TABLE 3.—Continued

Symptoms Reference	Age (mean)	Continuing smokers			Former smokers			Never smokers		
		Lost	No change[a]	Gained	Lost	No change[a]	Gained	Lost	No change[a]	Gained
Comstock et al. (1970)			Net change: 4.0			Net change: −15.0			Net change: 0.0	
Sharp et al. (1973)		15.4	86.2	6.4	10.2	77.0	12.8	8.0	85.0	7.0
Dyspnea > grade 2										
Woolf and Zamel (1980)[i]		17.0	69.0	13.0	18.0	75.0	8.0	7.0	91.0	2.0
Tashkin et al. (1984)[j]		4.6	89.9	5.5	4.2	89.8	6.0	—	–	—
Comstock et al. (1970)			Net change: 2.0			Net change: 11.0			Net change: 2.0	
Sharp et al. (1973)[k]		11.0	72.8	16.2	14.4	72.8	12.8	10.2	79.8	10.0
Friedman et al. (1973)										
White male ≥1 ppd			Net change: −8.9			Net change: −4.8				
White female ≥1 ppd			Net change: −11.8			Net change: −5.0				
Wheeze										
Woolf and Zamel (1980)[l]		18.0	71.0	11.0	0.0	96.0	5.0	5.0	91.0	4.0
Tashkin et al. (1984)[l]		11.2	77.8	11.0	13.7	82.1	4.2	–	–	—

TABLE 3.—Continued

Symptoms Reference	Age (mean)	Continuing smokers			Former smokers			Never smokers		
		Lost	No change[a]	Gained	Lost	No change[a]	Gained	Lost	No change[a]	Gained
Comstock et al. (1970)[m]			Net change: 5.0			Net change: −5.0			Net change: −2.0	
Sharp et al. (1973)[m]		13.4	77.0	9.6	11.1	78.7	10.2	7.3	88.4	4.3

[a]No change indicates that respiratory symptoms were either consistently absent or consistently present.
[b]Only females, cough and/or phlegm, 5-yr study period.
[c]Light=≤70 cig/wk; moderate=71–140 cig/wk; heavy=more than 140 cig/wk.
[d]Former smokers defined as those who stopped between baseline and followup.
[e]Males only, 5–6-yr followup.
[f]Males only, former studies defined as those who stopped between baseline and followup, 7-yr followup.
[g]Former studies defined as those who stopped between baseline and followup, 1.5-yr followup.
[h]ppd=packs/day.
[i]Grade 2 or 3 dyspnea.
[j]Dyspnea not defined.
[k]Dyspnea at ordinary pace.
[l]Wheeze not defined.
[m]Ever wheeze.

age; former smokers had a shorter duration of smoking in years than current smokers of 1/2 to 1 pack per day, but similar cumulative pack-years (11.5 vs. 15.0). More former and never smokers reported consistent absence of cough or sputum, dyspnea, or wheeze compared with current smokers. Thirteen percent of former smokers developed cough or phlegm during the study period compared with 9 percent of never smokers and 16 percent of smokers. At enrollment, smokers had more respiratory symptoms and were more likely to develop symptoms over the 5 years of the study.

Similarly, in a large population study in the Los Angeles area, respiratory symptoms diminished among former smokers after only 5 years of abstinence (Tashkin et al. 1984). In this study, the following 4 smoking groups were defined: 278 persistent smokers; 414 never smokers; 106 quitters, subjects who smoked regularly at baseline but were nonsmokers at the conclusion of the study; and 294 former smokers, individuals who were regular smokers but had quit at least 2 years prior to baseline. The mean age for female quitters (45.6 years) was comparable among the smoking categories; the mean age for male quitters (43.4 years) was similar to the mean ages for current and never smokers; however, it was 6.2 years less than that for former smokers. Quitters and former smokers had smoked similar numbers of cigarettes per day (26.3 vs. 24.6 for males; 19.1 vs. 19.0 for females), but quitters had higher pack-years (38.6 vs. 26.8 for males; 27.4 vs. 16.2 for females). In addition, quitters had pack-years comparable with current smokers (38.6 vs. 40.5 for males; 27.4 vs. 30.9 for females). Over the 5 years of the study, quitters recovered from the symptoms of cough, sputum, and wheeze more frequently than continuing smokers. No difference in shortness of breath was found between the two groups in the 5-year study period. Quitters and former smokers were not compared to determine the relative importance of cumulative exposure versus time since exposure on the observed reduction of symptoms among ex-smokers.

Comstock and coworkers (1970) reported comparable findings in a study of respiratory symptoms in 670 male telephone company employees studied for 5 to 6 years. Symptoms of chronic cough, phlegm production, and wheeze decreased significantly in quitters whose baseline prevalence for these symptoms was similar to persistent smokers but whose followup values were comparable to never smokers. Baseline and followup prevalence rates for breathlessness in quitters were equivalent to those of persistent smokers.

Sharp and colleagues (1973) found similar trends in respiratory symptoms in 1,263 middle-aged males from an industrial population surveyed in 1961 and again in 1968. Former smokers were defined as individuals who stopped smoking after entry into the study; previous smoking histories were not provided. Over the 7 years of the study, 72.3 percent of former smokers with persistent cough and 64.4 percent with persistent phlegm recovered from the symptoms. These rates of recovery were higher than for the other smoking groups with similar symptoms. Additionally, former smokers who originally complained of dyspnea and wheeze tended to lose these symptoms over the study period, but less dramatically (49-percent and 45.5-percent recovery, respectively). New reports of cough and phlegm were made by less than 10 percent of never and former smokers and 16 percent of continuing smokers, whereas new wheeze was found in 13.5 percent of former and 14.1 percent of continuing smokers. In contrast, dyspnea developed in 18.1 percent of former smokers and 22.4 percent of continuing smokers.

In a study of shorter duration, Friedman and Siegelaub (1980) confirmed the findings of Tashkin and coworkers (1984), Comstock and associates (1970), and Sharp and colleagues (1973). Over approximately 1.5 years of observation, 3,825 recent quitters more often reported decreased chronic cough but no exertional dyspnea when compared with 9,392 persistent smokers.

