Life expectancy and cause of death in men examined at medical check-ups in 1964

Summary

Background. The purpose of the study was to determine the associations between blood pressure, body mass index and smoking habits recorded at routine medical check-ups with the company medical officer, and life expectancy and cause-specific mortality through several decades.

Material and method. Participants in the Linseed Oil Trial were monitored from 1967 through 2005 with respect to all-cause and cause-specific mortality in the Cause of Death Register. The population studied consisted of 15 934 men who were born between 1905 and1914 and were in work in 1967. The analyses used various multivariate regression methods.

Results. A total of 15 535 participants (97.5 %) were dead, and the average age of death was 76.6 (SD 9.1). Blood pressure, body mass index and cigarette smoking were associated with the age of death and mortality due to cardiovascular disease, lung cancer and respiratory system diseases. High systolic blood pressure (≥ 160 mm Hg) was associated with a 5-year reduction in life expectancy, 15 cigarettes daily with 3.5 years, obesity with 1.4 years and a definite elevated sedimentation rate with a 3.3 year reduction in life expectancy. The excess mortality persisted through the entire follow-up period for all factors, but declined gradually for high blood pressure and high sedimentation rate. The associations for smoking and obesity did not change over time. The associations for smoking were weaker than in most early studies.

Interpretation. The results of routine medical check-ups in the occupational health service can predict lost years of life through several decades.

Tor Bjerkedal
tor.bjerkedal@getmail.no
Institute of Health and Society
University of Oslo
and
Institute of Epidemiology, Norwegian Armed Forces Medical Services

Petter Kristensen
National Institute of Occupational Health
and
Institute of Health and Society
University of Oslo

Randi Selmer
Norwegian Institute of Public Health

A hypothesis was postulated in the early 1960s that a dietary supplement of linseed oil, with a high content of the unsaturated fatty acid linolenic acid, could prevent ischaemic heart disease (IHD) (1). To test this hypothesis, a working group assisted by Norwegian company medical officers started a one-year controlled clinical trial in 1964. It was called the «Linseed Oil Trial», and encompassed over 16 000 men born in the period 1905–1914 (2, 3). Data on established and suspected risk factors for ischaemic heart disease were obtained from the notes of company medical officers and were essentially based on previous routine medical check-ups (3). This was a period during which some company medical officers were drawing attention to public health issues, not least cardiovascular disease (4, 5).

The Linseed Oil Trial was completed, even though it rapidly became clear that supplements of linseed oil did not have the expected effect (6). The treatment did not have any beneficial health effect compared with a placebo (2, 3). However, known risk factors such as high blood pressure (7), high body mass index (BMI) (8) and cigarette smoking (9) were associated with a higher risk of ischaemic heart disease (2, 3). The participants in the Linseed Oil Trial continued to be monitored from 1966 to 1982, and the same risk factors were found to be associated with higher all-cause mortality (10). Because it was suspected that sedimentation rate was also associated with the risk of ischaemic heart disease (4), this was also recorded and found to be associated with both this disease (3) and all-cause mortality (10).

The participants in the Linseed Oil Trial continued to be monitored through 2005 as an observation study linked to the Cause of Death Register. By this time almost all of them were dead. The survivors were 91–100 years old.

The benefit of routine medical check-ups for presumed healthy adults is open to debate (11). The purpose of this study was to determine whether and to what extent the results of these routine check-ups by company medical officers can predict lost years of life and mortality due to various causes. In addition to blood pressure, body mass index and smoking habits, we examined the association with sedimentation rate (3, 10).

The same year that the Linseed Oil Trial was carried out, a major blood pressure survey was also carried out in Bergen. This was subsequently followed up with respect to various causes of death, with special emphasis on cardiovascular disease (12). A few years later, the Oslo survey was conducted among men in their 40s. This has been followed up subsequently (13).

Various risk models for cardiovascular disease have been developed on the basis of data from national and international population studies. Blood pressure and cigarette smoking are factors in all of these. The SCORE risk model (14) is used in the European guidelines for prevention of cardiovascular disease, while the corresponding NORRISK model is used in the Norwegian guidelines (15). We will relate our findings to these Norwegian surveys and the NORRISK risk model.

