Respiratory effects of lowering tar and nicotine levels of cigarettes smoked by young male middle tar smokers.

I. Design of a randomised controlled trial

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Abstract

Study objective—The aim was to investigate the effect on respiratory health of male middle tar smokers changing the tar and nicotine levels of the cigarettes they smoke for a six month period.

Design—This was a randomised controlled trial. Middle tar smokers were randomly allocated to smoke one of three different types of cigarette (low tar, middle nicotine; middle tar, middle nicotine; and low tar, low nicotine) in place of their usual cigarette for a six month period. Main outcome measures were assessment of respiratory health by documenting respiratory symptoms and peak expiratory flow rates, and of nicotine inhalation by measuring the urinary excretion of nicotine metabolites.

Setting—21 local authority districts of England.

Subjects—Participants were male middle tar smokers aged 18–44 years.

Main results—Postal questionnaires were sent to 265 016 individuals selected from the electoral registers of 21 local authority districts of England; 64% of questionnaires were returned revealing 7736 men aged 18–44 years who smoked only middle tar cigarettes. Of these, 7029 (90%) were sent a health warning and 707 (10%) were not; the latter acted as a control group to assess the effect of the health warning. Of the 7029 men who had received a health warning and were visited at the recruitment stage, 2666 agreed and were eligible to participate in the trial although only 1541 (58% of those who agreed and were eligible) actually started smoking the study cigarettes; 643 men (24% of those willing to participate at the beginning of the trial and 42% of those who actually started smoking the study cigarettes) completed the trial smoking the study cigarettes. Of these, 213 were in the low tar middle nicotine group, 220 were in the middle tar middle nicotine group, and 210 were in the low tar low nicotine group.

Conclusions—This study shows the feasibility of identifying and recruiting sufficient numbers of male middle tar smokers, with adequate numbers completing the trial, to detect any changes in respiratory health over a six month period.

study was undertaken as part of a research programme sponsored by the Independent Scientific Committee on Smoking and Health (ISCSH) to determine whether this voluntary agreement between the health ministers and the tobacco industry resulted in the smoking of less harmful cigarettes and whether reducing the tar levels of cigarettes therefore reduced the harm to respiratory health. The decision to assess the effects of smoking only on respiratory health, and not on other aspects of health, was taken because other conditions such as heart disease and carcinoma of the lung were being addressed in different parts of the research programme.

Prior to the main study described, a feasibility study was carried out.¹ Male middle tar smokers selected from a postal questionnaire on smoking habits were randomly allocated to smoke either a middle tar, middle nicotine or a low tar, low nicotine cigarette in place of their usual one for a five week period. During this period, respiratory symptoms were documented, urine specimens collected for the measurement of urinary nicotine metabolites, and cigarette butts were collected to calculate their weight and number in order to detect any changes in patterns of smoking. The results of this initial study showed that there was no statistically significant change in the prevalence of respiratory symptoms over the five week period. The excretion of nicotine metabolites, numbers of cigarettes smoked, and average cigarette butt weight for men allocated to the low tar cigarettes were not significantly different from those of the men allocated to the middle tar cigarettes.

The results from the feasibility study suggested that those who had been allocated to smoke low tar, low nicotine cigarettes changed their pattern of smoking to compensate for the reduced nicotine yield of their cigarettes. The study concluded that it was feasible to recruit individuals for such a trial but that to assess the possible effects of compensation, a third type of cigarette should be included in the main study—a low tar, middle nicotine cigarette. It was thought that if the nicotine intake with this cigarette was similar to a middle tar cigarette there would be no need for compensation. Because of the lower tar:nicotine ratio, there would be a corresponding reduction in the tar intake and an improvement in respiratory symptoms would ensue in comparison with middle tar smokers.

The hypotheses being tested in the main study were that: (1) smoking low tar cigarettes will produce fewer respiratory symptoms than smoking middle tar cigarettes; (2) middle tar smokers who change to low tar, low nicotine

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In November 1980 the United Kingdom health ministers and the tobacco industry agreed to continue lowering the tar yield of cigarettes. This

cigarettes will compensate; and (3) middle tar, middle nicotine smokers who change to low tar, middle nicotine cigarettes will not compensate.