Findings from two Finnish studies and one British study support the results of these North American investigations (Huhti and Ikkala 1980; Poukkula, Huhti, Mäkaräinen 1982; Leeder et al. 1977). In the 10-year study of Huhti and Ikkala (1980), respiratory symptoms increased in all groups of smokers except male quitters, who had lower prevalence of phlegm production and wheezing (Table 4). Similarly, in a 10-year followup of male pulp mill workers, Poukkula, Huhti, and Mäkaräinen (1982) observed a decrease in respiratory symptoms only for quitters and only for cough and phlegm production. No explanation for the increase in symptoms over time for never smokers was provided in either study. During a 6-year period, Leeder and colleagues (1977) evaluated chronic cough and phlegm annually in 3,916 young married adults. Men who gave up smoking had a progressive decline in the reporting of cough and phlegm. Only a small number of female ex-smokers were included.

In summary, the findings from these longitudinal studies agree with those from the cross-sectional surveys and suggest that cough, phlegm production, and wheezing reverse after cessation, regardless of duration or quantity previously smoked. Dyspnea, however, may be less likely to resolve in subjects with longer smoking histories, possibly indicating irreversible damage induced by smoking up to time of cessation.

Clinical Studies of Possible Mechanisms

Few studies have investigated the mechanisms by which respiratory symptoms improve after smoking cessation. Reversal of mucous gland hyperplasia and reduction in airway inflammation have been considered likely mechanisms but have not been documented. Recovery of epithelial integrity has been shown in two small clinical studies of epithelial permeability (Minty, Jordan, Jones 1981; Mason et al. 1983). Improvement in tracheal mucous velocity, another possible mechanism by which respiratory symptoms may decrease after smoking cessation, has also been examined. Goodman and coworkers (1978) reported that five of nine young former smokers had tracheal mucous velocities that were comparable with age-matched never smokers. One subject had a minimally depressed velocity, and three had markedly depressed values. Only one subject was restudied 2 months after baseline and 9 months after cessation, and at that time, tracheal mucous velocity was found still to be reduced. Because subjects were not studied while smoking, the change after cessation could not be determined. Camner, Philipson, and Arvidsson (1973) studied tracheal velocity in subjects before and after smoking cessation. They found that in 11 of 17 male former smokers, tracheal mucous velocity improved 3 months after cessation and that in the remaining 6 former smokers, velocity was slower or similar when compared with baseline values. Improved tracheal mucous velocity may lead to less mucus in the airways and thereby reduce symptoms of cough and wheeze among former smokers.

TABLE 4.—Percentage of subjects with respiratory symptoms by smoking status, 1961 and 1971, in a cohort of middle-aged, rural Finns

	Smoking groups[a]							
	I		II		III		IV	
	Never smokers 1961 Never smokers 1971		Ex-smokers 1961 Ex-smokers 1971		Smokers 1961 Ex-smokers 1971		Smokers 1961 Smokers 1971	
Symptoms	Males (89)	Females (573)	Males (102)	Females (26)	Males (75)	Females (19)	Males (211)	Females (47)
Phlegm all day—winter								
1961	4	2	7	—	9	11	18	4
1971	6	4	7	4	7	—	27	13
Wheezing most days								
1961	—	3	—	—	3	—	4	2
1971	2	6	4	—	1	—	9	11
Weather affects chest								
1961	6	14	10	15	13	11	13	6
1971	19	27	25	23	24	16	39	19
Breathlessness grades 3–4								
1961	4	20	10	12	15	16	11	9
1971	10	24	17	12	16	21	21	6
Chronic bronchitis								
1961	9	5	14	15	29	16	36	21
1971	11	8	15	12	9	5	41	21
Mean age (yr) in 1961	50	51	50	49	50	47	49	46

[a]Figures in parentheses are number of subjects.
SOURCE: Huhti and Ikkala (1980).

Respiratory Infections

Numerous clinical studies have shown alterations in immune and inflammatory function among cigarette smokers compared with never smokers. Studies of peripheral blood have shown that current smokers have as much as 30 percent higher leukocyte counts than never smokers (Corre, Lellouch, Schwartz 1971; Friedman et al. 1973). Increases have been reported in polymorphonuclear leukocytes (Bridges, Wyatt, Rehm 1985), which appear to have normal chemotactic, microbicidal, and secretory functions (Nobel and Penny 1975; Abboud et al. 1983), and monocytes (Nielsen 1985), which may partially lack the ability to kill intracellular *Candida* (Nielsen 1985). Total

numbers of T lymphocytes are increased among smokers (Kaszubowski, Wysocki, Machalski 1981; Robertson et al. 1983; Burton et al. 1983; Smart et al. 1986). Light and moderate smokers have increases in OKT3+ (total T cells) and OKT4+ (T-helper cells) (Hughes et al. 1985; Ginns et al. 1982), and heavy smokers have decreases in OKT4+ and increases in OKT8+ (T-suppressor cells) (Ginns et al. 1982; Miller et al. 1982). Additionally, functional changes in T lymphocytes from smokers have been observed (Whitehead et al. 1974; Suciu-Foca et al. 1974; Onari et al. 1980), but these findings remain controversial.

Changes in serum components have also been reported. Smokers have higher levels of C5, C9, C1 inhibitor (Wyatt, Bridges, Halatek 1981), C-reactive protein, and autoantibodies (antinuclear and rheumatoid factors) (Heiskell et al. 1962), but lower levels of specific immunoglobulins (IgG, IgM, and IgA) (Ferson et al. 1979; Vos-Brat and Rumke 1969; Kosmider, Felus, Wysocki 1973; Dales et al. 1974; Wingerd and Sponzilli 1977; Gulsvik and Fagerhol 1979; Gerrard, Heiner et al. 1980; Leitch, Lumb, Kay 1981; Andersen et al. 1982; Bartelik, Ziolo, Bartelik 1984; McSharry, Banham, Boyd 1985). As previously described, IgE is elevated in smokers (Burrows et al. 1981; Zetterström et al. 1981; Hällgren et al. 1982; Warren et al. 1982; Bonini 1982; Stein et al. 1983), and this increase may result from suppression of regulatory T-lymphocyte function (Holt 1987).