Material and method

Participants

The participants in the Linseed Oil Trial were presumed healthy men in their 50s who were recruited in 1964–65 by the company medical officers at 280 companies. Over 40 % of them lived in Eastern Norway and were employed in secondary industry companies as manual workers. A total of 16 608 men were recruited, of whom 16 364 were

Main points

- The results of routine medical check-ups by the occupational health service can predict lost years of life through several decades.
- The associations for high blood pressure weakened over time, but not for smoking.

born between 1905 and 1914 (3). It is not clear how many of those who were invited declined to take part, but 208 men from four companies were not included because of their company medical officer's illness or death (3). The 15 934 who were born between 1905 and1914 and who were in work (had pensionable income) in 1967 took part in this follow-up.

Data sources

The company medical officers completed a registration form for each participant in early 1965. Amongst other things, the form contained information about current smoking habits and the results of health surveys conducted by the company in the previous two years. After obtaining national identity numbers, data from the 1960 Population and Housing Census and the Cause of Death Register were linked to this material. The Regional Committee for Medical Research Ethics recommended that the project be carried out.

Explanatory variables

Information on civil status, region of residence, industry group and occupational group were obtained from the 1960 Population and Housing Census. Systolic and diastolic blood pressure, height and weight recorded by the occupational health service in the course of the previous two years were included. Systolic blood pressure was grouped into nine categories, while diastolic blood pressure was not used in the main analyses (16).

Body mass index (BMI, kg/m^2) was calculated on the basis of height and weight, and grouped as underweight (< 18.5 kg/m^2), normal weight (18.5–24.99 kg/m^2, overweight (25.0–29.99 kg/m^2) or obese (≥ 30 kg/m^2). The number of cigarettes per day entered on the registration form was also included and grouped in four categories.

The form contained a record as to whether the participant had an elevated (> 15 mm) sedimentation rate in repeated measurements over a number of years. This was classified by the company medical officer as «definitely elevated» «possibly elevated» or «not elevated» (3). The explanatory variables and their distributions are indicated in table 1.

Outcome variables

The date and underlying cause of death were obtained from the Cause of Death Register. As well as all-cause deaths, cause-specific deaths were registered for circulatory system, including ischaemic heart disease and cerebrovascular disease (stroke), cancer, including cancer of the bronchi and lungs (lung cancer), respiratory system and death due to external causes. The causes of death were classified at different times according to ICD-7, ICD-8, ICD-9 and ICD-10. Codes and time intervals during which classifications applied are shown in table 2.

Statistical analyses

Version SE11.1 of the Stata statistical package was used. We present several different measures of the relationship between the risk factors and all-cause mortality and cause-specific mortality. We calculated the average age at death grouped according to the categories of the explanatory variables and used multiple linear regression, Cox regression and Kaplan-Meier curves.

Multiple linear regression analysis was carried out for all participants who died in the follow-up period 1967–2005. Estimated coefficients represent the relationship between life expectancy, the explanatory variables how many years more or less individuals with different risk factors lived on average compared with persons in a given reference group. Linear regression is possible because virtually all of the subjects are dead. Age at time of death represents the cumulative effect of the mortality rates from the age of 50.

Cox regression is central in survival analysis – it models the age-specific mortality rates. The results are estimated hazard ratios (HR), which are the ratios between the mortality rates in various categories of an explanatory variable. Hazard ratios are assumed to be the same for all ages/time intervals. In order to determine whether the relative effect of the risk factors declined with time/age, we calculated the hazard ratio for death from all causes in four observation periods (1967–76, 1977–86, 1987–96 and 1997–2005).

We entered all explanatory variables as categories. In addition we performed analyses with systolic blood pressure as a continuous risk factor and calculated the hazard ratio per 15 mm Hg increase for the whole period and for the first 20 years of the follow-up. When mortality rates for specific causes were modelled, participants were censored out at the time of death due to other causes, emigration or at the end of the observation period, 1 January 2006.

We followed all age cohorts from the age of 62. Survival from the time of turning 62 (1967–1976) until the end of 2005 was calculated using Kaplan-Meier curves for selected combinations of systolic blood pressure level and smoking habits. The curves show the percentage that are still alive at different ages after the start of the follow-up. The curves provided a basis for calculating median survival, i.e. the age when half of the group is dead.

In all the regression analyses, the 95 % confidence interval (CI) was calculated for the point estimates (coefficient for change in life expectancy and hazard ratio).

