smoked. The study of Canadian veterans (*9*) also contained evidence of a dose-response in mortality by amount smoked for cigar smokers. No dose-response relationship was observed among pipe smokers (table 8). Kahn (*50*) reported a consistent increase in overall mortality with an increase in the amount smoked for both pipe and cigar smokers (table 9). Hammond (*38*) found no consistent relationship between overall mortality and the number of cigars or pipefuls smoked (table 10).

TABLE 7.—*Mortality ratios for total deaths of cigar and pipe smokers by amount smoked—Hammond and Horn*

Amount smoked	Number of deaths		
	Observed	Expected	Mortality ratio
Nonsmoker	1, 664	1, 664	1. 00
Cigar only:			
Total	653	598	1. 09
1 to 4 cigars	410	400	1. 03
>4 cigars	229	185	1. 24
Pipe only:			
Total	609	560	1. 09
1 to 10 pipefuls	391	374	1. 05
>10 pipefuls	204	172	1. 19

Source: Hammond, E. C., Horn, D. (*40*).

TABLE 8.—*Mortality ratios for total deaths of cigar and pipe smokers by amount smoked—Best*

Amount smoked	Number of deaths		
	Observed	Expected	Mortality ratio
Nonsmoker	----------	----------	1. 00
Cigar only:			
Total	90	82. 07	1. 10
1 to 2 cigars	64	56. 05	1. 14
3 to 10 cigars	23	19. 40	1. 19
>10 cigars	1	1. 59	. 63
Pipe only:			
Total	570	566. 99	1. 00
1 to 10 pipefuls	374	370. 09	1. 01
10 to 20 pipefuls	141	140. 84	1. 00
>20 pipefuls	36	35. 90	1. 00

Source: Best, E. W. R. (*9*).

The above evidence suggests that a dose-response relationship may exist between the number of cigars and pipefuls smoked and overall mortality. However, because of the high-mortality rate of ex-smokers of cigars and pipes, it is difficult to interpret the data presented without including this group with the continuing smokers. Without data which examines patterns of both daily rate of smoking and inhalation at various age levels, no firm conclusions can be drawn as to the nature of this dosage relationship.

TABLE 9.—*Mortality ratios for total deaths of cigar and pipe smokers by age and amount smoked—Kahn*

Amount smoked	Mortality ratio, age	
	55 to 64	65 to 74
Nonsmoker	1. 00	1. 00
Cigar only:		
Total	1. 01	1. 08
1 to 4 cigars per day	. 89	1. 00
5 to 8 cigars per day	1. 14	1. 23
>8 cigars per day	1. 65	1. 28
Pipe only:		
Total	1. 08	1. 06
1 to 4 pipefuls per day	1. 16	. 91
5 to 19 pipefuls per day	1. 04	1. 10
>19 pipefuls per day	----------	1. 18

Source: Kahn, H. A. (*50*).

TABLE 10.—*Mortality ratios for total deaths of cigar and pipe smokers by amount smoked—Hammond*

Amount smoked	Mortality ratio	Amount smoked	Mortality ratio
Nonsmoker	1. 00	Current pipe smokers:	
Current cigar smokers:		Total	1. 04
Total	1. 09	1 to 9 pipefuls per day	1. 08
1 to 4 cigars per day	1. 03	>9 pipefuls per day	. 92
>4 cigars per day	1. 18		

Source: Hammond, E. C. (*58*).

Inhalation

Inhalation of tobacco smoke directly exposes the bronchi and the lungs to smoke and results in the absorption of the soluble constituents of the gas and particulate phases. Without inhalation tobacco smoke only reaches the oral cavity and the upper digestive and respiratory tracts and does not reach the lungs where further direct effects and systemic absorption of various chemical compounds can occur.

Although the smoker has some voluntary control over the inhalation of smoke, the physical and chemical properties of tobacco smoke to a degree determine its acceptability and "inhalability."

