

REVIEW 693

CONFIDENTIAL

Subject ref 2

"The Health Risks of Smoking
The Framingham Study: 34 Years of Follow-up"
K M Freund et al
Annals of Epidemiology (1993), 3, 417-424

The Framingham Heart Study is well known for the detail of the observations made and the frequency and length of follow-up, though the number of subjects involved is substantially less than in many other prospective studies. Starting in 1948 to 1952 it involved a cohort of some 5,000 men and women who have been examined biennially ever since. This paper describes results from 34 years of follow-up of 1,916 men and 2,587 women initially free of coronary heart disease (CHD) and aged 45 to 84 in at least one examination. (It is not quite clear why follow-up was for only 34 years - or put the other way round, why it took until 1993 to present analyses of data up to 1986).

Analyses related smoking habits to the prevalence or incidence of various endpoints - cough; forced expiratory volume in one second (FEV₁); lung cancer; CHD; stroke and transient ischemic attacks; intermittent claudication; cardiovascular disease (CVD); presence of any of the three preceding endpoints; or mortality. Analyses combined results for each successive two-year period of follow-up, subjects being classified as non-smokers or smokers based on their most recent examination. Subjects were also classified by cumulative amount smoked (pack-years) up to the

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most recent examination. Results in the tables are expressed as age-adjusted annual rates or as odds ratios adjusted for age and also (except in the case of lung cancer) blood pressure, cholesterol, glucose intolerance and ECG left ventricular hypertrophy. It should be noted that, for two of the three types of odds ratios cited, current smoker and amount smoked (20/day), risk is relative to a denominator (non-smokers) which includes ex-smokers. This is not strictly comparable to results from many prospective studies which give risk relative to lifelong never smokers. The odds ratios for cumulative pack-years (30 pack-years) are relative to lifelong never smokers. It is unfortunate that no separate results are given for ex-smokers.

As is reported by numerous other studies, there was an increase in prevalence of cough and a decrease in FEV_1 in relation to number of cigarettes smoked. Although there were only 94 lung cancer deaths, risk was clearly substantially increased in smokers of both sexes and age groups (results were separately presented for ages 45-64 and 65-84). All-cause mortality was also clearly elevated in smokers, with current smokers, compared to non-smokers, having a highly significant 60-80% increased risk in all four age group/sex considerations.

For coronary heart disease, based on a total incidence, fatal or non-fatal, of almost 1,300 cases a clearly significant relationship with smoking was interestingly evident only in men aged 45-64, although a marginally significant relationship was also seen for women aged 45-64. While the literature generally shows the association between smoking and CHD to be clearly stronger in younger than in older men and women, most

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other studies do report an increased risk in older men and women (and a larger relative risk than reported by Framingham in younger men and women). A possible explanation of the difference might lie in the fact that while other studies often only report deaths from CHD, Framingham includes a number of non-fatal types of the disease. These include angina, which Framingham, like other studies (see review 610) find to be not positively associated with smoking at all. The authors actually note in the text that if angina were excluded from the definition, then a significant relationship with smoking in both young and older women would be seen. It is a pity that the authors did not include results for fatal CHD only, which would have allowed more direct comparison with other evidence.

In general, although the association of CHD may perhaps be weaker than reported by other studies, I regard the Framingham results as broadly in line with those from the other major prospective studies. In 1989, Seltzer, in a paper in the Journal of Clinical Epidemiology (42, 743-750) suggested that the Framingham study data brought into question "established wisdom" (i.e. the 1983 US Surgeon-General's report) concerning smoking and CHD. In my review (480) of that paper I noted that I was not particularly impressed by it. Reading the paper reviewed here, partly written to counter Seltzer's paper, I retain my view that the Framingham Heart Study data do not in fact contradict in any important way the overall evidence on smoking and CHD which the Surgeon-General considered.

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