Results

All-cause mortality

In the follow-up period 1967–2005, 15 535 died (97.5 %). 27 participants emigrated during the period and 372 were still alive on 1 January 2006. The percentage of survivors grouped according to the explanatory variables is shown in table 1. The percentage of survivors was, as expected, positively associated with the civil status of married, living in Western Norway, non-manual occupation, low systolic blood pressure, normal weight, non-smoker and non-elevated sedimentation rate. The same pattern was reflected in the multivariate analysis of life expectancy (table 3). The associations were moderate for most categories (+/– 2 years of life), but the estimates for lost years of life were substantially higher for high systolic blood pressure – five years on average where the latter was ≥ 160 mm Hg. The estimates were also somewhat higher for the highest smoking categories (3.5 years for ≥ 15 cigarettes a day and for an elevated sedimentation rate (3.3 years). Obesity was associated with 1.4 years and underweight with 1.7 lost years of life compared with those of normal weight.

Figure 1 shows the survival function from the age of 62 for selected risk categories. On the basis of the curves, the estimated median survival for non-smokers with systolic blood pressure of < 140 mm Hg will be 81.2 years. Survival for smokers was estimated at 75.2 years for blood pressure of 140–159 Hg. Estimated survival with blood pressure of ≥ 180 mm Hg (irrespective of smoking habits) was 72.5 years. It can be read off figure 1 that the calculated percentage of participants alive at the age of 80 was 19 % for those with blood pressure ≥ 180 mm and 60 % for non-smokers with blood pressure < 140 mm Hg.

Figure 2 shows that the hazard ratio estimates for the risk factors associated with all-cause deaths had increased in all time intervals between 1967 and 2005. However, the effect of high systolic blood pressure and an elevated sedimentation rate showed a declining tendency, while the estimates for smoking and obesity were stable over time.

Cause-specific deaths

The number of deaths distributed among the various causes of death is shown in table 2. Half died of circulatory diseases and a quarter of cancer.

The associations between the risk factors and circulatory system diseases, including ischaemic heart disease and stroke, are presented in table 4. Rising systolic blood pressure was strongly associated with increasing hazard ratio estimates, more strongly for stroke than for heart disease. The mortality rates were 5.3 and 2.8 times, respectively, higher in the highest blood pressure category than in the baseline category. Obesity and smoking were only moderately associated with mortality due to circulatory diseases, including ischaemic heart disease and strokes. Definitely elevated sedimentation rates were associated with ischaemic heart disease, with a hazard ratio estimate of 1.7.

Cancer and lung cancer as causes of death

Table 3 Changes in life expectancy in association with sociodemographic factors 1960 and some results of company medical officers' check-ups of 15 535 participants in the Linseed Oil Trial who died between 1967 and 2005. Linear regression analysis

