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Autor: Wynder, Ernst L. / Hoffmann, Dietrich

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American Health Foundation, Naylor Dana Institute for Disease Prevention, New York

SMOKING AND HEALTH: PATHOGENIC AND PREVENTIVE CONSIDERATIONS*

ERNST L. WYNDER and DIETRICH HOFFMANN

Introduction

Although a symposium on smoking, alcoholism, and the maintenance of health obviously must address the issue of pathogenesis of disease development, its primary focus should be on how to avoid, modify exposure to, or reduce the deleterious health impact on such factors. Too little emphasis has been given to the preventive aspects of disease, while evidence continues to show that tobacco usage and excessive alcohol consumption significantly contribute to human illness.

In order to determine which cigarette smoke components must be reduced to decrease health hazards and to understand more fully how the consequences of alcoholism can be diminished, it is necessary to define the role of various tobacco smoke constituents with respect to specific diseases, and to study the synergistic effects of alcoholism and tobacco on the development of tobacco-related cancers and other diseases. This presentation summarizes available evidence relating specific tobacco smoke components to cancer, cardiovascular disease, and chronic obstructive pulmonary disease. The use of this evidence in the development of less harmful cigarettes is also discussed, although it is emphasized that the incidence of tobacco-related diseases for adults is best reduced by smoking cessation and that children should be convinced not to begin the habit.

Prevention of the Smoking Habit in Children

It has been the unfortunate experience in most countries that the smoking habits of adolescent boys have not decreased over the years, whereas smoking among girls of these ages has increased. During the six years, covered by the most recent DHEW survey, smoking among

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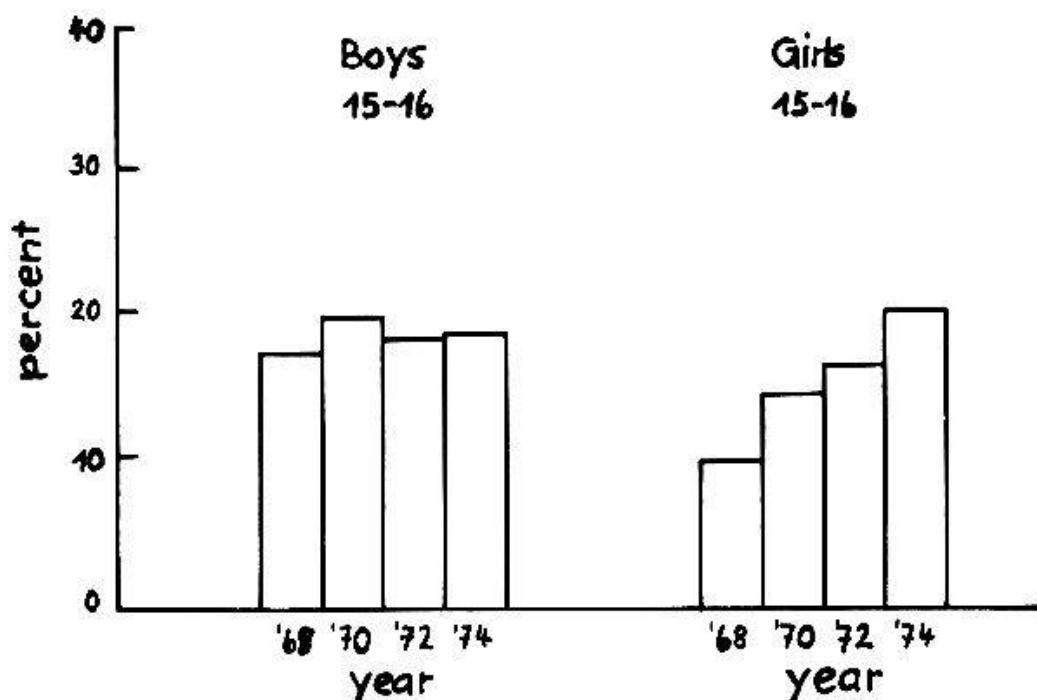


Fig. 1. Percent current regular smokers-teenage, 1968-1974.

boys (i.e., smoking one cigarette per week or more) has changed very little, while a gradual, but steady, increase in the proportion of smokers among the girls has led to the point where girls are smoking about as much as boys (Fig. 1) (1).

This finding reflects the relative ineffectiveness of current programs which attempt to educate children about the dangers of smoking. Such programs have had no appreciable impact, in part because a child finds it difficult to personally evaluate a future-oriented message, particularly one dealing with future health. The youngster's ability to cope with the various social influences compelling him to smoke (e.g., influences from family, friends, and the media), rather than lengthy lectures, will affect his decision. Thus, one of the basic tenets, accepted by the American Health Foundation, is that health education must be more than imparting information; it also must involve the active participation of the group being addressed. This belief is reflected in our Know Your Body ("KYB") program, directed toward the identification of risk factors for chronic diseases currently existing in children. This program combines the child's level of health knowledge, with reports of his/her health habits (including smoking and drinking), and the measuring of blood pressure, cholesterol, height and weight, and physical fitness. The test results are reported to the children, who record their specific data on individual Health Passports (Fig. 2) - a procedure which allows them to experience a personal involvement with their own health and/or risk factor scores. KYB, through an activistic health education and intervention program, involves also the teachers,