The condensate of pipe and cigar smoke is generally found to be alkaline when the pH is measured by suspending a Cambridge filter in CO_2-free water. Cigarette condensate is slightly acidic as measured by this method. Since alkaline smoke is more irritating to the respiratory tract, it has been assumed that the more alkaline smoke of pipes and cigars was in part responsible for the lower levels of inhalation reported by pipe and cigar smokers. Brunnemann and Hoffmann (*15*) have analyzed the pH of whole, mainstream smoke of cigarettes and cigars on a puff-by-puff basis using a pH electrode suspended in mainstream smoke. Smoke from several U.S. brands of cigarettes was found to be acidic throughout the entire length of the cigarette. Of interest was the finding that cigar smoke also had an acidic pH for the first two-thirds of the cigar and became alkaline only in the last 20 to 40 percent of the puffs from the cigar. Available epidemiological evidence indicates that most cigar smokers do not inhale the smoke and most cigarette smokers do. The fact that smoke from the first half or more of a cigar is acidic, near the range of pH values commonly found in cigarette smoke, and becomes alkaline only toward the end of the cigar might suggest that the pH of the smoke of a tobacco product may not be the only factor that influences inhalation patterns. Perhaps "tar" and nicotine levels as well as the concentration of other "irritating" chemicals also affect the degree to which a tobacco smoke will be inhaled.

Nicotine is rapidly absorbed into the blood stream from the lungs when tobacco smoke is inhaled. The amount of nicotine absorbed from the lungs is primarily a function of the nicotine concentration in the smoke and the depth of inhalation. Some nicotine may also be absorbed through the mucous membranes of the mouth. This is more likely to occur under alkaline conditions when nicotine is unprotonated (*3*, *15*, *79*). This suggests that cigar smokers may be able to absorb some nicotine through the oral cavity without having to inhale, particularly during the time that the smoke from the cigar is alkaline.

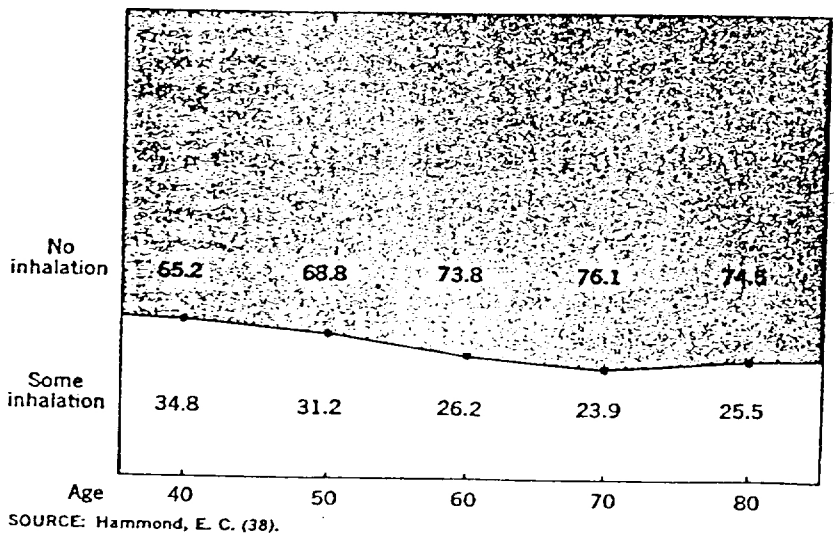
With the development of sensitive measures of serum nicotine levels (*48*) the extent to which nicotine is absorbed through the membranes of the mouth in pipe and cigar smokers can be more accurately determined.

Inhalation patterns of smokers were determined in several of the large prospective and some of the retrospective epidemiological studies. Inhalation was usually determined by the administration of a questionnaire that required a subjective evaluation of one's own patterns of inhalation. Although the accuracy of these questionnaires has not been confirmed by an objective measure of inhalation, such as carboxyhemoglobin or serum nicotine levels, their reliability is supported by mortality data which demonstrate higher overall and specific death rates with self-reported increases in the depth of inhalation.

Doll and Hill (*26*) and Hammond (*38*) presented information on inhalation patterns of pipe, cigar, and cigarette smokers (figs. 1, 2, 3, and table 12). Some 80 to 90 percent of cigarette smokers reported inhaling, with the majority of individuals inhaling moderately or deeply, whereas most pipe and cigar smokers denied inhaling at all. Pipe smokers reported slightly more inhalation than cigar smokers. For each type of smoking, less inhalation was reported by older smokers. This change may represent less awareness of inhalation, differences in smoking habits of successive cohorts of smokers, or it may reflect the operation of selective factors which favor survival of noninhalers.