Category	(Age at death (yrs) (average)	SD	Difference[1]	95 % CI
Total	76.6	9.1		
Civil status in 1960				
Married	76.8	9.1	0	Reference
Unmarried	75.3	8.9	–1.0	–1.6 to –0.4
Widower	75.1	8.8	–1.2	–2.4 to +0.1
Separated/divorced	74.3	8.5	–1.9	–3.0 to –0.8
Unknown	75.5	9.3	–0.5	–2.1 to +1.2
Region of residence				
Oslo-Akershus (03, 02)	76.5	9.0	0	Reference
Rest of Eastern Norway (01, 04–08)	76.6	9.0	+0.3	–0.1 to +0.6
Southern Norway (09–11)	76.6	9.4	+0.4	–0.1 to +0.9
Western Norway (12–14)	77.8	9.1	+1.3	+0.7 to +1.9
Central Norway (15–17)	76.2	9.0	–0.2	–0.7 to +0.4
Northern Norway (18–20)	76.0	9.0	–0.3	–1.1 to +0.6
Unknown	75.5	9.3	–2	
Industrial group 1960				
Primary	77.7	9.0	+0.9	–0.1 to +1.9
Secondary	76.5	9.0	–0.3	–0.7 to +0.1
Tertiary	76.9	9.1	0	Reference
Unknown	76.2	9.3	–0.3	–1.2 to +0.6
Occupational group 1960				
Non-manual	77.8	9.2	0	Reference
Manual	76.3	9.0	–1.3	–1.7 to –0.9
Unknown	75.7	8.9	–1.4	–2.1 to –0.8
Systolic blood pressure (mm Hg)				
< 125	78.2	9.1	0	Reference
125–134	77.6	8.9	–0.6	–1.0 to –0.2
135–144	76.8	8.9	–1.5	–1.9 to –1.1
145–154	75.1	8.7	–3.1	–3.6 to –2.6
155–164	74.3	9.0	–4.0	–4.6 to –3.4
165–174	73.1	8.5	–5.4	–6.2 to –4.7
175–184	73.5	8.7	–5.0	–5.9 to –4.1
185–194	71.6	8.4	–6.5	–7.9 to –5.1
≥ 195	71.0	8.4	–7.4	–8.7 to –6.2
Unknown	75.8	10.3	–3.6	–5.6 to –1.5
Body mass index (BMI) (kg/m^2)				
Underweight (< 18.5)	74.7	9.2	–1.7	–3.0 to –0.5
Normal weight (18.5–24.99)	76.8	9.0	0	Reference
Overweight (25.0–2.99)	76.6	9.1	+0.1	–0.2 to +0.3
Obesity (≥ 30)	74.2	8.7	–1.4	–2.1 to –0.7
Unknown	76.9	9.9	+1.7	–0.1 to +3.6
Cigarette smoking				
Non-smoker	77.9	9.1	0	Reference
1–4 cigarettes a day	76.9	8.9	–0.9	–1.5 to –0.4
5–14 cigarettes a day	75.3	8.7	–2.4	–2.8 to –2.0
≥ 15 cigarettes a day	74.1	8.7	–3.5	–4.0 to –3.0
Unknown	76.7	9.1	–1.0	–1.3 to –0.6
Sedimentation rate				
Not elevated	77.2	9.0	0	Reference
Possibly elevated	74.3	9.0	–2.4	–3.0 to –1.9
Definitely elevated	73.3	8.6	–3.3	–3.8 to –2.8
Unknown	75.6	9.2	–1.4	–2.5 to –0.4
Constant			82.6	82.1 to 83.2

[1] Adjusted for year of birth and all factors in the table | [2] Estimate dropped because of colinearity

were only moderately associated with the risk factors, with the exception of smoking (table 5). The hazard ratio estimate for lung cancer in smokers who smoked at least 15 cigarettes a day was 5.5. Lung cancer was also associated with a definitely elevated sedimentation rate. Death due to respiratory disease was associated with a lower body mass index, smoking and an elevated sedimentation rate. A similar pattern was found for deaths due to external causes, but with somewhat weaker hazard ratio estimates for body mass index and smoking.

The hazard ratio estimates in tables 4 and 5 were only moderately changed by the multivariate model including all the risk factors (data not shown). The only exception was the hazard ratio for circulatory diseases in association with obesity, where the estimate was 1.7 before adjustment and 1.4 after adjustment for systolic blood pressure.

In the survival analysis, where systolic blood pressure was included as a continuous variable, a 15 mm Hg increase in systolic blood pressure amounted to a hazard ratio of 1.27 (1.25–1.29) for circulatory diseases in the follow-up period as a whole. The effect on blood pressure was somewhat stronger during the first 20 years of the follow-up, when a 15 mm Hg increase was associated with a hazard ratio of 1.32 (1.30–1.35) for circulatory disease, 1.25 (1.22–1.28) for ischaemic heart disease and 1.48 (1.41–1.55) for death due to stroke.

