Cancer Causes and Control, 2, 239 - 246

A randomized trial of smoking cessation interventions in general practice in Italy

Nereo Segnan, Antonio Ponti, Renaldo N. Battista, Carlo Senore, Stefano Rosso, Stanley H. Shapiro, and Daniela Aimar

(Received 23 April 1991; accepted 1 May 1991)

The purpose of this study was to examine the effectiveness of different practice-based approaches to assist patients of primary care physicians to quit smoking and sustain cessation. Forty-four nonsmoking general practitioners volunteered for the study. After a period of training, they randomized 923 smoking clients, unselected for motivation toward quitting, to four different intervention groups: (i) minimal intervention, consisting of one single counselling session and a brief handout on quitting techniques; (ii) repeated counselling including reinforcing sessions at Months 1, 3, 6, and 9; (iii) repeated counselling and use of nicotine gum; and (iv) repeated counselling and spirometry. Biochemically validated smoking status was assessed at six and 12 months after recruitment. The proportion of verified quitters at 12 months was 4.8 percent among subjects randomized to the minimal intervention group, compared to 5.5 percent, 7.5 percent, and 6.5 percent among those randomized to the three repeated-counselling groups. In no treatment group was the outcome significantly different from that for one-time counselling at the ($P < 0.05$) level. Lack of power, contamination, and low attendance at reinforcing sessions should be taken into account in interpreting the results.

Key words: Biochemical verification, counselling, general practice, Italy, nicotine gum, randomized trial, smoking cessation, spirometry.

Introduction

The strong association between cigarette smoking and increased morbidity and mortality from respiratory, cardiovascular, and neoplastic diseases is well documented[1] and makes smoking an important public health problem.

Some interventions that have been proposed to curtail tobacco-use employ a community approach,[2] while others are targeted to individuals through clinical encounters.[3-5] The privileged position of primary care physicians in prevention has been recognized by many.[6] Studies from some countries indicate that 70 percent of patients in the average practice see their doctor at least once a year and 90 percent at least once every five years.[7] Several randomized, controlled trials suggest that physician intervention has a positive impact on the cigarette-smoking behavior of patients.[8-18] An overview of 39 such trials[19] evaluated the key elements of a smoking cessation intervention;

Drs Segnan, Ponti, Senore, and Rosso, and Ms Aimar are with the Epidemiology Unit, USL TORINO I, via S. Francesco da Paola 31, 10123 Torino, Italy. Dr Battista is in the Departments of Epidemiology and Biostatistics, of Family Medicine, and of Medicine, McGill University and the Division of Clinical Epidemiology, Department of Medicine, Montreal General Hospital. Dr Shapiro is in the Department of Epidemiology and Biostatistics, McGill University, Montreal, Quebec, Canada. Address correspondence to Dr N. Segnan. *This study was financed by a Health Education grant from the Piedmont Health Authority (Adm. Act 4195/41/86). Dr Battista is a Research Scholar of the National Health Research and Development Program, Ottawa, Canada.*

face-to-face advice followed by reinforcing sessions were identified as important components of success.

In Italy, 46 percent of males and 18 percent of females aged 14 years or older smoke. While the prevalence for males is relatively stable across the country, that for females varies; in Turin, 27 percent of women aged 14 or over are current smokers.[20] All residents of Italy are entitled to the service of primary care physicians (GPs) within the National Health Service. GPs practice on a capitation basis and are responsible for a defined group of individuals. They provide free and accessible primary care and act as gatekeepers to specialists and hospital care. The purpose of our study was to examine the effectiveness of different GP-based approaches to assist patients to quit smoking and sustain cessation.

Methods

Forty-four nonsmoking GPs, each having at least 400 individuals on his or her list, participated in the trial on a voluntary basis. They agreed to recruit male and female patients from 20 to 60 years of age who were smokers and free of any life-threatening disease.

