TABLE 1.—Case–control studies of CHD risk among former smokers

Reference	Population	Number of cases	Number of controls	Source of controls	Number of cases among former smokers	Relative risk as compared with never smokers[a]	
						Former smokers	Current smokers
Willett et al. (1981)	Nurses Health Study: women aged 30–55	263	5,260	Nested in cohort	29	Overall 1.0 (0.7–1.6) Quit 1–4 yr 1.5 (0.7–3.1) Quit 5–9 yr 1.5 (0.8–3.0) Quit ≥10 yr 0.6 (0.3–1.3)	3.0 (2.3–4.0)
Rosenberg, Kaufman, Helmrich, Shapiro (1985)	Eastern US men aged <55	1,873	2,775	Hospital-based	348	1.1 (0.9–1.4)	2.9 (2.4–3.4)
Rosenberg, Kaufman, Helmrich, Miller et al. (1985)	Eastern US women aged <50	555	1,864	Hospital-based	35	1.0 (0.7–1.6)	1.4–7.0 depending on cig/day
LaVecchia et al. (1987)	Italian women aged <55	168	251	Hospital-based	3	0.8 (0.2–3.8)	3.6–13.1 depending on cig/day

TABLE 1.—Continued

Reference	Population	Number of cases	Number of controls	Source of controls	Number of cases among former smokers	Relative risk as compared with never smokers[a]	
						Former smokers	Current smokers
Rosenberg, Palmer, Shapiro (1990)	Eastern US women aged <65	910	2,375	Hospital-based	149	Overall 1.2 (1.0–1.7) Quit <24 mo 2.6 (1.8–3.8) Quit 24–35 mo 1.3 Quit ≥36 mo 0.8–1.1	3.6 (3.0–4.4)

NOTE: CHD=coronary heart disease.

[a]95% confidence interval shown in parentheses when available.

be quite valuable in assessing the time course for the decline in risk. However, the lack of detailed data on fatal cases is a potential limitation of the case–control approach.

In a case–control study of women in the Nurses Health Study cohort, Willett and coworkers (1981) identified 263 women who reported a nonfatal MI on the baseline Nurses Health Study questionnaire in 1976 when they were 30 to 55 years of age. Their smoking histories were compared with randomly selected controls corresponding in age with a case–control ratio of 1:20. Women who were former smokers did not experience increased risk of MI, with a relative risk compared with never smokers of 1.0 (95-percent confidence interval (CI), 0.7–1.6). In contrast, current smokers had a significantly elevated threefold higher risk of MI. When duration of abstinence was assessed, it appeared that those who quit either 1 to 4 or 5 to 9 years earlier had a nonsignificantly elevated risk of 1.5, and those who quit 10 years or more earlier had a relative risk of 0.6. Because there were only 29 cases among former smokers, the estimates for risk by duration of abstinence are not precise.

Rosenberg, Kaufman, Helmrich, and Shapiro (1985) specifically analyzed the impact of smoking cessation on risk of first MI among 4,648 men less than 55 years of age, using a hospital-based case–control design. Men with known preexisting heart disease were excluded. The 2,775 controls were mostly persons with fracture or sprain, disk disorders, and gastrointestinal disorders thought not to be related to cigarette smoking. There were 1,873 cases and 2,775 controls. For current smokers (smoked within the past year), the age-adjusted relative risk was 2.9 (95-percent CI, 2.4–3.4) and for past smokers overall, it was 1.1 (95-percent CI, 0.9–1.4). The relative risk for those who had not smoked for 12 to 23 months was 2.0 (95-percent CI, 1.1–3.8). For those with longer durations of abstinence, the relative risk was 1.1 (95-percent CI, 0.9–1.4) (Figure 2). The risk was increased for those smoking more cigarettes per day among current smokers as well as recent quitters. For longer durations of abstinence, the amount previously smoked appeared to have little impact. These investigators also examined the effect of quitting within categories of other risk factors; in general, there were no marked differences other than for diabetics among whom the benefits of cessation appeared to be greater. The same group of investigators (Rosenberg, Kaufman, Helmrich, Shapiro 1985) addressed the possibility that continuing smokers and former smokers may differ in their underlying risk of heart disease. They found that those who quit had a slightly higher risk profile. Hence, the benefit of cessation in this study cannot be attributed to overall better health among those who quit.

Rosenberg and associates (1985) also conducted a hospital-based case–control study of first nonfatal MI among women less than 50 years of age (Rosenberg, Kaufman, Helmrich, Miller et al. 1985). Women who smoked in the year before admission were classified as current smokers. Participants consisted of 555 cases and 1,864 controls who were hospitalized for trauma, orthopedic disorders, and other conditions thought to be unrelated to smoking. Current smokers had relative risks increasing from 1.4 to 7.0, depending on the number of cigarettes smoked per day. In contrast, former smokers (at least 1 year of abstinence) had the same risk as never smokers, with a relative risk of 1.0 (95-percent CI, 0.7–1.6).

In a recent report, Rosenberg, Palmer, and Shapiro (1990) further examined the decline in risk of MI among women who stopped smoking. Cases included 910 women

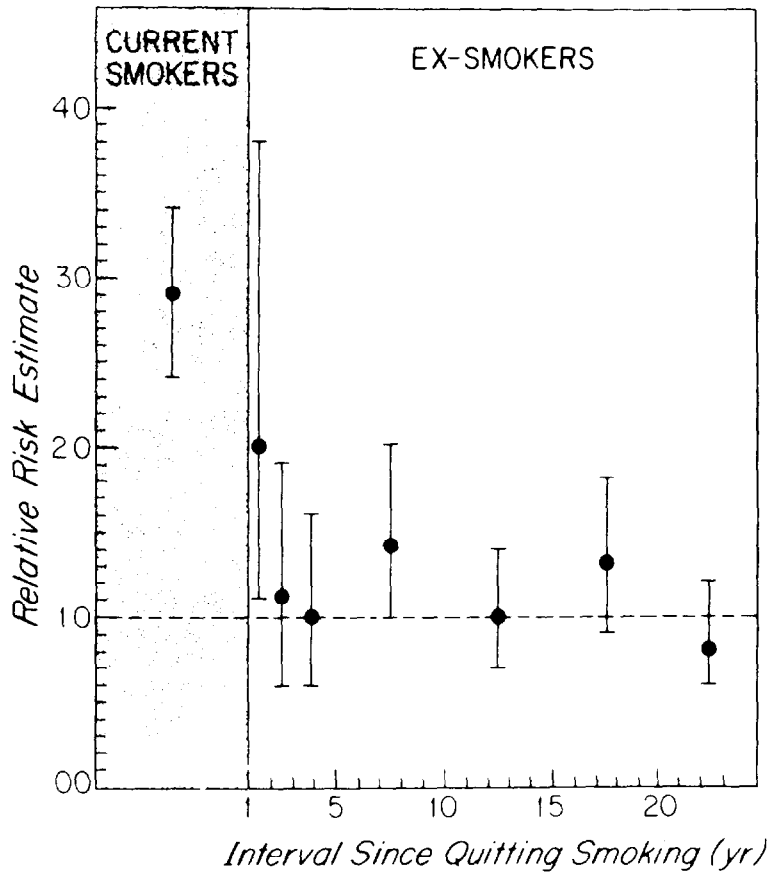

FIGURE 2.—Estimated relative risk of MI after quitting smoking among men under age 55, adjusted for age; 95% CIs are indicated by vertical line; relative risk for men who never smoked is 1.0

NOTE: MI=myocardial infarction; CI=confidence interval.