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<p>Sam Smith 301 Jones St. New York, New York JAN 10, 1964</p> <p>Dr. O'Reilly Hospital Pediatric Clinic</p> <p>741-4811 566-3488 561-6321</p>		<table border="1"> <tr><td>DATE</td><td>1/13/76</td></tr> <tr><td>AGE</td><td>7</td></tr> <tr><td>SEX</td><td>12</td></tr> <tr><td colspan="2">GENERAL</td></tr> <tr><td>WEIGHT</td><td>62 1/2"</td></tr> <tr><td>HEIGHT</td><td>123 1/2"</td></tr> <tr><td>BLOOD PRESSURE</td><td>100/60</td></tr> <tr><td colspan="2">PULMONARY CAPACITY</td></tr> <tr><td colspan="2">LAB. TESTS</td></tr> <tr><td>CHOLESTEROL</td><td>176</td></tr> <tr><td>HEMOGLOBIN</td><td>41</td></tr> <tr><td>BLOOD SUGAR</td><td>57</td></tr> <tr><td colspan="2">PHYSICAL FITNESS</td></tr> <tr><td>RECOVERY INDEX</td><td>136</td></tr> <tr><td colspan="2">EYE TEST</td></tr> <tr><td>HEARING TEST</td><td>11/75</td></tr> <tr><td colspan="2">DENTAL CHECK-UP</td></tr> <tr><td>HEALTH PASSPORT</td><td>11/75</td></tr> </table>		DATE	1/13/76	AGE	7	SEX	12	GENERAL		WEIGHT	62 1/2"	HEIGHT	123 1/2"	BLOOD PRESSURE	100/60	PULMONARY CAPACITY		LAB. TESTS		CHOLESTEROL	176	HEMOGLOBIN	41	BLOOD SUGAR	57	PHYSICAL FITNESS		RECOVERY INDEX	136	EYE TEST		HEARING TEST	11/75	DENTAL CHECK-UP		HEALTH PASSPORT	11/75
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Fig. 2.

who receive a detailed KYB Teacher's Guide, and the AHF health educators, who actually work with the children in the areas of smoking, nutrition, and exercise.

We are looking forward to a reduction of risk factors. Our results in this area are preliminary, but as can be seen in Fig. 3, fewer children are beginning to smoke in our study schools than in our control schools. Such reduction, of course, will ultimately determine the success of the program.

Similarly, a decrease in the number of overweight students was observed. Among seventh and eighth graders from four schools in the New York area, a significantly greater proportion of the students in the experimental group than in the control group shifted from being overweight to being within the normal weight range for their size, age, and sex (Table 1). In addition, 70 percent of the students in the experimental group had a lower skinfold measurement on the post-test than the pre-test, whereas only 29 (43 percent) of the students in the control group manifested such changes ($\chi^2 = 9.29$, $p < .01$). These data indicate that the personal involvement of the student, working together with teachers, parents, and members of the American Health Foundation, will likely result in a reduction of risk factors, i.e., smoking, weight reduction, etc. We suggest that similar activistic health education programs be implemented in schools around the world.

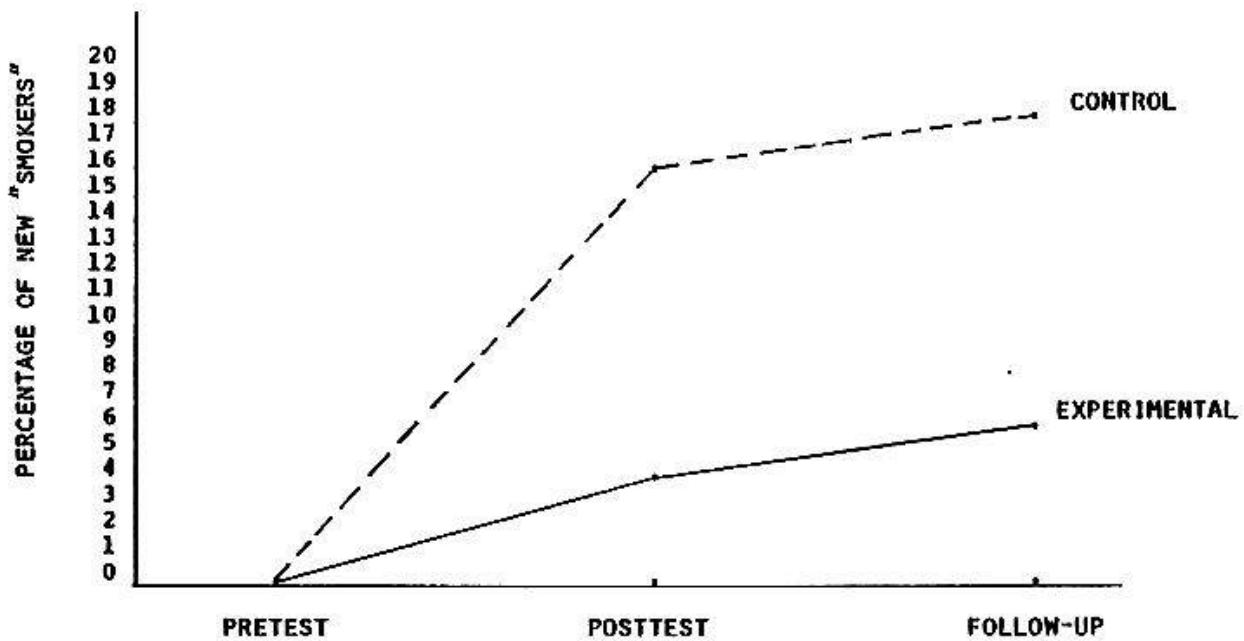


Fig. 3. Percentage of pretest nonsmokers who smoked one or more cigarettes during the month preceding the posttest and the 3 month follow-up.

Table 1. Comparison of Shift from $\geq 130\%$ of Ideal Weight to $<130\%$ of Ideal Weight on Pre- and Post-Screening for Study and Control Students

	Study				Control			
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
	N	%	N	%	N	%	N	%
$\leq 130\%$ of Ideal Weight	14	38	6	17	27	39	24	35
$<130\%$ of Ideal Weight	23	62	31	83	42	61	45	65

While the initial program involved ten to fourteen year olds, a similar program for six year olds is being established. We believe that if we are going to modify the health habits of our children, the awareness of good health practices must begin as early in life as possible.

Smoking Cessation Programs

A significant number of American adults have given up smoking - the percentage is greater in men than in women as is indicated in Fig. 4. Our own epidemiologic data show that, among men, the ability to give up the smoking habits, without professional help, is highly correlated with educational attainment: such an educational gradient for women is not apparent, however (Fig. 5 and 6).

