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Lung Cancer Trends. Part 1: North America

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1. INTRODUCTION

One of the most important steps in cancer prevention is to analyse long-term trends in cancer incidence and mortality. Epidemiology studies using case-control and cohort designs to evaluate exposure–disease associations have causally linked smoking to lung cancer in investigations reported since the 1950s [1–3].

The Doll and Hill cohort consisted of general practitioners in the United Kingdom. Of 34,439 male British doctors who replied to a postal questionnaire in 1951, 10,000 died during the first 20 years, and another 10,000 died during the second 20 years [4]. Another large case-control study centred on the year 1990 found that people who stopped smoking, even well into middle age, avoided more than 90% of the risk attributable to tobacco use [5].

As lung cancer incidence and mortality rates are followed over time, their rise and decline parallel past trends of cigarette smoking [6]. Biomarkers of exposure, dose, susceptibility, and genetic damage may allow epidemiology investigations to uncover specific pathways of human lung carcinogenesis. "Passive smoking"—the involuntary inhalation of tobacco smoke by non-smokers—has also been recognised as a cause of lung cancer [7].

For lung cancer, statistics have confirmed the clinical impression that the disease became more frequent during the first half of the 20th century. However, it is also well known that, in the 19th century, this malignancy was usually misdiagnosed as pulmonary tuberculosis or chronic bronchitis and emphysema. To illustrate, a report of the Prudential Insurance Company on international statistics of cancer mortality 1908–1912 never mentioned lung cancer [8,9]. At the end of the 20th century, lung cancer had become one of the world's leading causes of death—and the most preventable one.

Tobacco was widely used throughout the world for centuries, but the present lung cancer pandemic followed the introduction of manufactured cigarettes with addictive properties, which resulted in a new pattern of sustained exposure of the lung to inhaled carcinogens [10].

In January 1964, the first Surgeon General's report on smoking and health (*Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service*) was the first official recognition in the United States that cigarette smoking causes cancer and other serious diseases. That landmark report prompted a series of public health actions that reflected changes in societal attitudes toward the health hazards of tobacco use. Among the actions were the banning of tobacco advertising on broadcast media, the development of effective treatments for tobacco dependence, and the publishing of 27 further Surgeon General's reports on topics such as environmental (that is, second-hand) tobacco smoke, which led to creation of smoke-free public places, restaurants, and bars. As a result of those and other efforts, per capita annual consumption of cigarettes among adults aged 18 years and older declined during 1963–2002 to 1979 cigarettes from 4345, the lowest figure recorded since 1941 [11,12]. Current smokers in the United States are now outnumbered by former smokers. However, despite that progress, smoking remains the chief preventable cause of death in the United States. Each year approximately 440,000 people die from illnesses attributed to smoking [13].

In Canada, three types of cancer account for at least 50% of new cancer cases in each sex: prostate, lung, and colorectal cancers in males, and breast, lung, and colorectal cancers in females. Lung cancer incidence among men is declining: 2003 saw an estimated 12,200 new cases and 10,900 deaths [14]. However, lung cancer incidence continues to rise among women. With an estimated 9,000 new cases in 2003, lung cancer is the second-leading cancer in women. Lung cancer alone accounts for 30% of cancer deaths in men and 25% in women. Lung cancer will continue to be the leading cause of cancer deaths in Canadian women in 2003, accounting for an estimated 7900 deaths. That estimate reflects the rapid increase in the lung cancer mortality rate among women over the past three decades.

2. INCIDENCE AND MORTALITY

2.1 Sex Differences

Estimates of cancer incidence and mortality are usually presented both as numbers of cases and deaths and as annual incidence or mortality rates per 100,000 population. The rates are age-standardised to take into account differences in the age structures of the populations being compared. Because of the high case-fatality rate of lung cancer, the incidence and mortality rates are nearly equivalent.

In the United States, statistics indicate that lung cancer was rare until the disease began a sharp rise in the 1930s. That rise peaked by the mid 20th century, with lung cancer becoming the leading cause of cancer death among men. The epidemic among women followed that among men, with a sharp rise in rates from the 1960s to the present, resulting in lung cancer becoming the most frequent cause of female cancer mortality [15]. The epidemic among women not only occurred later, but did not reach as high a peak as that in men, because smoking prevalence crested at substantially higher levels among men than among women [16,17].

Mortality rates in older age groups with lung cancer continue to increase in both sexes, more significantly in men than in women. The mortality rate for lung cancer is now decreasing in younger age groups. The decreases are also more pronounced for men, but are now becoming evident in women [18]. As the younger birth cohorts age, their reduced risk of lung cancer should translate into substantial reductions in the overall occurrence of the disease.

In an analysis of lung cancer mortality in the United States for 1970–1997, Jemal *et al.* [16] found that the rates of decrease in younger men and women—that is, those born after 1950—were moderating. The authors suggested that that moderation could reflect patterns of smoking initiation in young adults.

In the United States, an estimated 173,770 new cases of lung cancer are expected in 2004 [19]. The incidence rate is declining significantly in men, to 79.8 in 2000 from a high of 102.1 per 100,000 population in 1984. In the 1990s, the increase among women reached a plateau, with an incidence rate of 52.8 per 100,000 population in 1998.

An estimated 160,440 lung cancer deaths are expected in the United States in 2004. Since 1991, mortality rates have continued to decline significantly (by about 1.8% per year) in men. However mortality rates have continued to rise in both white and African American women (although the rate of increase has slowed since the early 1990s). Decreasing lung cancer incidence and mortality rates reflect decreased smoking rates over the past 30 years.

In Canada, among women, lung cancer incidence and mortality rates are continuing to increase. Those rates are now 3–4 times as high as the rates in 1974. However, the estimated rates among women in 2003 were still much lower than those among men [14]. Among men, lung cancer rates levelled off in the mid 1980s. Those rates have since consistently declined, reflecting a drop in tobacco consumption among men beginning in the mid 1960s.

Between 1991 and 1999, mortality rates for lung cancer were showing their greatest increase among women, with a significant increase of 2.1% per year. Among women, smoking rates began to decline slightly only around the 1980s [20], and thus benefits in terms of declining lung cancer rates have yet to become apparent (Figures 1 and 2).