Methods

The study design was based partly on the observations made in the feasibility study. The main study took place between 1985 and 1988 in 21 local authority districts in England. Local authority districts were chosen as these were the smallest areas for which mortality data were available over the last 10 years. The areas were chosen on the basis of their standardised mortality ratios for asthma so that information on differences in asthma prevalence and treatment could also be collected for a separate study. The areas chosen had either high (167–396) or low (0–39) asthma standardised mortality ratios for 15–64 year old men for the period 1974–83.

Initial ethical approval was granted by West Lambeth Health Authority ethics committee and was also sought from the individual district health authorities in the local authority districts where the trial took place. Twenty four areas were initially chosen for the study. Where ethical approval was not granted, additional areas that had the closest standardised mortality ratios for asthma were then approached and the sampling ratios in the remaining and replacement areas adjusted to give the required numbers for the trial. A total of 34 district health authorities were approached through their regional and district directors of public health and each was sent an identical protocol and covering letter stating that ethical approval had been granted by West Lambeth Health Authority ethics committee. Most consulted with their own local ethics committees. As local authority district and district health authority boundaries did not always coincide, two district health authorities had to be consulted for some local authority districts. Permission was given for the study to be conducted within the boundaries of 21 local authority districts. Of the district health authorities which did not give permission, some simply stated that they did not wish to support the study. Other reasons for refusing permission were that the study was contrary to local antismoking policies or other health promotion activities. District health authorities were also consulted to ensure that the study did not overlap with other locally organised studies involving smoking.

SAMPLE SIZE

Estimates of the sample size needed for this study were based partly on the results of the feasibility study and on data from the Office of Population Censuses and Surveys *General household survey*.² To calculate the number of questionnaires to be mailed in the initial stage of the study so that sufficient numbers of middle tar smokers would be identified and recruited into the trial, it was necessary to estimate: (1) the response rates at the different stages of the study; (2) the prevalence of smoking and respiratory symptoms and changes likely to occur; (3) the population for each of the local authority districts, and (4) the size of the changes to be detected.

Table I shows the estimates made in calculating the sample size along with the actual numbers in the trial. The assumptions made for purposes of the sample size calculation, based on the findings of the feasibility study, were that changes due to individuals losing or developing symptoms, partly due to random fluctuation and partly due to the effect of smoking, would differ according to cigarette group. They were that, of the middle tar smokers classified as having respiratory symptoms at the beginning of the trial, 30% of those allocated to the low tar, middle nicotine cigarettes and 10% of those allocated to both the middle tar, middle nicotine and low tar, low nicotine cigarettes would lose their symptoms by the end of the trial. Of those without symptoms 10%, 30%, and 30% would develop symptoms in the low tar middle nicotine, middle tar middle nicotine, and low tar low nicotine groups, respectively.

To detect a difference of at least 20% between the proportion of respondents losing their symptoms (30% loss versus a 10% loss) with reasonable confidence ($\alpha=0.05$, $\beta=0.1$) 92 men who had respiratory symptoms initially would be needed to complete the trial in each of the three cigarette groups. Using the estimates made earlier, 264 000 questionnaires would need to be mailed to identify 7733 middle tar smokers of whom 2216 would start the trial.

SAMPLING

The sampling frame used for this study was the electoral register. The sample was obtained using systematic random sampling using sampling ratios of between 1 in 2 and 1 in 8 of the males on the local electoral registers of 21 local authority districts in England. If there was any doubt as to the sex of the elector on the electoral register then this person was included in the postal questionnaire stage as the gender was asked on the questionnaire and any woman incorrectly sent a questionnaire could subsequently be excluded from the study. In fact in only one district was there any difficulty in identifying the sex of subjects and here specialist advice was available to help distinguish them.

The study took place in three stages, a postal questionnaire stage, a recruitment stage, and a trial stage.

