

## Summary of Observational Studies

In a meta-analysis of cohort and case-control studies of cigarette smoking and stroke (Shinton and Beevers 1989), the overall relative risk of stroke among former smokers was 1.17 compared with never smokers (95-percent CI, 1.05–1.30). This estimate is based on a summary of 18 relative risks from 13 studies that separately identified former smokers (Kahn 1966; Doll and Peto 1976; Abbott et al. 1986; Colditz et al. 1988; Ostfeld et al. 1974; Kono et al. 1985; Khaw et al. 1984; Vessey, Lawless, Yeates 1984; Bell and Symon 1979; Bell and Ambrose 1982; Bonita et al. 1986; Bonita 1986; Taha, Ball, Illingworth 1982). As observed for the relation between current smoking and stroke, the risk among former smokers was greater when the analysis was repeated using only those studies with stroke occurring before age 75 (RR=1.47, 95-percent CI, 1.15–1.88 compared with never smokers). By comparison, the relative risks for current smokers were 2.9 for those younger than 55 years and 1.8 for persons aged 55 to 74 years. Thus, although a modest elevation in risk persisted among younger former smokers, this relative risk was substantially less than that which was observed among current smokers.

## Intervention Studies

Intervention trials described above provide little direct evidence relating to change in risk of stroke after smoking cessation. Only the trial of smoking cessation conducted among 1,445 British men used a single intervention (Rose et al. 1982). During 10 years of followup, five men in the normal care group died because of stroke, and seven men in the intervention group died because of stroke. The small numbers in each group and the small difference in smoking cessation rates between the intervention and control groups limit any conclusion regarding the impact of smoking cessation in this population.

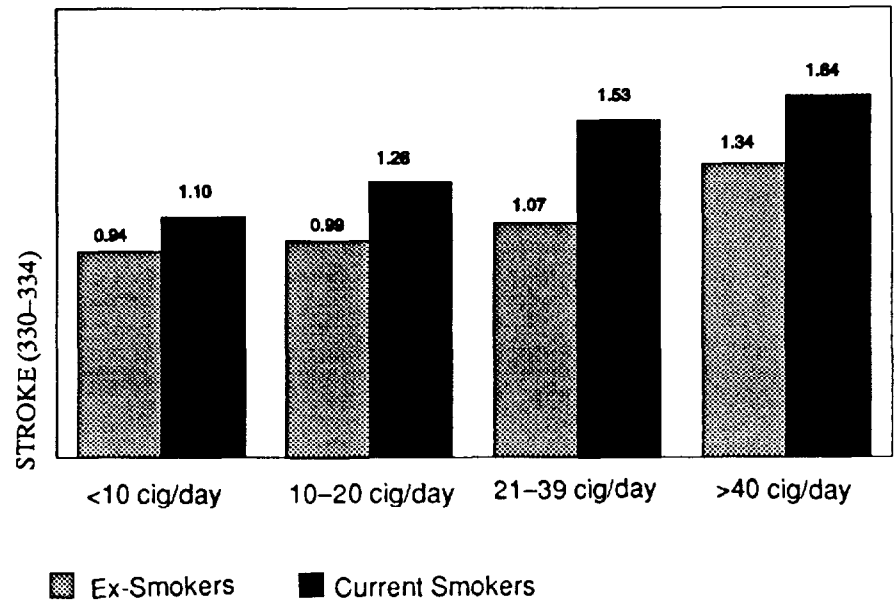
Other intervention studies have included management of hypertension and cholesterol as well as smoking cessation programs. As discussed under randomized trials of smoking cessation and CHD, these multiple interventions make drawing conclusions difficult regarding the relation between smoking cessation and risk of stroke (Steinbach et al. 1984; Wilhelmsen et al. 1986; MRFIT Research Group 1982, 1986; Salonen, Puska, Mustaniemi 1979; Hjermann 1980; Holme 1982).

In a nonrandomized intervention, Rogers and colleagues (1985) measured changes in cerebral artery blood flow among volunteers who were encouraged to abstain from cigarettes. Cerebral perfusion was improved after smoking abstinence.