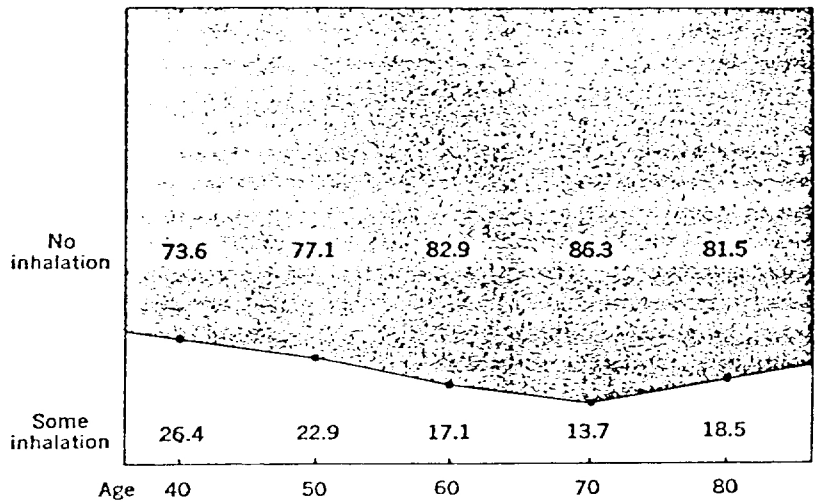
The Tobacco Research Council of the United Kingdom has, since 1957, periodically reported the use of tobacco products by the British.

Figure 1.—Inhalation among pipe smokers by age.



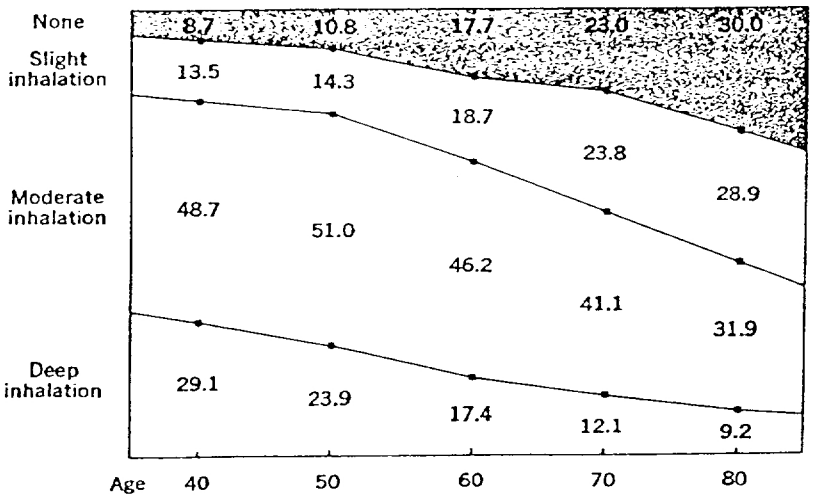
SOURCE: Hammond, E. C. (*38*).

Figure 2.—Inhalation among cigar smokers by age—Hammond.



SOURCE: Hammond, E. C. (38).

Figure 3.—Depth of inhalation among cigarette smokers by age.—Hammond.



SOURCE: Hammond, E. C. (38).

Recent reports edited by Todd have contained data on the inhalation pattern of cigar, pipe, and cigarette smokers (*92*, *93*, *94*). Table 11 shows that most cigarette smokers inhale a "lot" of "fair amount" whereas most pipe and cigar smokers do not inhale at all or "just a little." Little change is observed in the inhalation patterns of a given product since 1968.

Best (*9*) reported inhalation data among male cigarette smokers by smoking intensity and age group, but did not report the inhalation

patterns of pipe and cigar smokers. The overall mortality rates of current pipe smokers who inhaled at least slightly were reported by Hammond (*38*) as being somewhat higher than for men who never smoked regularly. The overall mortality rates of current cigar smokers who reported inhaling at least slightly were appreciably higher than for men who never smoked regularly (table 13).