Bronchoalveolar lavage has provided evidence on the noncellular and cellular components of the peripheral airways and alveoli among smokers and nonsmokers. Data have indicated that smokers appear to have normal or slightly elevated levels of IgA and IgG (Reynolds and Newball 1974; Warr and Martin 1977; Bell et al. 1981; Velluti et al. 1983; Pre, Bladier, Battesti 1980; Gotoh et al. 1983). Similarly, values for lysozyme (Harris et al. 1975), complement components (Robertson et al. 1976), and fibronectin (Villiger et al. 1981) are elevated in lavage fluid from smokers. The total number of cells retrieved from lavage of smokers is increased with marked elevation in the percentages of activated macrophages and neutrophils (Hunninghake et al. 1979; Harris, Swenson, Johnson 1970). Absolute lymphocyte numbers remain unchanged, although T-cell function may be altered (Daniele et al. 1977; DeShazo et al. 1983). Recovered macrophages have increased chemotactic function (Warr and Martin 1974; Labedzki et al. 1983; Richards et al. 1984) and increased release of damaging products such as superoxide anions (Hoidal et al. 1979; Hoidal et al. 1980; Joseph et al. 1980; Hoidal and Niewoehner 1982; Greening and Lowrie 1983; Razma et al. 1984), but diminished microbicidal activity (Martin and Warr 1977; Fisher et al. 1982; Ando et al. 1984).

Smokers have been shown to have reduced specific immune responses to inhaled antigens in several occupational studies. Farmers who were never smokers had higher levels of serum precipitins to *Micropolyspora faeni* than farmers who smoked (Morgan et al. 1973; Morgan et al. 1975; Gruchow et al. 1981; Cormier and Bélanger 1989; Kusaka et al. 1989), whereas pigeon breeders who had never smoked had higher precipitating antibodies to pigeon 7 globulin compared with their smoking counterparts (McSharry et al. 1984; Andersen and Christensen 1983; Boyd et al. 1977). Similar results have been found in poultry workers (Andersen and Schonheyder 1984) and processing workers (McSharry and Wilkinson 1986) in relation to IgG responses to hen

serum antigen and prawn antigen, respectively. Whether smokers have a lower incidence of hypersensitivity pneumonitis has not been adequately studied.

Finally, smokers manifest a blunted immune response to influenza vaccination. Although smokers and nonsmokers have similar postvaccination titers at 3 months (Knowles, Taylor, Turner-Warwick 1981), current smokers have reduced titers at 1 year when compared with nonsmokers (Finklea et al. 1971; Mackenzie, Mackenzie, Holt 1976). In a large clinical trial comparing responses to killed and live attenuated vaccine, smokers had a decreased primary immune response to the killed vaccine (Mackenzie, Mackenzie, Holt 1976).

Although effects of smoking on the immune system have been demonstrated, few studies have investigated the association between smoking and acute respiratory illnesses of presumed infectious etiology. Aronson and coworkers (1982) found that smoking was associated with an increased risk of acute respiratory tract illness. In addition, these investigators found that smoking increased the likelihood of having a lower respiratory tract illness and increased the duration of the symptom of cough. These findings corroborated the results of other investigations (Haynes, Krstulovic, Bell 1966; Peters and Ferris 1967; Parnell, Anderson, Kinnis 1966) that showed the same trend for increased respiratory infections among smokers compared with nonsmokers. In contrast, Pollard and associates (1975) found no difference in the incidence of respiratory illness observed among smokers compared with nonsmokers. Short follow-up of 9 weeks and selection of Naval recruits who had a high prevalence of acute respiratory disease as patients may explain the discrepancy in results.

Kark, Lebiush, and Rannon (1982) studied an outbreak of influenza among 336 men serving in a military unit in Israel. They found that 68.5 percent of 168 current and occasional smokers had clinically apparent influenza as compared with 47.2 percent of never and former smokers. Smokers and nonsmokers with influenza had comparable serologic response rates. Among smokers, the attributable risk percentage for severe influenza, defined as illness resulting in bedrest or loss of workdays, was 40.6 percent (95-percent confidence interval (CI), 21.6–54.8 percent). Similar results have also been reported by several other researchers (Finklea, Sandifer, Smith 1969; MacKenzie, Mackenzie, Holt 1976; Kark and Lebiush 1981).

Smoking Cessation and Respiratory Infection

The relationship between altered immune and inflammatory functions and the occurrence of respiratory infections among ex-smokers has not been extensively investigated. This Section reviews available relevant studies.

Studies of animals have shown a return to normal immune and inflammatory function after cessation of cigarette smoke exposure (Holt and Keast 1977). Investigations of humans have yielded similar findings. Specifically, among former smokers, serum concentrations of IgG, IgA, and IgM (Hersey, Prendergast, Edwards 1983) and bronchoalveolar lavage cell numbers and percentages return to those of never smokers (Holt 1987). Additionally, Miller and coworkers (1982) found that within 6 weeks of smoking cessation, the number and function of T lymphocytes reverted to normal. Finally, Raman, Swinburne, and Fedulla (1983) found that 3 years after smoking

cessation, former smokers had pneumococcal oropharyngeal adherence values comparable with those of never smokers. The significance of these changes in specific components of host defenses to the risk of subsequent respiratory infections among former smokers has not been characterized.

Mortality from influenza and pneumonia with respect to cigarette smoking has been assessed in several cohort studies (Table 5). Mortality from influenza and pneumonia was increased in ever smokers relative to never smokers in the American Cancer Society Cancer Prevention Study I (ACS CPS-I) followup from 1959 through 1963 (Hammond 1965). In the British Physicians Study, current and former smokers had small excesses of mortality from pneumonia, but annual mortality rates from pneumonia increased with the amount smoked (47/100,000 for 1–14 g tobacco/day, 62/100,000 for 15–24 g tobacco/day, 91/100,000 for ≥25 g/day) (Doll and Peto 1976). A similar exposure–response relationship was found in the U.S. Veterans Study (Rogot and Murray 1980).

Findings from ACS CPS-II on age-adjusted mortality from influenza and pneumonia have been examined for the effects of active smoking and smoking cessation (Table 5). Male former smokers of fewer than 21 cigarettes per day have mortality ratios after 10 years of abstinence that are approaching unity. Male former smokers of more than 21 cigarettes per day have mortality ratios approaching unity after 15 years of abstinence, but much higher for shorter periods of abstinence. Female former smokers of any amount have mortality ratios that approach those of never smokers within 3 to 5 years of abstinence.

The association between cigarette smoking status and mortality from influenza and pneumonia may partially reflect the effects of smoking on respiratory defense mechanisms including immune responses. The vulnerability of persons with cigarette-related cardiopulmonary diseases to respiratory infections may also contribute to the association. For example, Glezen, Decker, and Perrotta (1987) studied underlying diagnoses in patients hospitalized with acute respiratory disease during influenza epidemics in Houston, TX. Chronic pulmonary conditions were the most common underlying condition, and cardiac conditions were the next most frequent.