Postal questionnaire stage

The postal questionnaire stage took place between March and November 1986. During this stage a self administered questionnaire was sent to each of 265 016 individuals identified by the sampling

Table I The estimates made in determining sample size for the trial and the actual numbers involved in the trial

	Estimate	Number in trial
Number of mailed questionnaires	264 000	265 016
Response to postal questionnaire (as % of total mailed questionnaires)	171 600 (65%)	170 310 (64%)
Manufactured cigarette smokers in the 18–44 year age group	19 333	16 580
Middle tar smokers age 18–44 years (as % of cigarette smokers 18–44)	7733 (40%)	7736 (47%)
Number of men sent a health warning (as % of middle tar smokers 18–44)	7026 (90%)	7029 (90%)
Response to administered questionnaire at recruitment (as % of middle tar smokers sent health warning)	4562 (65%)	5153 (73%)
Number willing to participate in the trial (as % of response at recruitment)	2216 (49%)	2666 (52%)
Number with respiratory symptoms starting the trial (as % of number willing to participate)	554 (25%)	1241 (47%)
Number of participants completing the trial (as % of number willing to participate at beginning of trial)	1108 (50%)	643 (24%)
Number with respiratory symptoms finishing the trial	276	283

process. The questionnaire stated its purpose was to collect information about people's health; no mention was made of the trial at this stage. The questionnaire asked about age, gender, respiratory symptoms, medication, and smoking habits. Respondents who smoked were asked to include an empty cigarette packet of the brand they usually smoked when they returned the questionnaire so that the tar level could be identified. It has been found that requesting a cigarette packet is an efficient way of gaining accurate brand details.³ Male smokers within the age group who did not return an empty packet were sent a follow up letter asking for brand details and/or an empty cigarette packet.

If there was no response to the questionnaire, a postcard reminder was sent three weeks later, followed by a second questionnaire three weeks after that, if still no response. Reply paid envelopes were enclosed for the return of the questionnaires and cigarette packets.

Of the male smokers aged 18–44 years, 7029 (90%) were sent a health warning informing them of the dangers of smoking, the advantages of giving up, and providing addresses of where to find help, if needed, in giving up smoking. The remaining 707 (10%), who were acting as a control group, were not sent a health warning and subsequently were not asked to participate in the trial.

Recruitment stage

The recruitment stage took place between October 1986 and September 1987. Approximately three months after the health warning had been sent, the 18–44 year old male middle tar smokers who had been sent such a health warning were interviewed. A questionnaire was administered to assess their eligibility and willingness to participate in the trial. Information on smoking habits, brand details, and respiratory symptoms (using

the Medical Research Council respiratory symptoms questionnaire⁴) was collected. Peak expiratory flow rates were measured at this visit using a mini Wright peak flow meter.⁵ The peak flow meters were numbered and the number of the peak flow meter used initially was recorded. As far as possible subjects had peak expiratory flow rates measured using the same meter on the two occasions when this measurement was made.

Those eligible for inclusion in the trial were male middle tar smokers (classified as smokers whose usual brand of cigarette yielded > 12 mg of tar per cigarette) who regularly smoked only manufactured cigarettes (at least five per day) and who did not have a medical condition that might be made worse by smoking.

Interviewers were instructed to visit each potential recruit at least four times before classifying him as uncontactable unless there was evidence that he had moved from that address or he had refused to see them. Three out of the four visits had to be made out of normal working hours, ie, at night or at the weekend unless there was reliable evidence that he was a night worker.

Except for the three London areas, the areas were recruited in pairs at approximately fortnightly intervals. There was an interval between the first pair and subsequent pair to allow any organisational or other problems to be remedied.

Trial stage

The trial stage took place in the 21 areas between January 1987 and March 1988. Following their identification at the recruitment stage, eligible volunteers were then stratified according to the presence or absence of respiratory symptoms, taking any one positive response to the Medical Research Council questionnaire at recruitment as identifying the presence of respiratory symptoms. Within each area they were then randomly allocated to smoke one of three types of study cigarette which had the mean tar and nicotine levels shown in table II. The timing of the recruitment and trial stages in the 21 areas is shown in fig 1. The study outline is shown in fig 2.

