# Long term effect on mortality of stopping smoking after unstable angina and myocardial infarction

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## Abstract

**Subjects who stop smoking cigarettes after myocardial infarction have an improved rate of survival compared with those who continue, but to date it was not known whether the benefit persisted for more than six years. A total of 498 men aged under 60 years who had survived a first episode of unstable angina or myocardial infarction by two years were followed up by life table methods for a further 13 years. Mortality in those who continued to smoke was significantly higher (82·1%) than in those who stopped smoking (36·9%). These differences increased with time. Mortality in those who were non-smokers initially and who continued not to smoke was intermediate (62·1%). The adverse effect of continued smoking was most pronounced in those with unstable angina. Continuing to smoke increased the rate of sudden death to a greater degree in those with less severe initial attacks, while the effect of smoking on fatal reinfarctions was most apparent in those with a more complicated presentation.**

**These findings suggest that stopping cigarette smoking is the most effective single action in the management of patients with coronary heart disease.**

## Introduction

Improved survival in subjects who stop smoking cigarettes after myocardial infarction compared with those who continue was first reported in 1975.[1 2] Further studies have confirmed this finding,[3-7] but it is not known whether the benefit persists beyond six years.[4]

We examined the effects of giving up cigarette smoking on mortality in patients with confirmed unstable angina or myocardial infarction; the patients were studied for up to 15 years. We also discuss cause and mode of death in relation to smoking habits and severity of the initial attack.

## Materials and methods

From January 1965 to December 1975, 555 men who had survived a first attack of confirmed unstable angina or myocardial infarction (categorised as uncomplicated or complicated) by at least 28 days entered the study. Diagnostic criteria for these three groups have been published previously.[1] The men were consecutive patients and all were aged less than 60.

A uniform programme of rehabilitation and secondary prevention included antismoking advice in hospital and at follow up. Full information about the risk factors for each patient was obtained during the first admission and annually at a special follow up clinic. Those smoking five or more cigarettes daily during the six months before the initial attack were classed as smokers and all others, including ex-smokers, were defined as non-smokers. At each follow up a smoker who had ceased smoking for at least three months was defined as having stopped smoking. A high degree of veracity in the stated smoking habits of a sample of these patients has been reported.[8]

Cause and mode of death for those who died were derived from hospital records, necropsy reports, death certificates, and through contact with the family physician and patients' relatives. Our definitions of cause and mode of death have been previously reported.[9]

This report deals with the 498 subjects of the original cohort of 555 who were still alive two years after the initial attack. Those who died within the first two years were excluded from the analysis, as were those on whom no data were available and those who were non-smokers at entry but subsequently started smoking (fig 1).

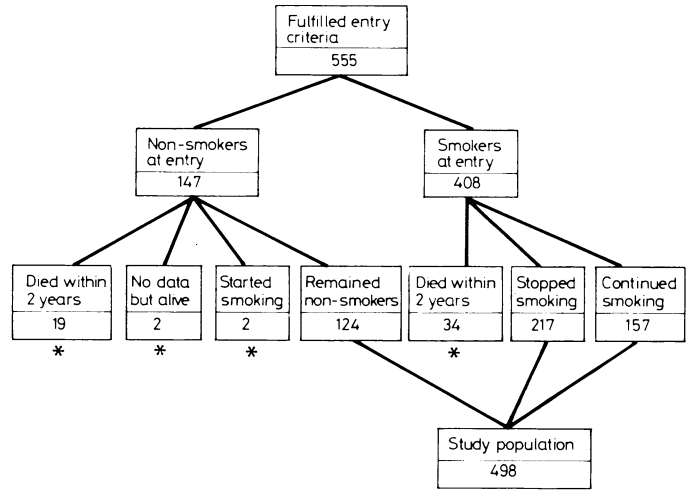


FIG 1—Derivation of study population.
*Excluded from this report.