Similar experiences have been reported from other countries. In England, for instance, it has been shown that smoking cessation is greater among physicians than in the general population

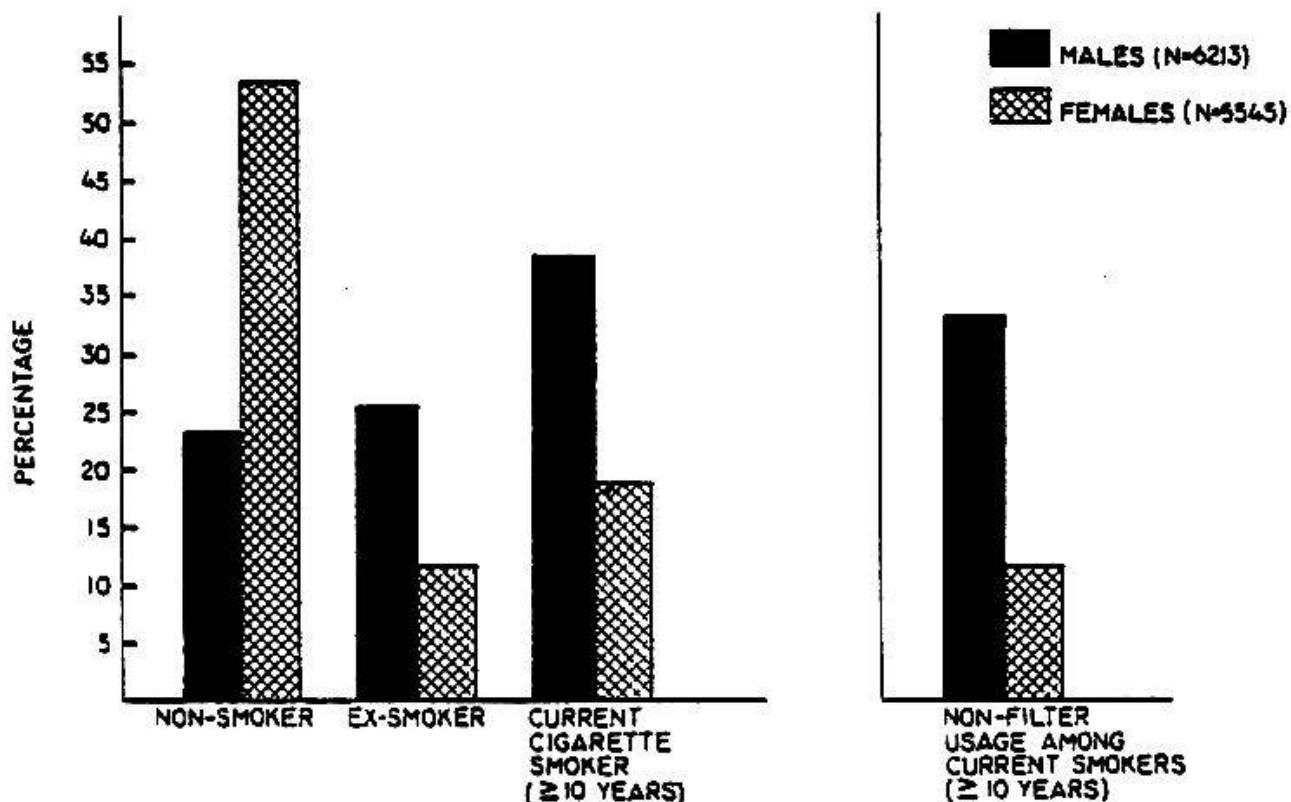


Fig. 4. Smoking habits for male and female controls.

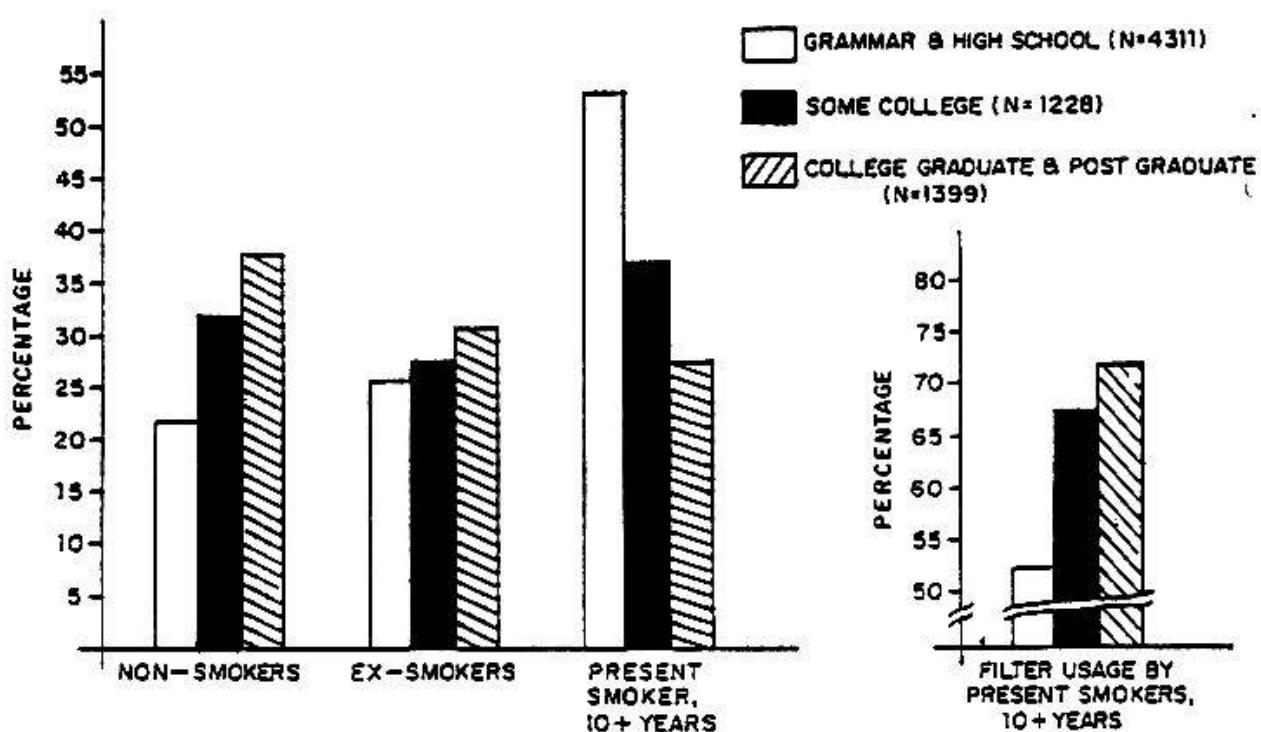


Fig. 5. Distribution of smoking habits of male controls.

