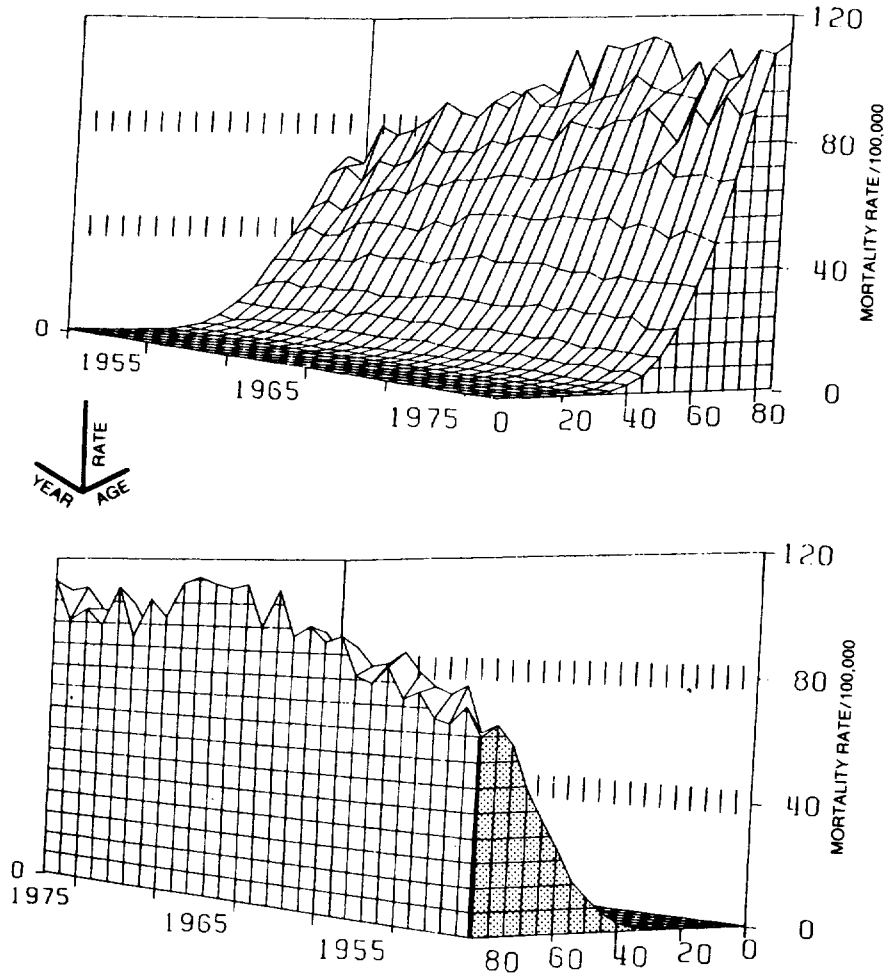

FIGURE 53.—Age-specific mortality rates by 5-year age groups for cancer of the pancreas for white males, United States, 1950–1977

SOURCE: National Cancer Institute (*198*).

groups without significant increases in the rates of the younger age groups, as is readily apparent when age-specific death rates for white males and females are plotted on a three-dimensional graph (Figures 53 and 54).

Pancreatic carcinoma is generally undetected until late in its course, due to difficulties in diagnosis and the nonspecific nature of the presenting symptoms. Metastasis occurs relatively early in the

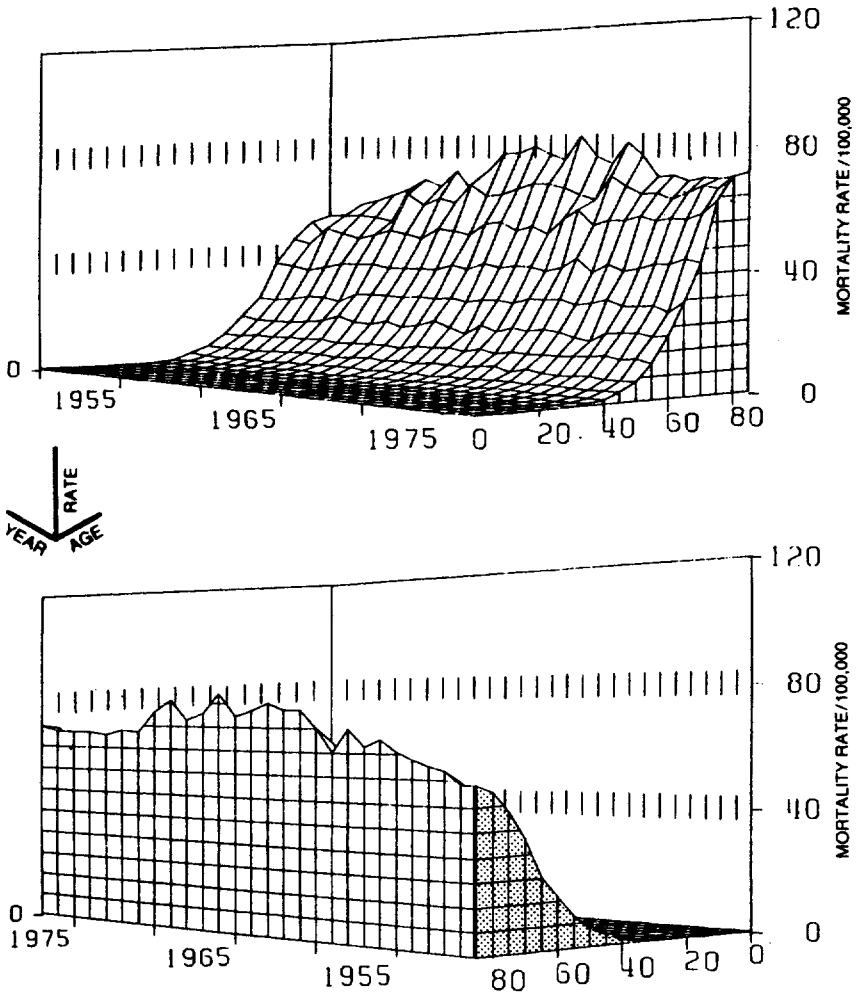

FIGURE 54.—Age-specific mortality rates by 5-year age groups for cancer of the pancreas for white females, United States, 1950–1977

SOURCE: National Cancer Institute (*198*).

course of this disease, contributing to the poor 3-year survival rate of 2 percent (*194*) and a mean survival time after diagnosis of less than 6 months (*187*). The most common form of pancreatic cancer is adenocarcinoma. Pancreatic cancer is more common among men than among women in the United States, but the male to female ratio has been decreasing steadily from 1.6:1 during the period of 1940–1949 to 1.2:1 estimated in 1980 (*270*).

Several epidemiological studies have established an association between cigarette smoking and pancreatic cancer.

Causal Significance of the Association

Consistency, Strength, and Specificity of the Association

A number of retrospective studies have examined the relationship between smoking and pancreatic cancer. In the Third National Cancer Survey (*299*) and in the Hawaiian Study of Five Ethnic Groups (*113*), there was a significant positive relationship between smoking and pancreatic cancer. An earlier retrospective case control study of 81 cases of pancreatic cancer (*320*) found a dose-response relationship with a relative risk of 5.0 for males smoking more than two packs of cigarettes per day (Figure 55). A recent report found a positive association for both males and females who had ever smoked and cancer of the pancreas (relative risk of 1.4), but not for pipe or cigar smokers. They also reported a significant dose-response relationship for females. A similar but not significant dose-response relationship was noted for males (*169*).