Available evidence indicates that cigarette smokers inhale smoke to a greater degree than smokers of cigars or pipes. Once a smoker has learned to inhale cigarettes, however, there appears to be a tendency to also inhale the smoke of other tobacco products. For cigars, this is evidently true whether one smokes both cigarettes and cigars or switches from cigarettes to cigars (tables 14, 15, 16).

Bross and Tidings (*14*) examined the inhalation patterns of smokers of large cigars, cigarettes, and those who switched from one tobacco product to another (table 15). Nearly 75 percent of those who were currently smoking only cigarettes reported inhaling "almost every puff" and only 7 percent never inhaled. The opposite was true for persons who had always smoked only cigars among whom 4 percent re-

TABLE 11.—*The extent of inhaling pipes, cigars, and cigarettes by British males aged 16 and over in 1968 and 1971*

Amount of inhalation	Tobacco product					
	Cigars		Pipes		Cigarettes	
	1968	1971	1968	1971	1958	1971
Inhale a lot	23	19	8	8	47	47
Inhale a fair amount	16	19	10	8	31	30
Inhale just a little	27	27	24	26	13	15
Do not inhale at all	34	35	59	58	9	8
Total	100	100	100	100	100	100

Source: Todd, G. F. (*93, 94*).

TABLE 12.—*Inhalation among cigar, pipe, and cigarette smokers by age—Doll and Hill*

Smoking type	Percentage of inhalers, age					
	25 to 34	35 to 44	45 to 54	55 to 64	65 to 74	>74
Cigar and pipe	12.00	10.00	7.00	5.00	4.00	4.00
Mixed (cigarette and other)	74.00	60.00	47.00	36.00	30.00	26.00
Cigarette only	90.00	85.00	75.00	66.00	58.00	41.00

Source: Doll, R., Hill, A. B. (*26*).

ported inhaling almost every puff and 89 percent said they never inhaled. Cigar smokers who also smoked cigarettes reported intermediate levels of inhalation between the cigar only and cigarette only categories. Inhalation patterns were similar whether the individual continued to smoke both products, stopped smoking cigarettes but continued smoking cigars, or stopped smoking cigarettes and switched to cigars. In all three groups, about 20 percent reported inhaling "almost every puff." This suggests that once an individual's inhalation patterns are established on cigarettes, he may be more likely to inhale cigar smoke if he switches to cigars, or uses both cigars and cigarettes, than the cigar smoker who has not smoked cigarettes.

Todd (*93*) reported similar data for a sample of smokers in the United Kingdom (table 16). The prevalence of inhaling a "lot" or "fair amount" of smoke was highest among cigarette smokers who were currently smoking cigarettes (77 percent) and lowest among current cigar smokers who had previously smoked only cigars or pipes (18 percent). Individuals who switched from cigarettes to cigars main-

TABLE 13.—*Mortality ratios for total deaths of cigar and pipe smokers by age and inhalation—Hammond*

Inhalation	Mortality ratio, age	
	45 to 64	65 to 84
Nonsmoker	1.00	1.00
Cigar only:		
Total	1.09	.98
No inhalation	1.02	.91
Some inhalation	1.28	1.37
Pipe only:		
Total	1.04	.95
No inhalation	.98	.87
Some inhalation	1.21	1.11

Source: Hammond, E. C. (*55*).

TABLE 14.—*Percentage of British male cigar smokers who reported inhaling a lot or a fair amount by type of product smoked*

Type of product	1968		1971	
	Number of individuals	Percent	Number of individuals	Percent
Cigars only	706	23.0	111	27.0
Cigars and cigarettes	1,193	42.0	277	44.0
Cigars and pipes	596	35.0	109	32.0
Cigars, cigarettes, and pipes	26	52.0	15	32.0

Source: Todd, G. F. (*93, 94*).

tained somewhat higher levels of cigar smoke inhalation than those cigar smokers who had never smoked cigarettes (30 percent).

Todd (*93*) examined further the relationship between the inhalation of cigarette and cigar smoke. In general, cigarette smokers who switched to cigars were much less likely to report inhaling cigar smoke than cigarette smoke; however, those who in the past reported inhaling cigarette smoke a "lot" or "fair amount" were much more likely to report inhaling cigar smoke to the same degree than those ex-cigarette smokers who in the past did not inhale the smoke of their cigarettes (table 17).