SOURCE: Rosenberg, Kaufman, Helmrich, Shapiro (1985).

with first infarction: their smoking histories were compared with those of 2,375 hospitalized controls. Among former smokers overall, the relative risk of MI was 1.2 (95-percent CI) compared with never smokers; for current smokers the relative risk was 3.6. When former smokers were subdivided according to duration of abstinence, women who had stopped smoking within the previous 24 months had a relative risk of 2.6 (95-percent CI, 1.8–3.8). The relative risk was 1.3 for those who stopped smoking 24 to 35 months earlier. After 3 years of abstinence, relative risks ranged from 0.8 to 1.1 and were indistinguishable from that of women who had never smoked.

Cohort Studies

Data from prospective cohort studies are summarized in Table 2. The British Physicians Study of Doll and Hill (1954, 1956) was one of the important early studies that established the link between smoking and risk of CHD and the health benefits of cessation. The study is based on a survey of 40,637 British physicians who responded to a 1951 questionnaire inquiring about smoking behavior. A second questionnaire was mailed to men in 1957–58 and to women in 1960–61; the response rate was 98 percent. The 10-year followup (Doll and Hill 1964) used the updated data to assess risk among former smokers. Additional questionnaires were distributed in 1966 and 1972, with response rates of 96 and 98 percent, respectively. The 20-year followup of 34,440 men (Doll and Peto 1976) showed a reduction in CHD mortality among former smokers. The benefits were more apparent in the younger age group, and the excess risk declined with increasing duration of abstinence. In men aged 30 to 54 years, the relative risk among former smokers of 1 to 4 years' duration was 1.9 compared with never smokers; relative risk further declined to 1.4 to 1.3 with a maximum of 20 years' duration of abstinence. In contrast, persistent smokers had a relative risk of 3.5. In this study, those who quit had smoked about 10 percent fewer cigarettes per day before quitting than did persistent smokers.

The British Physicians Study also included 6,194 women, for whom the data were reported separately (Doll et al. 1980). These women completed questionnaires in 1951, 1961, and 1973. In contrast to most studies among adults, a substantial minority of nonsmoking women in this cohort initiated cigarette smoking between 1951 and 1961. Thus, the rates of smoking-related diseases among those classified as never smokers are likely to be overestimated because never smokers, defined according to the 1951 data, included a proportion of subsequent current smokers. Overall, the relative risk of CHD mortality among former smokers was 0.9 compared with 1.0 to 2.2 among current smokers, depending on the amount smoked. Because there were only 26 cases among former smokers, a detailed analysis was not performed.

The first large-scale American Cancer Society (ACS) cohort was assembled in 1952 when 187,783 men aged 50 to 69, living in 9 States, completed a questionnaire related primarily to smoking (Hammond and Horn 1958a,b). The men were enrolled by over 22,000 ACS volunteers each of whom was asked to enroll 10 individuals, excluding those who were seriously ill. There was no further update of cigarette use. These men were studied for fatal outcomes for an average of 44 months, for a total of 667,753 person-years. Cause of death for 11,870 individuals was determined by death certificate. Compared with never smokers, the relative risk of death due to CHD among current smokers of less than 1 pack per day was 1.75. Among former smokers of less than 1 pack per day, those quitting within the previous year had a relative risk of 2.09, those quitting 1 to 10 years earlier had a risk of 1.54, and those quitting for more than 10 years had a relative risk of 1.09. A similar pattern was observed among smokers of 1 pack or more per day: among current smokers, the relative risk was 2.2; among quitters within the past year, 3.00; among quitters of 1 to 10 years, 2.06; and among quitters of more than 10 years, 1.60 (Figure 3). The authors speculated that the elevated

TABLE 2.—Cohort studies of CHD risk among former smokers

Reference	Population	Followup	Number of cases among former smokers	Relative risks compared with never smokers[a]		Comments
				Former smokers	Current smokers	
Doll and Hill (1964)	British physicians: 34,445 men	10 yr for CHD deaths	28	Quit 1–4 yr 1.05	1.41	Smoking ascertained 1951, updated 1958
			61	5–9 yr 1.25		
			59	10–14 yr 1.16		
			40	≥15 yr 1.12		
Doll and Peto (1976)	British physicians: 34,440 men	20 yr for CHD deaths		Aged 30–54	3.5	Smoking data assessed at baseline and after 7 yr
			7	Quit 1–4 yr 1.9		
			10	5–9 yr 1.3		
			10	10–14 yr 1.4		
			7	≥15 yr 1.3		
				Aged 55–64	1.7	
			19	Quit 1–4 yr 1.9		
			34	5–9 yr 1.4		
			38	10–14 yr 1.7		
			45	≥15 yr 1.3		
				Aged ≥65	1.3	
			24	Quit 1–4 yr 1.0		
			76	5–9 yr 1.3		
			62	10–14 yr 1.2		
			148	≥15 yr 1.1		

TABLE 2.—Continued

Reference	Population	Followup	Number of cases among former smokers	Relative risks compared with never smokers[a]		Comments
				Former smokers	Current smokers	
Doll et al. (1980)	British physicians: 6,194 women	22 yr for CHD deaths	26	0.91	1.0–2.2 depending on amount smoked	Smoking assessed at baseline and after 9 yr
				Previously <1 ppd		
Hammond and Horn (1958a,b)	187,783 men aged 50–60	44 mo for CHD deaths			1.75 (143 cases)	
			23	Quit < 1 yr 2.09		
			80	1–10 yr 1.54		
			40	>10 yr 1.09		
				Previously ≥1 ppd		
					2.20 (122 cases)	
			18	Quit < 1 yr 3.00		
			64	1–10 yr 2.06		
			40	>10 yr 1.60		
				Previously 1–19 cig/day		
Hammond and Garfinkel (1969)	ACS CPS-I: 358,534 men free of diagnosed CHD	6 yr for CHD mortality			1.90 (1,063 cases)	
			29	Quit <1 yr 1.62		
			57	1–4 yr 1.22		
			55	5–9 yr 1.26		
			52	10–14 yr 0.96		
			70	≥20 yr 1.08		