PART II: PULMONARY FUNCTION AMONG FORMER SMOKERS

Cross-Sectional Population Studies of FEV_1

Epidemiologic studies have generally evaluated airflow obstruction based on FEV_1, a spirometric parameter sensitive to airways and parenchymal effects. Cross-sectional population studies, that is, studies in which lung function and cigarette smoking are measured at a single point in time, have demonstrated that cigarette smoking is a strong determinant of FEV_1 level (U.S. DHHS 1984). In those studies in which results from former smokers have been reported, the level of FEV_1 has generally been between that of never smokers and current smokers (Table 6).

Several studies have shown that the level of FEV_1 declines with increasing cumulative smoking among former smokers as well as current smokers (Burrows et al. 1977; Beck, Doyle, Schachter 1981; Dockery et al. 1988). Burrows and colleagues (1977)

TABLE 5.—Age-standardized mortality ratios for influenza and pneumonia for current and former smokers compared with never smokers

Reference	Population	Followup	Cause of death	Standardized mortality ratios by smoking status			
				Gender, age group (yr)	Never smokers	History of smoking	
Hammond (1965)	1,045,087 US men and women (ACS CPS-I)	4 yr	Influenza and pneumonia	Men 45–64	1.0	1.9	
				Men 65–79	1.0	1.7	
				Women 45–64	1.0	1.3	
				Never smokers	Former smokers	Current smokers by amount (g/day)	
Doll and Peto (1976)	34,440 male British doctors	20 yr	Pneumonia	1.0	1.1	1–14	0.9
						15–24	1.1
						≥25	1.7
				Smoking amount (cig/day)	Former smokers[a]	Current smokers	
Rogot and Murray (1980)	293,958 US veterans	16 yr	Influenza and pneumonia	<10	0.8	1.2	
				10–20	1.0	1.7	
				21–39	1.0	2.2	
				≥40	1.3	2.4	
				Never smokers	Former smokers	Current smokers by amount (g/day)	
Carstensen, Pershagen, Eklund (1987)	25,000 Swedish men	16 yr	Pneumonia	1.0	0.6	1–7	1.3
						8–15	1.0
						>15	1.7

TABLE 5.—Continued

Reference	Population	Followup	Cause of death	Standardized mortality ratios by smoking status							
				Total former smokers	Former smokers by years of abstinence						Current smokers
					<1	1–2	3–5	6–10	11–15	≥16	
American Cancer Society (unpublished tabulations)	1,080,555 US men and women (ACS CPS-II)	4 yr	Influenza and pneumonia								
			Men, total	1.3	—[b]	—	—	—	—	—	1.8
			Men <21 cig/day	1.3	3.4	2.1	1.8	1.8	1.1	1.1	2.0
			Men ≥21 cig/day	1.3	2.4	—	2.2	2.1	2.1	0.9	1.2
			Women total	1.2	—[b]	—	—	—	—	—	2.7
			Women <20 cig/day	1.0	—	—	1.3	0.6	0.3	1.2	3.4
			Women ≥20 cig/day	1.1	1.3	2.4	0.6	2.4	1.3	0.2	2.0

NOTE: ACS CPS-I and -II=American Cancer Society Cancer Prevention Studies I and II.
[a]Former cigarette smokers who stopped smoking for reasons other than a physician's orders.
[b]Not calculated.

TABLE 6.—Association between cigarette smoking status and FEV_1 levels in selected cross-sectional studies of adult populations

Reference	Year of study	Location	Population	Findings
Goldsmith et al. (1962)	1961	San Francisco, CA	3,311 longshoremen	Mean FEV_1 % of predicted value
				Never smokers 100
				Former smokers 97
				Current smokers 93
Edelman et al. (1966)		Baltimore, MD	410 male volunteers, aged 20–103	By partial regression analysis, significant reduction of FEV_1 among current and former cigarette smokers
Higgins and Kjelsberg (1967)	1959–60	Tecumseh, MI	5,140 men and women, aged 16–79	Age-adjusted mean FEV_1 (L)
				Men / Women
				Never smokers 3.3 / 2.3
				Former smokers 3.3 / 2.3
				Current smokers 3.1 / 2.3
Higgins et al. (1968)	1963	Marion County, WV	926 white men, aged 20–69	Mean FEV_1 (L)
				Never smokers 3.6
				Former smokers 3.3
				Current smokers 3.5
Wilhelmsen, Orha, Tibblin (1969)	1963	Göteborg, Sweden	331 men, age 50	Mean FEV_1 (L)
				Never smokers 3.8
				Former smokers 3.7
				Current smokers 3.5

TABLE 6.—Continued

Reference	Year of study	Location	Population	Findings
Woolf and Suero (1971)		Toronto, Canada	298 female volunteers, aged 25–54, employed at commercial firms	Adjusted mean levels
				FEV_1 / FEV_1/FVC ratio
				Never smokers: 2.7 / 86.7
				Former smokers: 2.6 / 85.0
				Current smokers: 2.5 / 84.6
Schlesinger et al. (1972)	1968	Israel	4,331 male civil servants, aged 45 and older	Mean value of the FEV_1/FVC ratio
				Never smokers: 76.0
				Former smokers: 74.3
				Current smokers: 73.6
Fletcher et al. (1976)	1961	London, England	1,136 men, aged 30–59, employed at bank or in maintenance of transportation equipment	Adjusted FEV_1 (L)
				Never smokers: 3.3
				Former smokers: 3.2
				Current smokers: 3.0
Higgins, Keller, Metzner (1977)	1962–65	Tecumseh, MI	4,669 men and women, aged 20–74	Mean normalized FEV_1 score
				Men / Women
				Never smokers: 10.2 / 10.1
				Former smokers: 9.9 / 10.0
				Current smokers: 9.6 / 9.8

TABLE 6.—Continued

Reference	Year of study	Location	Population	Findings
Anderson (1979)		Lufa, Papua New Guinea	733 men and women aged 25 and older	Age and height-adjusted mean FEV_1 (L)
				Men / Women
				Never smokers: 2.6 / 2.4
				Former smokers: 2.6 / 2.3
				Current smokers: 2.6 / 2.4
Higenbottam et al. (1980)		London, England	18,403 male civil servants, aged 40–64	Age and height-adjusted mean FEV_1 (L)
				Former smokers: 3.2
				<7 yr abstinent: 3.2
				7–12 yr abstinent: 3.2
				≥13 yr abstinent: 3.1
				Current smokers: 3.1
Huhti and Ikkala (1980)	1961	Rural commune, Finland	473 men and 569 women, followed for 10 yr	FEV_1 at initial examination
				Men / Women
				Never smokers: 3.5 / 2.5
				Former smokers: 3.5 / 2.5
				Current smokers[a]: 3.3 / 2.8
Bossé et al. (1980)	1963	Boston, MA	703 healthy male veterans followed for 10 yr	Initial FEV_1 adjusted for age
				Never smokers: 3.6
				Former smokers: 3.6
				Current smokers: 3.3