2.2 Race and Ethnicity

The 2000 U.S. population census report found that about 36.6 million African Americans resided in the United States, representing more than 12% of the total U.S. population [23]. The African American population increased by about 6.7 million between 1990 and 2000. Before the 1960s in the United States, lung cancer mortality rates were significantly lower in non-white patients than in white patients [24]. However, in recent years, higher incidence rates and lower survival rates for lung cancer were found in African American men than in white men.

Lung cancer incidence rates were similar among African American and white women, but lung cancer occurred about 40% more frequently among African American men than among white men in the United States between 1995 and 1999 [21,22,25] (Figures 3 and 4).

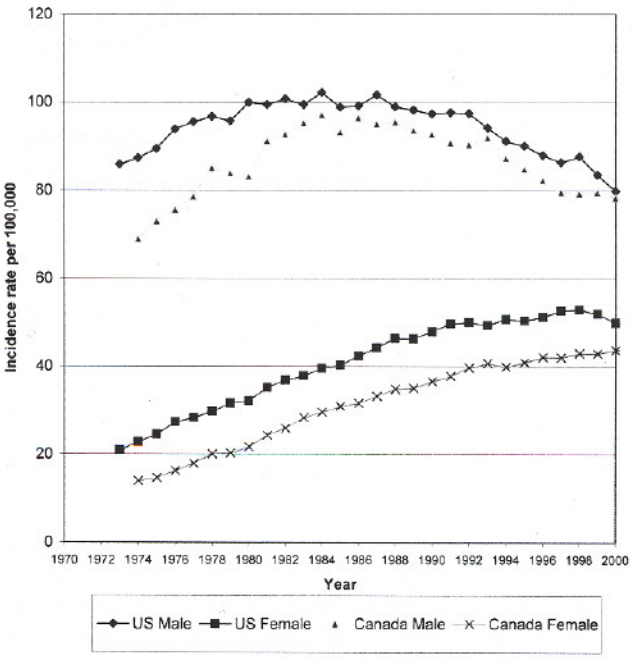

FIGURE 1 *Lung cancer incidence rates for the United States (1973–2000) and Canada (1974–2000) for men and women* [14,21,22].

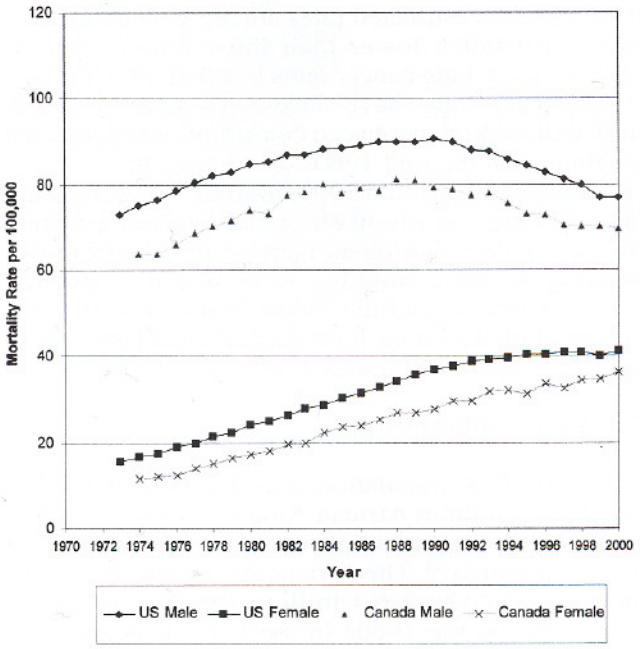

FIGURE 2 *Lung cancer mortality rates for the United States (1973–2000) and Canada (1974–2000) for men and women* [14,21,22].

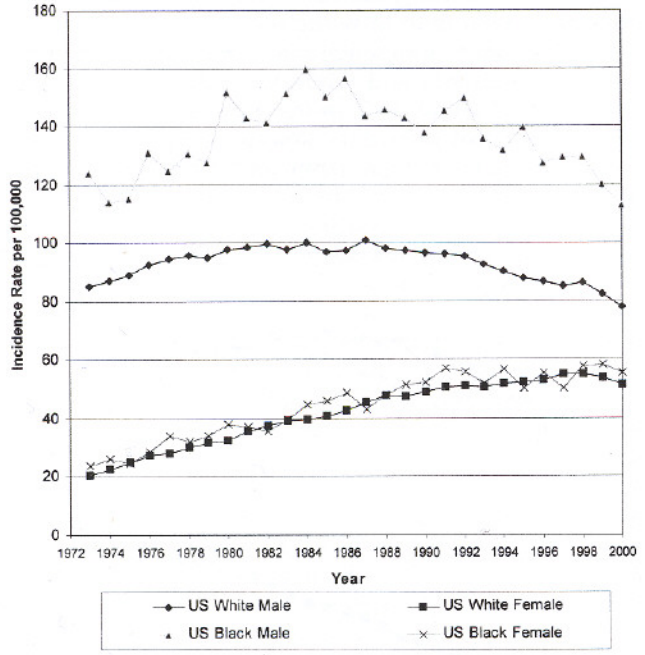

FIGURE 3 *Lung cancer incidence rates per 100,000 for the United States (1973–2000) for white and black men and women* [21,22].