TABLE 2.—Continued

Reference	Population	Followup	Number of cases among former smokers	Relative risks compared with never smokers[a]		Comments
				Former smokers	Current smokers	
Hammond and Garfinkel (1969) (continued)				Previously ≥20 cig/day	2.55	
			62	Quit <1 yr 1.61	(2,822 cases)	
			154	1–4 yr 1.51		
			135	5–9 yr 1.16		
			133	10–14 yr 1.25		
			80	≥15 yr 1.05		
ACS (unpublished tabulations)	ACS CPS-II: 1.2 million men and women	4 yr for CHD deaths		Men <21 cig/day	1.93	Persons with cancer, heart disease, and stroke excluded at baseline
			14	Quit <1 yr 1.43		
			48	1–2 yr 1.61		
			47	3–5 yr 1.49		
			88	6–10 yr 1.28		
			90	11–15 yr 0.99		
			359	≥16 yr 0.88		
				Men ≥21 cig/day	2.02	
			19	Quit <1 yr 2.56		
			33	1–2 yr 1.57		
			36	3–5 yr 1.41		
			67	6–10 yr 1.63		
			71	11–15 yr 1.16		
			182	≥16 yr 1.09		

TABLE 2.—Continued

Reference	Population	Followup	Number of cases among former smokers	Relative risks compared with never smokers[a]		Comments
				Former smokers	Current smokers	
ACS (unpublished tabulations) (continued)				Women <20 cig/day	1.76	
			3	Quit <1 yr 2.13		
			7	1–2 yr 0.87		
			11	3–5 yr 1.31		
			12	6–10 yr 0.74		
			17	11–15 yr 1.20		
			82	≥16 yr 1.17		
				Women ≥20 cig/day	2.27	
			9	Quit <1 yr 1.41		
			10	1–2 yr 1.16		
			16	3–5 yr 0.96		
			24	6–10 yr 1.88		
			12	11–15 yr 1.37		
			32	≥16 yr 1.12		
Dorn (1959); Kahn (1966); Rogot and Murray (1980)[b]	US veterans: 248,046 men	16 yr for cardiovascular deaths	9,027	Stopped (overall) 1.15	1.58	Those who quit on doctor's orders were excluded
				<5 yr 1.40		
				5–9 yr 1.40		
				10–14 yr 1.30		
				15–19 yr 1.20		
				≥20 yr 1.00		

TABLE 2.—Continued

Reference	Population	Followup	Number of cases among former smokers	Relative risks compared with never smokers[a]			Comments
				Former smokers		Current smokers	
Dorn (1959); Kahn (1966); Rogot and Murray (1980)[b] (continued)		For CHD deaths		Stopped (overall) <5 yr 5–9 yr 10–14 yr 15–19 yr ≥20 yr	1.16 1.40 1.40 1.30 1.20 1.10	1.58	No update of smoking information
Doyle et al. (1962)	Framingham and Albany cohorts 4,120 healthy men aged 30–62	6-8 yr for fatal and nonfatal MI	10	0.9		2.3	Only baseline smoking data used
Doyle et al. (1964)	Framingham and Albany cohorts of 4,120 healthy men aged 30–62	10 yr (Framingham) 8 yr (Albany) MI and CHD deaths	13	1.1 (0.5–2.2)		2.0–3.0 depending on amount smoked	No data on duration
Gordon, Kannel, McGee (1974)	2,336 men in Framingham Heart Study, aged 29–62	18 yr for CHD excluding angina	24	0.7		1.3	Smoking information updated biennially
Rosenman et al. (1975)	3, 154 healthy California men aged 39–59	8–9 yr for fatal and nonfatal CHD	16	Aged 39–40 Aged 50–59	1.9 1.1	2.5	Only baseline smoking data used

TABLE 2.—Continued

Reference	Population	Followup	Number of cases among former smokers	Relative risks compared with never smokers[a]			Comments
				Former smokers	Current smokers		
Cederlof et al. (1975)	Sample of 51,911 Swedish men aged 18–69	10 yr	97	Quit 1–9 yr	1.5 total	1.7	Only baseline smoking data used
				Smoked <20 cig/day	0.9		
				Smoked ≥20 cig/day	1.6		
			86	Quit ≥10 yr	1.0 total		
				Smoked <20 cig/day	0.9		
				Smoked ≥20 cig/day	1.1		
Fuller et al. (1983)	Whitehall civil servants: 18,403 men aged 40–64	10 yr for CHD deaths	208	171 normo-glycemic	1.3	2.5	Prevalent cases of CHD not excluded
				23 glucose intolerant	0.7	1.5	
				14 diabetics	3.8	2.9	
Friedman et al. (1981)	25,917 Kaiser-Permanente subscribers in the San Francisco area, aged 20–79	4 yr for CHD deaths	31		0.9	1.6	Prevalent cases of CHD not omitted; exclusion of those cases increased the apparent benefit of quitting

TABLE 2.—Continued

Reference	Population	Followup	Number of cases among former smokers	Relative risks compared with never smokers[a]		Comments
				Former smokers	Current smokers	
Keys (1980)	7-Countries Study of 12,096 men free of CHD	10 yr for CHD deaths	About 13[c] (Northern Europe)	2.3	2.4–4.5 depending on amount	Relative risk based on only about 5 cases in never smokers, very small numbers
			About 9 (Italy, Greece, Yugoslavia)	0.8	0.7–1.8 depending on amount	
			About 7[c] (US)	0.7	1.6–3.0 depending on amount	Numbers extrapolated from figures
Shapiro et al. (1969)	HIP cohort about 39,000 men aged 35–64	3 yr for MI	NR	1.0	1.8	
Jajich, Ostfeld, Freeman (1984)	2,674 poor persons in Cook County, IL aged 64–75	4.5 yr for CHD deaths	20	1.11	1.94	Stroke excluded but prevalent CHD not excluded at baseline
Willett et al. (1987)	Nurses Health Study: 121,700 US women aged 30–55	6 yr for nonfatal MI and CHD deaths	55	1.5 (1.0–2.1)	2.1–10.8 depending on amount smoked	

TABLE 2.—Continued

Reference	Population	Followup	Number of cases among former smokers	Relative risks compared with never smokers[a]		Comments
				Former smokers	Current smokers	
Floderus, Cederlof, Friberg (1988)	10,495 Swedish twins aged 36–75	21 yr for CHD deaths	188 men 10 women	1.0 (0.8–1.1) 0.6 (0.4–1.0)	1.4–1.8 depending on amount smoked	No reassessment of smoking during followup; no data on duration
Lannerstad, Isacsson, Lindell (1979)	703 Malmö men, age 55	5 yr	0	CHD deaths	2.0	No cases among former smokers; only 2 in never smokers
Holme et al. (1980)	14,816 healthy Oslo men, aged 40–49	4.7	NR			Never and ex-smokers had about 40% of the risk of cigarette smokers
Netterstrom and Juel (1988)	2,465 Danish bus drivers	7.75 yr for MI and CHD death	9	3.2 (0.4–25.6)	5.0 (0.7–36.0)	

NOTE: CHD=coronary heart disease; ppd=packs/day; ACS CPS-I and -II=American Cancer Society Cancer Prevention Studies I and II; HIP=health insurance plan; MI=myocardial infarction; NR=not reported.

