue. As shown in table 3, 1 h glucose significantly predicted mortality in the intervention group but not in the control group, despite similar baseline glucose concentrations and significant weight reduction in the intervention group during the intervention period.² The fact that the effect of group on total and coronary heart disease mortality was no longer significant when the group by 1 h glucose interaction term was added to the model suggests that factors related to glucose tolerance explain a part of the excess mortality in the intervention group compared with the control group. Aspects of the intervention methods—possibly mental stress induced by intense health education in the dominant executives, or blood pressure medications^{8, 30}—may have made individuals with impaired glucose tolerance especially vulnerable.

In conclusion, this study shows that the traditional cardiovascular risk factors³¹ are also important predictors of mortality among men of the highest social class. Cholesterol was specifically associated with cardiac deaths and its impact on total mortality seemed to be determined by the proportion of coronary deaths to total deaths. In this population, where confounding factors (initial diseases, different life styles, or social class) were minimised, no evidence was found for an association between low cholesterol and non-vascular or non-illness deaths. The value of studying homogeneous populations to enhance internal validity has also recently been discussed in the context of body weight and mortality.³² However, the important questions remain: what is the optimal treatment to lower the risk factors in primary prevention and what are the target levels for intervention? Apparently the intervention methods were not optimal in the Helsinki Businessmen Study. Consequently, the unconventional results of this trial should—rather than calling for pessimism—stimulate more research to find better intervention methods for the primary prevention of cardiovascular diseases.

We thank Soile and Marja Aarnio for technical assistance. Sigrid och Ane Gyllenbergs Stiftelse is acknowledged for financial support. Presented in part at the 66th Scientific Sessions of the American Heart Association, November 8–11, 1993, Atlanta, Georgia, USA.

- Miettinen TA, Strandberg TE. Implications of recent results of multifactorial primary prevention. *Ann Med* 1992;24:85–9.
- Miettinen TA, Huttunen JK, Naukkarinen JK, Strandberg T, Mattila S, Kumlin T, *et al*. Multifactorial primary prevention of cardiovascular diseases in middle-aged men. Risk factor changes, incidence and mortality. *JAMA* 1985;254:2097–102.
- Strandberg TE, Salomaa VV, Naukkarinen VA, Vanhanen HT, Sarna SJ, Miettinen TA. Long-term mortality after 5-year multifactorial primary prevention of cardiovascular diseases in middle-aged men. *JAMA* 1991;266:1225–9.
- Paul O, Hennekens CH. The latest report from Finland: a lesson in expectations. *JAMA* 1991;266:1267–8.
- Should clinical trials carry a health warning? [Editorial] *Lancet* 1991;338:1495–6.
- Oliver MF. Doubts about preventing coronary heart disease. *BMJ* 1992;304:393–4.
- Bassler TJ, Bassler TJ, Newman TJ, *et al*. Long-term mortality after primary prevention for cardiovascular diseases. *JAMA* 1992;267:2183–6.
- Salomaa V. Long-term effect of primary prevention measures of