Several of the large prospective investigations have reported mortality ratios of approximately 2.0 for smokers as compared with nonsmokers. These data are presented in Table 36. The dose-response relationships from four of the major prospective studies are presented in Table 37. Smokers consuming more than one pack of cigarettes per day had mortality ratios two to three times greater than those of nonsmokers.

These data consistently support an association between smoking and pancreatic cancer, although the strength of the association is less than that noted for smoking and cancer of the lung, larynx, oral cavity, and esophagus.

Temporal Relationship of the Association

Support for the temporal relationship of the association is provided by the prospective studies that observed subjects over varying periods of time for the development of pancreatic cancer. Support for the temporality of the association is advanced by a histological study showing a greater frequency of premalignant changes in pancreatic tissue of smokers when compared with tissue of nonsmokers (*162*), and by cohort analysis showing correlation between trends in smoking patterns and pancreatic cancer mortality (*22, 128*).

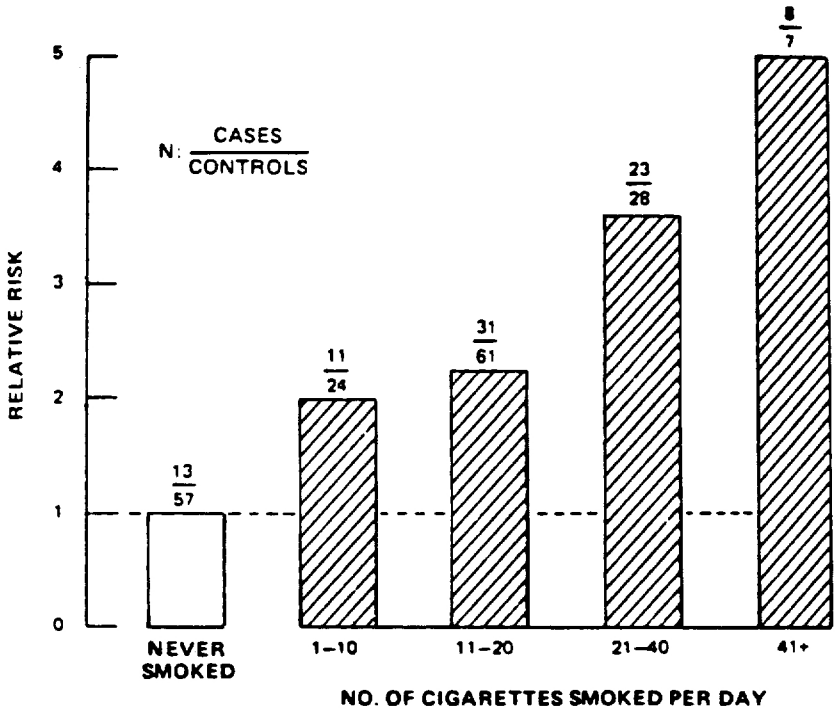

FIGURE 55.—Relative risk of pancreatic cancer in males, by number of cigarettes smoked

SOURCE: Wynder (*320*).

Coherence of the Association

Dose-Response Relationship

The coherence of the association is supported by the dose-response relationship noted above, although it is not as marked as those noted for smoking and other cancers.

Correlation of Pancreatic Cancer Among Populations With Different Tobacco Consumption

The finding of a low incidence of pancreatic cancer in special groups (e.g., Mormons and Seventh Day Adventists) with a small proportion of smokers (*79, 165, 166, 211, 294*) is consistent with a causal relationship.

TABLE 36.—Pancreatic cancer mortality ratios—prospective studies

Study	Size of Population	Nonsmokers	All Cigarette Smokers	Comments
ACS 9-State Study	188,000 white males	1.00	1.50	Based on 117 microscopically proved cases
Canadian Veterans	78,000 males	1.00	1.96	
ACS 25-State Study	358,000 males 483,000 females	1.00 1.00	2.14 1.42	
U.S. Veterans	290,000 males	1.00	1.79	
Japanese Study	122,000 males 143,000 females	1.00 1.00	1.57 males 1.94 females	
California occupations	68,000 males	1.00	2.43	
Swedish Study	55,000 males and females	1.00 1.00	3.1 males 2.5 females	
British Physicians	34,000 males	1.00	1.60	

TABLE 37.—Mortality ratios for cancer of the pancreas by amount smoked—prospective studies

Study	Population	Amount Smoked per Day				Comments
		Males		Females		
Swedish Study	55,000 males and females	NS	1.00	NS	1.00	
		1–7	1.60	1–7	2.40	
		8–15	3.40	8–15	2.50	
		15 +	5.90	15 +	3.00	
British Physicians	40,000	NS	1.00	NS	1.00	Males based on grams of tobacco per day
		1–14	1.35	1–14	0.44	
		15–24	1.42	15–24	2.66	
		25 +	2.07	25 +	1.77	
Japanese Study	265,000 males and females	NS	1.00	NS	1.00	
		1–19	1.42	1–19	1.00	
		20–39	1.57	20–29	1.60	
		40 +	0.69	30 +	1.90	
U.S. Veterans	290,000 males	NS	1.00			
		1–9	1.60			
		10–20	1.71			
		21–39	2.00			
		40 +	2.20			

NOTE: NS: Nonsmoker.

Correlation of Sex Differences in Pancreatic Cancer With Different Smoking Habits

The declining male to female mortality ratio discussed above is consistent with the delayed initiation of cigarette smoking by women as compared to men.

Two studies have performed cohort analyses of the relationship of time trends in smoking patterns among males and females and mortality rates from carcinoma of the pancreas. Bernard and Weiss (*22*) examined the relationship in the United States for the period of 1939 to 1969; Moolgavkar and Stevens (*185*) examined these relationships in England and Wales for the period of 1941 to 1975. Both studies found a positive association between changes in smoking habits in males and females and pancreatic cancer death rates.

Smoking and Histologic Changes in the Pancreas

A recently reported study (*162*) found evidence for premalignant changes in pancreatic tissue of smokers. The authors collected 108 specimens of pancreatic tissue. In 44 percent of the series, there were some focal acinar cell abnormalities, which the authors state were similar to atypical acinar cell nodules in carcinogen-treated animals. These findings were more common in tissue from patients with a history of smoking as compared with tissue from nonsmokers. Tissue from heavy smokers (67 to 100 pack-years) showed a 1.8 times higher incidence of such nodules than tissue from all smokers.

Pancreatic Cancer and Non-Cigarette Tobacco Use

The U.S. Veterans Study found an elevated risk of 1.5 for pancreatic cancer in cigar, but not pipe, smokers.

Experimental Studies

Dietary factors, the presence of underlying diseases, such as chronic pancreatitis and diabetes mellitus, and chemical exposures have been suggested as potential determinants for this disease (*187*).