Four interventions were delineated, none of which entailed any charge to the patient:

(i) *Minimal intervention.* This consisted of one session of face-to-face counselling on the day of the patient's recruitment. An explanatory brochure was provided to the patient during the session;

(ii) *Repeated counselling (RC).* Subjects recruited to this group were to receive the same counselling as the first group, but also were invited to follow-up appointments at months 1, 3, 6 and 9, when the antismoking message would be reinforced. The appointment dates were recorded by the physician on the brochure provided to the patient. Patients were also reminded of their return visits by a telephone call two days before the appointments. This call was made only to subjects who had attended the previous return visit;

(iii) *RC plus nicotine gum.* On the first visit, subjects were instructed by the doctor on the correct use of the drug, including the advised daily dose. The gum was provided in a quantity sufficient to last until the first follow-up visit. On that occasion, more gum could be given, but subjects were recommended not to use it for a period longer than three months;

(iv) *RC plus spirometry.* Subjects received a written prescription and were asked to set an appointment for a spirometric test in a specialized center of the National Health Service. The report form showed an estimate of the 'lung age' of the subject.[21] The physician was expected to discuss the result with the patient at the follow-up visit, stressing the need to maintain lung function or not to damage it further.

Participating physicians attended two three-hour training sessions; one was given by experts in interpersonal communication to introduce counselling techniques, the other was devoted to the organizational aspects of the study. Another session was offered three months after the beginning of the study; this was attended by 40 percent of the participating GPs.

Physicians scheduled recruitment on specific days of the week. At that time, the GPs were to offer recruitment to all eligible subjects who came to their office, following a predetermined randomized sequence of the four interventions. A package of closed, numbered envelopes containing the material pertaining to the interventions was provided to each GP at the beginning of the study. The envelopes were indistinguishable from the outside and blocked treatment-allocation was based on a sequence of random numbers. The research staff checked physicians' compliance with the procedure for assignment by comparing envelope numbers and dates of recruitment. Physicians requested subjects' informed consent before randomization.

Interventions started immediately after recruitment. Recruitment lasted from February to October 1988. Shortly after recruitment, the subjects were contacted by telephone by trained interviewers, independent of the study staff, and questioned about their smoking habits and other characteristics. Two additional telephone interviews were performed at months 6 and 12 after recruitment to collect information about subjects' smoking status, compliance with the intervention, and changes from baseline characteristics.

The primary outcome of the study was biochemically verified smoking-cessation at 12 months after recruitment, sustained for at least three months before the follow-up interview. Self-reported smoking status was validated by determination of urinary cotinine levels. Subjects who reported they had quit smoking at least one week before the sixth-month and twelfth-month interviews were asked to provide a urine sample. Samples were taken at the research center an average of one or two weeks after self-reported smoking cessation. A home visit was also offered.

Analyses of cotinine concentration were performed by radioimmunoassay and were validated for a sample of one-fifth by gas chromatography. Cotinine values

Table 1. Selected characteristics of the 44 participating physicians, compared with a sample of all Turin general practitioners

Variable	Study GPs		Sample of all GPs[a]	
	n	%	*n*	%
Age				
< 40	28	63.6	114	50.7
⩾ = 40	16	36.4	111	49.3
Sex				
Male	34	77.3	189	84.0
Female	10	22.7	36	16.0
Smoking habits				
Current smoker	0	0.0	77	34.2
Ex-smoker	17	38.6	52	23.1
Never smoker	24	54.6	80	35.6
Missing	3	6.8	16	7.1
Number of patients in their list				
⩽ = 400	0	0.0	46	20.4
401 - 800	15	34.1	86	38.2
801 - 1500	20	45.5	56	31.3
> 1500	9	20.4	37	20.7

[a] Random sample of 225 general practitioners (GPs), drawn in the Spring of 1986 from the file of all Turin GPs (n = 1,158). Data on smoking habits were obtained by personal interviews, while information on age, sex and number of clients are kept on the larger file for administrative purposes.

were adjusted by computing cotinine/creatinine ratios, standardized to creatinine excretion and urine flow.[22] Based on the shape of the distribution of cotinine/creatinine ratios and on experiences of cotinine determination in larger data sets[23,24] the cut-off value for distinguishing current smokers from quitters was set at 100 ng/mg.