[a]95% confidence interval shown in parentheses when available.

[b]Breakdowns of relative risk derived from figure presented in paper cited.

[c]Extrapolated from figure presented in paper cited.

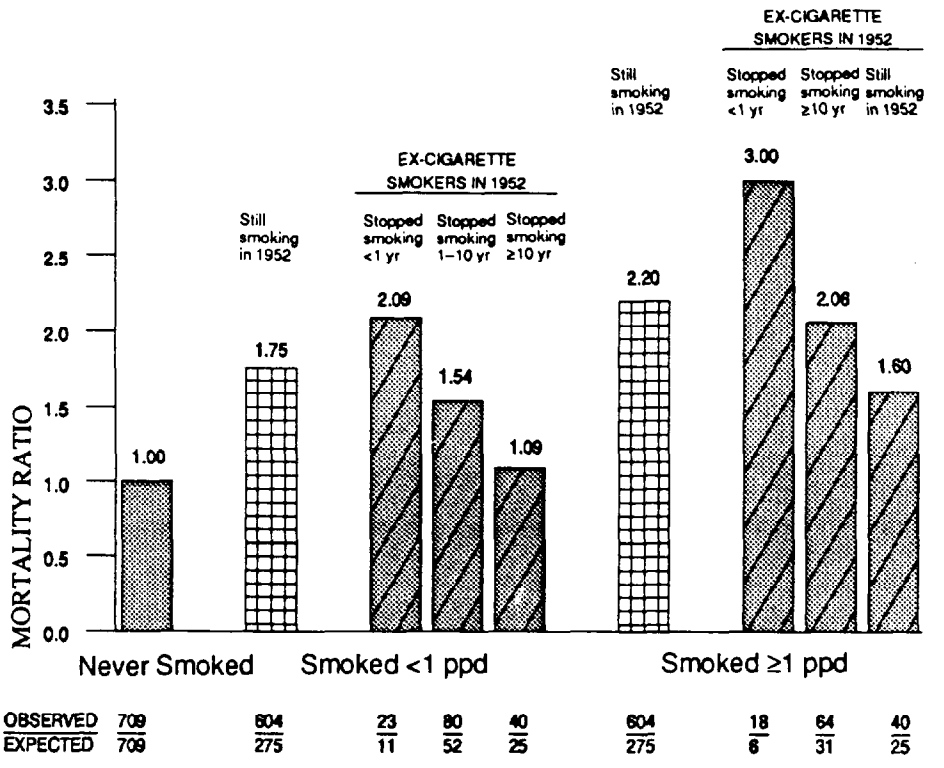

FIGURE 3.—Mortality ratios due to coronary artery diseases; rates for men who have stopped smoking are compared with those for men who never smoked and those for men still smoking in 1952

NOTE: ppd=packs/day.

SOURCE: Hammond and Horn (1958b).

risk among recent quitters reflected the inclusion of men who stopped smoking because of early symptoms of heart disease.

A second cohort study, the ACS Cancer Prevention Study I (CPS-I) (formerly called the ACS 25-State Study), was undertaken between 1959 and 1972. Recruitment was by family, and eligible families had at least one person aged 45 or older. All family members aged 35 or older were asked to participate in the study; more than 1 million persons were enrolled. In a 6-year followup of 358,534 men free of diagnosed serious illness, clear reductions in risk of CHD mortality were observed among former smokers compared with current smokers (Hammond and Garfinkel 1969). Among those smoking less than 1 pack per day, the relative risk among current smokers was 1.90. Among those who stopped in the previous year, the relative risk was 1.62, and among those

with 10 years or more of abstinence, the risk was nearly the same as that for never smokers. A similar pattern was observed among those smoking 1 pack or more per day. Current smokers at that level had a relative risk of 2.55. Quitters of less than 1 year had a relative risk of 1.61, and those with between 10 and 20 years of abstinence had only a slightly elevated relative risk of 1.25. Because of the very large number of deaths and the careful followup, the estimates of effect are relatively precise. In this period, cigarette smoking declined substantially, especially in the predominantly white, middle- to upperclass groups represented by the study population. Hence, some misclassification of the current smoking group may have occurred, but the relative risks among former smokers, apart from the most recent quitters (some of whom inevitably resumed smoking), are likely to be accurate.

In 1982, a third ACS cohort, CPS-II, was initiated in 50 States. The methods for recruitment and the population enrolled were similar to CPS-I, but the cohort was larger, with more than 1.2 million participants (Chapter 3). Preliminary data based on 4 years of followup were published in the 1989 Surgeon General's Report (US DHHS 1989). Among men, former smokers aged 35 or younger had relative risks of CHD of 1.41, those aged 36 to 64 had 1.75, and those 65 or older had 1.29; the relative risks among current smokers were 1.94, 2.81, and 1.62, respectively. A generally similar pattern was seen among women.

When the data are examined by amount of previous smoking and time since quitting, the pattern of changing risk is influenced by the presence of disease at enrollment. When those who reported themselves as sick or as having previously diagnosed cancer, heart disease, or stroke at baseline were not excluded from the analysis, men who previously smoked fewer than 21 cigarettes per day and who had quit smoking within the previous 3 years experienced a CHD mortality rate that was about 6 percent higher than that among current smokers. However, with increasing duration of abstinence, the risk among former smokers came very close to that of never smokers; after 16 years or more, the relative risk was 1.01 (US DHHS 1989). It is likely that the early peak in mortality among recent quitters partly reflects the effect of having included those who quit because of smoking-related illness. After excluding those with cancer, heart disease, and stroke at baseline, this early excess mortality is less apparent (Table 2). In all categories, those who quit 1 to 2 years earlier had relative risks substantially lower than those of current smokers. Findings are less consistent for those who quit within the past year, presumably because of a high incidence of smoking resumption in that group and the possible inclusion of persons who stopped smoking as a result of symptoms due to undiagnosed illness. A very similar pattern was observed among men who smoked 21 cigarettes or more per day, except that the relative risks were higher for all but those with the shorter period of abstinence. The absolute rates were lower for women, as expected, and the relative risks are thus statistically unstable. Nevertheless, the overall patterns among female smokers were generally similar to those among male smokers.