The follow up examination two years after the attack (mean time to follow up: 2·04 years) was used as the basis of our study because information on smoking was complete at this stage, changes in smoking habits were rare afterwards, and the confounding effect of the severity of the initial attack on mortality was largely eliminated by this time.[10]

The mean time to follow up or death for the 498 subjects was 7·4 years. However, using actuarial life table methods[11] with a review date of 1 January 1980[12] mortality could be estimated up to 15 years after the initial attack, 13 years from the two year examination. A total of 148 subjects died during the study period and 317 were alive at the review date. Data on the remaining 33 were unavailable at review date; all were alive at last follow up, which, in all but seven cases, was within two years of the review date. Such losses before review were treated as a competing risk according to the model of Dorn.[13]

Our analysis required a summary measure that could be applied to a single life table and used to compare different groups. The commonly used log-rank test[14] is unsuitable for analysis of cause specific mortality.[15] We therefore used a system based on a weighted average of the interval hazard rates.[15] This is referred to as an average annual mortality and the ratio of two such measures defines an average relative risk. Significance was calculated by an appropriate significance test[15] and confidence intervals for the relative risk were calculated using test based limits.[16] The $\chi^2$ and $t$ tests were used to calculate significance of other differences.

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## Results

Of the various characteristics and risk factors measured at the time of the initial attack[1] only exercise was significantly associated with giving up smoking in the 374 who were smokers at entry; those who continued to smoke took less exercise before entry ($p=0.02$). With this exception none of the differences between those who continued and those who stopped smoking were large or significant. The mean age of those who continued smoking was 50·3 years compared with 50·5 years in those who stopped ($p=0.79$). As initial exercise was not related to prognosis the analysis of those who stopped and those who continued smoking was not adjusted for any other factors.

The 124 who were non-smokers at entry were also compared with the 374 who were smokers at entry. The non-smokers took less exercise ($p<0.01$), had a significantly higher diastolic blood pressure at the time of the attack (80·5 mm Hg compared to 77·6 mm Hg, $p=0.04$), and had more than double the proportion of those with defined hypertension (22·6% compared with 10·2%, $p<0.01$). The non-smokers had a mean age of 51·8 years at time of attack compared with 50·4 years for the smokers ($p=0.03$). The two groups had similar systolic blood pressure and cholesterol concentrations, and the same prevalence of preinfarction angina.

Figure 2 shows cumulative mortality from all causes, starting two years after the initial attack, for the three surviving groups defined by smoking habit. The mortality at 13 years was 82·1% among those who continued to smoke, 36·9% in those who had ceased smoking, and 62·1% in non-smokers who remained non-smokers. In terms of the average annual mortality over the full period of follow up, those who continued to smoke had a mortality 2·8 times higher than that of those who stopped ($p<0.01$).

On the basis of the 13 years' cumulative rates, vascular causes accounted for 68% of the total mortality among the 498 survivors at two years; 24% was due to fatal infarction and 35% to sudden death. There were no significant differences between the three smoking groups.

The relative risk of death for those who continued to smoke compared with that for those who stopped in terms of cause specific mortality showed that those who continued to smoke had higher average annual mortalities than those who stopped smoking for all vascular causes (relative risk = 2·4; $p<0.01$), fatal reinfarctions (relative risk = 2·6; $p=0.02$), and sudden death (relative risk = 1·6; $p=0.14$). For each of these causes of death the average mortality of the 124 non-smokers lay between the two extremes of those who continued and those who stopped smoking. When the first (0-6 years) and second (7-13 years) periods of follow up were examined separately, relative risks for all causes, fatal reinfarction, and, to a lesser extent, sudden death were seen to increase with time. The relative risk for all causes was 1·7 in the first period (95% confidence interval 1·1-2·4) and 5·0 in the second (95% confidence interval 2·2-11·1). The relative risks for fatal reinfarction and sudden death did not reach significance as regards this time trend. The effect of continuing to smoke was not only long term but actually increased with duration of follow up.

Relations between the severity of the presenting attack, smoking, and mortality were also examined. Table I shows the average annual death rates of the 374 who smoked initially and the number who had ceased smoking at two years in three groups defined by the severity of the initial attack. Though a larger proportion of those who had had complicated myocardial infarctions ceased smoking, the average annual mortality was also highest in this group (both differences non-significant).

Table II presents the average annual cause specific and total mortality for those who continued and those who stopped smoking broken down by severity of initial attack, together with the relative risks for continuing smoking. The total mortality increased with severity in both smoking groups but the overall effect of continuing to smoke was highest in those with unstable angina. Among those who continued to smoke the sudden death rate was not related to severity but the rate increased with increasing severity in those who stopped cigarette smoking. Thus, as for total mortality, the effect of continued smoking on sudden death was most pronounced in those with unstable angina but no effect on sudden death was apparent in those with a complicated myocardial infarction.