During the six month trial, participants were visited approximately fortnightly. Each period of 14 days was divided into an initial five "target" days, followed by two "reserve" days, and finally the remaining seven days. The aim was to visit each participant on the same day each fortnight, preferably on one of the target days, thus spacing visits at 14 day intervals. Where this was not possible another of the target or reserve days was used, using the remaining seven days only if absolutely essential. At these visits interviewers administered questionnaires which enquired about respiratory symptoms and smoking habits. Peak expiratory flow rate was measured at the end of the trial. At each visit, trial cigarettes were provided at a cost of £1.15 per packet of 20 king size filter tip cigarettes. At the time of pricing this was 1p per packet cheaper than any king size filter tip cigarette available for purchase within the United Kingdom. Evidence from the feasibility study suggested that this chosen price did not dissuade men from participating in the trial nor did it alter their smoking habits. The cigarettes were supplied in blank white packets all carrying a

Table II Mean tar and nicotine levels in study cigarettes

Cigarette type	Tar (mg/cigarette)	Nicotine (mg/cigarette)
Low tar, middle nicotine (LM)	9.5	1.16
Middle tar, middle nicotine (MM)	13.8	1.24
Low tar, low nicotine (LL)	9.7	1.04

Figure 1 The time schedule for the recruitment and trial stages in the 21 areas

standard health warning and identifiable only by means of a horizontal, vertical, or diagonal line. If participants stopped smoking the study cigarettes they were asked to remain in the trial and answer the respiratory symptoms questions but not be supplied with trial cigarettes. It was stressed to interviewers that participants must not be allowed to change brands of study cigarette if, for example, they disliked the brand they had been allocated.

All three stages began in the 21 areas at staggered intervals of time so that post sent and returned did not coincide, and to allow for easier administration. For the recruitment and trial stages this also ensured that briefings did not all take place at the same time.

TRAINING

Interviewers were trained on two occasions, first for the recruitment stage and then for the trial stage, in 11 centres in England. They were taught the use of standardised techniques including the administration of the Medical Research Council questionnaire on respiratory symptoms, Field's card system,⁶ and the measurement of peak expiratory flow rate. All interviewers were given a training manual which contained detailed instructions. Training was essential to ensure standardisation of the administration of the questionnaires and measurement of peak expiratory flow rate and thus to minimise variation between and among interviewers.

QUALITY CONTROL

Teaching of the Field's card system took approximately one hour during the training day. For each interviewer, their gradings of the card system made on the first few interviews were checked by the research team at St Thomas's Hospital. Team leaders were informed if there were problems with these gradings. Apart from the training days, interviewers were initially accompanied by a team leader who was an experienced interviewer who checked their work. The interviewers also reported fortnightly to their team leader throughout the trial, who notified them of any errors made and of the general quality of their work.

OUTCOME MEASURES

Changes in respiratory health

Four outcome measures were used to assess changes in respiratory health during the six month trial. Three measures assessed changes in respiratory symptoms and the fourth assessed changes in peak expiratory flow rate. The respiratory symptoms measures have been previously described in detail⁷; a brief description only is given here.

(1) The first measurement was a method described by Field known in this study as Field's card system based on a technique developed by Ingham⁸ for giving a quantitative and sensitive assessment of frequency of cough. This produced a score of between 1 and 8, with 1 indicating no cough and 8 the maximum frequency of cough.

(2) The second measure used was a series of graded statements on cough and phlegm in which participants chose one of five statements for each symptom which best described their symptoms over the preceding two weeks. Each symptom produced a score of between 1 and 5, with a score of 1 indicating the minimum level of symptoms and 5 indicating the maximum. Both measures were obtained on eight occasions throughout the trial.

(3) Questions 1, 3, 5, 6, 8, 10, and 12 of the Medical Research Council questionnaire on cough, phlegm, and chest illness were asked at recruitment and at the end of the trial. Question 12 was modified to cover a period of 12 months instead of three years.