The pathogenic mechanisms by which tobacco smoking influences the development of pancreatic cancer are obscure. It has been suggested that a carcinogen derived from tobacco smoke (either directly or after metabolism by the liver) is excreted into the bile (*321*). It is then refluxed into pancreatic ducts and induces cancer. One group of investigators (*145*) has reported that nicotine inhibits pancreatic bicarbonate secretion in the dog by direct action on the organ. This has led to speculation that inhibition of duct cell secretion of bicarbonate could lead to intracellular pH changes and subsequently play a role in carcinogenesis. It has also been suggested that a protease-antiprotease imbalance may be capable of promoting carcinogenesis. Cigarette smoke is known to affect the protease-

antiprotease balance *in vivo* and *in vitro*. In a study of beagle dogs smoking 12 cigarettes per day for 600 days, the authors reported significant changes in pancreatic proteases as compared with their sham-exposed controls (*189*).

Conclusion

Cigarette smoking is a contributory factor in the development of pancreatic cancer in the U.S. The term "contributory factor" by no means excludes the possibility of a causal role for smoking in cancers of this site.

Stomach Cancer

It is estimated that in the United States there will be 24,200 new cases of stomach cancer and 13,800 deaths in 1982 (*2*). For unknown reasons, mortality rates and the number of deaths have fallen dramatically over the last 28 years.

The age-adjusted mortality rate for stomach cancer has continued to decline for both males and females. Since the period of 1951–1953 through 1976–1978, the age-adjusted rate has decreased by 59 percent in males and 65 percent in females. Rates for both males and females adjusted to the 1970 population are presented in Figure 56. Figures 57 and 58 give age-specific death rates for cancer of the stomach for four separate time periods by race and sex.

In 1950, cancer of the stomach was fatal to 24,257 persons; in 1977, 14,440 died from this cancer in the United States. Death rates are higher for races other than white than for whites; other males have higher death rates than any of the other color sex groups.

The age-adjusted rate for other than white males was 31.16 in 1950 compared to 23.86 for white males. The corresponding rates for females were 16.05 and 13.13, respectively. By 1977, the rate for other than white males had decreased to 15.18; the corresponding rate for white males was 8.25. The age-adjusted rate for females other than white was 7.46 in 1977 compared to 3.83 for white females.

These differences may represent variations in exposure to undetermined dietary and other environmental factors or genetic differences.

A limited number of epidemiological studies have examined the relationship between smoking and stomach cancer. The data are not consistent, but overall, the evidence points to a possible association between cigarette smoking and stomach cancer. Olearchyk (*204*) noted that alcoholism (26.7 percent) and smoking (26 percent) were common habits of 243 patients with stomach cancer. In the population-based Third National Cancer Survey (*299*), there was a significant positive association between smoking and stomach cancer. A few other retrospective studies have also reported a statistical association between smoking and stomach cancer (*122, 151, 302*).

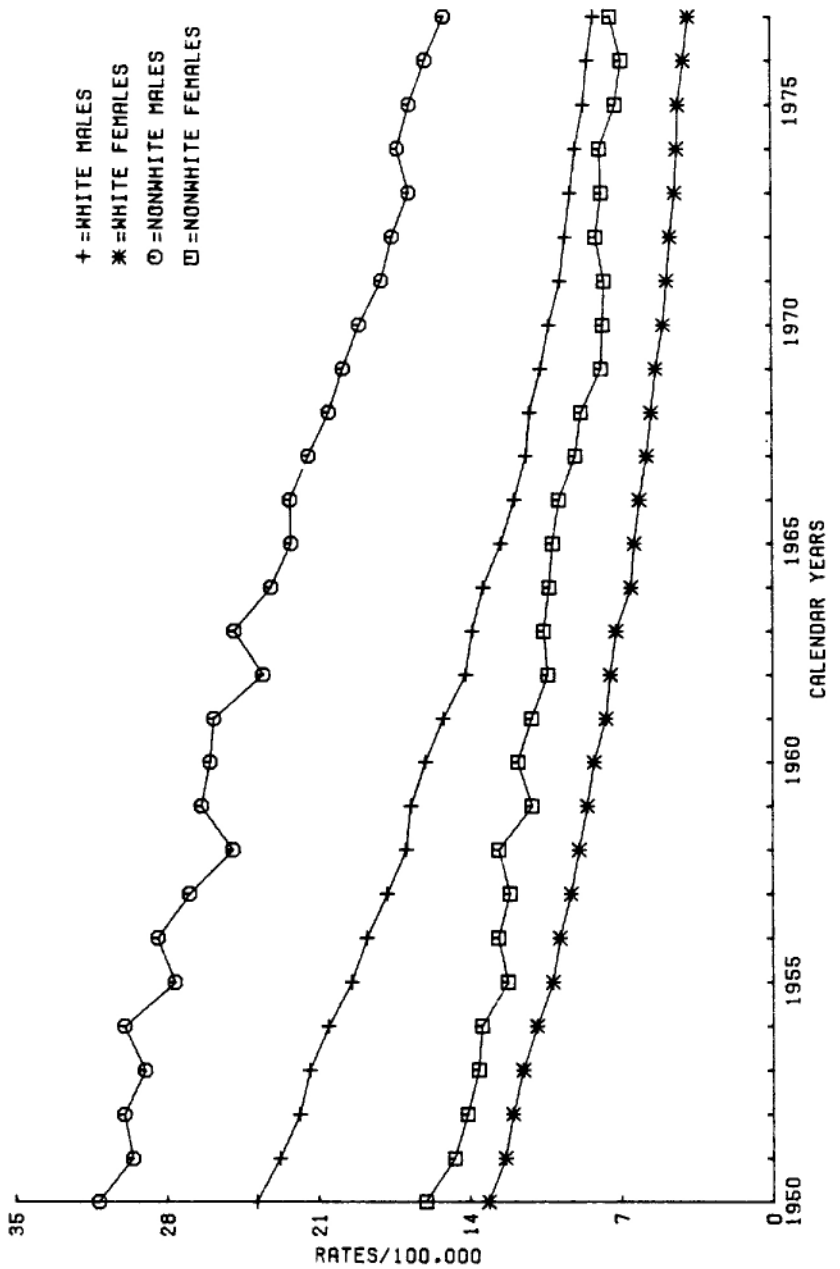

FIGURE 56.—Age-adjusted* mortality rates for cancer of the stomach, by race and sex, United States, 1950–1977

* This graph is age-adjusted to the U.S. population as enumerated in 1970; all rates cited within the text of this Report, however, are adjusted to the population as enumerated in 1940.

SOURCE: National Cancer Institute (*198*).