An estimated 19,100 cases of lung cancer are expected to occur among African Americans in 2003 [26], accounting for about 14% of all cancer diagnoses in that group. Lung cancer is the second most common cancer in both African American men and women. The incidence rate for lung cancer among African Americans has decreased in men since 1984

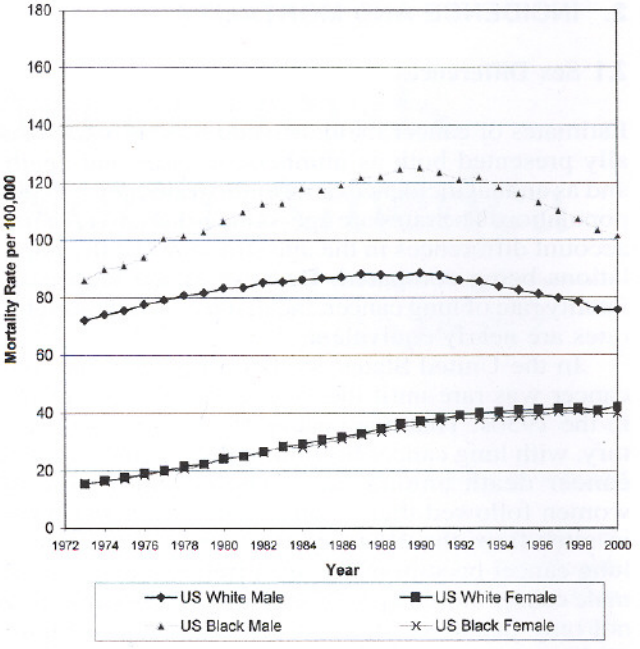

FIGURE 4 *Lung cancer mortality rates per 100,000 for the United States (1973–2000) for white and black men and women* [21,22].

(on average, 1.6% per year) [22], but has remained stable among African American women since 1990. An estimated 15,800 lung cancer deaths are expected to occur among African Americans in 2003.

In the 1970s, lung cancer mortality rates increased by an average of 3.1% per year among African American men and 6.2% per year among African American women. Lung cancer mortality rates increased in the 1980s as well. However, during 1993–1999, the lung cancer mortality rate in African American men decreased substantially (by 2.6% per year); in women, the rate increased by 1.2% per year from 1991. The decline in mortality rate among men is a result of decreases in smoking prevalence over the preceding 30 years.

Lung cancer mortality rates among Hispanics and Native Americans and Asians and Pacific Islanders are significantly lower than rates among African Americans and non-Hispanic whites [27]. In 2000, approximately 35.3 million Hispanics/Latinos comprised about 12.5% of the total United States population [28], a sharp increase from 9% in 1990, making Hispanics the fastest growing minority group in the country [29]. An estimated 4500 Hispanics are expected to be diagnosed with lung cancer in 2003 [30]. Because of the traditionally lower rates of cigarette smoking among Hispanics, lung cancer rates between 1992 and 1999 were approximately 50% lower in that group than in non-Hispanics. During the same years, a significant decrease (3.1% per year on average) occurred in the rates of new lung cancer cases among Hispanic men and women [22]. An estimated 3900 deaths from lung cancer are expected to occur

among Hispanics in 2003. Lung cancer is the leading cause of cancer death among Hispanic men; it is second among Hispanic women. During 1992–1999, the mortality rate from lung cancer declined among Hispanic men (on average, 1.9% per year); the mortality rate for Hispanic women did not decrease significantly. The decline in the mortality rate among men most likely resulted from decreases in the prevalence of smoking over the past 30 years. The decline was not as pronounced in women because the smoking patterns of women lag behind those of men.

For American Indians and Alaska Natives in the United States, lung cancer was the leading cause of cancer death in 1994–1998. The mortality rates vary by region. The mortality rate per 100,000 population in the Alaska region was 78.1. The rate in the Northern Plains region was highest at 96.9, with the average rate for all racial/ethnic populations in the United States combined being 57.8. The rate was lowest in the Southwest region at 14.1 [31]. All rates for lung cancer mortality were consistent with known regional patterns of cigarette smoking for American Indian and Alaska Native communities across the United States [32]. For lung cancer among women during 1992–2000, incidence rates for American Indian and Alaska Native populations appeared to be declining significantly, but death rates were rising [33].

The prevalence of cigarette smoking among adults aged 18 years and older ranged from 40.4% for American Indians and Alaska Natives to 12.3% for the Chinese population. The prevalence among youth aged 12–17 years ranged from 27.9% for American Indians and Alaska Natives to 5.2% for the Japanese population. Among both youth and adults, American Indians and Alaska Natives show the highest prevalence of cigarette smoking [34].

2.3 Socioeconomic Factors

In the United States, the poverty rate (percentage of the population below the poverty level) was chosen as the preferred measure for describing socioeconomic inequalities in cancer. Areas with a poverty rate of 20% or higher are often considered to be distressed or severely disadvantaged areas.

Compared with the lung cancer mortality rate for men in low-poverty areas, the rate for men in high-poverty areas was 7% higher in 1975 and 25% higher in 1999 [35]. However, in 1975, women in high-poverty areas had a 7% lower lung cancer mortality rate than did women in low-poverty areas. But the socioeconomic differences diminished in the 1990s: the 1999 data indicated no statistically significant difference between the poverty groups.

During 1995–1999, lung cancer mortality among men increased with increasing area poverty rates for non-Hispanic whites, blacks, and Hispanics, but did not change significantly with poverty rates for Asians and Pacific Islanders. In high-poverty areas, lung cancer mortality rates were about 16%, 29%, and 56% higher than in low-poverty areas for black, non-Hispanic white, and Hispanic men respectively. In high-poverty areas, the lung cancer mortality rates for non-Hispanic white women and Hispanic women were respectively about 6% and 29% higher. In high-poverty areas as compared with low-poverty areas, the mortality rates for Asian and Pacific Islander and American Indian and Alaska Native women were respectively about 26% and 24% lower.

The lung cancer incidence rate for men in high-poverty counties during 1975–1999 was at least 12% higher than the rate for men in low-poverty counties. The lung cancer incidence rates increased with increasing area poverty for non-Hispanic white and black men and women and for Asian and Pacific Islander men. Compared with the lung cancer incidence rates for their counterparts in low-poverty areas, the rates for non-Hispanic white, black, and Asian and Pacific Islander men were respectively about 45%, 46%, and 23% higher in high-poverty areas. In high-poverty areas as compared with low-poverty areas, the incidence rates for non-Hispanic white and black women were respectively about 23% and 19% higher. In contrast, in low-poverty areas as compared with high-poverty areas, lung cancer incidence rates for Hispanic men and women were about 21% and 34% higher respectively [35] (Figures 5–8).