The above three sets of questions were all piloted and found to be highly repeatable.⁷

(4) In addition to the three sets of measures for respiratory symptoms, peak expiratory flow rates were measured at recruitment and at the end of the trial. On each occasion five readings were taken with the subject seated and the mean of the last three readings was used in the analysis.

Compliance and compensation

It was possible that participants might change their pattern of smoking to compensate for the change in cigarette. They could do this in several ways—by not complying with the study cigarettes and smoking non-trial ones, by changing their consumption of cigarettes, or by changing the way they smoked such as by taking larger or more puffs from their cigarette, inhaling more frequently or deeply, or smoking the cigarette to a shorter butt length. Data were therefore collected to measure the degree to which compensation occurred.

Figure 2 Study design

At the fortnightly interviews all participants reported on the quantities of study and non-study cigarettes they had smoked since their last interview. To assess the extent to which participants might have smoked non-study cigarettes a random sample of 60% of participants were asked to collect the cigarette butts of all the cigarettes they smoked for three one week periods. As the study cigarettes could be identified by a thin white line around the filter, the proportion of study cigarettes smoked could be calculated. The cigarettes were indistinguishable from one another and neither the interviewer nor the participant knew which cigarette had been allocated.

To assess the inhalation of nicotine, the same sample of participants who provided butts were also asked to provide urine samples. These were collected in thymolised tubes on five occasions throughout the trial for the measurement of nicotine metabolites (as cotinine) and creatinine by automated versions of the barbituric and alkaline picrate methods, respectively,^{9 10} on a ChemLab System 4 analyser. These samples were collected in plastic tubes on the day of the visit and the tubes were sent to St Thomas's Hospital in first class prepaid padded bags where they were frozen upon receipt. For both the urine sample and butt collection, a pretrial sample was collected at visit 1 to give information on usual smoking habits.

Initial findings of study

POSTAL QUESTIONNAIRE STAGE

The total response to the 265 016 postal questionnaires after 12 weeks was 64%. The cumulative responses were: 39% after the first mailing; 52% after a postcard reminder three weeks later; and 64% after a second questionnaire three weeks after the postcard reminder. There was no response from 33% of the sample and, in addition, 3% of questionnaires were returned uncompleted.

The questionnaire yielded 16 580 men aged 18–44 years who reported smoking only manufactured cigarettes, of whom 7736 smoked middle tar cigarettes. Of these, a random sample of 7029 was sent a health warning and 707 acted as the control group to evaluate the effect of the health warning.

RECRUITMENT STAGE

Of the 7029 middle tar smokers identified by the initial questionnaire and sent a health warning, 5153 (73%) were interviewed at recruitment and 1876 (27%) could not be contacted after four visits. Of the 5153 who were interviewed, 3650 (71%) were eligible to participate in the trial, 369

(7%) were excluded for health reasons, and 1134 (22%) were ineligible because they had either given up smoking, had switched to low tar cigarettes or other forms of tobacco, or were smoking less than five manufactured cigarettes a day. Of the 3650 who were eligible, 2666 (73%) agreed to take part in the trial, 879 (24%) refused, and 105 (3%) could not take part in the trial because they were moving out of the study area. The 2666 willing participants were randomly allocated to the three cigarette types.

The prevalence of respiratory symptoms, as determined by responses to the Medical Research Council questionnaire, among the 2666 men agreeing to participate was 47%. Those who agreed to participate in the trial had a higher prevalence of symptoms than those who refused, and they also smoked more cigarettes per day and smoked lower tar brands (table III). No statistically significant association was found with age, nicotine level of the usual cigarette, or duration of smoking. The differences which were found were not large and the subsequent randomisation makes it very improbable that they could have biased the findings.

TRIAL STAGE

Continuation in the trial

Of 2666 individuals who initially agreed to take part in the trial, 1125 (42%) withdrew on the first visit and only 1541 (58%) actually began smoking the trial cigarettes, with 517 in the low tar middle nicotine (LM) group, 506 in the middle tar middle nicotine (MM) group, and 518 in the low tar low nicotine (LL) group.