To examine the effects of smoking cessation at different ages, CPS-II data on cumulative mortality rates due to CHD were tabulated for 5-year categories of age at cessation. (See Table 3 and Chapter 3 for a description of the methods used to calculate these rates.) The mortality rates used for these calculations were based on subjects not

TABLE 3.— Estimated probability of dying from ischemic heart disease in the next 16.5-year interval (95% CI) for quitting at various ages compared with never smoking and continuing to smoke, by amount smoked and sex

Age at quitting or at start of interval	Never smokers	Continuing smokers		Former smokers	
		<21[a]	≥21[a]	<21[a]	≥21[a]
MEN					
40–44	0.01 (.01–.01)	0.03 (.02–.03)	0.03 (.03–.04)	0.01 (.00–.02)	0.02 (.01–.02)
45–49	0.02 (.01–.02)	0.04 (.04–.05)	0.04 (.04–.05)	0.02 (.01–.03)	0.02 (.01–.03)
50–54	0.04 (.03–.03)	0.07 (.06–.07)	0.06 (.06–.07)	0.04 (.03–.05)	0.04 (.02–.05)
55–59	0.05 (.05–.06)	0.10 (.08–.11)	0.09 (.07–.10)	0.05 (.04–.07)	0.08 (.06–.10)
60–64	0.10 (.09–.11)	0.14 (.12–.16)	0.16 (.10–.21)	0.12 (.09–.15)	0.10 (.06–.15)
65–69	0.15 (.13–.17)	0.20 (.16–.25)	0.13 (.08–.19)	0.14 (.07–.21)	0.12 (.00–.24)
70–74[b]	0.13 (.11–.14)	0.17 (.13–.22)	0.10 (.05–.16)	0.19 (.10–.29)	0.11 (.02–.20)

sick at interview or giving a history of heart disease, cancer, or stroke. For both women and men, during the next decade-and-a-half cumulative CHD mortality for those who stopped smoking before age 60 was about half that of those who continued to smoke. This same pattern of reduced risk extended to those who stopped smoking between ages 60 and 64. After age 65, few persons stopped smoking, as indicated by wide confidence intervals, so that no clear patterns could be determined.

Because the methods used in CPS-I and CPS-II are similar, it is appropriate to compare the results of the two studies. In CPS-II, the relative risks of CHD for current smoking among men and women are substantially higher at every age than those observed in CPS-I. The higher relative risks for CHD and other smoking-related diseases among women in CPS-II are possibly due to the earlier age of smoking

TABLE 3.—Continued

Age at quitting or at start of interval	Never smokers	Continuing smokers		Former smokers	
		<20[a]	≥20[a]	<20[a]	≥20[a]
WOMEN					
40–44	0.00 (.00–.00)	0.01 (.00–.01)	0.01 (.01–.01)	0.00 (.00–.01)	0.00 (.00–.01)
45–49	0.00 (.00–.01)	0.01 (.01–.01)	0.01 (.01–.02)	0.00 (.00–.00)	0.01 (.00–.01)
50–54	0.01 (.01–.01)	0.02 (.02–.03)	0.03 (.02–.03)	0.01 (.00–.02)	0.02 (.01–.02)
55–59	0.02 (.02–.02)	0.04 (.03–.05)	0.05 (.04–.06)	0.01 (.00–.02)	0.02 (.01–.04)
60–64	0.04 (.03–.04)	0.06 (.04–.07)	0.08 (.06–.10)	0.02 (.00–.05)	0.04 (.01–.06)
65–69	0.07 (.07–.08)	0.11 (.07–.15)	0.12 (.07–.18)	0.12 (.03–.21)	0.09 (.01–.17)
70–74[b]	0.07 (.06–.07)	0.09 (.05–.13)	0.11 (.05–.16)	0.03 (.00–.08)	0.02 (.00–.05)

NOTE: Based on subjects not sick at enrollment or giving a history of cancer, heart disease, or stroke; 95% confidence interval (CI) shown in parentheses.

[a] Cig/day.

[b] Estimates for quitting at this age are estimates of the probability of dying in the next 12.5-yr interval.

SOURCE: Unpublished tabulations, American Cancer Society.

initiation in the more recent cohort (US DHHS 1989). The higher relative risks among men are more difficult to explain because the age of initiation has not changed substantially among men over time (US DHHS 1989).

The large size and careful methodology of the three ACS cohorts provide considerable evidence for the benefit of quitting in reducing risk of CHD. These studies also provide strong evidence that there is some residual risk of CHD attributable to past smoking that persists for a considerable duration after cessation.

The U.S. Veterans Study (Dorn 1959; Kahn 1966; Rogot 1974; Rogot and Murray 1980) has also provided useful information on the health effects of smoking. The population was drawn from 293,958 U.S. veterans who held Government life insurance policies in December 1953. In 1954, a total of 198,820 individuals returned mailed

questionnaires about their smoking behavior, and in 1957, an additional 49,226 responded. Those who stopped smoking on a physician's orders were excluded from the analysis. Mortality in this cohort was monitored, and death certificates were obtained to assess cause of death. Smoking status after the baseline questionnaire was not ascertained. After 16 years of followup, quitters at enrollment when compared with never smokers had relative risks of 1.15 for all cardiovascular mortality and 1.16 for CHD death specifically (Rogot and Murray 1980). In contrast, men who were current smokers at baseline had relative risks of 1.58 for these two categories. Among past smokers, risk of death due to CVD increased with higher previous usual daily cigarette consumption. The relative risks among past smokers, compared with never smokers, ranged from 1.02 for less than 10 cigarettes per day to 1.34 for 40 cigarettes or more per day. This gradient was more pronounced among current smokers (Figure 4).

A gradient was also apparent for decreasing risk with increasing duration of smoking abstinence. For both cardiovascular and coronary mortality, there was a moderate decrease in risk with short duration of abstinence and a smaller, but consistent decline in risk with longer periods of abstinence (Figure 5). After 20 years or more of abstinence, the relative risk of CVD was 1.04, and for coronary death, the risk was 1.05.

The major strength of the U.S. Veterans Study is the large numbers, with 21,413 deaths from CVD among smokers and 9,027 among former smokers. The long followup period without reclassification of smoking status is a limitation, which will tend to lead to an underestimate of the effect of sustained smoking and an underestimate of the benefits of quitting (Chapter 2). This source of potential bias may not have markedly distorted the estimates in this study: in the followup of this cohort (Rogot and Murray 1980), the relative risk for cardiovascular mortality associated with current smoking at enrollment was 1.62 at 8.5 years and 1.58 at 16 years; for coronary disease, the relative risk was 1.61 at 8.5 years and 1.58 at 16 years. Thus, the impact of misclassification of current smokers who quit (and therefore lowered their risk) as persistent smokers appears to be slight. A similar comparison of the relative risks among former smokers is less informative in assessing the impact of misclassification. Most quitters who resume smoking do so within 2 years after cessation. Therefore, misclassification of ex-smokers between 8.5 and 16 years of cessation is likely to be small. For both cardiovascular mortality and coronary mortality, the relative risks among ex-smokers declined slightly from 1.21 at 8.5 years of followup to 1.15 and 1.16 at 16 years of followup. This is consistent with the inverse relation between duration of smoking cessation and mortality ratio.