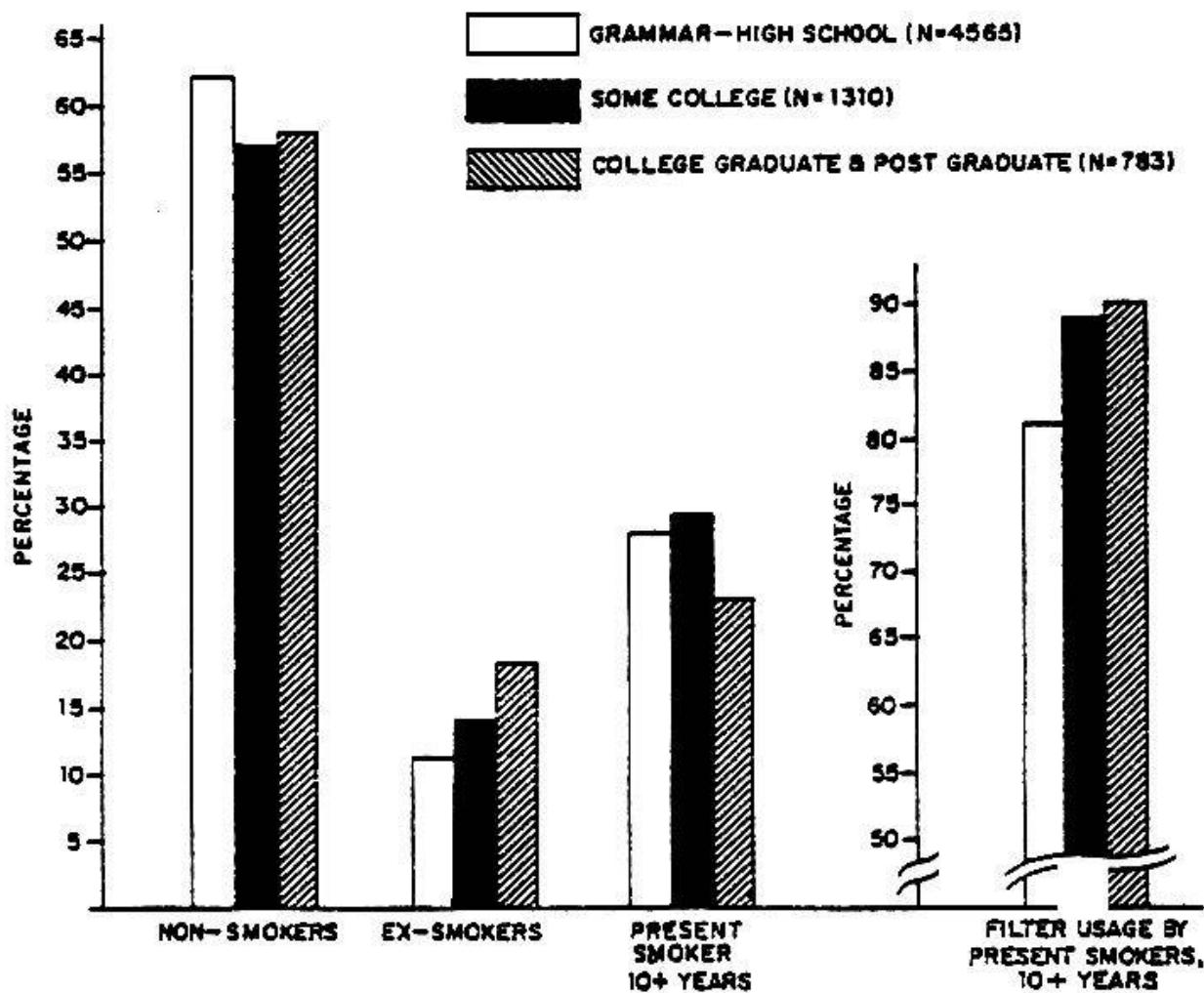


Fig. 6. Distribution of smoking habits of female controls.

(2). These studies indicate that it is possible to give up smoking by oneself and that most ex-smokers who initially experienced withdrawal symptoms can overcome them without any outside help. The willingness or ability to give up smoking is probably not entirely related to education in general and increased health knowledge in particular. Most studies have suggested that nearly all population groups are aware of the health risks associated with smoking. But we believe that among male populations, it is primarily a question of peer pressure. This pressure is less intense or less successful among women, perhaps largely due to the fact that many women are more concerned about the immediate likelihood of gaining weight than about the long-term risk of developing a smoking-related disease. The medical profession's effort to assist patients in smoking cessation has been very disappointing. Whether for economic or academic reasons, physicians make poor health educators in the areas of weight control, excessive alcohol intake, or smoking. In addition, it is disappointing that hospitals, with their many specialty clinics, are rarely involved in successful