In the case of fatal reinfarctions the situation was reversed. The infarct rate increased with severity in those who continued to smoke but remained more or less constant in those who stopped smoking. Continuing to smoke affected the fatal reinfarction rate most severely in those with a previous complicated myocardial infarction and did not affect the reinfarction rate in those who had unstable angina.

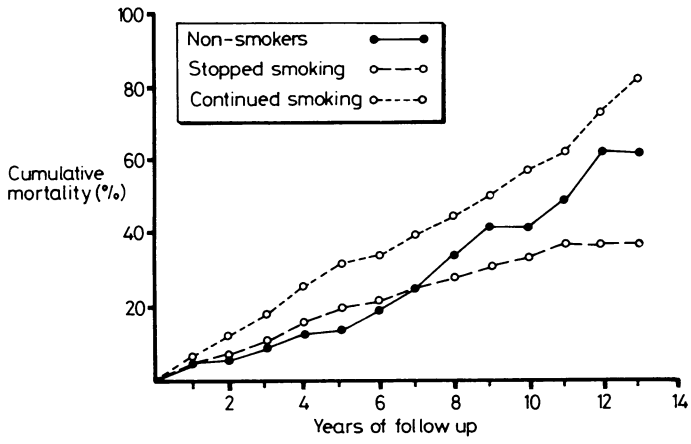


FIG 2—Cumulative mortality for 498 survivors of a coronary attack by smoking habit. Life table curves start two years after attack. Average annual mortality was 6·5% in non-smokers, 3·7% in those who stopped smoking, and 10·2% in those who continued smoking.

TABLE I—*No of patients who stopped smoking and average annual death rate by severity of initial attack*

| Severity of attack | No of patients | No who stopped smoking* | Average annual death rate* |
|---|---|---|---|
| Unstable angina | 63 | 33 | 6·2% |
| Uncomplicated myocardial infarction | 219 | 126 | 6·0% |
| Complicated myocardial infarction | 92 | 58 | 8·9% |
| Total | 374 | 217 | 6·9% |

*Differences between groups not significant.

TABLE II—*Average annual total and cause specific mortality and relative risks for those continuing and those who stopped smoking by severity of attack*

| | Average annual mortality (%) | | |
|---|---|---|---|
| | Continued smoking | Stopped smoking | Relative risk |
| | *All causes* | | |
| Severity of attack: | | | |
| Unstable angina | 10·0 | 1·9 | 5·4** |
| Uncomplicated infarction | 8·6 | 3·9 | 2·2* |
| Complicated infarction | 12·4 | 4·7 | 2·7** |
| | *Sudden death* | | |
| Severity of attack: | | | |
| Unstable angina | 2·3 | 0·8 | 2·7 |
| Uncomplicated infarction | 2·3 | 1·2 | 2·0 |
| Complicated infarction | 2·6 | 2·7 | 1·0 |
| | *Fatal reinfarction* | | |
| Severity of attack: | | | |
| Unstable angina | 0·6 | 0·6 | 1·1 |
| Uncomplicated infarction | 1·9 | 0·8 | 2·4* |
| Complicated infarction | 3·4 | 0·7 | 4·9** |

*$p<0.05$, **$p<0.01$.

## Discussion

Previous reports on the benefits of giving up cigarette smoking after myocardial infarction were based on six years' observation or less.[1-7] This study, with a follow up of up to 15 years from the time of the initial attack and with negligible losses to follow up, shows that the deleterious effect of continuing to smoke cigarettes persisted over the long term and related to cause specific as well as total mortality. This influence of smoking appears to be cumulative so that giving up even some years after a first coronary attack may have a useful impact on prognosis.

The anomalous position of non-smokers, who have a poorer prognosis than smokers who stopped after infarction, has been noted previously.[4,5] A probable explanation, supported by our results, is that this group had more coronary risk factors, other than smoking, compared with initial smokers and that these factors may be less amenable to intervention than smoking.