## Influence of Prior Levels of Smoking

Using data from the followup of 248,046 U.S. veterans monitored for 15 years, Rogot and Murray (1980) reported the mortality ratio for stroke among former cigarette smokers who stopped smoking for reasons other than a physician's orders according to the level of prior cigarette smoking. Based on 1,279 strokes among past smokers, the mortality ratio for stroke among former smokers relative to never smokers increased

with higher previous daily cigarette consumption from 0.94 for those smoking less than 10 cigarettes per day to 1.34 for those smoking 40 cigarettes or more per day compared with never smokers (Figure 7). Data from ACS CPS-II also address this relationship (Table 8). Within each level of previous smoking, the risk of stroke was clearly lower for former smokers than for continuing smokers, except among men who smoked 21 cigarettes or more per day. Other studies have had too few former smokers to classify them according to previous number of cigarettes smoked.



**FIGURE 7.—Mortality ratios for stroke for current smokers and ex-smokers compared with never smokers, by daily cigarette consumption, US Veterans Study, 1954-69**

SOURCE: Adapted from Rogot and Murray (1980).

#### Effect of Duration of Abstinence

The relation between duration of abstinence and risk of stroke has been addressed in only a few studies. In a case-control study that included 145 former smokers who suffered stroke, Donnan and coworkers (1989) observed that the relative risk of stroke declined monotonically over the 10 years following quitting: at the end of 10 years, a significant excess risk of stroke was still evident.

Using 5-year intervals, Rogot and Murray (1980) reported the mortality ratios for those who had abstained. Assuming that an individual classified as a former smoker at the beginning of the study would remain a former smoker throughout the 15 years of

**TABLE 8.—Prospective cohort studies of smoking cessation and risk of stroke**

Reference	Population	Followup	Cases among former smokers	Outcome	Relative risk compared with never smokers <sup>a</sup>	
					Former smokers	Current smokers
Ostfeld et al. (1974)	2,748 Cook County, IL residents receiving old age assistance aged 65–74	3 yr	23	All strokes	0.91 <sup>b</sup>	1–9 cig/day: 1.29 10–19 cig/day: 0.85 ≥20 cig/day: 0.81
Nomura et al. (1974)	47,423 Washington County, MD residents	2 yr morbidity	27 (men)	Thrombosis	1.03 <sup>b</sup>	0.79
				Hemorrhage	0.79	0.86
				Undifferentiated	1.00	1.30
				Total	0.97	0.90
			8 (women)	Thrombosis	1.08	1.14
				Hemorrhage	2.00	0.91
				Undifferentiated	1.14	0.36
				Total	1.26	0.92
Doll and Peto (1976)	British physicians: 34,440 men	20 yr	NR	Cerebral thrombosis mortality	1.22	1.24
Okada et al. (1976)	4,186 Japanese	6 yr	NR	Cerebrovascular attacks	Relative risk of cerebral hemorrhage in nonsmokers was lower than in smokers or ex-smokers, but the difference was not statistically significant	

TABLE 8.—Continued

Reference	Population	Followup	Cases among former smokers	Outcome	Relative risk compared with never smokers <sup>a</sup>	
					Former smokers	Current smokers
Doll et al. (1980)	British physicians: 6,194 women	22 yr	NR	Death due to cerebral thrombosis	1.18	1-14 cig/day: 0.93 14-24 cig/day: 0.45 ≥25 cig/day: 0.19
Rogot and Murray (1980)	US veterans: 248,046 men	15 yr	1,279	Stroke ICD 330-343 (7th revision)	1.02	1.32
Fuller et al. (1983)	Whitehall civil servants: 18,403 men aged 40-64	10 yr	34	Stroke mortality	1.52	1-9 cig/day: 1.0 <sup>c</sup> 10-19 cig/day: 2.0 ≥20 cig/day: 2.3
Vessey, Lawless, Yeates (1984)	17,000 UK women aged 25-39	10-16 yr	2 4	Subarachnoid Nonhemorrhagic	2.3 <sup>b</sup> 1.3	3.0 1.4
Abbott et al. (1986)	Honolulu Heart Study: 7,895 men of Japanese origin; 658 smokers who quit in first 6 yr	12 yr; 6 yr	11 3	Thromboembolic Hemorrhagic Total	1.6 (0.7-3.8) 1.8 (0.4-9.0) 1.5 (1.0-2.3)	3.00 6.10 3.50
Welin et al. (1987)	789 men living in Gothenburg, 678 examined	18.5 yr; 11 yr	NR	Excluded subarachnoid hemorrhage	1.18 <sup>b</sup>	1.67
Carstensen, Pershagen, Eklund (1987)	25,159 Swedes	16 yr	124	Cerebrovascular mortality ICD 430-438	1.10	1-7 g/day: 0.9 8-15 g/day: 0.9 >15 g/day: 1.1