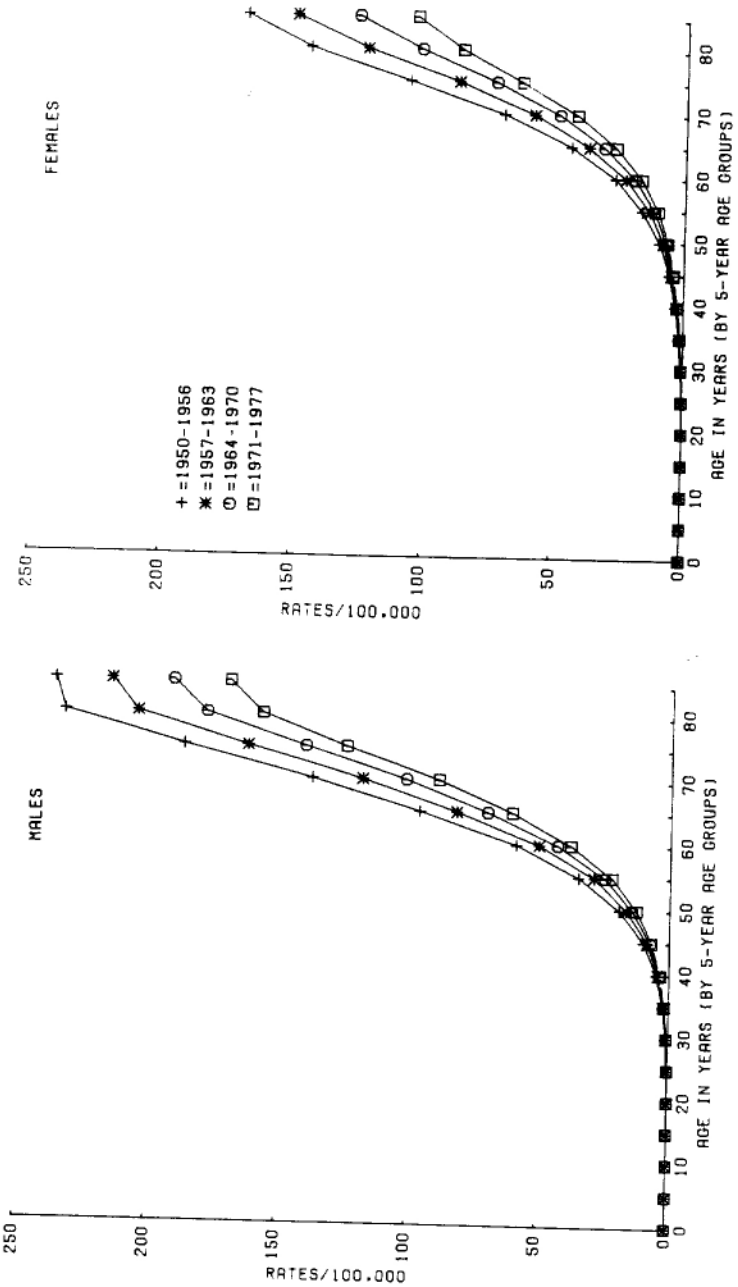

FIGURE 57.—Age-specific mortality rates for whites in the United States for cancer of the stomach

SOURCE: National Cancer Institute (*198*).

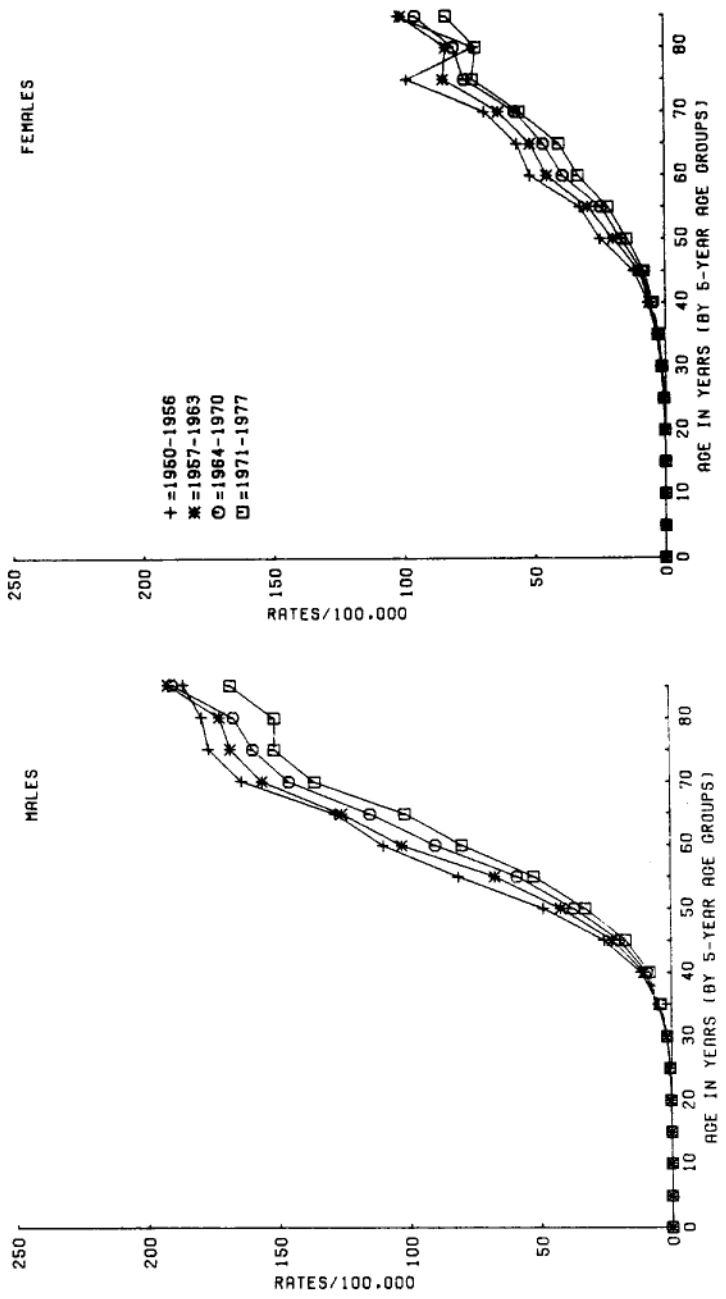

FIGURE 58.—Age-specific mortality rates for nonwhites in the United States for cancer of the stomach

SOURCE: National Cancer Institute (*198*).

TABLE 38.—Stomach cancer mortality ratios—prospective studies

Population	Study size		Non-smokers	All cigarette smokers	Comments
ACS 9-State Study	188,000 white males		1.00	1.61	Based on 176 microscopically proved cases
U.S. Veterans	290,000		1.00	1.52	
Swedish Study	55,000 males and females	(men)	1.00	1.80	Cigarette and pipe smokers
		(women)	1.00	2.30	
Japanese Study	265,000 males and females	(men)	1.00	1.59	
		(women)	1.00	1.31	
California males in 9 occupations	68,000		1.00	1.04	
ACS 25-State Study	358,400 males	45–64	1.00	1.42	
		65–79	1.00	1.26	
British Physicians	34,000		1.00	1.39	All current smokers

TABLE 39.—Stomach cancer mortality ratios by amount smoked—prospective studies

Study	Population size	Amount smoked per day	Mortality ratio	Comment
U.S. Veterans	290,000 males	Nonsmoker	1.00	
		1–9	1.47	
		10–20	1.49	
		21–39	1.55	
		40+	1.83	
British Physicians	34,000 males	Nonsmoker	1.00	Based on grams of tobacco per day
		1–14	1.20	
		15–24	1.65	
		25+	1.39	
California males in 9 occupations		Nonsmoker	1.00	
		about ½ pk	1.09	
		about 1 pk	0.94	
		about 1 ½ pk	1.25	
Japanese Study	122,000 males	Nonsmoker	1.00	
		1–19	1.46	
		20–39	1.53	
		40+	1.78	

In contrast with the above investigations, the Hawaiian Study of Five Ethnic Groups failed to show a statistically significant association between smoking and stomach cancer (*113*). Haenszel et al. (*91*)

reported an increased relative risk for stomach cancer among smokers in a series of 783 patients living in the Hiroshima and Miyagi prefectures of Japan; however, these findings were not statistically significant. In a similar study of Japanese living in Hawaii, these same authors (*92*) found a statistically significant increased risk among Issei smokers but not among Nissei. The absence of a significant association between cigarette smoking and gastric cancer has been reported by other authors (*236, 318*).