3. SURVIVAL

In the United States, African American patients are less likely than white patients to be diagnosed with cancer at a localised stage; they are more likely to be diagnosed at a regional or distant stage of the disease. Furthermore, for all stages combined, African Americans have lower 5-year relative survival rate than do white patients. The 5-year relative survival rates in African American and white men with lung

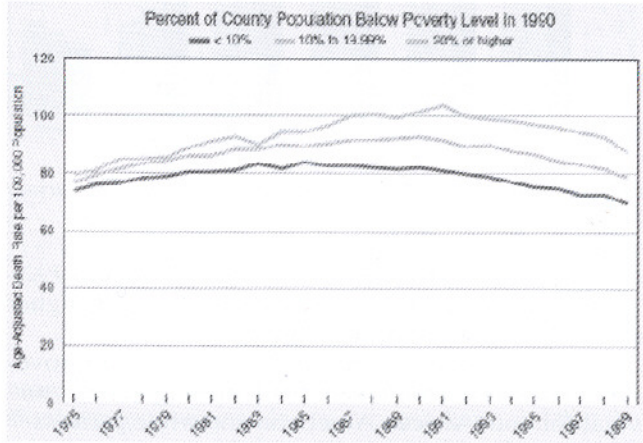

FIGURE 5 *Trends in the lung cancer death rate among U.S. men, 1975–1999* [35].

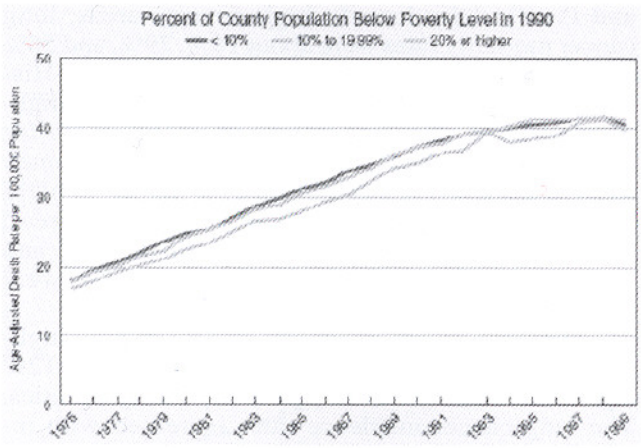

FIGURE 6 *Trends in the lung cancer death rate among U.S. women, 1975–1999* [35].

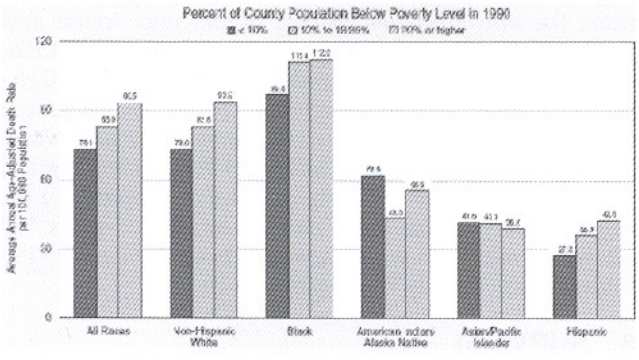

FIGURE 7 *Lung cancer death rate among U.S. men of various races, 1995–1999* [35].

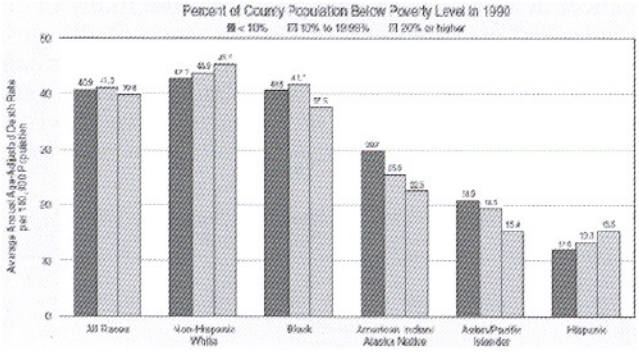

FIGURE 8 *Lung cancer death rate among U.S. women of various races, 1995–1999* [35].

cancer were respectively 10.8% and 13.3% in 1992–1998. The African American men also had higher cancer incidence and mortality rates.

Despite much research into cancer, little improvement has been seen since 1974 in lung cancer survival for both African American and white patients [36] (Table I). Generally, small-cell lung cancer has a poorer prognosis than non-small-cell lung cancer (Table II).

4. FACTS ABOUT TOBACCO SMOKING

Cigarette smoking, the leading cause of lung cancer, accounts for approximately 90% of lung cancer cases in the United States and in other countries where cigarette smoking is common [37,38]. Smokers have a lung cancer risk about 20 times that of non-smokers.

4.1 Disease Occurrence Reflects Smoking Patterns

In general, trends of lung cancer occurrence closely reflect patterns of smoking, but the mortality rates lag behind the smoking rates by about 30 years. The delayed health effects of smoking became very much apparent by the late 1940s, with rapidly rising rates of smoking-related cancer incidence and mortality in women and a continuing rise in the rates in men [39]. The prevalence of current cigarette smokers was estimated to be 56% in 1930. That percentage rose steadily to 65% in 1940, maintained a rough plateau until 1955 [40], and then began to progressively decline, reaching 28.1% in 1991 [11]. The lung cancer mortality rate among men was only 4.9 per 100,000 in 1930. That rate rose slowly at first and then more rapidly until 1980. Thereafter, it slowed and peaked at 90.6 in 1990. The mortality rate then fell to 76.9 in 2000 (Figure 9).

Historically, the rate of smoking was much higher among men than among women, but the sex difference diminished over time (the rate among men declined and the rate among women rose). For women, the prevalence of cigarette smoking rose above 2% after 1930, increasing steadily to a peak of 38% in 1960. It then declined—more slowly than in men—to 24.1% in 2000. The lung cancer mortality rate in women began to rise substantially from 1960, approximately 30 years after the rise in smoking prevalence. From 1965 to 1990, the increase was linear; however, it seems to have slowed a little between 1990 and 2000 (Figure 10).