**TABLE 8.—Continued**

Reference	Population	Followup	Cases among former smokers	Outcome	Relative risk compared with never smokers <sup>d</sup>	
					Former smokers	Current smokers
Wolf et al. (1988)	Framingham Study: 4,255 men and women	26 yr	N/A	Stroke and transient ischemic attack	Risk significantly lower than that of current smokers	Men: 1.42 stroke 1.56 brain infarction  Women: 1.61 stroke 1.86 brain infarction
Colditz et al. (1988)	Nurses Health Study: 118,539 US women aged 30–55	8 yr	65	Subarachnoid hemorrhage	3.0 (1.3–6.6)	1–14 cig/day: 4.3 15–24 cig/day: 5.1 ≥25 cig/day: 10.3
				Thromboembolic stroke	1.3 (0.7–6.6)	1–14 cig/day: 1.8 15–24 cig/day: 3.2 ≥25 cig/day: 3.1
				Total stroke	1.5 (1.1–2.2)	1–14 cig/day: 2.5 15–24 cig/day: 2.9 ≥25 cig/day: 3.8
US DHHS (1989)	ACS CPS-I (25-State Study)	6 yr (1959–65)	NR		Men <sup>d</sup> 35–64 yr: 1.02 (0.83–1.25) <sup>d</sup> ≥65 yr: 0.93 (0.80–1.08) <sup>d</sup>	1.79 (1.55–2.08) <sup>d</sup> 1.15 (1.02–1.30) <sup>d</sup>

TABLE 8.—Continued

Reference	Population	Followup	Cases among former smokers	Outcome	Relative risk compared with never smokers <sup>a</sup>			
					Former smokers	Current smokers		
ACS (unpublished tabulations)	ACS CPS-II (50-State Study) <sup>c</sup>	4 yr (1982-86)	NR	Mortality due to cerebrovascular disease	Men <21 cig/day			
					Quit <1 yr	3.94	2.43	
					1-2 yr	1.11		
					3-5 yr	1.55		
					6-10 yr	1.64		
					11-15 yr	0.62		
					≥16 yr	0.72		
					Men ≥21 cig/day			
					Quit <1 yr	0.37	2.07	
					1-2 yr	1.43		
					3-5 yr	1.39		
					6-10 yr	2.27		
					11-15 yr	2.34		
					≥16 yr	1.92		
					Women <20 cig/day			
					Quit <1 yr	NR	1.77	
					1-2 yr	1.92		
					3-5 yr	0.79		
6-10 yr	0.59							
11-15 yr	1.23							
≥16 yr	0.93							

**TABLE 8.—Continued**

Reference	Population	Followup	Cases among former smokers	Outcome	Relative risk compared with never smokers <sup>a</sup>		
					Former smokers	Current smokers	
ACS (unpublished tabulations) (continued)					Women $\geq 20$ cig/day		
					Quit <1 yr	0.29	2.33
					1-2 yr	0.51	
					3-5 yr	0.71	
					6-10 yr	0.84	
					11-15 yr	0.23	
					$\geq 16$ yr	0.73	

NOTE: N/A=not applicable; ACS CPS-I and -II=American Cancer Society Cancer Prevention Studies I and II; NR=not reported; ICD=International Classification of Disease.

<sup>a</sup>95% confidence interval shown in parentheses when available.