Completeness of recruitment and follow-up interviews

A total of 923 subjects were randomized to the four treatment groups. Eighty-six subjects refused recruitment. For most physicians, the number of subjects recruited was considerably lower than anticipated: 52 percent of GPs recruited less than 20 smokers; 41 percent recruited 20-39; and only three GPs (seven percent) recruited 40 or more subjects. The initial telephone interview subsequent to recruitment was carried out for 91 percent of the 923 subjects (six percent refused, three percent could not be traced), while follow-up interviews at months 6 and 12 were completed for, respectively, 91 percent (two percent refused, seven percent were untraced) and 87 percent (six percent refused, seven percent were untraced) of subjects.

Physicians' and subjects' characteristics

Selected characteristics of physicians who volunteered for the study are reported in Table 1, along with those of a random sample of all GPs practising in Turin. The volunteers included a slightly larger proportion of younger and female physicians. The Table also shows differences by smoking habits and number of clients.

In Table 2, characteristics of patients are presented by treatment group. The database covering all persons enlisted in any National Health Service general practice provided data on age and sex for all recruited subjects. The remaining information was obtained by telephone interview. Data show similar distribution by treatment for all variables, including potential confounders such as smoking habits, number of previous attempts to quit, and health status. Although eligibility criteria included ages 20-60, 44 recruited subjects were either younger (seven subjects) or older (37 subjects), but were retained in the analysis.

Content of interventions

The sixth-month questionnaire asked subjects what their physician prescribed during the recruitment visit (Table 3). Seventy-five percent of subjects randomized to the minimal intervention group (MI) reported receiving only the advice to quit. Physicians proposed the correct interventions, according to subjects' reports, in 67 percent of the cases in the repeated counselling group (RC) and in 93 percent and 84 percent, respectively, in the nicotine gum (RCN) and spirometry (RCS) groups. In the MI group, however,

Table 2. Subjects' characteristics by randomized treatment group, and proportion of subjects by level of the variables considered

Variable	Treatment groups (%)			
	Minimal intervention $n = 62$	Repeated counselling $n = 275$	Nicotine gum[a] $n = 294$	Spirometry[a] $n = 292$
Age				
< 31	12.9	21.8	23.5	18.5
31 - 40	25.8	27.3	21.8	28.8
41 - 50	37.1	26.2	30.3	27.4
> 50	24.2	24.7	24.5	25.3
Gender				
Female	32.3	39.6	36.7	40.1
Male	67.7	60.4	63.3	59.9
Education[b]				
≤ 5th grade	30.2	25.5	25.7	29.6
6th - 12th grade	45.3	48.2	48.9	42.7
≥ 13th grade	24.5	26.3	25.4	27.7
Marital status[b]				
Ever married	88.7	77.3	79.8	83.5
No. cigarettes smoked daily[b]				
≤ 10	14.8	18.3	19.9	15.2
11 - 20	63.0	52.4	47.6	57.8
> 20	22.2	29.3	32.6	27.0
No previous attempts to quit				
0	35.2	34.8	36.1	35.2
1	25.9	29.2	27.5	25.1
≥ 2	38.9	36.0	36.4	39.7
Symptoms related to smoking[b]				
Any	51.9	51.4	50.9	52.3
Self-perceived health				
Excellent	13.2	16.6	17.8	14.6
Good	43.4	38.9	45.0	39.3
Fair	37.7	36.8	28.6	37.5
Poor	5.7	7.7	8.6	8.6

[a] In combination with repeated counselling.
[b] Missing values: (MI) 1 for education, marital status, and self-perceived health; (RC) 1 for number of cigarettes; (N) 1 for education and marital status and 2 for number of cigarettes; (S) 4 for number of cigarettes and 1 for symptoms and self-perceived health.