A review of the effects of tobacco smoking on cancer (specifically lung cancer) incidence and mortality was published in 1999 [4]. Analyses using statistical modelling techniques show a tight association between national mortality rates and smoking [42]. The risk of lung cancer among cigarette smokers increases with the duration of smoking and the number of cigarettes smoked per day [43,44].

The composition of cigarettes has evolved considerably since the 1950s. The cigarette type has shifted from mainly unfiltered cigarettes to predominantly filtered cigarettes. Substantial changes have also occurred in the design of cigarettes and in the tobacco used. Reconstituted tobacco has been used increasingly since the 1960s, and changes have been made to the cigarette papers and additives used [45].

Estimates indicate that passive smoking accounts for approximately 3000 lung cancer deaths per year in the United States [46]. Passive smokers inhale a

TABLE I Trends in 5-year relative survival rates (%) for lung cancer, adjusted for normal life expectancy, and based on cases diagnosed during 1974–1998 and followed through 1999, United States [22]

Year of diagnosis	*All races*			*White*			*Black*		
	Total	*Men*	*Women*	*Total*	*Men*	*Women*	*Total*	*Men*	*Women*
1974–1976	12.4	11.2	15.8	12.5	11.1	16.0	11.4	11.0	13.1
1977–1979	13.4	11.7	17.1	13.6	12.0	17.2	11.1	9.1	17.2
1980–1982	13.4	12.1	16.1	13.5	12.2	16.2	12.1	10.9	15.5
1983–1985	13.6	11.9	16.7	13.8	12.1	17.0	11.3	10.3	14.1
1986–1988	13.3	12.0	15.4	13.5	12.0	15.8	11.9	11.9	11.7
1989–1991	13.9	12.4	16.2	14.3	12.7	16.6	10.7	9.5	13.0
1992–1998	14.7	13.1	16.7	15.0	13.3	17.0	12.3	10.8	14.7
1992–1998									
All stages	14.7	13.1	16.7	15.0	13.3	17.0	12.3	10.8	14.7
Localised	48.5	44.6	52.8	49.2	45.2	53.3	42.9	38.4	49.1
Regional	21.7	20.2	23.8	22.1	20.7	24.0	18.1	16.5	20.6
Distant	2.5	2.3	2.9	2.4	2.1	2.8	2.8	2.3	3.6
Unstaged	8.4	7.5	9.5	8.5	7.5	9.6	8.9	9.0	8.9

TABLE II Trends in 5-year relative survival rates (%) for small cell and non-small-cell lung cancer, adjusted for normal life expectancy, and based on cases diagnosed during 1974–1998 and followed through 1999, United States [22]

Year of diagnosis	*All races*			*White*			*Black*		
	Total	*Men*	*Women*	*Total*	*Men*	*Women*	*Total*	*Men*	*Women*
Small-cell lung and bronchus cancer (invasive)									
1974–1976	3.6	3.0	5.0	3.6	2.9	5.0	3.4	3.6	3.1
1977–1979	4.5	3.3	6.7	4.5	3.3	6.7	3.8	3.4	4.8
1980–1982	4.7	3.8	6.2	4.8	4.0	6.2	4.0	3.0	6.4
1983–1985	4.8	3.5	6.6	4.8	3.6	6.6	4.7	2.5	8.5
1986–1988	5.0	3.9	6.5	5.2	4.0	6.8	3.9	3.4	4.6
1989–1991	5.4	4.5	6.5	5.5	4.4	6.8	3.7	4.3	2.9
1992–1998	6.4	5.4	7.4	6.4	5.4	7.4	5.3	3.7	7.1
1992–1998									
All stages	6.4	5.4	7.4	6.4	5.4	7.4	5.3	3.7	7.1
Localised	20.4	17.7	23.5	21.7	18.9	24.9	10.3	2.7	18.4
Regional	13.1	11.7	14.4	13.2	11.9	14.3	10.0	8.3	11.3
Distant	2.5	2.1	3.0	2.4	2.1	2.7	2.4	1.0	4.4
Unstaged	8.7	7.5	9.9	8.9	7.3	10.4	11.3	16.0	5.7
Non-small-cell lung and bronchus cancer (invasive)									
1974–1976	13.8	12.4	17.8	13.9	12.4	18.1	12.3	11.7	15.0
1977–1979	15.0	13.2	19.3	15.4	13.6	19.5	12.1	9.8	19.4
1980–1982	15.1	13.6	18.4	15.4	13.8	18.6	13.2	11.9	16.9
1983–1985	15.5	13.5	19.2	15.9	13.8	19.6	12.3	11.2	15.0
1986–1988	15.1	13.6	17.6	15.4	13.7	18.2	13.1	13.1	13.1
1989–1991	15.7	13.9	18.6	16.3	14.4	19.1	11.8	10.1	14.8
1992–1998	16.3	14.5	18.8	16.7	14.8	19.2	13.2	11.7	16.0
1992–1998									
All stages	16.3	14.5	18.8	16.7	14.8	19.2	13.2	11.7	16.0
Localised	50.5	46.6	54.9	51.2	47.2	55.4	44.9	40.4	51.3
Regional	23.0	21.3	25.6	23.5	21.8	25.9	19.0	17.2	22.1
Distant	2.6	2.3	2.9	2.4	2.1	2.9	2.9	2.6	3.4
Unstaged	8.3	7.4	9.4	8.4	7.5	9.5	8.7	8.4	9.3

complex mixture of smoke that is now widely referred to as "environmental tobacco smoke" (ETS). The U.S. National Research Council reviewed the epidemiologic evidence and concluded that non-smoking spouses married to cigarette smokers were about 30% more likely to develop lung cancer than were non-smoking spouses married to non-smokers, and that the relationship was biologically plausible. Almost one fourth of lung cancer cases among never-smokers were estimated to be attributable to passive smoking [47].