<sup>b</sup>Relative risk calculated from data presented in original paper.

<sup>c</sup>Relative risk reported by Shinton and Beevers (1989)

<sup>d</sup>Data for women former smokers not presented separately.

<sup>e</sup>Excluding those with a history of cancer, heart disease, or stroke at enrollment.

followup, these investigators reported mortality ratios close to 1.0 for all durations except for 5 to 9 years after quitting.

Based on 26 years of studying 4,255 men and women in the Framingham Study (Wolf et al. 1988), the risk of stroke among persons who stopped was significantly lower than that among persons who continued to smoke cigarettes. Furthermore, persons who quit smoking developed stroke at the rate of never smokers soon after discontinuing cigarette smoking (Figure 8). Wolf and coworkers (1988) estimated that the risk of stroke among smokers had decreased significantly 2 years after quitting and reverted to the level of never smokers within 5 years. These results persisted after controlling for age, blood pressure, serum cholesterol level, relative weight, left ventricular hypertrophy on electrocardiogram, and blood glucose level. Thus, the reduction in risk after smoking cessation is not attributable to differences in other risk factors for stroke between those who quit and those who continue to smoke.

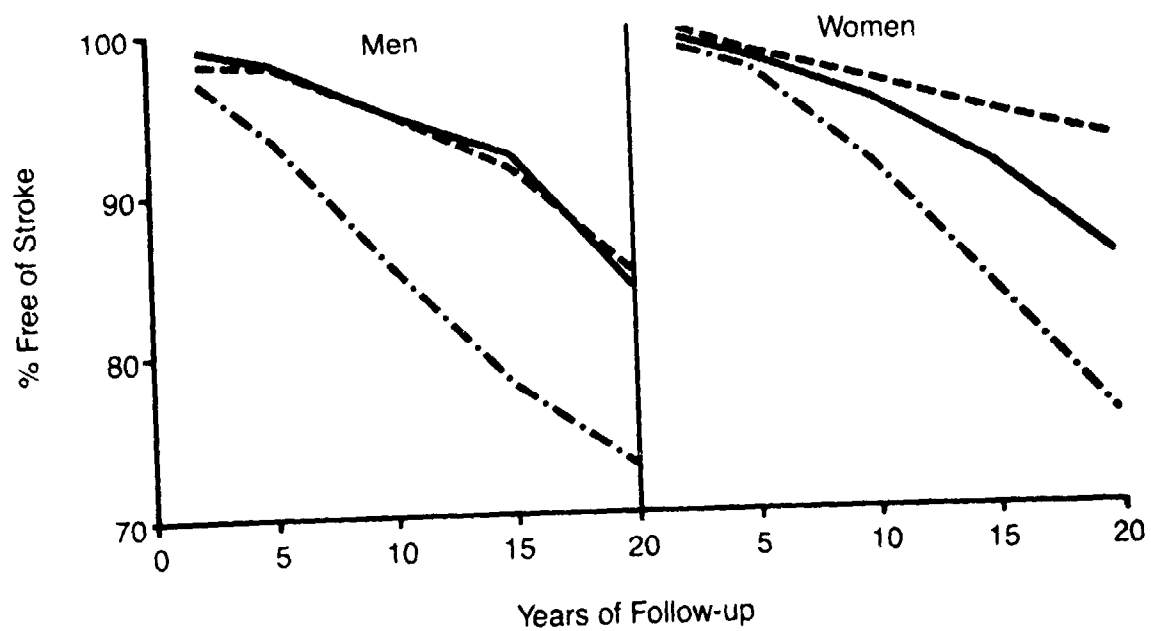
In the Nurses Health Study (Colditz et al. 1988), a lower risk of stroke was observed with increasing time from cessation. Compared with the risk among never smokers, the relative risk was 2.6 among women who had stopped for less than 2 years (95-percent CI, 1.4–4.7). However, among women who had stopped for 2 years or more, the relative risk was reduced to 1.4 (95-percent CI, 1.0–2.0). Women currently smoking 15 to 24 cigarettes per day had a relative risk of 2.9 compared with never smokers. Again, the elevation of the relative risk during the first 2 years after cessation is consistent with high recidivism among these women.