Continuation in the trial was positively associated with age and daily cigarette consumption, but was not found to be significantly associated with tar or nicotine levels, age at onset of smoking, or presence of respiratory symptoms. Continuation in the trial did not vary significantly between the three types of cigarette. Figure 3 shows the continuation in the trial for all participants and fig 4 shows the continuation in the trial for each cigarette group. It can be seen that there was a large drop out initially before the participants had smoked any of the study cigarettes. In fact, only 58% of participants started smoking the trial cigarettes. The numbers dropping out initially and at each stage of the trial were very similar in each of the three cigarette groups.

Six hundred and forty three men completed the trial smoking the study cigarettes, with 213, 220

Table III Characteristics of individuals interviewed at the recruitment stage. Values are means (SD)

	Eligible for trial		All middle tar smokers interviewed (n = 5153)
	Recruited (n = 2666)	Refusals (n = 984)	
Age (years)	31.1 (7.7)	31.3 (7.8)	31.1 (7.7)
Age started smoking (years)	16.0 (2.9)	16.2 (3.0)	16.0 (2.9)
Tar level of usual cigarette (mg/cigarette)	15.3 (1.2)	15.4 (1.4)	15.1 (1.7)
Nicotine level of usual cigarette (mg/cigarette)	1.4 (0.12)	1.4 (0.15)	1.4 (0.17)
Cigarettes consumed per day	19.5 (8.6)	18.2 (9.2)	17.8 (9.6)
Prevalence of respiratory symptoms (MRC questionnaire)	47%	39%	45%

Figure 3 Continuation in the trial for all subjects

and 210 participants in the LM, MM, and LL groups respectively. These figures represented 24% of those willing to participate at the beginning of the trial, but 42% of those who actually started smoking the study cigarettes.

Characteristics of participants

The mean age of the 1541 participants who started smoking the study cigarettes was 31.9 years (SD 7.6) and the mean tar and nicotine levels per cigarette prior to the trial were 15.3 (1.2) mg and 1.4 (0.13) mg respectively. On average participants smoked 20 (8.5) cigarettes per day and started smoking at the age of 15.9 (2.8) years. Seven hundred and nine (46%) were found to have respiratory symptoms prior to the trial. The three cigarette groups were very similar with respect to age, daily cigarette consumption, tar and nicotine levels of usual cigarettes, age at onset of smoking, and presence of respiratory symptoms (table IV).

Discussion

This study was undertaken to determine the effect on respiratory health of reducing the tar level of cigarettes. The feasibility study undertaken prior to this had suggested that middle tar, middle nicotine cigarette smokers who changed to low tar, low nicotine cigarettes compensated for this change in cigarette. To look at both changes in respiratory health and the effect of compensation which might occur when changing cigarette, it was decided to use the three types of cigarette previously described. The measures chosen for assessing change in respiratory health were designed to identify changes in respiratory symptoms, namely cough and phlegm, and in lung function, namely measuring peak expiratory flow rates. The period of six months has been shown in previous studies to be sufficient to detect a change in respiratory symptoms.¹¹

Because an observational study comparing high and low tar smokers may be affected by selection bias if a smoker's choice of cigarette was affected by any existing symptoms he might have, it was decided to undertake an intervention study where smokers were randomly allocated to one of the three types of cigarette.

National prevalence figures were used to estimate the numbers of male middle tar smokers aged 18-44 years on the electoral registers. The sampling ratios were then calculated accordingly to give the necessary numbers for the trial. The age group 18-44 years was chosen for the study because it is believed that in this age group pathological changes associated with respiratory symptoms or falling peak expiratory flow rate are more likely to be reversible. Using the electoral register as a sampling frame inevitably has some limitations as a proportion of people will have died or moved after the register had been compiled and some people will not have registered at all. If the questionnaires were returned with substituted names in place of the name that had appeared on the electoral register, they were accepted for recruitment if eligible.

Information given on the postal questionnaire from some respondents could not always be used, as insufficient details were sometimes given regarding gender, age, symptoms, or brands, and not all participants enclosed an empty cigarette packet for confirmation of tar level, despite being sent a reminder letter.