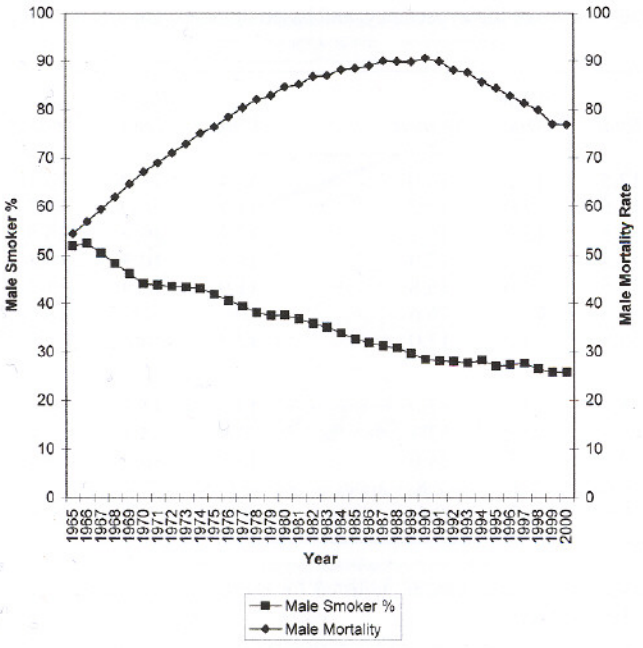

FIGURE 9 *Percentage of adult smokers and mortality rate among U.S. men, 1965–2000* [11,21,22,41].

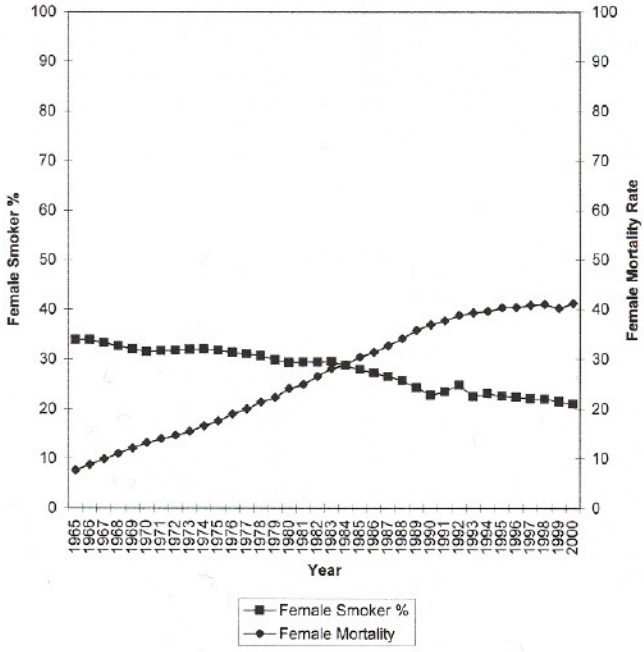

FIGURE 10 *Percentage of adult smokers and mortality rate among U.S. women, 1965–2000* [11,21,22,41].

4.2 Smoking Cessation and Initiation Prevention

The prevention of smoking initiation among nonsmokers and the encouragement of smoking cessation among smokers both lead to declines in lung cancer incidence and mortality. That relationship was recently seen in U.S. states that instituted aggressive antismoking campaigns. State-wide comprehensive tobacco control programs typically involve some mix of public education, print media campaigns, prevention of youth access to tobacco, restriction of advertising, creation of smoke-free environments, work-site antismoking programs, training for health professionals on cessation techniques, and school-based smoking prevention curricula.

Lung cancer mortality rates in young adults (aged 30–39 years) during the two time intervals 1990–1994 and 1995–1999 correlated strongly and inversely with the index of state tobacco control efforts. Lung cancer mortality rates decreased in states with high tobacco control efforts, but increased in states with low tobacco control efforts. Tobacco control indices were strongly and positively correlated with cessation of smoking by age 30–39 years [48].

It seems that smoking intervention and education programs have effectively reversed the upward trend in smoking-related cancer incidence that occurred through the 1990s. Although a majority of the adults in the United States are current or former smokers, smoking cessation and prevention efforts have been successful. Nevertheless, about one in four adults still currently smokes cigarettes, the decline in ever-smoking has reached a plateau in recent years, and rates of teenage smoking have begun to increase.

A key to maintaining the decreasing trend of smoking-related cancer incidence and deaths is the prevention of smoking in young people. Although the number of high-school students that started smoking decreased from 1983 to 1993, evidence suggests that the rate of smoking is on the rise again. In 1997, the smoking rate among high-school students in the United States was 32% higher as compared with the rate in 1991. The use of tobacco by young female adolescents is on the rise, and those who are current smokers typically began smoking before high school graduation [49].

Adult smokers who quit or die are being replaced by young adolescents who smoke. Until recently, lung cancer control efforts have focused primarily on smoking prevention in youth and cessation among adults (Figures 11–13). Ultimately, the preferred disease control strategy is the prevention of lung cancer through the elimination of tobacco use altogether [53].

5. AGE-SPECIFIC TRENDS

Trends of age-specific lung cancer mortality rates in the United States are showing varying epidemic patterns in men and in women [15]. In older age groups, mortality rates continue to rise in both sexes, but the rate of increase is decelerating more significantly in men than in women [16]. In younger age groups, the rate of lung cancer is now decreasing. Those decreases are more pronounced for young men, but are now also becoming evident in young women [18]. A recent analysis of lung cancer mortality in the United States for 1970–1997 [16] found that the rates of

FIGURE 11 *Anti-tobacco posters: "Strike Back Against Tobacco"* [50].

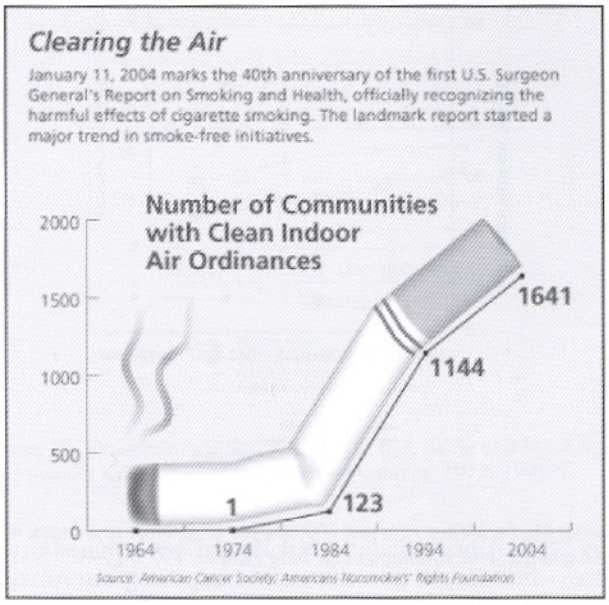

FIGURE 12 *Anti-tobacco picture: "Clearing the Air"* [51].

decrease in younger men and women were moderating, but that the decline is continuing.