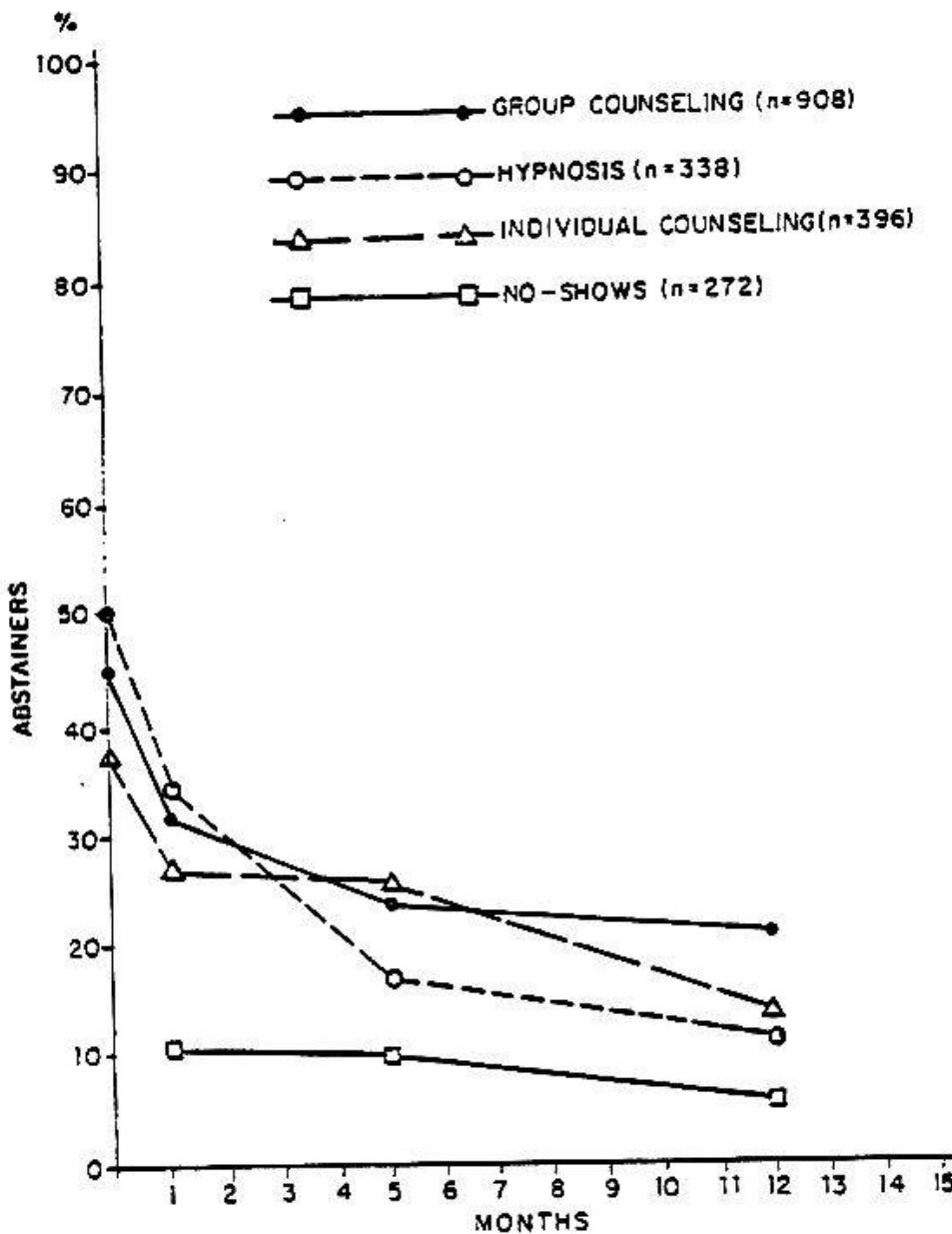


Fig. 7. Results of intensive intervention AHF smoking clinic programs.

smoking cessation programs. And yet, we know that virtually any organized attempt to help an individual quit smoking is a cost-effective procedure. We have shown that group therapy results in approximately a 25 percent success rate for one year (Fig. 7), and in studies where we were able to provide long-term maintenance, the success rate for one year has even risen to 44 percent. This indicates that the success of a smoking cessation program is directly related to its intensity.

While our initial group therapy consisted of seeing participants every week for one and one-half hours, it appeared to be more cost-effective for participants to attend a single

Table 2. Tumor Initiating Agents in the Particulate Phase of Tobacco Smoke*

Compound	Rel. Activity as complete carcinogen**	ng/cig***	References
Benzo(a)pyrene	+++	10-50	4
5-Methylchrysene	+++	0.6	5
Dibenz(a,h)anthracene	++	40	4
Benzo(b)fluoranthene	++	30	4
Benzo(1)fluoranthene	++	60	4
Dibenzo(a,h)pyrene	++	pr	4
Dibenzo(a,i)pyrene	++	pr	4
Dibenzo(a,j)acridine	++	3-10	4,6
Indeno(1,2,3,-cd)pyrene	+	4	4
Benzo(c)phenanthrene	+	pr	4
Benzo(a)anthracene	+	40-70	4
Chrysene	+	40-60	5
Benzo(e)pyrene	+?	5-40	4
2-,3-Methylchrysene	+	7	5
1-,6-Methylchrysene	-	10	5
2-Methyl fluoranthene	+	34	7
3-Methyl fluoranthene	?	40	7
Dibenzo(a,c)anthracene	(+)	pr	8
Dibenzo(a,h)acridine	(+)	0.1	6
Dibenzo(c,g)carbazole	(+)	0.7	6

* Incomplete list; all mentioned compounds are active as tumor initiators on mouse skin.

** Relative carcinogenic activity on mouse skin as measured in our own laboratory on Swiss albino (Ha/ICR/Mil) mice. ? = Carcinogenicity unknown; (+) = not tested in own laboratory.

*** pr = present, but no quantitative data given.

marathon session of 14 hours (3). We realize the difference in the ability to stop smoking for a single day compared to that of long-range cessation. Long-term maintenance, thus, is an important area for any cessation program if it is to excel. The key factor for the success of such programs is to motivate people, and above all, to work with committed and trained health educators who care for their participants on a long-term basis.

If hospitals and communities would incorporate these programs in an organized manner, a high success rate will more likely be achieved.