Prospective data from ACS CPS-II showed that among men who quit smoking, the risk of stroke returned to that of never smokers after 11 years or more of smoking abstinence for those originally smoking fewer than 21 cigarettes per day. However, for men who previously smoked 21 cigarettes or more per day, the risk among former smokers did not return to the level of never smokers, even after 16 years or more of cessation. Among women who quit, the rate of decrease was much more rapid; by 3 to 5 years after cessation, the risk of stroke was similar to that of never smokers (Table 8).

### **Oral Contraceptives and Smoking Cessation**

In two studies the risk of subarachnoid hemorrhage was augmented among cigarette smokers who also take oral contraceptives (Petitti and Wingerd 1978; Collaborative Group for the Study of Stroke in Young Women 1975). In the Collaborative Group Study of stroke among young women (1975), the category of former smokers was not clearly defined; rather, a group of “once regular smokers” was compared with “never regular smokers.” In this study there was no association between current smoking or former smoking and risk of thrombotic stroke. Overall, the relative risk for hemorrhagic stroke was 1.8 among once regular smokers and 3.3 among current smokers. Within the group of once regular smokers, women currently using oral contraceptives had approximately twice the risk compared with women not using oral contraceptives. The Royal College of General Practitioners study of oral contraceptives did not separate former smokers from never smokers (Layde, Beral, Kay 1981). Hence, data to address the relationship among oral contraceptives, smoking cessation, and risk of subarachnoid





**FIGURE 8.—Survival free of stroke in cigarette smokers (dotted line), never smokers (solid line), and former smokers (dashed line), aged 60, using Cox proportional hazard regression model, among men and women**

SOURCE: Wolf et al. (1988).

hemorrhage are not available from that study. Because oral contraceptive preparations used today provide substantially lower doses, the risk of cardiovascular disease associated with their use and their interaction with cigarette smoking may be different than observed for the early high-dose preparations.

### **Effect of Smoking Cessation After Stroke**

In contrast with CHD, in which the focus after MI is prevention of recurrent disease, the center of attention after a major cerebrovascular event is rehabilitation. For CHD, substantial evidence shows the benefits of abstaining from smoking after onset of CHD. Comparable data are not available on the benefits of abstinence after stroke.

### **Summary**

Risk of stroke resulting from occlusion of the cerebral arteries and from subarachnoid hemorrhage is increased approximately twofold to fourfold among current smokers compared with never smokers. After cessation, the excess risk decreases steadily. In some studies, the risk of stroke among former smokers becomes indistinguishable from that of never smokers within 5 years; in other studies, this decrease did not occur until after 10 years or more of smoking abstinence. The reduced risk of stroke among persons who stop smoking is independent of the amount previously smoked and other known risk factors for stroke. Similar reductions in risk of stroke after cessation are seen among men and women, but few data are available for minority populations.

### **CONCLUSIONS**

1. Compared with continued smoking, smoking cessation substantially reduces risk of coronary heart disease (CHD) among men and women of all ages.
2. The excess risk of CHD caused by smoking is reduced by about half after 1 year of smoking abstinence and then declines gradually. After 15 years of abstinence, the risk of CHD is similar to that of persons who have never smoked.
3. Among persons with diagnosed CHD, smoking cessation markedly reduces the risk of recurrent infarction and cardiovascular death. In many studies, this reduction in risk of recurrence or premature death has been 50 percent or more.
4. Smoking cessation substantially reduces the risk of peripheral artery occlusive disease compared with continued smoking.
5. Among patients with peripheral artery disease, smoking cessation improves exercise tolerance, reduces the risk of amputation after peripheral artery surgery, and increases overall survival.
6. Smoking cessation reduces the risk of both ischemic stroke and subarachnoid hemorrhage compared with continued smoking. After smoking cessation, the risk of stroke returns to the level of never smokers; in some studies this has occurred within 5 years, but in others as long as 15 years of abstinence were required.

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**CHAPTER 7**  
**SMOKING CESSATION AND**  
**NONMALIGNANT RESPIRATORY DISEASES**