Table 3. Percentage of physicians' compliance with the study protocol, according to subjects' reports, by treatment group

Prescription	Treatment group[a]			
	MI ($n = 60$)	RC ($n = 257$)	RCN ($n = 268$)	RCS ($n = 264$)
Advice to quit, only	75.0	24.5	1.9	8.3
Follow-up visits, only	10.0	67.3	4.5	2.7
Follow-up visits + gum	15.0	7.8	92.5	1.1
Follow-up visits + spirometry	0.0	0.4	0.4	83.7
Follow-up visits + spirometry + gum	0.0	0.0	0.7	4.2
	100.0	100.0	100.0	100.0

[a] Missing values by group are 1 for minimal intervention (MI) and repeated counselling and nicotine gum (RCN), 3 for repeated counselling (RC), and 6 for repeated counselling and spirometric test (RCS).

25 percent of the subjects were told to return for further counselling. Nicotine gum was prescribed in more than one-half of these cases. In the RC group, on the other hand, 25 percent did not mention any prescription of follow-up visits and eight percent reported prescription of gum or spirometry.

According to the study protocol, physicians were supposed to set a specific date for follow up and write the time and date in the study leaflet given to the subject. Among subjects who were invited to see the doctor again, according to their recollection, physicians complied fully with the protocol in 53 percent (RCS), 58 percent (RCN) and 66 percent (RC) of the cases. In 29 percent (RCS), 17 percent (RCN) and nine percent (RC) of the cases, no appointment was made and the subject was only generically invited to come back for follow-up visits.

Subjects' compliance with interventions

Two sources of information are available: physicians' records of the follow-up visits for the treatment groups, and subjects' reports from the sixth-month and twelfth-month interviews for both the treatment groups and the MI group.

According to both physicians' and subjects' reports, the RCN group was characterized by a slightly greater number of follow-up visits. According to physicians' reports, little more than one-third of subjects in the three treatment groups with follow-up visits had at least two of the three follow-up visits that they could potentially attend during the six months following recruitment. On the other hand, 54 percent of subjects in the MI group reported never having discussed smoking with their doctor during the six months following recruitment, compared with 31 percent (RCN), 37 percent (RC), and 38 percent (RCS) in the other three groups. Also, 38 percent of subjects in the MI group discussed smoking with their doctor at least twice during the same period, compared to 45 percent (RCS), 46 percent (RC), and 52 percent (RCN) of subjects randomized to groups with scheduled reinforcing sessions.

Examination of physicians' records showed that when patients claimed not to have received a prescription for nicotine gum (24 subjects), the doctor had recorded some conditions contradicting use of the gum (cardiovascular problems, peptic ulcer, dental prosthesis). No such information was available for 19 subjects reporting not to have had a prescription of spirometry. Information on refusals was taken from physicians' records and is concordant with subjects' reports.

Eighty-five percent of subjects in the nicotine-gum group who received the prescription tried the gum; of the same group of subjects, 55 percent reported having taken at least one gum per day for one or more weeks. Of the 133 subjects who reported having taken nicotine gum for at least one week, 21 percent took the gum for just one week, 34 percent took it for more than one month, and 45 percent for an intermediate period of time. The average number of pieces of gum consumed per day by these subjects was 4.8.

One hundred and twenty-four subjects in the spirometry group (50.2 percent of those who had the test prescribed) reported having had the spirometry for which they were referred. For 111 of these, taking of the test was confirmed by the testing center.

Results

Smoking cessation rates at 12 months are presented in Table 4. They range from 4.8 percent (MI) to 7.5 percent (RCN). No difference is significant at the 0.05 level.

Two subjects could not be traced at one-year follow-up because of death, and six because of serious illnesses. Exclusion of these subjects from the analysis does not change the results.

Cessation rates at six months are higher than at twelve months in three of four groups and are reported in Table 5.

On average, the prevalence of self-reported quitting at the sixth-month and twelfth-month follow-up was about twice the prevalence of ex-smokers after biochemical validation. For example, at one-year follow-up, 128 subjects (16 percent) reported smoking cessation, but 44 refused the test, nine relapsed before biochemical verification, and 11 had a cotinine value above the cut-off level.