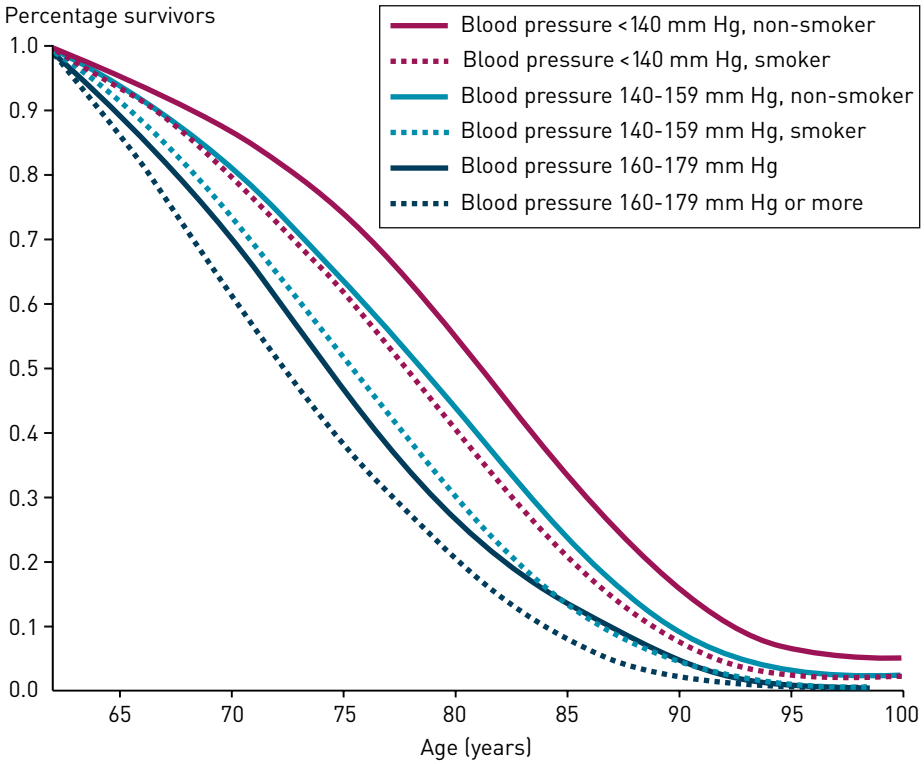

Figure 1 *Survival with follow-up from age of 62 grouped by selected categories of systolic blood pressure and smoking habits of participants in the Linseed Oil Trial who were in work in 1967*

Discussion

This study shows that even after several decades of follow-up, well-known risk factors such as blood pressure, cigarette smoking and obesity measured at routine medical check-ups by the company medical officer were associated with lost years of life – both all-cause deaths and cause-specific deaths. The results indicate that there is a socioeconomic gradient in life expectancy, although the material is too homogeneously composed of manual workers in secondary industry for it to be possible to determine this in more detail.

The unique aspect of this study is that we have been able to follow the study population until almost all of them were dead. Since very few of them emigrated, we were able to analyse predictors for age at time of death by means of simple multiple regression. A number of diagnostic tests have shown that an additive model (not presented) fits well and that the combined effect of various covariates can be found by means of effect summation. For example, men with baseline values for all factors had an average life expectancy of 82.6 years. The estimated life expectancy of men with systolic blood pressure of between 165 mm Hg and 174 mm Hg and reported smoking of at least 15 cigarettes a day was 73.9 on average, i.e. almost nine years lower. Presented in this manner, average life expectancy is intuitively easy to understand and provides information additional to the hazard ratios presented by survival analyses.

The health surveys in the Linseed Oil Trial were carried out almost 50 years ago among men who were able to work. Most of them were manual workers in Eastern Norway, and they all worked in companies with an occupational health service. The question of how far the findings in the study can be generalised can therefore be raised. The fact that we do not know about later changes with respect to risk factors is also a weakness, and we therefore cannot estimate the importance of any blood pressure medication, smoking cessation or weight changes.