The "Less Harmful Cigarette"

Considerable research has been done on identifying agents in tobacco smoke that relate to specific diseases (4-36). In tobacco carcinogenesis, a significant number of established animal carcinogens, tumor promoters, accelerators, and co-carcinogens have been identified (Tables 2-4). As can be seen from these data, specific carcinogens may differ for various

Table 3. Cocarcinogenic Agents in the Particulate Matter of Tobacco Smoke*

Compound **	Cocarcinogenic Activity ***	ng/cig.	References
1. Neutral Fraction			
Pyrene (-)	+	50-200 (4)	9,10
Methylpyrenes (?)	?	50-300 (4)	-
Fluoranthene (-)	+	100-260 (4,7)	9
Methylfluoranthene (+;?)	?	180 (7)	-
Benzo(ghi)perylene (-)	+	60 (4)	10
Benzo(e)pyrene (+)	+	30 (4)	10
Other PAH (+)	?	?	-
Naphthalenes (-)	+	360-6300 (4,11)	12
1-Methylindoles (-)	+	830 (13)	14
9-Methylcarbazoles (-)	+	140 (15)	14,16
4,4-Dichlorostilbene (-)	+	1500 (17) §	14,16
Other neutral compounds (?)	?	?	-
2. Acidic Fraction			
Catechol (-)	+	200,000-500,000	10
4-Alkylcatechols (?)		>10,000	-
Other phenols (?)	?	?	-
Other acidic agents (?)	?	?	-

* Incomplete list

** In parenthesis carcinogenic activity on mouse skin; (?) = unknown

***+ = active; ? = unknown

§ Value from 1968 USA cigarette; today values will be lower, because DDT and DDD decreased in the US tobaccos.

cancer sites. While we can never be certain that these compounds are, in fact, responsible for the increased risk of specific cancers, it is desirable that those substances known or suspected to have toxic properties be specifically reduced. There has been an overall reduction in tar yield of cigarettes in the United States and in other countries (Fig. 8). In recent years, efforts have been directed toward reducing tar yields below 10 mg. and nicotine to 0.6 mg., and less. These newer low tar/nicotine cigarettes are increasing in popularity as can be seen by the market share of sales they represent (Fig. 9). In terms of cardiovascular disease, the question remains whether it is carbon monoxide and/or nicotine which relates to the pathogenesis of arteriosclerosis and the development of particular cardiovascular events. Though carbon monoxide has been suggested to increase distress, particularly in those who have a very severe history of angina (37, 38), there is no conclusive evidence that CO relates to cardiovascular attacks in the general population.

ASTRUP et al. showed that carbon monoxide increased atherosclerosis in cholesterol-fed rabbits (39-41). BIRNSTINGL and associates (42) also found this effect, and WEBSTER et al. showed similar effects with squirrel monkeys (43). In a repeat study, however, ASTRUP et al.

Table 4. Organ Specific Carcinogens in Tobacco Smoke Particulates*

Carcinogen	Conc/cig. **	Carcinogenicity ***
1. Esophagus		
N-Nitrosornicotine	137 ng (18)	+ (19)
Nitrosopiperidine	0-9 ng (20)	(21,22)
Unknown unsymmetrical nitrosamines	?	+ (21,22)
2. Lung		
Polonium-210	0.03-1.3 pCi (4,23)	+ (24)
Nickel compounds	0-600 ng (4,25,26)	+ (27,28)
Cadmium compounds	9-70 ng (26,29)	(30)
Unknowns	?	?
3. Pancreas		
Nitrosamines	?	+ (31)
Unknowns	?	?
4. Kidney and Bladder		
β-Naphthylamine	22 ng (32)	+ (33,34)
α-Aminofluorene	+ (35)	+ (33,34)
α-Aminostilbene	+ (35)	+ (33,34)
o-Tuluidine	+ (35)	+ (33)
Unknown aromatic amines	?	?
o-Nitrotoluene	21 ng (36)	?
Unknown nitro compounds	?	?
Di-n-butylnitrosamine	0-3 ng (20)	+ (21,20)
Other nitrosamines	?	+ (21,22)

* List is incomplete; data are based on experimental data only.