The relationship between smoking and stomach cancer was examined in several prospective studies (Table 38). Although mortality ratios were increased for smokers as compared with nonsmokers, these increases were small. Three of the four major prospective studies noted a consistent dose-response relationship as measured by the number of cigarettes smoked per day. However, the magnitude of these relationships was moderate compared to that between smoking and other cancer sites (Appendix Tables A and B).

Conclusion

1. Epidemiological studies have noted an association between cigarette smoking and stomach cancer. The association is small in comparison with that noted for smoking and some other cancers.

Cancer of the Uterine Cervix

Slightly over 8,300 women died of cancer of the uterine cervix in 1950. By 1977, the total number of deaths attributed to this site had decreased to 5,165. The age-adjusted rate for white females is only about one-third that observed for races other than white (3.53 versus 9.63) (Figure 59).

The age-specific rate for races other than white was 17.92 in 1950 and decreased to 7.99 by 1977. The age-specific rate for white females decreased from 10.12 to 4.12 over the same time period (Figure 60). Squamous cell carcinoma is the major cell type. The overall 5-year survival for patients with carcinoma of the cervix is 60 percent, but survival ranges from 86 percent for those with localized disease, to 50 percent for those with regional involvement, and to 22 percent for those with distant metastases (*2*).

Cervical cancer appears to be more common among women who have early and frequent coitus, who have early or multiple marriages or partners, and who become pregnant at an early age or frequently (*140, 264*). In addition, a number of other variables have been studied that may affect the risk for cervical cancer, including

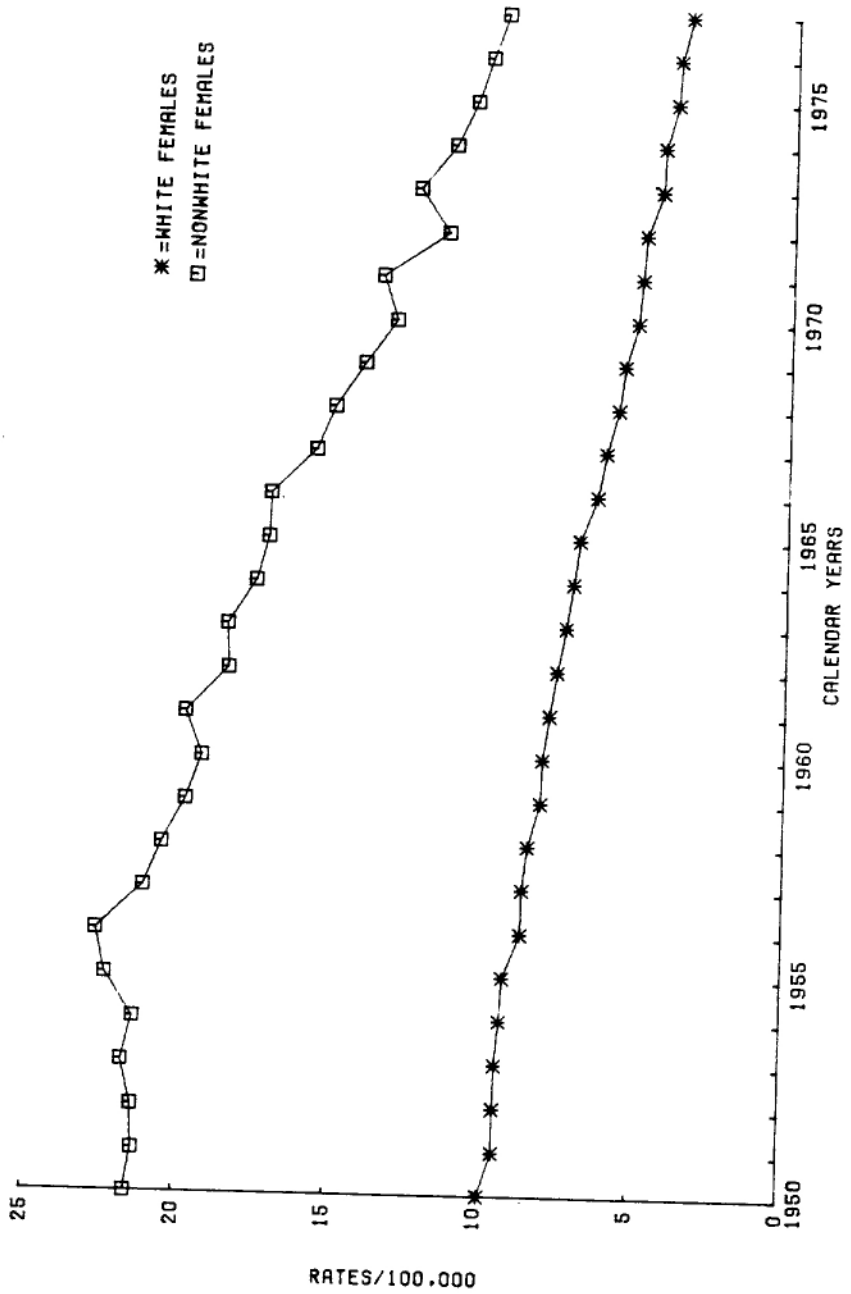

FIGURE 59.—Age-adjusted* mortality rates for cancer of the uterine cervix, by race, United States, 1950–1977

* This graph is age-adjusted to the U.S. population as enumerated in 1970; all rates cited within the text of the Report, however, are adjusted to the population as enumerated in 1940.

SOURCE: National Cancer Institute (*198*).