- coronary heart disease on the risk factor levels in middle-aged men [thesis]. Helsinki: University of Helsinki, 1988: 1-78.
- 9 Dixon WJ. *BMDP statistical software manual*. Berkeley: University of California Press, 1992.
 - 10 Keys A, Aravanis C, Blackburn H, *et al*. Probability of middle-aged men developing coronary heart disease in five years. *Circulation* 1972;45:815-28.
 - 11 Muldoon MF, Manuck SB, Matthews KA. Lowering cholesterol concentrations and mortality: a quantitative review of primary prevention trials. *BMJ* 1990;301: 309-14.
 - 12 Davey Smith G, Pekkanen J. Should there be a moratorium on the use of cholesterol-lowering drugs? *BMJ* 1992;304:431-3.
 - 13 Jacobs D, Blackburn H, Higgins M, *et al*. Report of the conference on low blood cholesterol: mortality associations. *Circulation* 1992;86:1046-60.
 - 14 Stamler J, Stamler R, Brown WV, *et al*. Serum cholesterol—doing the right thing. *Circulation* 1993;88:1954-60.
 - 15 Lewis B, Tikkanen MJ. Low blood total cholesterol and mortality: causality, consequence and confounders. *Am J Cardiol* 1994;73:80-5.
 - 16 Law MR, Thompson SG, Wald NJ. Assessing possible hazards of reducing serum cholesterol. *BMJ* 1994;308: 373-9.
 - 17 The Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study. *Lancet* 1994;344:1383-9.
 - 18 Salonen J. Risk of cancer and death in relation to serum cholesterol: a longitudinal study in an Eastern Finnish population with high overall cholesterol level. *Am J Epidemiol* 1982;116:622-30.
 - 19 Pekkanen J, Nissinen A, Punsar S, Karvonen MJ. Short- and long-term association of serum cholesterol with mortality. *Am J Epidemiol* 1992;135:1251-8.
 - 20 Frank JW, Red DM, Grove JS, Benfante R. Will lowering population levels of serum cholesterol affect total mortality? *J Clin Epidemiol* 1992;45:333-46.
 - 21 Chen Z, Peto R, Collins R, MacMahon S, Lu J, Li W. Serum cholesterol concentration and coronary heart disease in population with low cholesterol concentrations. *BMJ* 1991;303:276-82.
 - 22 Kromhout D, Bosschietter EB, Drijver M, Lezenne Coulander C. Serum cholesterol and 25-year incidence of and mortality from myocardial infarction and cancer. *Arch Intern Med* 1988;148:1051-5.
 - 23 Davey Smith G, Shipley MJ, Marmot MG, Rose G. Plasma cholesterol concentration and mortality. The Whitehall Study. *JAMA* 1992;267:70-6.
 - 24 Chyou PH, Nomura AM, Stemmermann GN, Kato I. Low serum cholesterol and cancer among Japanese American men. *J Clin Epidemiol* 1992;45:287-92.
 - 25 Strandberg TE, Miettinen TA. Fatal and non-fatal violent events in 15-year follow-up of multifactorial primary prevention of cardiovascular diseases: the Helsinki Businessmen Study. In: *Low blood cholesterol—health implications*. Proceedings of a Meeting held in Milan, July 1993. London: Current Medical Literature, 1993:40-2.
 - 26 Lindberg G, Råstam L, Gullberg B, Eklund GA. Low serum cholesterol concentration and short-term mortality from injuries in men and women. *BMJ* 1992;305:277-9.
 - 27 Vartiainen E, Puska P, Pekkanen J, Tuomilehto J, Lönnqvist J, Ehnholm C. Serum cholesterol concentration and mortality from accidents, suicides, and other violent deaths. *BMJ* 1994;309:445-7.
 - 28 Chen Z, Keech A, Collins R, *et al*. Prolonged infection with hepatitis B virus and association between low blood cholesterol concentration and liver cancer. *BMJ* 1993; 306:890-4.
 - 29 Iribarren C, Dwyer JH, Burchfiel CM, Reed DM. Can the U-shaped relation between mortality and serum cholesterol be explained by confounding? [abstr] *Circulation* 1993;87:7.
 - 30 Salomaa VV, Strandberg TE, Vanhanen H, Naukkarinen V, Sarna S, Miettinen TA. Glucose tolerance and blood pressure: a long-term follow-up study in middle-aged men. *BMJ* 1991;302:493-6.
 - 31 Manson JE, Tosteson H, Ridker PM, *et al*. The primary prevention of myocardial infarction. *N Engl J Med* 1992; 326:1406-16.
 - 32 Lee IM, Manson JE, Hennekens CH, Paffenbarger RS. Body weight and mortality. A 27-year follow-up of middle-aged men. *JAMA* 1993;270:2823-8.