The effects of extreme risk factor levels

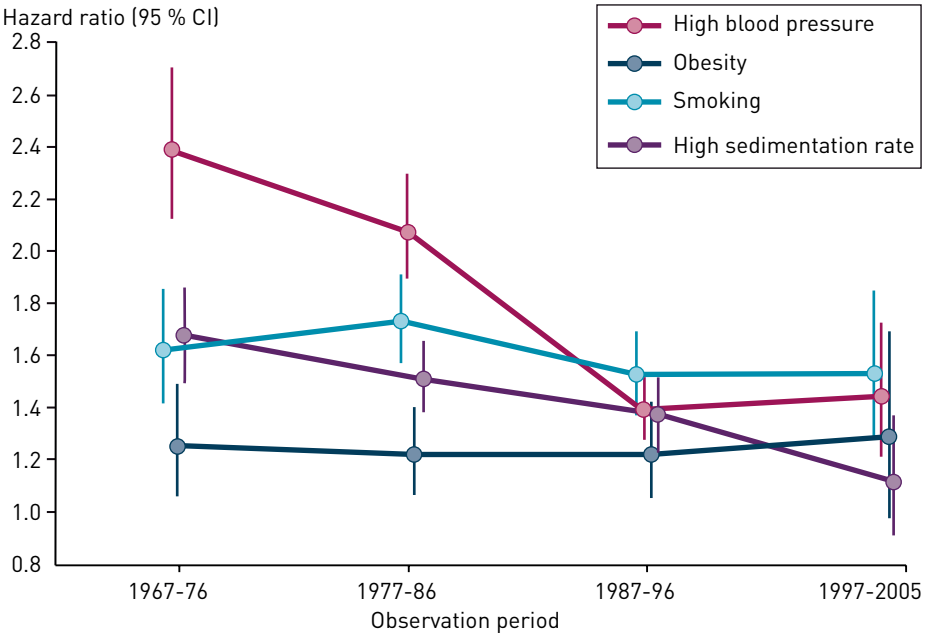

Figure 2 *Hazard ratio with 95 % confidence interval (CI) for death in four follow-up periods between 1967 and 2005 distributed by selected risk factors among participants in the Linseed Oil Trial who were in work in 1967. High blood pressure: systolic blood pressure ≥ 160 mm Hg versus < 125 mm Hg; obesity: BMI ≥ 30 kg/m² versus 18.5–24.99 kg/m²; smoking: ≥ 15 cigarettes a day versus non-smoker; high sedimentation rate: definitely elevated versus not elevated*

will be underestimated in the calculations of lost years of life because the 372 who were alive at the end of 2005 are not included in the linear regression analyses. Most of them had a favourable risk profile (table 1). If they had been included, they would have pushed up the estimated age at death for those with a favourable profile. Given that all 372 lived to be 100, the regression analysis would have yielded estimates for lost years of life that were 0.4 year higher for blood pressure ≥ 195 mm Hg and 0.7 year higher for smoking of ≥ 15 cigarettes a day than the corresponding estimates in table 3.

Blood pressure effects

We found that high blood pressure had a significant effect, with five lost years of life for participants with systolic blood pressure ≥ 160 Hg compared with participants with < 125 mm Hg. The blood pressure effect waned over time. This is consistent with the results of 33 years of follow-up in the Oslo survey (13). The strength of the associations between a 15 mm Hg increase in systolic blood pressure and death due to ischaemic heart disease or stroke found through follow-up over a 20-year period was almost identical to similar follow-up in the Bergen blood pressure survey (table 4 in ref. 12). This may imply that the blood pressure measurements had the same predictive value as the blood pressure data from the Bergen survey, even though the Linseed Oil Trial was based on routine medical examinations in advance of the project and probably encumbered with larger random measurement errors.

Blood pressure in the Bergen study was based on the second of two measurements; in the Linseed Oil Trial it was based on a non-standardised and imprecisely described measuring method; in addition, there were far more people carrying out the measurements. Random measuring errors and intra-individual variations in blood pressure lead to underestimation of the association with mortality. In the NORRISK risk model, the hazard ratio per 15 mm Hg systolic blood pressure is 1.35 for circulatory diseases as a whole (15), i.e. slightly higher than the value of 1.27 that we found. This may be due to some random measuring errors in our study.

We observed a weaker association between blood pressure and mortality after 20 years of follow-up. This may be due to blood pressure changing and to the subjects being 20 years older, with an average age of almost 80. It may also be due to the fact that some subjects have been put on blood pressure treatment. During the first part of the follow-up period, the general population received far less blood pressure treatment than is the case today. One interpretation of our findings may be that the effect of high blood pressure among persons who have not received treatment is at least what we have observed. This is also of relevance to present day medicine.

Effects of smoking

The negative effects of smoking were weaker than in other surveys (9, 17), with hazard ratio estimates associated with smoking at least 15 cigarettes a day of 1.3 for ischaemic heart disease and 5.5 for lung cancer. By way of comparison, follow-up of men in large Norwegian health surveys yielded hazard ratio estimates for death from lung cancer of 17 and 3 for daily smokers and former smokers, respectively, in relation to never-smokers (table 4.25 and table 4.17 in ref. 18).

The corresponding hazard ratio estimates for mortality due to ischaemic heart disease for daily smokers and former smokers were 3.3 and 1.5, respectively, for subjects younger than 65 and 1.7 and 1.3 for those over 65 (table 4.17 in ref. 18). The long follow-up time cannot be the explanation, as the hazard ratio estimates for all-cause deaths remained stable over time, as was the case in the Oslo survey (13).