Though the smoking habits of our patients were carefully determined at entry and after two years by direct interview, data on subsequent smoking habits of the groups have not been taken into consideration in this report. Nevertheless, if some of those who had stopped smoking resumed the habit and some of those who continued to smoke subsequently gave up this would be expected to conceal an even greater divergence of the mortality curves. In our experience patients who have stopped smoking two years after a coronary attack seldom resume the habit although those still smoking at this time may eventually stop, particularly if they suffer a further non-fatal coronary episode.

A strong interaction between stopping smoking and the severity of the initial attack was apparent in terms of total mortality and mode of death. The effect of continued smoking on total mortality was greatest in those with unstable angina, suggesting that antismoking advice should be at least as compelling in those with less severe attacks. The greater benefit of stopping smoking in patients at lowest risk after infarction was also noted by Salonen.[6] An earlier analysis of our patients suggested a greater benefit from stopping smoking in subjects with a complicated myocardial infarction.[3] This finding, however, seems to have been heavily influenced by a small number of cases who died soon after discharge from hospital and re-examination of the data raises doubts about the accuracy of information on their smoking habits. In contrast, the choice of the two year follow up examination for the present report has yielded reliable information on smoking habits.

In terms of mode of death smoking had its strongest effect on sudden death in the patients with unstable angina and on fatal reinfarction in patients with complicated myocardial infarction. This may suggest that different pharmacological interventions may be appropriate in groups defined by severity of illness and smoking habit. There is no doubt, however, that stopping cigarette smoking is the most effective single action in the management of patients with coronary heart disease. Future trials of drug and surgical treatment in those surviving myocardial infarction should provide details of smoking habits at presentation and at follow up.

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# SHORT REPORTS

## Acupuncture needles as a cause of bacterial endocarditis

The incidence of infective endocarditis has remained unchanged during the past 40 years.[1] There are several reasons for this. Many patients at risk of infective endocarditis are unaware that they have a cardiac lesion, and others have poor dental health despite knowing of their susceptibility to infective endocarditis.[2] Medical and dental practitioners could do more to extend dental prophylaxis.[3] Physicians should also be aware, however, of possible new ways of inducing endocarditis in at risk patients, so that appropriate advice and prophylaxis may be given. We report the development of bacterial endocarditis after the insertion and manipulation of acupuncture needles.

### Case report

A 57 year old woman with a prosthetic Starr-Edwards valve in the mitral position presented at the outpatient department with a 10 day history of night sweats, fever, fast irregular palpitations, anorexia, lassitude, and increasing dyspnoea. She also complained of sudden weight gain with ankle and abdominal swelling. She had contracted rheumatic fever as a child and undergone mitral valvotomy in 1970 with valve replacement in 1972. Eighteen days before presentation acupuncture needles had been inserted in both ears in an attempt to stop her smoking. These needles had remained in situ for one week and had then been replaced by a second set after which she complained of irritation and a discharge from the skin around the needle.

On examination she was feverish, in fast atrial fibrillation and gross right heart failure, and with an enlarged pulsatile liver and tricuspid incompetence. There was also appreciable splenomegaly. An ejection systolic murmur was heard in the mitral area with clear prosthetic valve sounds. Two splinter haemorrhages and two Osler's nodes were noted, but no Roth spots were seen. Microscopic sterile haematuria was found. The erythrocyte sedimentation rate was 68 mm in the first hour. *Pseudomonas aeruginosa* (sensitive to gentamicin) was grown from two out of eight blood cultures, although no growth was obtained from an ear skin swab culture. Serological tests for other causes of endocarditis yielded negative results. An echocardiogram (M mode and sector) suggested two possible vegetations around the valve. Bacterial endocarditis was diagnosed. Treatment was started with increased diuretics and intravenous antibiotics (penicillin 3 MU every four hours and gentamicin 80 mg every eight hours). The gentamicin and intravenous penicillin were continued for four weeks and then oral amoxycillin was given to complete a six week course.

She made a full and uneventful recovery and was well six months later with no heart failure.

### Comment

The patient was well aware of the need for prophylaxis against bacterial endocarditis and regularly received antibiotics before dental treatment. She had not considered acupuncture to be a procedure needing antibiotic cover; nor, presumably, had her acupuncturist. There was little doubt that clinically she had bacterial endocarditis. The source of infection was probably the acupuncture needle site, which was clearly inflamed. It is perhaps important that the needles were in situ for a long period and had been manipulated several times each day on instruction. The relevance of the growth of *P aeruginosa*