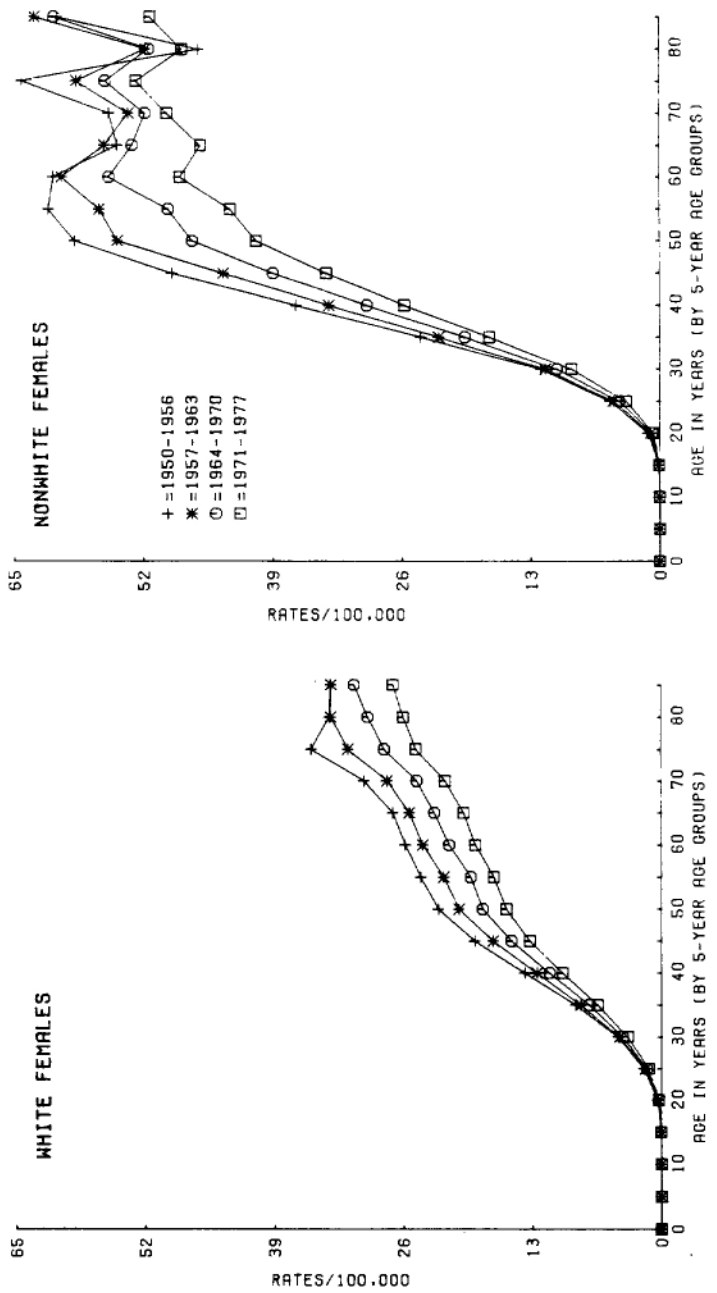

FIGURE 60.—Age-specific mortality rates for whites and nonwhites in the United States for cancer of the uterine cervix

SOURCE: National Cancer Institute (*198*).

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venereal infections, circumcision status of consort, and exogenous hormones (*264*).

A limited number of studies have attempted to identify an association between cigarette smoking and cervical cancer. One study (*192*) reported a relationship between smoking status (never smoked, ex-smokers, present smokers) and suspicious or positive cervical cytology. Thomas (*264*) administered a home questionnaire to 324 females with abnormal cervical cytology and reported that the prevalence of smoking was 70 percent in cases with carcinoma *in situ* and 58 percent in controls ($0.02 \leq p \leq 0.05$). When adjusted for thirteen other variables (including ≥ 3 births, first pregnancy prior to age 20, husband's circumcision and prior marriage history, and marital instability, among others), he reported a "borderline" significant relative risk ($0.02 \leq p \leq 0.05$) for carcinoma *in situ*, and non-significant differences for dysplasia. A case-control study among 350 Moslems and non-Moslems in Yugoslavia found that cervical cancer patients were more likely to smoke and to smoke more than one pack per day; the differences were statistically significant ($p < 0.01$) for Moslems (*140*). Subsequently, three other retrospective studies in Germany (*201*), England (*38, 305*), and Canada (*297*) have reported that smoking was a risk factor for cervical cancer. The English study (*108*) examined 31 women with dysplasia, carcinoma *in situ*, or invasive carcinoma, and attempted to control for known risk factors such as age at first intercourse and number of sexual partners of both wife and husband. They reported no effect of husband's smoking habit on the relative risk of cervical abnormalities, but a statistically significant excess risk among wives who were current smokers (RR 7.9), and an elevated risk for women who were former smokers (RR 3.7) over that for women nonsmokers (RR 1.0). Conversely, however, the Canadian study reported age-adjusted relative risks for *in situ* and invasive cancers for current smokers of 3.8 and 2.0, but no adjustment was made for other known risk factors for the disease. In the Third National Cancer Study (*299*), Williams and Horm have reported a significant positive association between cigarette smoking and both invasive and *in situ* cervical cancer, as well as between nonsmoking tobacco use (snuff and chewing tobacco) and invasive cervical cancer. A dose-response relationship was evident. The Swedish (*42*) and the Japanese (*119, 120*) prospective studies included data on smoking and cervical cancer. Cigarette smokers had increased mortality ratios, and a dose-response relationship was noted (Table 40). None of these studies controlled for other known risk factors.

Stellman et al. (*256*) examined the records of 332 patients with cervical cancer (stages not identified) who were controls for another study of smoking and health at different hospitals in several cities. The controls were patients hospitalized for non-smoking-related

TABLE 40.—Cervical cancer mortality ratios for women by current number of cigarettes smoked per day—prospective studies

Population	Cigarettes/day	Mortality ratio
Japanese Study	Nonsmokers	1.00
	1–19	1.00
	20–29	1.85
	30+	3.50
	All smokers	1.72
Swedish Study	Nonsmokers	1.00
	1–7	2.80
	8–15	3.00
	≥16	3.40
	All smokers	3.00

diseases and matched for age, race, hospital, and hospital status (semi-private versus ward). Socioeconomic status was determined by the subject's education and occupation and by the husband's occupation. Their analysis showed an overall positive association between cigarette smoking and cervical cancer. However, after Mantzel-Haenszel adjustment for age and socioeconomic status, the authors did not find a statistically significant association. The authors suggest that the association between smoking and cervical cancer is highly confounded and not consistent with a causal hypothesis. This study also, however, failed to include direct measures of potential confounding variables, such as sexual activity. It should be noted that in the Swedish (*42*) and German (*201*) studies, differences in socioeconomic status did not affect cervical cancer incidence.

The associations described between cervical cancer and many other variables, in addition to the variation in results of studies of the possible association of cigarette smoking and cervical cancer, do not permit a conclusion on the character of this relationship at this time.

Conclusion

1. There are conflicting results in studies published to date on the existence of a relationship between smoking and cervical cancer; further research is necessary to define whether an association exists and, if so, whether that association is direct or indirect.

Smoking and Overall Cancer Mortality

Introduction

Several investigators have estimated the proportion of all cancer deaths attributable to tobacco use in the United States to range from 22 percent to 38 percent of all cancer deaths (*70, 78, 106*). The authors of a recent review of cancer causes (*70*), commissioned by the Congressional Office of Technology Assessment, concluded that 30 percent of all U.S. cancer deaths are attributable to tobacco use (Appendix Table C). These estimates reflect a growing consensus that smoking is the single largest contributor to cancer mortality in the United States.

Overall Cancer Mortality

As early as 1928, Lombard and Doering (*160*), in a study of 217 cancer patients and 217 controls in Massachusetts, identified an association between heavy smoking (defined as all types of smokers) and cancer in general. This study is of historical significance in light of our present day knowledge about the relationship between smoking and specific cancer sites. Over the last two decades, four of the eight major prospective studies have examined the relationships between smoking to overall and site-specific cancer mortality. Two of these studies (*98, 120*) included observations on females as well as males.