Lung cancer incidence rates initially began to decline in men diagnosed with the disease before 50 years of age. The rates then peaked and declined for each older age group in succession over time [6]. The earliest decline in incidence rates in men occurred in the mid-to-late 1970s among men diagnosed at ages 20–49 years. The incidence rates peaked in the period from 1979 through 1981 for males 50–59 years old at diagnosis, in the mid 1980s for males 60–79 years old, and in the early 1990s for males 80 years of age and older. Age-specific mortality rates for men followed patterns similar to those for incidence rates, but the peak years generally occurred later.

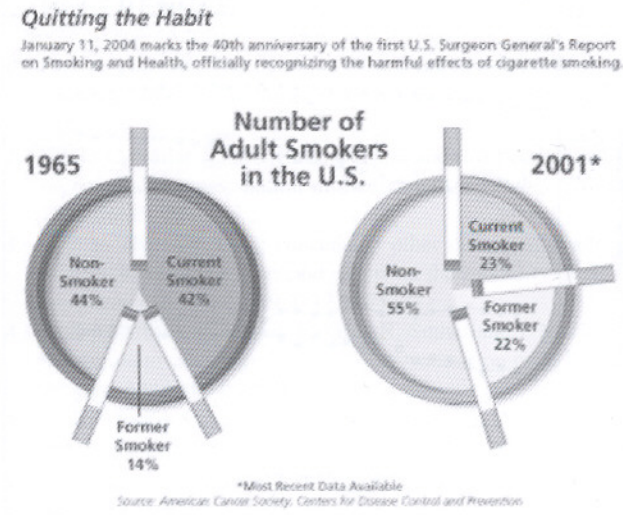

FIGURE 13 *Anti-tobacco picture: "Quitting the Habit"* [52].

A downturn in lung cancer incidence rates among women was most apparent for those aged 40–49 years and 50–59 years at diagnosis. Incidence rates for those age groups peaked in the mid 1970s and the late 1980s respectively. From 1990 through 1996, incidence rates for women aged 60–69 years were approximately level; for older women, those rates continued to increase. Age-specific patterns in lung cancer mortality rates among women were similar to those in incidence rates [6] (Figure 14). The lung cancer trends are similar for Canada (Figure 15).

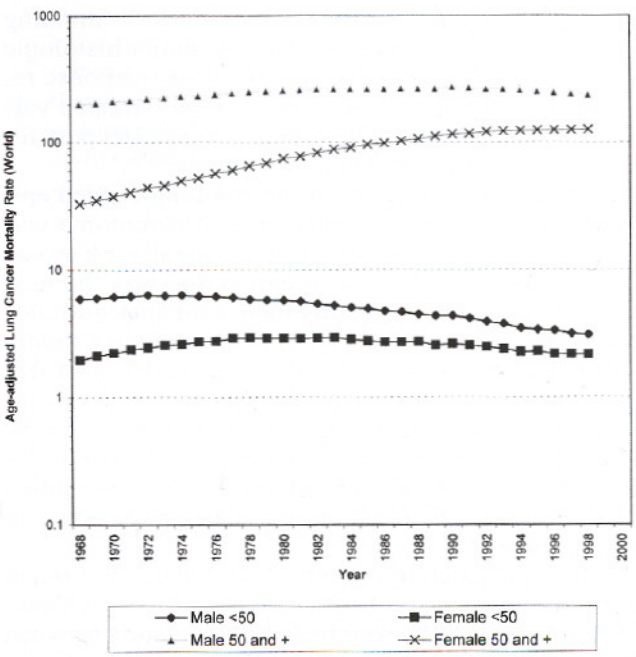

FIGURE 14 *Lung cancer mortality rates in the United States among men and women aged below 50 years and 50 years or more, 1968–1998* [54].

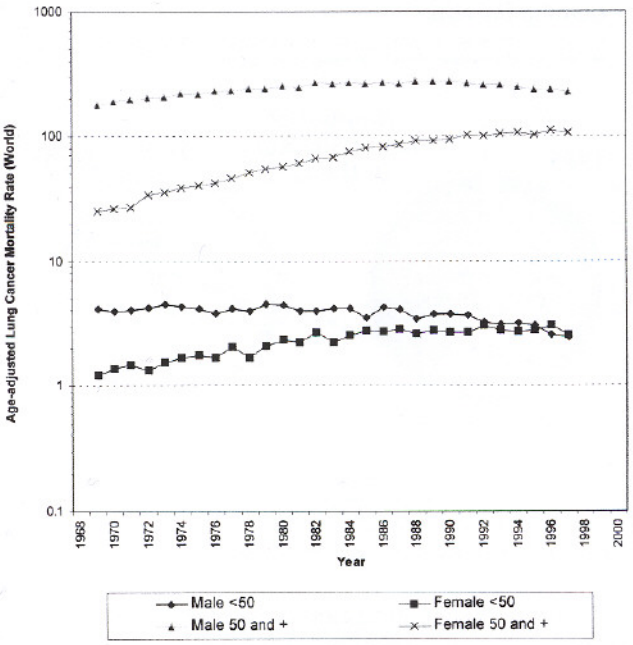

FIGURE 15 *Lung cancer mortality rates in Canada among men and women aged below 50 years and 50 years or more, 1969–1997* [54].

6. HISTOLOGIC SUBTYPE

As classified by conventional light microscopy, the four major lung cancer types are squamous cell carcinoma, adenocarcinoma, large-cell carcinoma, and small-cell undifferentiated carcinoma. Together, those four types of lung cancer account for more than 90% of lung cancer cases in the United States [55]. Smoking has been shown to cause each of the major histologic types of lung cancer, although the dose–response relationship with the number of cigarettes smoked varies across the types. The relationship is steepest for small-cell undifferentiated carcinoma [56,57].