In practice we identified almost exactly the number of eligible subjects as predicted, although we slightly overestimated the prevalence of smoking in this group and underestimated the proportion smoking middle tar cigarettes. The number continuing to smoke after the health warning who were willing and eligible to participate in the trial was larger than predicted. Of these, however, 42% withdrew from the trial before they had smoked any of the study cigarettes. It was originally estimated that 50% of participants would complete the trial. In fact 24% of those originally agreeing to participate and 42% of those actually starting the study cigarettes did finish the trial. In view of the higher number starting the trial than originally estimated, the number of participants completing the trial in each of the three cigarette groups was very close to the number initially estimated as necessary to give the statistical analyses sufficient power. Thus while changes in smoking habits overtook the spread of tar product available, it was feasible to conduct a randomised trial. The number of participants starting the trial and compliance were both lower than expected. This did not affect the

Figure 4 Continuation in the trial for each cigarette group. LM = low tar, middle nicotine; MM = middle tar, middle nicotine; LL = low tar, low nicotine

Table IV Characteristics of the 2666 individuals who agreed to participate in the trial. Values are means (SD)

	Did not start the trial (n=1125)	Started the trial (n=1541)	Cigarette groups*		
			LM (n=517)	MM (n=506)	LL (n=518)
Age (years)	30.1 (7.7)	31.9 (7.6)	31.4 (7.7)	31.7 (7.4)	31.4 (7.6)
Age started smoking (years)	16.0 (2.8)	15.9 (2.8)	16.0 (3.0)	15.8 (2.6)	15.9 (2.9)
Tar level of usual cigarette (mg/cigarette)	15.4 (1.2)	15.3 (1.2)	15.3 (1.2)	15.2 (1.3)	15.4 (1.1)
Nicotine level of usual cigarette (mg/cigarette)	1.4 (0.12)	1.4 (0.13)	1.4 (0.13)	1.4 (0.13)	1.4 (0.12)
Cigarettes consumed per day	18.9 (8.6)	20.0 (8.5)	20.3 (8.9)	19.9 (8.5)	19.9 (8.1)
Prevalence of respiratory symptoms (MRC questionnaire)	47%	46%	46%	47%	46%

*For those starting the trial
LM = low tar, middle nicotine; MM = middle tar, middle nicotine; LL = low tar, low nicotine

study design but it confirmed that extension of the study beyond six months was not viable. Reasons for withdrawing from the trial included participants moving, disliking the trial cigarettes, objecting to being visited every fortnight, and finding it inconvenient to buy a fortnightly cigarette supply. Participants were allowed to pay for their cigarettes in arrears if a large outlay initially caused them financial hardship. If the participant had not paid any money for five consecutive visits or ran up a debt of £50 and was not willing to pay some of the cost, he was no longer supplied with trial cigarettes. This was not a large problem however and only 1% of the value of distributed cigarettes was not recovered by the end of the trial.

There were several practical aspects to consider in conducting a multicentre trial on this scale. Training had to take place at several centres, at staggered intervals of time for both the recruitment and trial stages. This was mainly for administrative reasons. However, 299 fieldworkers were employed for the recruitment stage and 186 for the trial stage and it would have been impossible to train such numbers adequately at the same time with the number of researchers available. It was necessary to ensure quality control also for the multicentre trial and the fieldworkers' work was checked locally by the team leader and also centrally by the central office.

Ethical approval was sought for this study, which is accepted medical practice for intervention trials, even though in this study participants were not asked to smoke cigarettes with higher tar levels than their usual cigarette and they had resisted advice to give up smoking following the health warning. The nature of this trial involved contacting a large number of district health authorities. Although the same protocol was sent to each, the response varied from approval to rejection without explanation. This may reflect

the varied approach taken by their ethics committees to this study and suggests that guidelines for assessing medical research should be uniform.

This study shows the feasibility of conducting a large nationwide randomised controlled trial and despite the need for large initial numbers and considerable withdrawal from the trial, sufficient numbers of volunteers were recruited for and completed the trial to detect changes in respiratory health, if present, with reasonable confidence.

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