Table 4. One-year prevalence of biochemically verified smoking-cessation by treatment group

	$n1$[a]	$n2$[b]	%	CI[c]
Minimal intervention	62	3	4.8	1.0 - 13.5
Repeated counselling	275	15	5.5	2.6 - 8.4
Repeated counselling plus nicotine gum	294	22	7.5	4.3 - 10.7
Repeated counselling plus spirometry	292	19	6.5	3.5 - 9.5
Total	923	59	6.4	4.8 - 8.0

[a] $n1$ = number of subjects randomized to each treatment group.
[b] $n2$ = number of validated quitters.
[c] CI = 95% confidence interval.

Table 5. Number and proportion of validated quitters by randomized treatment group at the six-months follow-up

	$n1$[a]	$n2$[b]	%	CI[c]
Minimal intervention	62	3	4.8	1.0 - 13.5
Repeated counselling	275	16	5.8	2.9 - 8.7
Repeated counselling plus nicotine gum	294	23	7.8	4.6 - 11.0
Repeated counselling plus spirometry	292	23	7.9	4.6 - 11.2
Total	923	65	7.0	5.3 - 8.7

[a] $n1$ = number of subjects randomized to each treatment group.
[b] $n2$ = number of validated quitters.
[c] CI = 95% confidence interval.

Discussion

The outcome in no single treatment group differed significantly from that in the MI group. Nevertheless, in all three repeated counselling groups, a higher rate of smoking cessation was observed compared to MI, with ratios of 1.2, 1.4, and 1.6, respectively. The power of the study was much lower than anticipated.

Combining repeated counselling with nicotine gum or spirometric testing did not result in an important difference in smoking cessation rates in our study. Cessation rates in the RCN group are the highest, but the 95 percent confidence interval is wide (four to 11 percent).

Comparisons of results with randomized studies conducted in general practice in different countries,[8-18] employing partially different designs, are difficult for a number of reasons. First, one should take into account that cessation rates in the Italian general population are lower, especially among females, than in most other industralized countries.[25] In 1986, we interviewed a random sample of 1,421 persons in Turin about their smoking habits. Three percent and four percent, respectively, of ever-smokers reported to have quit smoking at an age equal to or one year younger than their current age. Our trial also was specifically designed, in contrast to some of the cited studies,[12,13,15,17] to assess the effect of physicians' advice to a population not selected for its motivation to quit smoking. Furthermore, in our study all unverified self-reported quitters have been counted as continuing smokers, and a further requirement of three months' abstinence has been applied.

The proportion of reported quitters who were validated biochemically varies from 47 percent to 53 percent in the four groups. Although attempts to enhance attendance included positive advice by the subject's physician, several reminders, and the offer of free parking, it may be that some of the refusers were true quitters. Our study had the greatest number of subjects tested for biochemical verification among the trials cited above, and both attendance and deception rates fall within the range of other studies.

Compliance (Table 3) was low in the RCN and RCS groups, while one-third of subjects in the RC group and one-fourth in the MI group reported that physicians did not comply with prescriptions of the protocol. Moreover, repeated counselling groups had a greater number of visits to the doctor during which smoking was discussed, but the difference was not as high as one might have expected: only about 50 percent more subjects did not have any such visit in the minimal intervention group in comparison with the other groups. If this had any effect on the results of the study, it would have diminished the difference in cessation rates between MI and the other groups. Table 3 also shows that a larger number of subjects randomized to simple repeated counselling do not recall the advice to return, even if attendance at follow-up visits does not show the same pattern.

An additional analysis was performed taking into consideration the treatments which subjects reported receiving, rather than those to which they had been randomized. Among the 106 subjects who reported to have received MI only, regardless of the group to which they had been randomized, only three (three percent) were validated quitters at 12 months. Potential selective recall by subjects or selective contamination of treatment groups by physicians may be responsible for the low quit-rate in this group.

Only two of the previous studies reviewed report data on compliance. Wilson[16] reported that subjects randomized to nicotine-gum treatment recalled receiving the prescription from the physician in 59 percent, and in 63 percent, of the cases in two treatment groups. In the same study, physicians' adherence to the protocol in prescribing return visits was 83.3 percent. Russell[14] reported that in ten percent to 16 percent of the cases in three different intervention groups, physicians did not follow the correct study procedures.