Among current smokers in the U.S. Veterans Study, the relative risks of coronary disease were slightly higher after 8.5 years of followup (relative risk (RR)=1.95 for >20 cig/day) than after 2.5 years of followup (RR=1.75) (Dorn 1959). As expected, those who stopped smoking on a physician's orders were at higher risk of death regardless of their smoking status.

An early report of combined data from the Framingham and Albany Heart Studies (Doyle et al. 1962) included 4,120 men free from coronary disease at entry into the study. The Framingham Study data were based on 6 years of followup and the Albany Heart Study data on 8 years of followup. Among the 411 former smokers in the combined cohort, the relative risk of MI (age-adjusted) was 0.9 compared with never

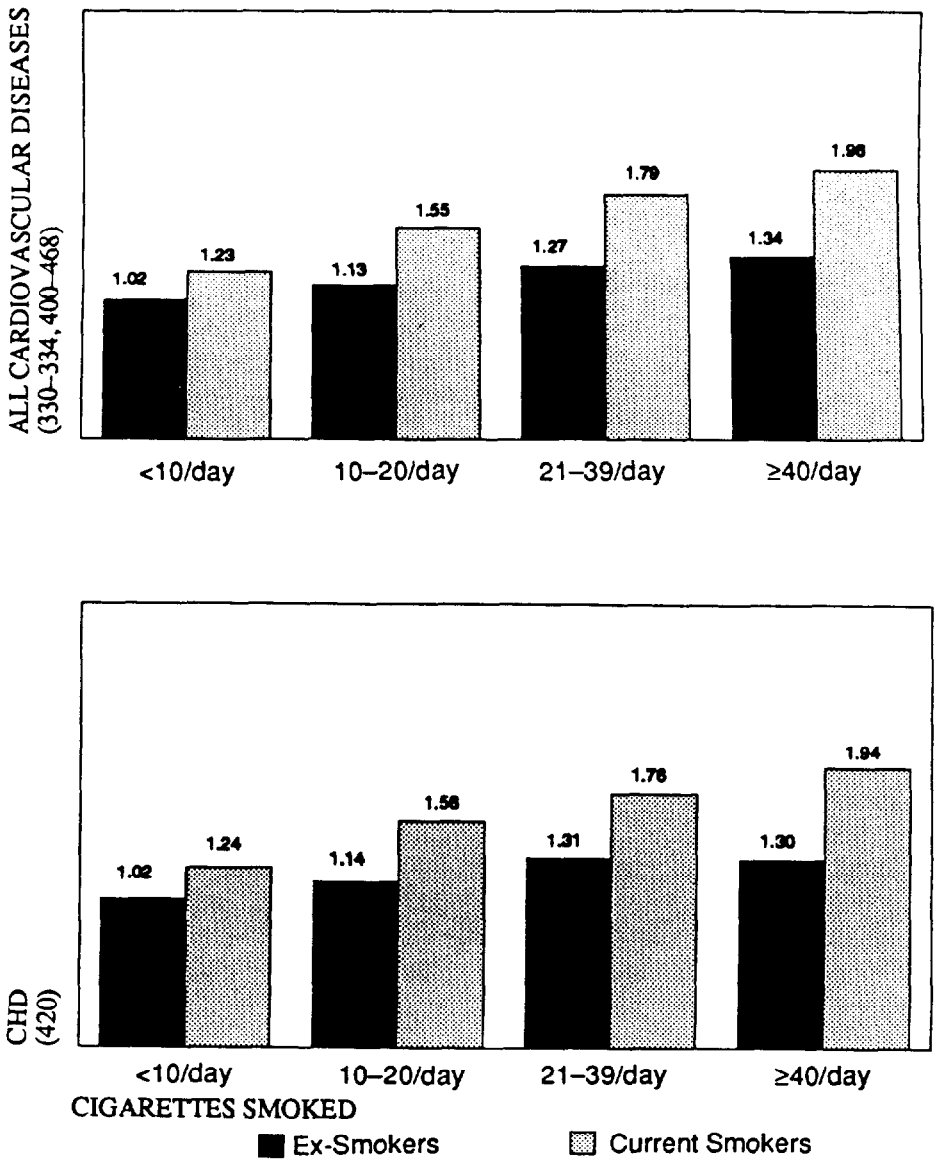

FIGURE 4.—Mortality ratios for all cardiovascular diseases and CHD, by daily cigarette consumption, US Veterans Study, 1954–69

NOTE: Ex-smokers includes only former cigarette smokers who stopped smoking for reasons other than physician's orders.

SOURCE: Rogot and Murray (1980).

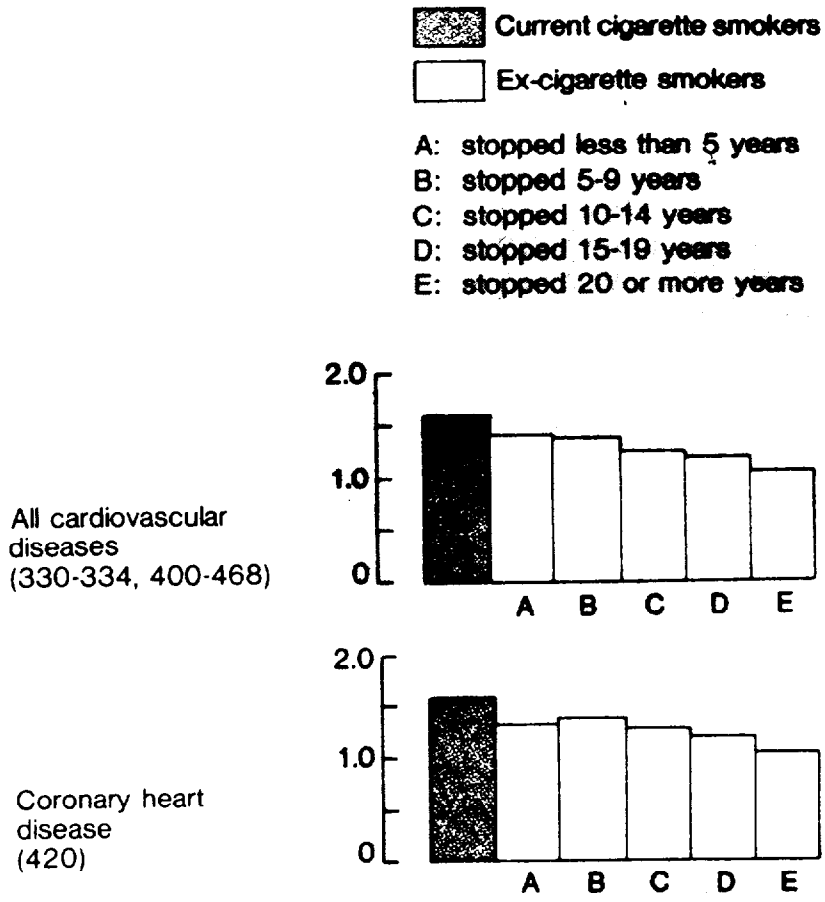

FIGURE 5.—Mortality ratio for current and former cigarette smokers by years of smoking cessation, US Veterans Study, 1954–69

NOTE: Ex-smokers includes only former cigarette smokers who stopped smoking for reasons other than physician's orders.