Male smokers, regardless of the amount smoked, have approximately twice the risk of dying from cancer than do their nonsmoking counterparts (Table 41). Data from these studies also showed a gradient increase in overall cancer mortality with the amount smoked. These data are presented in Table 42. Males who consumed more than one pack of cigarettes daily had overall cancer mortality rates almost three times greater than did nonsmokers. Mortality

TABLE 41.—Smoking and overall cancer mortality ratios—prospective studies

Study	Nonsmokers	Smokers	
		Male	Female
ACS 25-State Study	1.00	1.79 1.18 pipe and cigar	1.21
U.S. Veterans	1.00	2.12 1.32 cigars 1.29 pipes	
Japanese Study	1.00	1.62	1.41
ACS 9-State Study	1.00	1.97 cigarettes 1.44 pipe 1.34 cigar	

TABLE 42.—Smoking and overall cancer mortality ratios in males by amount smoked

Study	Amount smoked per day	Mortality ratio
ACS 9-State Study	Nonsmoker	1.00
	1–9	1.87
	10–20	1.92
	20+	2.94
	All smokers	1.97
U.S. Veterans	Nonsmoker	1.00
	1–9	1.42
	10–20	1.95
	21–39	2.66
	40+	3.31
	All smokers	2.12
Japanese Study	Nonsmoker	1.00
	1–19	1.53
	20–39	1.81
	40+	2.06
	All smokers	1.62

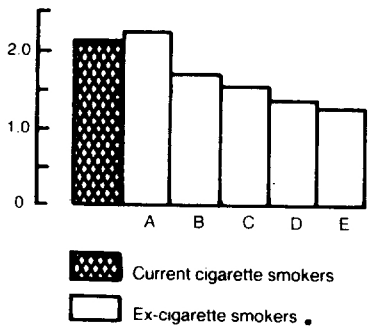

FIGURE 61.—Mortality ratios for all cancer sites for ex-cigarette smokers by number of years of smoking cessation, U.S. Veterans Study

NOTE: A: Stopped less than 5 years.
B: Stopped 5–9 years.
C: Stopped 10–14 years.
D: Stopped 15–19 years.
E: Stopped 20 or more years.
SOURCE: Rogot and Murray (*224*).

ratios for male pipe smokers and male cigar smokers were 1.44 and 1.34, respectively (*224*). Female smokers had overall cancer mortality rates 20 to 40 percent greater than female nonsmokers. Hammond (*106*) calculated that 34.5 percent of all cancer deaths in males were smoking related. These are in close agreement with estimates made by other investigators (*70, 216*).

Rogot and Murray (*224*) examined overall cancer mortality in ex-cigarette smokers compared to continuing cigarette smokers and

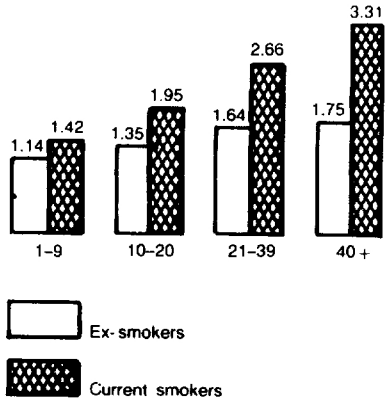

FIGURE 62.—Mortality ratios for all cancer sites for current and ex-smokers by number of cigarettes smoked daily, U.S. Veterans Study

SOURCE: Rogot and Murray (224).

found declining cancer mortality ratios for ex-smokers by the number of years off cigarettes. For those former smokers who had quit for 20 years or more, the overall cancer mortality rate was approximately 25 percent above those of nonsmokers but substantially below those of continuing smokers (1.27 versus 2.12) (Figure 61). These investigators also noted that cancer mortality among former cigarette smokers was correlated to the number of cigarettes smoked per day. A clear gradient by the amount smoked is evident for ex-smokers as well as continuing smokers for overall cancer mortality (Figure 62). Overall cancer mortality rates for former cigarette smokers were 40 percent greater than for nonsmokers.

Conclusion

1. Cigarette smokers have overall mortality rates substantially greater than those of nonsmokers. Overall cancer death rates of male smokers are approximately double those of nonsmokers; overall cancer death rates of female smokers are approximately 30 percent higher than nonsmokers, and are increasing.

2. Overall cancer mortality rates among smokers are dose-related as measured by the number of cigarettes smoked per day. Heavy smokers (over one pack per day) have more than three times the overall cancer death rate of nonsmokers.
3. With increasing duration of smoking cessation, overall cancer death rates decline, approaching the death rate of nonsmokers.

Summary

1. Cigarette smoking is the major cause of lung cancer in the United States.
2. Lung cancer mortality increases with increasing dosage of smoke exposure (as measured by the number of cigarettes smoked daily, the duration of smoking, and inhalation patterns) and is inversely related to age of initiation. Smokers who consume two or more packs of cigarettes daily have lung cancer mortality rates 15 to 25 times greater than nonsmokers.
3. Cigar and pipe smoking are also causal factors for lung cancer. However, the majority of lung cancer mortality in the United States is due to cigarette smoking.
4. Cessation of smoking reduces the risk of lung cancer mortality compared to that of the continuing smoker. Former smokers who have quit 15 or more years have lung cancer mortality rates only slightly above those for nonsmokers (about two times greater). The residual risk of developing lung cancer is directly proportional to overall life-time exposure to cigarette smoke.
5. Filtered lower tar cigarette smokers have a lower lung cancer risk compared to nonfiltered, higher tar cigarette smokers. However, the risk for these smokers is still substantially elevated above the risk of nonsmokers.
6. Since the early 1950s, lung cancer has been the leading cause of cancer death among males in the United States. Among females, the lung cancer death rate is accelerating and will likely surpass that of breast cancer in the 1980s.
7. The economic impact of lung cancer to the nation is considerable. It is estimated that in 1975, lung cancer cost $3.8 billion in lost earnings, $379.5 million in short-term hospital costs, and $78 million in physician fees.
8. Lung cancer is largely a preventable disease. It is estimated that 85 percent of lung cancer mortality could have been avoided if individuals never took up smoking. Furthermore, substantial reductions in the number of deaths from lung cancer could be achieved if a major portion of the smoking population (particularly young persons) could be persuaded not to smoke.
9. Cigarette smoking is the major cause of laryngeal cancer in the United States. Cigar and pipe smokers experience a risk for laryngeal cancer similar to that of a cigarette smoker.
10. The risk of developing laryngeal cancer increases with increased exposure as measured by the number of cigarettes smoked daily as well as other dose measurements. Heavy smokers have laryngeal cancer mortality risks 20 to 30 times greater than nonsmokers.

11. Cessation of smoking reduces the risk of laryngeal cancer mortality compared to that of the continuing smoker. The longer a former smoker is off cigarettes the lower the risk.
12. Smokers who use filtered lower tar cigarettes have lower laryngeal cancer risks than those who use unfiltered higher tar cigarettes.
13. The use of alcohol in combination with cigarette smoking appears to act synergistically to greatly increase the risk for cancer of the larynx.
14. Cigarette smoking is a major cause of cancers of the oral cavity in the United States. Individuals who smoke pipes or cigars experience a risk for oral cancer similar to that of the cigarette smoker.
15. Mortality ratios for oral cancer increase with the number of cigarettes smoked daily and diminish with cessation of smoking.
16. Cigarette smoking and alcohol use act synergistically to increase the risk of oral cavity cancers.
17. Long term use of snuff appears to be a factor in the development of cancers of the oral cavity, particularly cancers of the cheek and gum.
18. Cigarette smoking is a major cause of esophageal cancer in the United States. Cigar and pipe smokers experience a risk of esophageal cancer similar to that of cigarette smokers.
19. The risk of esophageal cancer increases with increased smoke exposure, as measured by the number of cigarettes smoked daily, and is diminished by discontinuing the habit.
20. The use of alcohol in combination with smoking acts synergistically to greatly increase the risk for esophageal cancer mortality.
21. Cigarette smoking is a contributory factor in the development of bladder, kidney, and pancreatic cancer in the United States. This relationship is not as strong as that noted for the association between smoking and cancers of the lung, larynx, oral cavity, and esophagus. The term "contributory factor" by no means excludes the possibility of a causal role for smoking in cancers of these sites.
22. In epidemiological studies, an association between cigarette smoking and stomach cancer has been noted. The association is small in comparison with that noted for smoking and some other cancers.
23. There are conflicting results in studies published to date on the existence of a relationship between smoking and cervical cancer; further research is necessary to define whether an association exists and, if so, whether that association is direct or indirect.