Compliance with return visits and lung function testing was particularly low in this experience; less than 40 percent of subjects attended at least two return visits (less than reported by most other studies), and 50 percent complied with the spirometric test. As was found in other trials,[12,16] those who attended more return visits also had higher cessation rates.

Compliance with nicotine-gum use, on the other hand, was higher than compliance levels reported by other authors, with the exception of Fagerström,[15] who had 90 percent compliance. In our study, the gum

was handed out directly by the doctor, which possibly enhanced compliance. No comparison is possible for the spirometric test, but it should be noted that compliance has been reported to be very low every time the prescribed intervention required a visit outside the physician's office, such as attending smoking cessation classes[18] or a health visitor.[9] Within the spirometry group, those who did not have the test had a lower cessation rate than compliers. On the other hand, within the nicotine group, excluding subjects presenting contraindications, the small group of those who did not try nicotine gum did better than those who tried it.

Of the five reviewed trials evaluating nicotine gum prescription,[12-16] two put contraindications for the use of the gum in the exclusion criteria.[12,13] We did not ask GPs to take these contraindications into account at the time of recruitment. The physicians judged that 24 percent of subjects randomized to the nicotine-gum group had contraindications for the use of the drug and did not prescribe the gum to them. In the analysis, we maintain these subjects in the nicotine-gum group: eight (33 percent) self-reported smoking cessation at 12 months, but only two (eight percent) were biochemically verified quitters. We believe that the exclusion of contraindications for nicotine-gum from the eligibility criteria is not likely to have substantially diluted the effect of the nicotine-gum treatment.

The authors of a recent trial on smoking cessation,[26] designed to evaluate the effect of different degrees of physicians' involvement, pointed out the need for intensive physician training to individualize interventions, to increase the number of cessation attempts by patients, and particularly to prevent relapse. Our training program for participating GPs focused on specific objectives: (i) to individualize communication with patients on smoking and reasons to quit; (ii) to propose a quit-date for those who agree to try; (iii) to discuss problems encountered if attempts fail and discuss individual strategies to prevent relapse, before and after cessation had been accomplished. The less than anticipated success of interventions may be partially due to the short duration of training. Moreover, any effect of physicians' training is diluted by the fact that control subjects had the same initial intervention in terms of counselling as those in the other groups.

Despite its limitations, the present study is consistent with the view that repeated counselling by general practitioners has a positive effect on cessation rates among their clients. To the best of our knowledge, this is the first such trial conducted in Italy, and it has shared the same methodologic problems encountered by similar studies in Canadian, British, and Australian general practice settings.

Acknowledgements—The authors gratefully acknowledge the support of SIMG (Italian Association of General Practice) as well as the advice of Drs G. Ventriglia and M. Nejrotti and the contribution of all physicians involved in this trial. Particularly useful contributions came also from Drs S. Quadrino, P. G. Maggiorotti, and W. Arossa. Dr G. Scherer of the Analytisches Forschungslabor in Munich, Germany, Dr P. Voria of the Ospedale Maggiore San Giovanni A. S. in Torino, Italy, and Dr R. Puntoni of the Laboratory of Clinical Physiology of the Italian Research Council in Pisa, Italy, performed the urine analyses for biochemical verification of smoking status. Serono SPA provided the nicotine gum used in the study. The Anti-Smoking Committee of the Municipality, Torino, and ACI (Automobile Club Italiano) also helped in various ways. The authors are grateful to Dr P. Ernst for his input at an earlier stage of the study and to Ms Azana Endicott and Ms Diane Telmosse for technical assistance.