SOURCE: Rogot and Murray (1980).

smokers, 60 percent lower than among current smokers. A more detailed analysis was not possible because only 10 cases occurred among former smokers.

In a second report using the combined data from the Framingham Study and the Albany cohort (Doyle et al. 1964), the relative risk for former versus never smokers

was 1.1 (95-percent CI, 0.5–2.2). Current smokers had significantly elevated relative risks ranging from 2.0 to 3.0, depending on the amount smoked.

In a later report from the Framingham Study based on 18 years of followup biennial examinations, Gordon, Kannel, and McGee (1974) assessed the effects of smoking cessation. In this analysis, anyone who smoked for 1 year or more during the most recent 2-year interval between examinations was considered a current smoker. Approximately 20 percent of men who reported that they had quit smoking at entry into the study resumed smoking; about half of those smoked very little or only intermittently after resumption. Compared with current smokers, former smokers had a 30-percent reduction in fatal and nonfatal CHD (excluding angina); the relative risk among current smokers compared with that among never smokers was 1.3. Other coronary risk factors were examined in detail; there were no significant differences between persistent smokers and those who quit, but those who quit were more likely to be ill. Hence, it would be expected that adjustment for confounding would have revealed even greater benefit from cessation. The benefit of quitting seemed more marked in younger men. However, there were only 24 cases of CHD among the quitters so that a detailed analysis could not be performed.

The Western Collaborative Group Study monitored a cohort of 3,524 men for an average of 8.5 years for CHD incidence (Rosenman et al. 1975). Information collected at baseline among men aged 39 to 49 indicated that former smokers had a relative risk of 1.9 compared with that of never smokers, 20 percent lower than among current smokers. For men aged 50 to 59, former smokers had a relative risk of 1.1 compared with never smokers, 40 percent less than among current smokers. This effect of cessation was slightly greater than that observed after 4.5 years of followup (Jenkins, Rosenman, Zyzanski 1968). The difference between the age groups could be a true effect or may reflect different levels of misclassification; it is possible that a greater proportion of the quitters in the younger group than in the older group resumed smoking.

In 1963, a prospective study of smoking and mortality was conducted in Sweden by sending questionnaires to a probability sample of men aged 18 to 69 (Cederlof et al. 1975). A total of 51,911 respondents provided some information; a subsample of 11,739 were sent followup questionnaires in 1969. In that interval, 12 percent of the former smokers had resumed cigarette smoking, and an additional 8 percent initiated pipe or cigar smoking. The men were monitored for 10 years for mortality and cancer morbidity. Men who quit within the past 9 years had a significantly elevated relative risk (RR=1.5) that was nearly as high as the relative risk for current smokers (RR=1.7). In contrast, those with a longer duration of abstinence had a relative risk of 1.0. Men with diseases at baseline were not excluded, so it is likely that the benefits of recent cessation are obscured by the inclusion of men with disease-induced quitting.

The Whitehall Civil Servants Study (Rose et al. 1977; Fuller et al. 1983) is another important source of data on risk factors for CHD. Between 1967 and 1969, a total of 18,403 male civil servants aged 40 to 64 were examined. In the 19-year followup, the age-adjusted CHD mortality rate among 17,051 persons with normal blood sugar was 50 percent lower for quitters than for current smokers. When compared with never smokers, the relative risk for former smokers among normoglycemics was 1.3. Among the 999 men with glucose intolerance (but not diabetes), the risk for former smokers

was 30 percent lower than that for current smokers. Overall, the 224 diabetic men experienced a very high risk of CHD; among this group the risk for former smokers was 30 percent higher than for current smokers (based on 10 cases among the current smokers). These data are generally consistent with other studies in the overall findings, but suggest that smoking cessation may not have the same benefit for diabetics as for the general population; however, this finding is based on small numbers, and the severity of diabetes was not considered in the analysis. This study did not provide any information on the time course of the decline in risk after cessation. It is also likely that during the long followup period, a substantial percentage of current smokers quit smoking.

The effect of differences in coronary risk factors other than smoking was examined in quitters and persistent smokers by Friedman and colleagues (1979). As expected, there were a number of differences between quitters and persistent smokers when they were studied at a time in which individuals in both groups were smoking. A followup analysis of this same population was conducted to assess the impact of quitting on risk of CHD and to evaluate the effect of differences between these groups that might alter CHD risk (Friedman et al. 1981). Smoking was assessed by questionnaire at approximately annual multiphasic health checkups given at the Kaiser-Permanente Medical Centers in San Francisco and Oakland, CA. There were 9,394 persistent smokers, 2,856 persistent quitters (those who denied smoking at 2 sessions after an examination when they were currently smoking), and 12,697 never smokers. The cohort was monitored for an average of 4 years for a total followup of 188,436 person-years. The age-, sex-, and race-adjusted death rates (per thousand person-years) associated with CHD were 2.6 among smokers, 1.4 among quitters, and 1.6 among never smokers. After adjustment for baseline differences, quitters had a risk of fatal CHD that was 55 percent lower (95-percent CI, 74–22) compared with persistent smokers. By excluding individuals with frank coronary disease at baseline, a slightly higher benefit for quitting was demonstrated. Further adjustment for measures of smoking intensity slightly attenuated the reduction in risk to 47 percent, suggesting that only a small part of the apparent benefit of quitting is attributable to the fact that quitters were less intense smokers at initiation of smoking. Only the number of cigarettes smoked had any measurable impact; depth of inhalation and duration of smoking had no effect. Except for women during the first half of this century, most smokers begin to smoke during adolescence; thus, duration is very highly correlated with age in most populations. These findings generally confirmed previous results from the same study (Friedman, Dales, Ury 1979).

The Seven Countries Study (Keys 1980) provided a valuable resource for analysis of risk factors for CHD. A total of 16 cohorts of men, aged 40 to 59, living in 7 countries, were examined and monitored for 10 years for CHD incidence. The cohorts were assembled between 1958 and 1964, and consisted of 12,096 men free from CVD. In each grouping of cohorts, former smokers had a lower risk of CHD than did current smokers. However, only about 28 cases of CHD death among former smokers were reported; therefore, no detailed analysis was possible.

Data on the health effects of smoking cessation are also available from the Health Insurance Plan of Greater New York. The incidence of MI was ascertained over a

3-year interval among 110,000 individuals (Shapiro et al. 1969). A total of 613 cases of MI were reported among men aged 35 to 64 in this group. Compared with current smokers, those who quit in the preceding 5 years had a 50-percent lower risk; compared with never smokers, the relative risk was 1.0. As in other studies, the percent reduction in risk associated with smoking cessation tended to be lower in the older age groups, but a decreased risk associated with quitting was apparent among all ages.