TABLE 6.—Continued

Reference	Year of study	Location	Population	Findings
Bossé et al. (1981)	1963	Boston, MA	850 healthy male veterans followed for 5 yr	Initial FEV_1 adjusted for age Never smokers 4.0 Former smokers 3.7 Current smokers 3.8
Beck, Doyle, Schachter (1981)	1972–74	Lebanon and Ansonia, CT; Winnsboro, SC	4,690 men and women, aged 7 and older	Residual FEV_1 (L) adjusted for age, height, weight Men / Women Never smokers –0.02 / 0.02 Former smokers –0.12 / 0.20 Current smokers –0.22 / 0.27
Tashkin et al. (1984)	1973–75	Los Angeles, CA	1,092 men and 1,309 women aged 25–64 followed for 5 yr	Initial adjusted level of FEV_1 Men / Women Nonsmokers 3.9 / 2.7 Former smokers 3.8 / 2.7 Current smokers[a] 3.6 / 2.5
Taylor, Joyce et al. (1985)	1981–82	London, UK	227 men followed for 7.5 yr	FEV_1 as percentage of predicted All / Reactors / Nonreactors Nonsmokers 119.1 / 92.0 / 121.4 Former smokers 107.8 / 96.4 / 111.4 Current smokers 100.5 / 84.6 / 108.5

TABLE 6.—Continued

Reference	Year of study	Location	Population	Findings
Camilli et al. (1987)		Tucson, AZ	654 men and 893 women aged 20 and older, who had FEV_1 at baseline and followup exams	Initial FEV_1 as percentage of predicted
				Men / Women
				Nonsmokers: 99.8 / 97.8
				Former smokers: 93.7 / 95.6
				Current smokers[a]: 91.8 / 91.6
Dockery et al. (1988)	1974–77	6 US communities	8,191 men and women aged 25–74	Deficit of FEV_1 (L) compared with expected
				Men / Women
				Nonsmokers: 0.03 / –0.02
				Former smokers: –0.26 / –0.05
				Current smokers: –0.51 / –0.23

NOTE: FEV_1=1-sec forced expiratory volume; FVC=forced vital capacity.

[a]At initial examination, which includes continuing smokers and those who subsequently quit.

reported that the level of FEV_1 had a highly significant quantitative relationship with pack-years in a general population sample of 2,369 subjects in Tucson, AZ, and that smokers and former smokers had comparable levels accounting for pack-years.

Higenbottam and coworkers (1980) assessed lung function in the 18,000 males in the Whitehall Civil Servants Study. Mean FEV_1 values among former smokers, adjusted for age and height, were lower than those for never smokers, but greater than those for current smokers. FEV_1 among former smokers decreased with increasing total consumption of cigarettes, but length of abstinence had little effect on FEV_1 among former smokers, although the minimum period considered was less than 6 years. The authors suggested that the depression of lung function associated with cigarette smoking has two components—an irreversible component related to total consumption and a component rapidly reversible on cessation.

Beck, Doyle, and Schachter (1981) analyzed FEV_1 data from 4,690 subjects, aged 7 years and older, in 3 separate U.S. communities. These investigators also found that the deficit in FEV_1 compared with that expected for never smokers increased with cumulative smoking as measured by pack-years and duration of smoking. After adjusting for cumulative smoking, FEV_1 was 147 mL lower among male smokers and 78 mL lower among female smokers compared with former smokers.

Dockery and coworkers (1988) studied 8,191 randomly selected adults in 6 U.S. communities. These researchers found that the deficit of observed FEV_1 compared with expected age-, height-, and sex-specific values increased linearly with cumulative pack-years among former smokers and current smokers (Figure 7) (Dockery et al. 1988). For the same pack-years, FEV_1 was 123 mL higher among male former smokers and 107 mL higher among female former smokers compared with current smokers.

In a followup study of 227 men, Taylor, Joyce, and coworkers (1985) reported that percent-predicted FEV_1 for former smokers (107.8 percent predicted) was between that of smokers (100.5) and never smokers (119.1). Within each smoking category, men with increased bronchial reactivity to inhaled histamine had lower levels of percent-predicted FEV_1 than did nonreactors. These differences were statistically significant among smokers (84.6 vs. 108.5 percent predicted for reactors and nonreactors, respectively) and former smokers (96.4 vs. 121.5 percent predicted for reactors and nonreactors, respectively).

The results of these studies suggest that permanent loss of FEV_1 occurs with smoking and that the extent of the loss is associated with the cumulative amount smoked. However, before the development of overt COPD, cessation is associated with an average improvement of 75 to 150 mL, implying that smoking also causes reversible decrements of function.

Pulmonary Function Studies After Smoking Cessation

Studies in which the lung function of smokers was measured before and after smoking cessation are reviewed in this Section; tests of pulmonary function included spirometry, nitrogen washout, and other techniques potentially sensitive to the effects of cessation. Inflammatory lesions of the small airways have been demonstrated to occur in young adult smokers before the appearance of clinically significant airflow obstruction