As in many other surveys, the smoking data were based on self-reporting, and we have no reason to suppose that the data differed in terms of quality from those in other studies. However, it is possible that the specification of daily cigarette consumption in the 1960s is deficient – in that it systematically overestimates the participants' historical exposure to tobacco. This may be the case because the participants grew up during the early phases of the smoking epidemic. They were in their 30s when the war ended and therefore probably made their debut as smokers relatively late in life and with more moderate consumption when they were young compared with those who came in at later stages of the smoking epidemic (19, 20).

This interpretation is underpinned by the results of 50 years of follow-up of British doctors, where the increase in mortality for smokers was more moderate for doctors born before 1900 than for doctors born in the period 1900–1930 (14). The interpretation was that the later cohorts started smoking earlier and with higher intensity (17). Another possible explanation may be that our reference category included former smokers. We do not know how many of the non-smokers had smoked previously.

Effects of body mass index

Like other studies, this study also showed a U-shaped association between body mass index and all-cause deaths, with estimated lost years of life of 1.7 and 1.4 for underweight (< 18.5 kg/m^2) and obese (≥ 30 kg/m^2), respectively, whereas there was little variation in mortality for a body mass index of between 18.5 kg/m^2 and 30 kg/m^2.

The risk of dying of circulatory diseases increased steadily with rising body mass index, whereas there was a negative association for respiratory diseases and external causes. This is consistent with earlier findings (21–24). The increase in risk of death due to lung cancer with low body mass index was weaker in our study than in the large international Prospective Studies Collaboration (24). This may be due to the relatively weak association with smoking habits in our study.

Associations with elevated sedimentation rate

Previous follow-up in the Linseed Oil Trial has shown that there was excess risk of coronary heart disease (3) and death (10) among participants with a persistently high sedimentation rate. Our study indicates that these associations persisted for several decades, although they declined gradually. These findings are consistent with the results of other studies (25, 26). The most likely interpretation is that chronic inflammation processes may be a causal factor or constitute part of the pathogenic process in atherosclerosis (26, 27).

This can also be seen in connection with level of C-reactive protein (CRP). This is a non-specific inflammation marker where elevated concentration levels have been linked to increased risk of *inter alia* cardiovascular disease (28). A single CRP reading has proven to improve risk predictions for coronary heart disease other than the traditional risk factors (29). The associations with death due to lung cancer and to respiratory system disease could be explained by similar chronic inflammation processes.

However, it is more difficult to explain the association with external causes. This may be a random finding, but it may also be due to unidentified or unknown confounding factors.

Conclusion

After more than 15 000 men, originally in their fifties, had been followed up for 40 years, almost all of them were dead. Age at the time of death was associated throughout the follow-up with well documented risk factors measured before the start of the study. This shows that the results of routine medical check-ups by the occupational health service can predict survival through several decades. The documentation of this fact may be an argument for conducting these medical check-ups, which may have a preventive potential – provided that the findings are followed up medically.

We thank Ola Thune of the Norwegian Labour and Welfare Administration, and Geir Skjeret of the Norwegian Armed Forces Medical Serviceswho prepared the data files for analysis.

Tor Bjerkedal (born 1926)
Dr. Med., Master of Public Health (Harvard). Professor Bjerkedal has been professor at the Institute of Hygiene and Social Medicine at the

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University of Bergen and the University of Oslo, medical consultant for the Norwegian National Insurance Administration, researcher at the Institute of Epidemiology, Norwegian Armed Forces Medical Services, and has been Professor Emeritus at the Institute of Health and Society at the University of Oslo since 1996.
Conflicts of interest: None declared

Petter Kristensen (born 1944)
Dr. Med., Senior Consultant and Head of Research at the Department of Occupational Medicine and Epidemiology, National Institute of Occupational Health, and Professor at the University of Oslo.
Conflicts of interest: None declared

Randi Selmer (born 1953)
PhD, statistician and senior researcher at the Division of Epidemiology, Norwegian Institute of Public Health.
Conflicts of interest: None declared

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Received 2 May 2011, first revision submitted 28 September 2011, approved 20 October 2011. Medical editor Erlend T. Aasheim