In the initial decades of the smoking-caused epidemic of lung cancer, squamous cell carcinoma was the type of lung cancer most frequently observed among smokers. Small-cell carcinoma was the next most frequent. After steadily increasing in occurrence during the period 1973–1987, adenocarcinoma finally surpassed squamous cell carcinoma as the most frequent form of lung cancer. Adenocarcinoma has increased markedly in all race–sex subgroups [58]. In the late 1970s, evidence was seen of a shift toward adenocarcinoma predominance. Now, adenocarcinoma of the lung is the most common histologic type of lung cancer [59,60].

In a prospective cohort of 41,836 Iowa women aged 55–69 years, with 13 years of follow-up (1986–1998), Yang *et al.* [61] examined the association between cigarette smoking history and three common histologic subtypes of lung cancer (123 small-cell, 115 squamous cell, and 234 adenocarcinoma). The researchers estimated four epidemiologic measures of effect: age-adjusted incidence rate, relative risk, excess risk (or risk difference), and population attributable risk. Of the three major lung cancer subtypes, the excess risk for heavy smokers as compared with never-smokers was higher for adenocarcinoma than for squamous cell and small-cell carcinoma. Adenocarcinoma of the lung is more strongly associated with tobacco smoke exposure than previously recognised.

The decline in lung cancer incidence rates has been more rapid for squamous cell and small-cell carcinomas than for adenocarcinoma, which is just beginning to show a lower rate [4]. In women, the Surveillance, Epidemiology and End Results data for 1973–1998 indicate that the incidence rates of squamous cell, small-cell, and large-cell carcinoma are reaching a plateau; the rate for adenocarcinoma is still rising (Figures 16–19) [62].

In Canada, lung cancer data were extracted from the Alberta Cancer Registry for the years 1979–1998 [63]. In women, incidence over that calendar

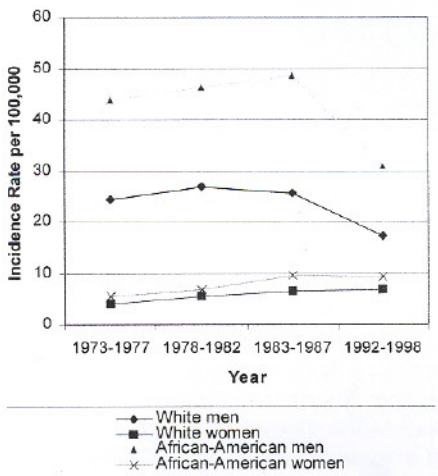

FIGURE 16 *Incidence rate per 100,000 for U.S. white and black men and women with squamous cell lung cancer, 1973–1998* [62].

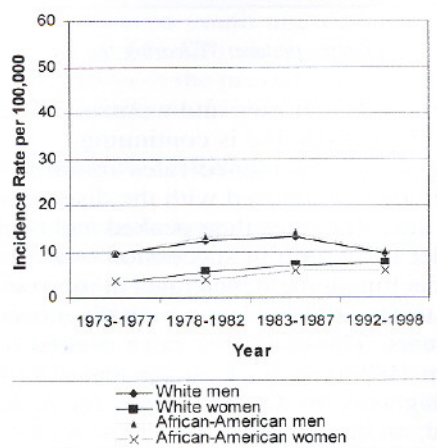

FIGURE 17 *Incidence rate per 100,000 for U.S. white and black men and women with small-cell lung cancer, 1973–1998* [62].

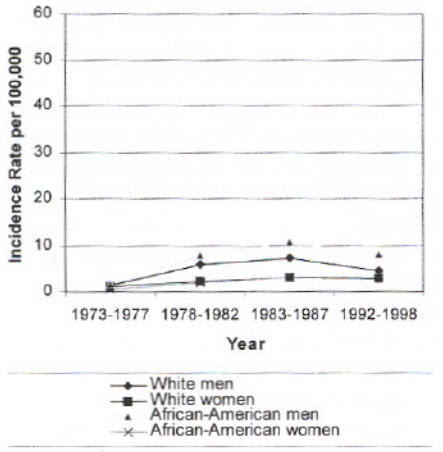

FIGURE 18 *Incidence rate per 100,000 for U.S. white and black men and women with large-cell lung cancer, 1973–1998* [62].

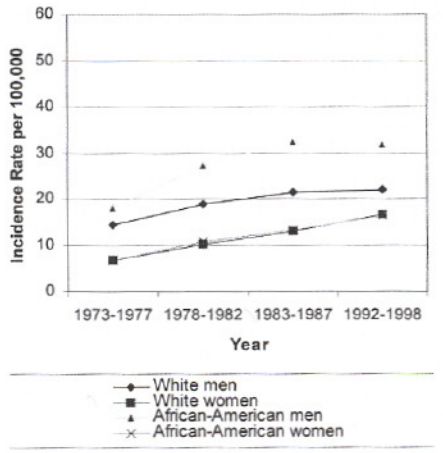

FIGURE 19 *Incidence rate per 100,000 for U.S. white and black men and women with adenocarcinoma lung cancer, 1973–1998* [62].

period increased for all lung cancer and for the adenocarcinoma, squamous cell, and small-cell carcinoma histologic types. In men, incidence of all lung cancer increased until 1988; it then decreased. Adenocarcinoma incidence in men increased over the entire time period; squamous cell and small-cell carcinoma incidence decreased. For women born before 1939, the incidence of all lung cancer and of the three histologic types increased across birth cohorts for all age groups. For women born after 1939, a slight decline was seen. Lung cancer incidence among men showed no marked increases across birth cohorts. In men born after 1929, incidences of all lung cancer and of squamous cell and small-cell carcinoma decreased across birth cohorts for all age groups. The incidence of adenocarcinoma increased across all birth cohorts in men. Those trends may reflect changes in smoking habits. However, the exact reason that adenocarcinoma has emerged as the most common histologic type is still uncertain.

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