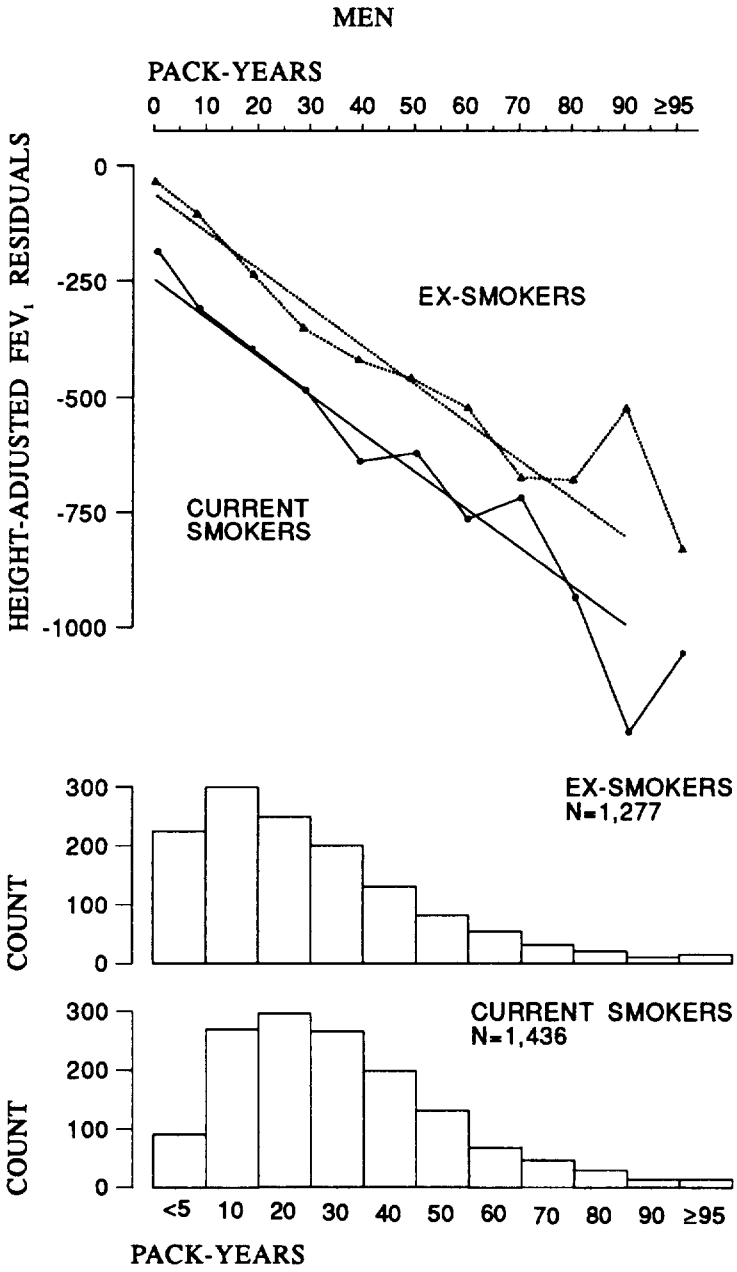

FIGURE 7.—Sex-specific mean height-adjusted FEV_1 residuals versus pack-years for current and ex-smokers, and distributions of number of subjects by pack-years

NOTE: FEV_1=1-sec forced expiratory volume.

SOURCE: Dockery et al. (1988).

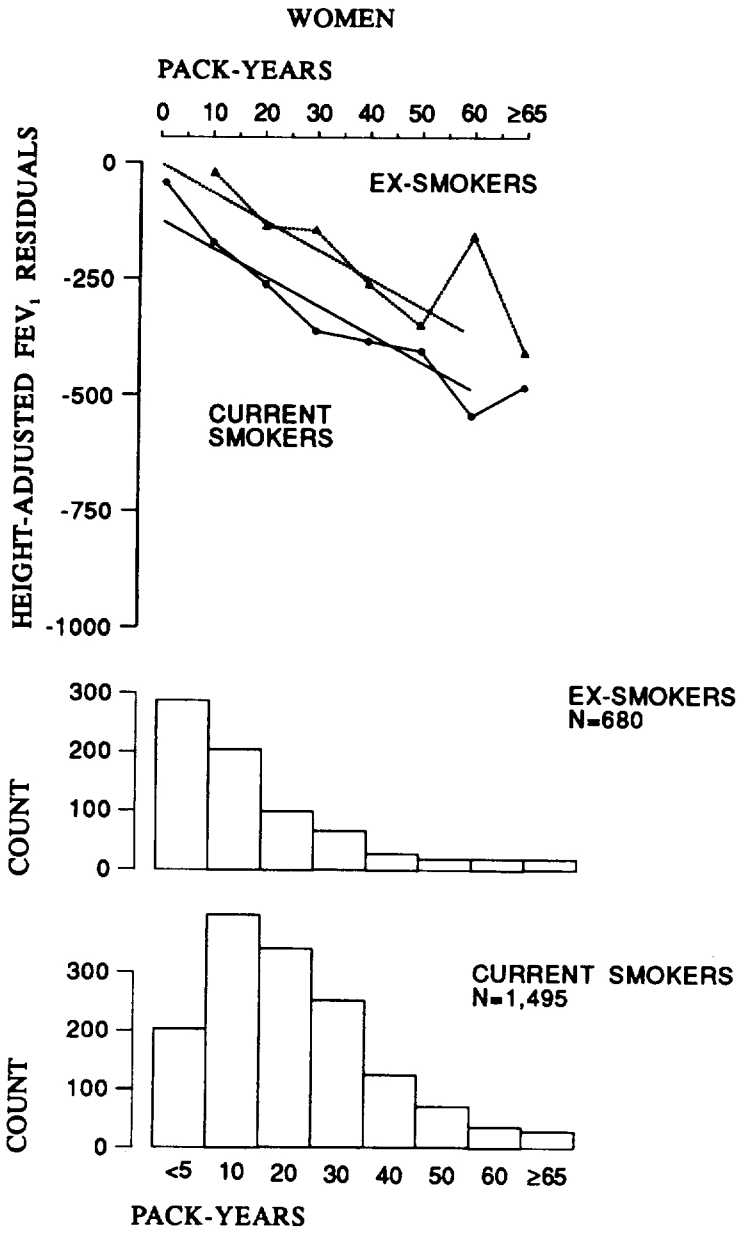

FIGURE 7. (Continued)—Sex-specific mean height-adjusted FEV_1 residuals versus pack-years for current and ex-smokers, and distributions of number of subjects by pack-years

NOTE: FEV_1=1-sec forced expiratory volume.

SOURCE: Dockery et al. (1988).

(Niewoehner, Kleinerman, Rice 1974). Tests sensitive to abnormalities of the small airways (e.g., helium-oxygen flow volume curves, the single breath nitrogen test or other tests of closing volume, and frequency dependence of compliance) would be expected to be particularly sensitive for detecting changes in function after cessation. In most of the studies reviewed in this Section, participants were enrolled through smoking cessation clinics and subsequently monitored for pulmonary function and smoking status. The data from these studies can assess reversible effects of smoking through documentation of functional change coincident with cessation; irreversible effects can be estimated by comparison of lung function level with predicted values for normal function.

Changes in Spirometric Parameters After Cessation

Studies of spirometric measurements of pulmonary function before and after smoking cessation are summarized in Table 7. Many of these studies suggested an improvement in pulmonary function following cessation, although the magnitude of the improvement was small in some of the studies.