24. Cigarette smokers have overall mortality rates substantially greater than those of nonsmokers. Overall cancer death rates of male smokers are approximately double those of nonsmokers; overall cancer death rates of female smokers are approximately 30 percent higher than nonsmokers, and are increasing.
25. Overall cancer mortality rates among smokers are dose-related as measured by the number of cigarettes smoked per day. Heavy smokers (over one pack per day) have more than three times the overall cancer death rate of nonsmokers.
26. With increasing duration of smoking cessation, overall cancer death rates decline, approaching the death rate of nonsmokers.

Technical Notes

Age-Adjusted Death Rates

Age-adjusted death rates show what the level of mortality would be if there were no changes in the age composition of the population from year to year. The age-adjusted death rates for the U.S. as a whole presented in this Report were computed by the Direct Method, that is, by applying the age-specific death rates for all causes of death or for deaths for a given cause to the standard population distributed by age. The total U.S. population as enumerated in 1940 is used as the standard population by the National Center for Health Statistics for presentation of mortality statistics. Standard populations other than 1940 have been used by other agencies, organizations, and researchers in presenting mortality data. This introduces some problems of comparability in the presentation of the statistical findings drawn from a variety of sources.

Cause-of-Death Classification

National mortality statistics from the National Center for Health Statistics for the U.S. presented in this Report are classified in accordance with the World Health Organization (WHO) Regulations, which specify that member nations classify causes of death in accordance with the International Statistical Classification of Diseases, Injuries, and Causes of Death. The deaths are tabulated and presented in *Vital Statistics of the United States, Volume II, Mortality* by cause-of-death categories that are consistent with WHO recommendations. Other organizations and researchers whose work is cited in this Report may use different cause-of-death categories. This introduces some problems of comparability in the presentation of the statistical findings drawn from a variety of sources.

Another problem of comparability in mortality rates is introduced when comparisons are made over time for specific causes of death. This is because of the practice to periodically revise the International Classification of Diseases (ICD) by which causes of death are

classified and tabulated. The ICD has been revised approximately every 10 years since 1900 to keep abreast of medical knowledge. Each decennial revision has produced breaks in the comparability of cause-of-death statistics. For many of the causes of death described in this Report, the reader may refer to the NCHS report (*199*) for information about comparability in cause of death statistics due to revisions in the ICD during 1950–1977.

Appendix Tables

APPENDIX TABLE A.—Mortality ratios (smokers vs. never smoked regularly) for smoking-related cancers among females—ACS 25-State Study and Japanese Study

Underlying cause of death	Mortality ratios	
	ACS	*Japanese*
Cancer (total)	1.21	1.41
Lung (excl. trachea, pleura)	3.58	2.03
Buccal cavity, pharynx, larynx, and esophagus	3.25	6.52
Pancreas	1.42	—
Uterus	1.18	—
Uterine cervix	—	1.72
Esophagus	4.89	—
Stomach	1.21	1.31
Bladder	2.58	2.00

APPENDIX TABLE B.—Mortality ratios (smoker vs. never smoked regularly) for smoking-related cancers among males—ACS 25-State Study and U.S. Veterans Study

Underlying cause of death	Mortality ratios		
	ACS		*U.S. Veterans*
	Age 45–64	Age 65–79	All
Cancer (total)	2.14	1.76	2.12
Lung (excl. trachea, pleura)	7.84	11.59	11.28
Buccal cavity, pharynx	9.90	2.93	4.22
Larynx	6.09	8.99	11.49
Esophagus	4.17	1.74	6.43
Bladder and other urinary	2.00	2.96	2.16
Kidney	1.42	1.57	1.41
Prostate	1.04	1.01	1.31
Pancreas	2.69	2.17	1.79
Liver, biliary passages	2.84	1.34	—
Stomach	1.42	1.26	1.52

APPENDIX TABLE C.—Cancer deaths caused by tobacco: United States, 1978

Certified cause of death[a]	Number of deaths			
	Observed	Estimated, had Americans not smoked	Approximate excess number and percent of deaths attributed to tobacco (percent in parentheses)	
Cancer, males				
Lung	71,006	6,439[b]	64,567	(90.9)
Mouth, pharynx, larynx, or esophagus	14,282	1,792 × 2[c]	10,698	(74.9)
Bladder	6,771	2,960[b]	3,811	(56.3)
Pancreas	11,010	6,585[b]	4,425	(40.2)
Other specified sites	100,799	—	5,000[d]	(5.0)
Unspecified sites	14,469	8,188[e]	6,281	(43.4)
Total, males	218,337		94,782[f]	(43.4)
Cancer, females				
Lung	24,080	5,454[b]	18,626	(77.4)
Mouth, pharynx, larynx, or esophagus	5,100	1,458 × 2[c]	2,184	(42.8)
Bladder	3,078	2,170[b]	908	(29.5)
Pancreas	9,767	7,291[b]	2,476	(25.4)
Other specified sites	127,642	—	1,000[d]	—
Unspecified sites	13,951	11,879[e]	2,072	(14.9)
Total, females	183,618		27,266[f]	(14.8)
Total, males and females	401,955		122,048[f]	(30.4)

[a] Site of origin of cancer.

[b] Number estimated by applying the nonsmoker mortality rates reported by Garfinkel (86) to the U.S. population of 1978.

[c] Double the number estimated by the procedure described in footnote b. This number was doubled to allow for the possibility that the subjects in the ACS prospective study were less exposed to alcohol or to some other cause(s) of cancer of the upper respiratory or digestive tracts than were average people in the United States. [Some evidence that this was indeed the case is that even the cigarette smokers in the ACS study had mortality rates for these types of cancer that were somewhat below the national U.S. rates (98).] However, it makes little difference to our grand totals whether the small number of cancers of the mouth and throat "expected" from the ACS nonsmoker experience are left unaltered, are doubled, or are trebled.

[d] Other specified sites include some, such as kidney, that may truly be affected by tobacco, and some, such as stomach or liver, that include a proportion of misdiagnosed cases of cigarette-induced cancer of the lung, pancreas, and other organs. Some fraction of the cancers certified as being of other specified sites is thus due to smoking, which in part explains the excess mortality among smokers in the aggregate of all such cancers that is found in the American prospective studies (Appendix Tables A and B). We have suggested, without firm evidence, that of these other cancers, perhaps 5,000 male and 1,000 female cases may have been due to tobacco. These suggested figures, totaling 6,000, may slightly underestimate the actual figures, but readers may substitute any estimate that they consider more plausible, e.g., some other estimate between 1,000 and 20,000, leading to an estimate of 29 to 34 percent of 1978 cancer deaths ascribable to tobacco.

[e] Estimated to match the proportions (43 percent male, 15 percent female) of specified sites attributed to tobacco.

[f] The percentage ascribable to tobacco is gradually increasing as lung cancer death rates are increasing among older Americans.

SOURCE: Doll and Peto (70).

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