References

1. Fielding JE. Smoking: health effects and control. *N Engl J Med* 1985; **313(8)**: 491-555.
2. Bettinghaus EP. Using the mass media in smoking prevention and cessation programs: an introduction to five studies. *Prev Med* 1988; **17**: 503-621.
3. Pederson L. Compliance with physician advice to quit smoking: a review of the literature. *Prev Med* 1982; **11**: 71-84.
4. Ockene JK. Smoking intervention: the expanding role of the physician. *Am J Publ Health* 1987; **77**: 782-3.
5. Greene HL, Goldberg RG, Ockene JK. Cigarette smoking: the physician role in cessation and maintenance. *J Gen Intern Med* 1988; **3**: 75-87.
6. Roemer MI. The value of medical care for health promotion. Commentary. *Am J Publ Health* 1984; **74**: 243-8.
7. Kohn R, White KL, eds. *Health Care, an International Study: Use of Physician Service*. Geneva: World Health Organization, 1979.
8. Russel MAH, Wilson C, Taylor C, Baker CD. Effect of general practitioner's advice against smoking. *Br Med J* 1979; **2**: 231-5.
9. Jamrozik K. Vessey M, Fowler J, Wald N, Parker J, Vunakis HV. Controlled trial of three different antismoking interventions in general practice. *Br Med J* 1984; **288**: 1499-502.
10. Wilson D, Wood G, Johnston N, Sicurella J. Randomized clinical trial of supportive follow-up for cigarette smokers in family practice. *Can Med Assoc J* 1982; **126**: 127-9.
11. Richmond RL, Webster IW. A smoking cessation programme for use in general practice. *Med J Austr* 1985; **142**: 190-4.
12. Marshall A, Raw M. Nicotine chewing gum in general practice: effect of follow-up appointments. *Br Med J* 1985; **290**: 1397-8.
13. Jamrozik K, Fowler G, Vessey M, Wald N. Placebo

controlled trial of nicotine chewing gum in general practice. *Br Med J* 1984; **289**: 794-7.
14. Russell MAH, Merriman R, Stapleton J, Taylor W. Effects of nicotine chewing gum as an adjunct to general practitioner's advice against smoking. *Br Med J* 1983; **287**: 1782-5.
15. Fagerström KO. Effects of nicotine chewing gum and follow-up appointments in physician based smoking cessation. *Prev Med* 1984; **13**: 517-27.
16. Wilson DM, Taylor DW, Gilbert RJ, *et al.* A randomized trial of a family physician intervention for smoking cessation, *JAMA* 1988; **260**: 1570-85.
17. Porter AMW, McCullough DM. Counselling against cigarette smoking. A controlled trial from a general practice. *The Practitioner* 1972; **209**: 686-9.
18. Thompson RS, Michnich ME, Friedlander L, Gilson B, Grathaus LC, Staser B. Effectiveness of smoking cessation interventions integrated into primary care practice. *Med Care* 1988; **26**: 62-76.
19. Kottke TE, Battista RN, DeFriese GH, Brekke ML. Attributes of successful smoking cessation interventions in medical practice: a meta-analysis of 39 controlled trials. *JAMA* 1988; **259**: 2883-9.
20. Istituto Centrale di Statistica. Indagine statistica sulle condizioni di salute della popolazione e sul ricorso ai servizi sanitari. *Notiziario ISTAT* 1987; **8**: 17.
21. Morris JF, Temple W. Spirometric 'lung age' estimation for motivating smoking cessation. *Prev Med* 1985; **14**: 660-2.
22. Haley NJ, Colosimo SG, Axelrad CM, Harris B, Sepkovic DW. Biochemical validation of self-reported exposure to environmental tobacco smoke. *Environmental Research* 1989; **49**: 127-35.
23. Haley NJ, Axelrad CM, Tilton KA. Validation of self-reported smoking behavior: biochemical analyses of continine and thiocyanate. *Am J Publ Health* 1983; **73**: 1204-7.
24. Riboli E, Preston-Martin R, Saracci R, *et al.* Exposure of nonsmoking women to environmental tobacco smoke: a 10-country collaborative study. *Cancer Causes and Control* 1990; **1**: 243-52.
25. Negri E, La Vecchia C. Determinants of stopping smoking in Italy: Italian National Health Survey. *Am J Publ Health* 1989; **79**: 1307.
26. Kottke TE, Brekke ML, Solberg LI, Hughes JR. A randomized trial to increase smoking interventions by physicians: doctors helping smokers quit, round I. *JAMA* 1989; **261**: 2101-6.