** Number in parenthesis indicates references.

*** Animal data on carcinogenicity.

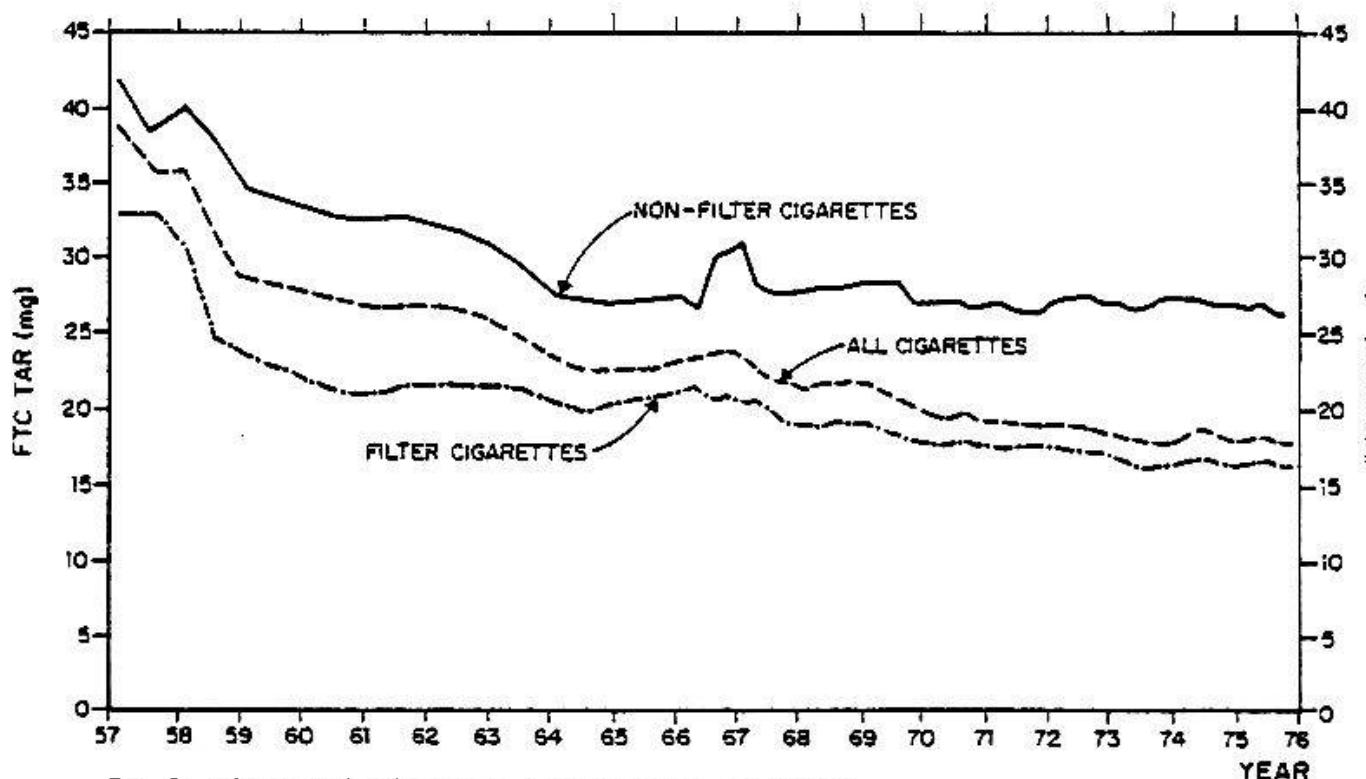


Fig. 8. Sales-weighted average tar deliveries, 1957-1976.

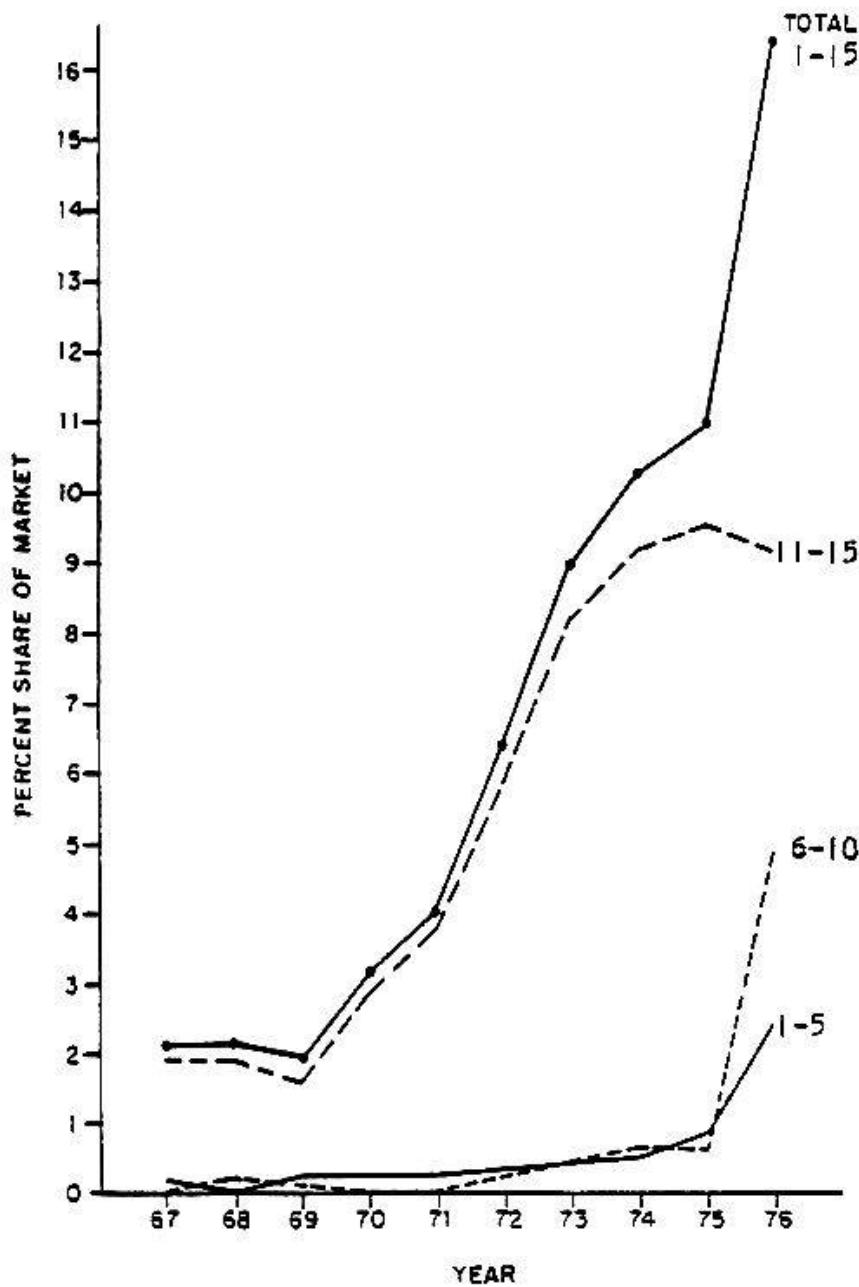


Fig. 9. Market share for low-tar (1-15 mg) cigarettes, 1967-1976.

were unable to confirm their earlier findings (44). In general, however, the specific role of carbon monoxide in the development of arteriosclerosis and cardiovascular disease remains in doubt. The effect of nicotine on cardiovascular events has been correlated to the effect that nicotine has on catecholamines, which are known to affect ventricular fibrillation (45, 46). It remains to be determined which tobacco smoke components relate to peripheral vascular disease and to aortic aneurysm. The relation of cigarette smoking to these diseases is of relatively greater order of magnitude than for myocardial infarction. In any case, we urge manufacturers to continue reducing the amount of nicotine, as well as of carbon monoxide, in cigarettes as a possible step towards the prevention of tobacco-related heart diseases. The