Dirksen, Janzon, and Lindell (1974) studied a randomly selected sample of men born in 1914 in Malmö, Sweden. Fifty-eight heavy smokers were solicited to participate in a smoking cessation program, with 31 abstaining for 2 months. Vital capacity (VC) and FEV_1/FVC improved 8 to 10 days after cessation.

Bode and coworkers (1975) studied 10 healthy subjects who participated in a smoking cessation program and remained abstinent for 6 to 14 weeks. Small and nonsignificant improvements were found for VC (0.3 percent change) and FEV_1 (0.9 percent change). Maximum expiratory flow rates with helium at 50 and 25 percent of VC significantly increased.

Martin and colleagues (1975) observed 12 successful subjects from a smoking cessation clinic for 1 to 3 months. Changes of $\dot{V}_{max50}$ and $\dot{V}_{max25}$ after smoking cessation were variable and not statistically significant. Residual volume and total pulmonary resistance were also unchanged.

McCarthy, Craig, and Cherniack (1976) studied a group of smokers who volunteered to participate in a smoking cessation program. At 25 to 48 weeks after cessation, only 15 participants were still not smoking. Among these subjects, FVC increased from 3.92 L to 4.04 L (3.1 percent change), but FEV_1 (–0.3 percent change) and mid-maximum expiratory flow (MMEF) (–9.6 percent change) decreased. Fifty-nine subjects were evaluated between 6 and 24 weeks following cessation. Significant improvements were noted for FVC (2.3 percent of initial value) and the peak expiratory flow rate (6.7 percent of initial value). The FEV_1, $\dot{V}_{max50}$, and $\dot{V}_{max25}$ did not change significantly.

Bake and colleagues (1977) observed 17 subjects who were abstinent from cigarettes for at least 5 months. During this interval, VC and FEV_1 improved by 4.4 and 4.8 percent predicted, respectively, while $\dot{V}_{max50}$ and $\dot{V}_{max25}$ were reduced by 2.5 percent predicted and 7.3 percent predicted, respectively. At 2-year followup, only nine subjects were still smoking. No significant differences from baseline function were found in this group.

TABLE 7.—Spirometric studies of participants in smoking cessation programs

Reference	Population	Followup	Measure	TLC	FVC or VC	FEV_1	FEV_1/FVC	MMEF	$\dot{V}_{max50}$	$\dot{V}_{max75}$
Dirksen, Janzon, Lindell (1974)	31 men born in 1914, Malmö, Sweden	8–10 days 52–60 days	Change from initial		110 mL 20 mL		0.7% −1.3%			
Bode et al. (1975)	3 men and 7 women, aged 29–61, smoking clinic	6–14 wk	% change[a]	−0.8%	−0.2%	−0.7%		−2.7%	−2.0%	−10.6%
McCarthy, Craig, Cherniack (1976)	15 subjects, smoking clinic	25–48 wk	% change[b]		3.1%	0.3%		−9.6%		
Bake et al. (1977)	9 men and 8 women, aged 24–69, smoking clinic	5 mo 2 yr	Change in % predicted		4.4 2.2	4.8 −1.6			−2.5 0.7	−7.3 −11.1
Buist et al. (1976)	6 men and 7 women, aged 24–53, smoking clinic	1 mo 3 mo 6 mo 12 mo	Change from initial values	+10 mL 100 mL −240 mL −50 mL	−40 mL −310 mL −120 mL −70 mL	−40 mL −70 mL +30 mL +60 mL		60 mL/sec 110 mL/sec +40 mL/sec 160 mL/sec		
Buist, Nagy, Sexton (1979)	3 men and 12 women, aged 24–52, smoking clinic	3–4 mo 6–8 mo 30 mo	Change in % predicted		2.4 6.5 6.5	1.5 4.6 3.3				

TABLE 7.—Continued

Reference	Population	Followup	Measure	TLC	FVC or VC	FEV_1	FEV_1/FVC	MMEF	$\dot{V}_{max50}$	$\dot{V}_{max75}$
Zamel, Leroux, Ramcharan (1979)	12 men and 14 women, mean age 36±9 yr	62±6 days	% change	1.2%	3.0%	4.0%				
Pride et al. (1980)	8 male smokers who thought easy to stop	4 yr	No improvement in spirometric tests or MMEF							

NOTE: TLC=total lung capacity; FVC=forced vital capacity; VC=vital capacity; FEV_1=1-sec forced expiratory volume; MMEF=mid-maximum expiratory flow.
[a]Average percentage change recalculated from individual values.
[b]Percentage change in reported mean values.

Buist and coworkers (1976) observed a group of six men and seven women who stopped smoking for at least 1 year after a smoking cessation program. Small changes were noted in spirometric parameters. The authors reported that MMEF distinguished between smokers and quitters in that over a 1-year period MMEF declined significantly among smokers but not among quitters.

Buist, Nagy, and Sexton (1979) supplemented this sample with participants from another smoking cessation program and extended followup to 30 months for both groups. Significant improvements were observed in VC, FEV_1, and MMEF among the quitters during the first 6 to 8 months (Figure 8). No further improvement was observed up to 30 months.

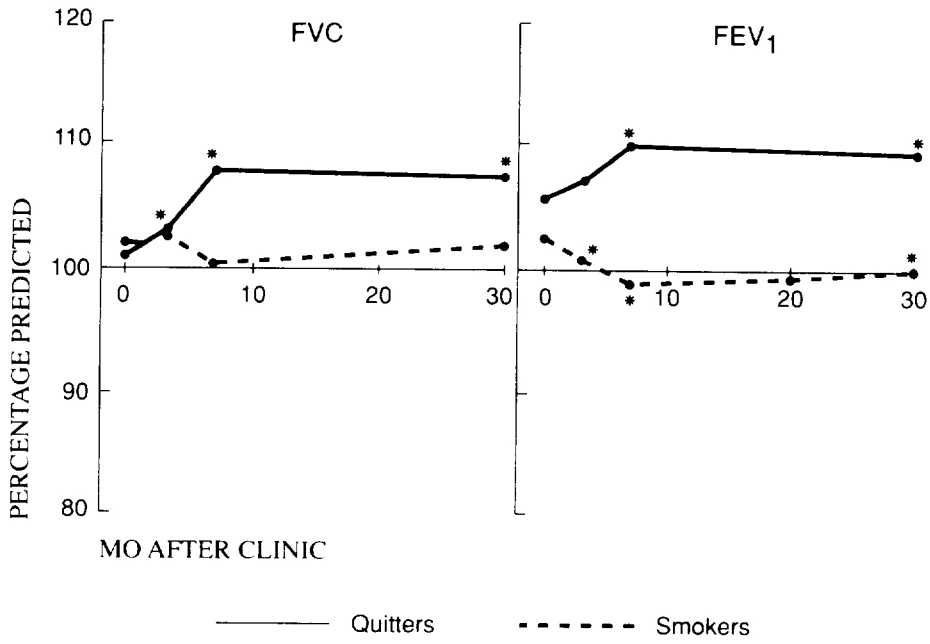

FIGURE 8.—Mean values for FVC and FEV_1, expressed as a percentage of predicted values, in 15 quitters and 42 smokers during 30 months after 2 smoking cessation clinics