Many studies of smoking cessation have focused on middle-aged men and women. Even as recently as the late 1970s, current smoking was considered to be a minor risk factor for CHD beyond age 65 (US DHEW 1979), and the benefits of cessation among older persons have been questioned (Seltzer 1974, 1975). Jajich, Ostfeld, and Freeman (1984) assessed the effect of quitting among 2,674 recipients of public assistance aged 64 to 75 in Cook County, IL. Of the 2,674 individuals studied, 270 were past smokers, 873 were current smokers, and 1,248 were never smokers. Participants were screened at baseline and monitored for 4 years for CHD mortality. Overall, former smokers had a relative risk of CHD mortality of 1.11 (based on 20 exposed cases), whereas current smokers had a relative risk of 1.94. The number of cases was inadequate for a detailed analysis of the effect of duration of abstinence. Persons with heart problems were not excluded at baseline. Approximately one-third of the CHD deaths were among those with such a history; therefore, it is likely that the apparent benefits of quitting may be understated because of the tendency of such individuals at high risk to quit because of illness. These data provide some evidence that the benefits of cessation extend to older adults.

The British Regional Heart Study (Cook et al. 1986) monitored 7,735 men aged 40 to 59 who were randomly selected from general practice lists in the United Kingdom. The men were screened at baseline and studied for 5 to 7.5 years for incidence of fatal and nonfatal CHD; in this interval, there were 336 CHD outcomes. Those with CHD at baseline were not excluded. Compared with never smokers, quitters had a relative risk of approximately 2.5; compared with current smokers, the relative risk was approximately 30 percent lower. Men who quit smoking within the previous 5 years had a relative risk of approximately 3.3, compared with 3.6 among persistent smokers. Those who had quit more than 5 years earlier had a relative risk of approximately 2.3, but there was no evidence for a trend of decreasing risk with increasing duration since cessation. Even those who had quit 20 or more years earlier had an elevated risk. After adjustment for other risk factors, the relative risk in this group was 1.6 ($p=0.11$).

As expected, the prevalence of CHD at baseline among quitters was significantly higher than for either current or never smokers. Presumably, the diagnosis of disease provided a motivation to quit. When these men were excluded, the relative risks were attenuated. Nonetheless, for those who had quit in the previous 5 years, the relative risk was still elevated at 3.2. The total years of smoking was suggested as the most important variable. It was also suggested that cessation lowered risk primarily by preventing the accumulation of further years of smoking. It is noteworthy that although results of this study are adequate to show an elevated risk among past smkers, the number of cases among former smokers is too small to provide precise estimates of risk at the various durations since quitting. For example, there are only 11 cases in the group that quit 20 or more years earlier.

Many studies of large cohorts examined the effects of smoking primarily among men. However, the Nurses Health Study investigators reported on smoking and CHD in a cohort of 121,700 women monitored through biennial questionnaires from 1976 to 1982 (Willett et al. 1987). Women with previously diagnosed CHD were excluded from the analysis. Compared with never smokers, former smokers had a relative risk of 1.5 (95-percent CI, 1.0–2.1). In contrast, current smokers had a substantially elevated relative risk, ranging from 2.1 for smokers of 5 to 14 cigarettes per day to 10.8 for those who smoked 45 cigarettes or more per day. There was no further analysis for the effect of duration of abstinence. The authors suggested that the slight elevation in risk of ex-smokers was due, in part, to resumption of smoking by some fraction of the former smokers. Adjustment for age; obesity; menopausal status; estrogen use; family history of MI; and personal history of diabetes, hypertension, and high cholesterol in a multivariate analysis led to an identical relative risk of 1.5, demonstrating the absence of confounding by these coronary risk factors in this population.

In another cohort study, Floderus, Cederlof, and Friberg (1988) monitored 10,945 twins born in Sweden between 1886 and 1925. Smoking behavior was ascertained at baseline in 1961, and the cohort was studied for mortality for 21 years using matched-pair analysis. Among the males, former smokers compared with never smokers had a risk of coronary mortality of 1.0 (95-percent CI, 0.8–1.1). In contrast, current smokers had relative risks ranging from 1.4 to 1.8 depending on amount smoked. There were no data on duration of abstinence at baseline, and there may have been changes in smoking prevalence during the long followup that would tend to attenuate the relative risk.

In a unique cohort design, Raichlen and coworkers (1986) examined progression of atherosclerosis among 32 men who underwent coronary angiographies at least 2 years apart. Among current smokers, progression of disease was statistically significant and was correlated with pack-years smoked during the interval. Among past smokers, the degree of progression of atherosclerosis was far less than among current smokers; it was not statistically different from lack of progression.

Several other cohort studies have reported on the relation of smoking cessation with risk of CHD; however, the number of subjects was generally too small to contribute substantially to knowledge in this area (Table 2).

Intervention Trials

In several clinical trials, an attempt has been made to evaluate the effect of altering risk factors for CHD, including smoking (Chapter 3). Most of the trials including smoking cessation have also incorporated interventions for other CHD risk factors making it difficult to assess the independent effect of quitting. Nonetheless, these data have extended the understanding of the effects of smoking cessation on CHD risk. Assessing self-report of smoking cessation or decrease in cigarette consumption is another potential difficulty. There may be a tendency for subjects in a trial to seek approval and avoid negative feedback by reporting less cigarette use than is actually the case (Chapter 2). Such a tendency would have the effect of misclassification and would yield an underestimate of the benefits of cessation (Table 4).

TABLE 4.—Intervention trials of smoking cessation and CHD risk

Reference	Population	Intervention	Outcome	Cases among former smokers	Overall effect of intervention	Effect of smoking cessation (nonrandomized)
Hughes et al. (1981); MRFIT Research Group (1982,1986); Grimm (1986);	MRFIT: 12,866 healthy US men aged 35–57 at high CHD risk	Diet, reduction in weight, hypertension, and smoking	CHD deaths	15	7% decline in intervention group	44% reduction compared with persistent smokers
Ockene et al. (1990)	MRFIT: 7,663 participant smokers at entry	Diet, reduction in weight, hypertension, and smoking	CHD deaths	33	–	Quitters had 42% reduction (16–60%) comparing quitters at first annual exam to smokers at that time
	MRFIT: 6,943 participant smokers at entry	Diet, reduction in weight, hypertension, and smoking	CHD deaths	12	—	Quitters had 65% reduction (37–80%) comparing 3-yr persistent quitters with persistent smokers
Hjermann et al. (1981)	Oslo study: 1,232 healthy Oslo men aged 40–49 at high CHD risk	Diet and smoking	Fatal and nonfatal MI	16	47% decline in intervention group	Smoking cessation accounted for about 25% of the difference between the groups
Kornitzer et al. (1983)	19,409 male Belgian factory workers, aged 40–59	Antismoking, hypertension control	Fatal and nonfatal MI	169	24.5% reduction in intervention group	No specific analysis conducted for effect of smoking cessation