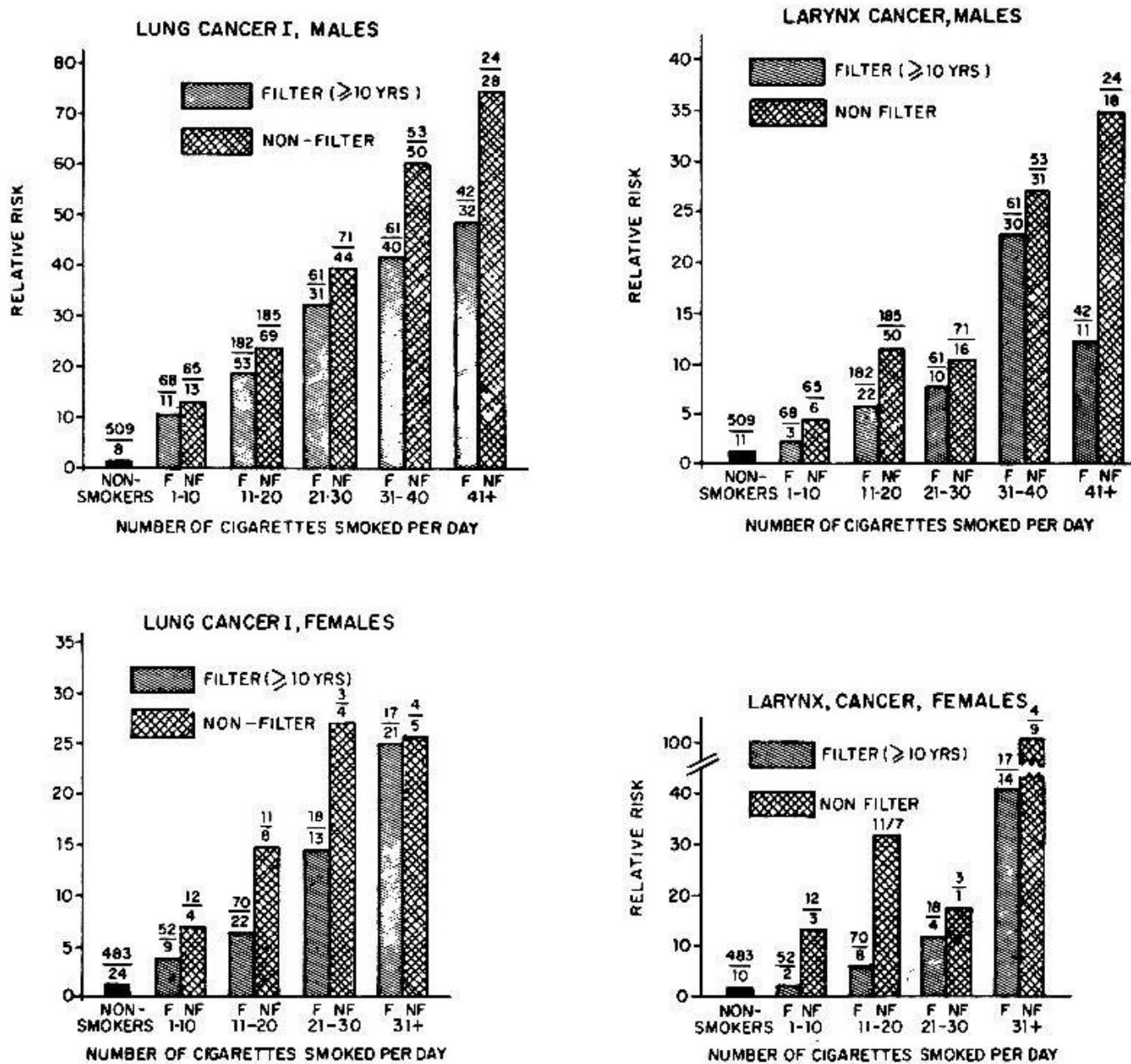


Fig. 10.

issue which remains to be determined is whether such a reduction will lead to an actual reduction in coronary events. While reduced nicotine in cigarettes may not have a significant effect on nicotine and cotinine levels in the blood, it is likely to have an effect on catecholamine (47).

In terms of chronic obstructive pulmonary disease, the extent to which the particulate and/or volatile components (particularly NO_2 and components of the acidic portion) relate to ciliastasis, mucus coagulation, and ultimately emphysema has yet to be determined (48, 49).

Studies in this field are particularly difficult to conduct in animals, but since charcoal filters tend to remove certain gaseous components of cigarette smoke, epidemiologic leads could be obtained by studying individuals who have smoked such cigarettes for the longest term of their years as smokers.

The final evaluation of the less harmful cigarette depends, of course, on epidemiologic studies. Such studies have already shown that smoking filter cigarettes for ten years or more results not only in a reduction of smoke exposure, but leads also to a reduction of lung and larynx cancer risk (Fig. 10). The reduction in risk for persons whose smoking history includes only filtered cigarettes remains to be measured. As yet, inspite of an initial study by HAMMOND of the American Cancer Society (50), we are uncertain about the relationship between filter cigarette smoking and reduction of coronary disease. This is a complex issue to study physiologically, and also because other risk factors, such as hypertension and hyperlipidemia, must be controlled for.

At the present time, we cannot draw a conclusion about the effects of filter cigarettes with regard to chronic obstructive pulmonary disease (COPD). This is another difficult area to study, in part, because COPD appears to be non-reversible. At our Institute, we are continually monitoring the incidence rates of tobacco-related diseases, and we include information on specific brands smoked by subjects in our prospective studies so that we will be able to report further on the long-term effect of tar reduction.

In summary, the prevention of tobacco-related diseases requires more action by the scientific and medical community than it has received in the past. In comparison to industry-related diseases, it is evident that not enough attention is being paid to this important public health problem. A successful solution would obviously have a pivotal impact on longevity, as well as on health care costs, and, thus, deserves our continued attention. But to accomplish what we believe can and should be accomplished requires more than occasional conferences ... it requires the practice of the best there is in preventive medicine.

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Author's address: Ernst L. Wynder M.D., President Naylor Dana Institute for Disease Prevention, American Health Foundation, 320 East 43rd Street, New York, N.Y. 10017 (USA)