NOTE: Asterisks (*) denote a significant difference from the initial value at $p<0.05$. FVC=forced vital capacity; FEV_1=1-sec forced expiratory volume.

SOURCE: Buist, Nagy, Sexton (1979).

Zamel, Leroux, and Ramcharan (1979) studied 26 healthy smokers for 2 months after cessation. They reported significant increases in VC and FEV_1 of 3.0 and 4.0 percent change, respectively. In contrast, Pride and coworkers (1980) in a 4-year study of eight male smokers "who thought they would find it easy to give up smoking," reported no improvement in spirometric tests of MMEF.

Taken together, these studies suggest that smoking cessation quickly results in small improvements in lung function, as assessed by spirometry. Although the changes were not uniformly statistically significant in the investigations reviewed in this Section, the number of subjects was small in most of the studies. Compared with baseline before cessation, FVC or VC and FEV_1 may improve by about 4 or 5 percent at 4 to 8 months after cessation. In absolute value, this improvement is comparable with the approximately 100-mL improvement reported by Beck, Doyle, and Schachter (1981) and Dockery and coworkers (1988) based on cross-sectional comparison of former smokers to current smokers.

Tests of Small Airways Function

Several investigators have studied the effects of smoking cessation using measures of small airways function as determined by the single breath nitrogen test (Table 8) and other tests. In the single breath nitrogen test, the subject breathes one breath of 100 percent oxygen from residual volume to total lung capacity (TLC). A concentration gradient of nitrogen is thus established with the highest concentrations at the apex. Subsequently, the subject exhales, and the nitrogen concentration of the exhaled air is monitored. The indices of small airways function provided by this test include the closing volume (CV) expressed as a percentage of the vital capacity (CV/VC percent), the closing capacity (CC) expressed as a percentage of TLC (CC/TLC percent), and the slope of the nitrogen concentration during the alveolar plateau (slope of phase III). Both CV and CC are increased by abnormalities of the small airways, whereas the slope of the nitrogen concentration reflects the evenness of the ventilation distribution.

Buist and colleagues (1976) studied a group of 25 cigarette smokers who attended a smoking cessation clinic. Cessation resulted in significant improvements in CV, CC, and the slope of alveolar plateau at 6 and 12 months after cessation. Participants in a second smoking cessation clinic were added, and the followup continued to 30 months (Buist, Nagy, Sexton 1979). At the 6- to 8-month followup, CV had improved by 33 percent predicted among those who quit, CC by 20 percent predicted, and the slope of the alveolar plateau by 52 percent. No further improvements were evident at the 30-month followup (Figure 9).

Similar improvements have been reported by several other investigators. Bode and coworkers (1975) found that CV improved by 20 percent 6 to 14 weeks after cessation compared with initial values among 10 subjects. These investigators reported that the slope of phase III was unchanged by cessation. McCarthy, Craig, and Cherniack (1976) observed 131 smokers aged 17 to 66 years who volunteered to attend a smoking cessation clinic. For 15 persons abstinent from 25 to 48 weeks, cessation resulted in a significant 13-percent reduction in CC and a 27-percent reduction in the slope of phase III.

Bake and coworkers (1977) showed a 33-percent reduction in the percent-predicted slope of phase III among 17 subjects at 5 months after cessation. On the other hand, only small changes in CV and CC were observed. Zamel, Leroux, and Ramcharan (1979) investigated 26 smokers for an average of 62 days after cessation. Similarly,

TABLE 8.—Studies of closing volume (CV/VC%), closing capacity (CC/TLC%), and slope of alveolar plateau (SBN_2/L) among participants in smoking cessation programs

Reference	Location	Population	Followup	Measure	CV/VC %	CC/TLC %	SBN_2/L
Dirksen, Janzon, Lindell (1974)	Malmö, Sweden	31 men born in 1914	8–10 days	Change from initial	+1.0%	–1.0%	
			52–60 days		–0.6%	–1.6%	
Bode et al. (1975)	Smoking clinic	3 men, 7 women	6–14 wk	% change[a]	–35.7%		5.9%
Martin et al. (1975)	Smoking clinic	12 subjects	1–3 mo	Plots, quantitative data unpublished			
McCarthy, Craig, Cherniack (1976)		15 subjects	25–48 wk	% change	0.0%	–13.2%	–26.6%
Buist et al. (1976)	Smoking clinic	6 men, 7 women	1 mo	Change from initial	–1.6%	–0.8%	–0.3%
			3 mo		–1.9%	+1.6%	0.0%
			6 mo		–4.1%	–5.7%	–0.4%
			12 mo		–3.6%	2.6%	–0.3%
Bake et al. (1977)	Smoking clinic	9 men, 8 women	5 mo	Change in % predicted	2.8	–1.8	–33.2
			2 yr		–2.5	0.3	–43.8
Buist, Nagy, Sexton (1979)	Smoking clinic	3 men, 12 women	3–4 mo	Change in % predicted	–23.1	–1.6	–25.6
			6–8 mo		–33.0	–19.5	–51.9
			30 mo		–25.4	–15.4	–48.4

TABLE 8.—Continued

Reference	Location	Population	Followup	Measure	CV/VC %	CC/TLC %	SBN_2/L
Zamel, Leroux, Ramcharan (1979)		12 men, 14 women	62±6 days	% change	−4.1%	−1.9%	−10.3%
Pride et al. (1980)		8 male smokers who thought easy to stop	4 yr		No improvement		Significant decline

NOTE: CV=closing volume; VC=vital capacity; TLC=total lung capacity.

[a]Average percentage change recalculated from individual values.