TABLE 15.—*Percentage of individuals reporting inhalation of "almost every puff" of tobacco smoke by current and previous tobacco usage and type of tobacco used*

Type of tobacco smoked		Number of patients	Type inhaled	Percentage inhaled	Confidence limits	
Current usage	Previous usage				Lower	Upper
Cigarettes only	Cigarettes only	2,359	Cigarette	74.8	73.1	76.6
Cigars only	Cigars only	649	Cigars	4.5	3.0	6.0
Cigarettes and cigars.	Cigarettes and cigars.	520	do	20.4	10.5	28.0
Cigars	Cigarettes and cigars.	93	do	18.3	9.0	30.0
None	Cigarettes and cigars.	186	do	21.5	17.8	24.2
Cigars	Cigarettes only	64	do	17.2	16.0	28.0

Source: Bross, I. D. J., Tidings, J. (*14*).

TABLE 16.—*Percentage of British males who reported inhaling a lot or fair amount of cigar smoke by current and previous tobacco usage and type of tobacco previously smoked (1968)*

Type of tobacco smoked		Number of individuals	Type inhaled	Percentage inhaled
Current usage	Previous usage			
Cigarettes only	Cigarettes only	2,586	Cigarette	77.7
Cigars only	Nonsmoker	306	Cigars	18.0
Cigars only	Cigarettes only	321	do	30.0

Source: Todd, G. F. (*94*).

TABLE 17.—*Extent of reported inhalation of cigar smoke by British male cigar smokers who were ex-cigarette smokers in 1968, analyzed by extent of reported inhalation of cigarette smoke when previously smoking cigarettes*

Extent of inhaling cigars	Extent of inhaling cigarettes	
	Inhale a lot or fair amount	Inhale a little or not at all
	Percent	*Percent*
Inhale a lot or fair amount	44. 0	5. 0
Inhale a little or not at all	56. 0	95. 0
Total	100. 0	100. 0
Sample size	244	56

Source: Todd, G. F. (*85*).

Specific Causes of Mortality

Cancer

Several prospective epidemiological studies have shown a significantly higher overall cancer mortality among pipe and cigar smokers compared to the cancer mortality of nonsmokers (table 18).

Pipe and cigar smokers have much higher rates of cancer at certain sites than at others. The upper airway and upper digestive tracts appear to be the most likely target organs. The relationship of pipe and cigar smoking to the development of specific cancers is detailed in the following sections.

TABLE 18.—*Mortality ratios for total cancer deaths in cigar and pipe smokers. A summary of prospective epidemiological studies*

Author, reference	Type of smoking				
	Nonsmoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only
Hammond and Horn (*40*)	1. 00	1. 34	1. 44	-------	1. 97
Best (*9*)	1. 00	1. 13	1. 38	-------	2. 06
Hammond (*38*)	1. 00	-------	-------	1. 21	1. 76
Kahn (*60*)	1. 00	1. 22	1. 25	1. 25	2. 21

Cancer of the Lip

Approximately 1,500 new cases of cancer of the lip are reported each year. Because of the possibility of early detection and surgical accessibility of cancers in this area, there are less than 200 deaths from cancer of the lip each year in the United States. Some of the earliest scientific investigations exploring the association between tobacco use and disease examined the smoking patterns of individuals with cancer of the lip.

Broders (*13*) in 1920 examined the smoking habits of patients in a retrospective study of 526 cases of epithelioma of the lip and 500 controls. Of the cancer cases, 59 percent smoked pipes, whereas this was true for only 28 percent of the controls. No association was found between cigar or cigarette smoking and cancer of the lip.

In a restrospective study of 439 clinic patients with cancer of the lip and 300 controls conducted in Sweden, Ebenius (*32*) reported a significant association between pipe smoking and cancer of the lip. A total of 61.8 percent of the lip cancer cases smoked pipes, while only 22.9 percent of the controls smoked pipes. No association was found between the use of cigarettes, cigars, or chewing tobacco and cancer of the lip.

In other retrospective studies, Levin, et al. (*60*) reviewed a series of 143 cases of cancer of the lip, and Sadowsky, et al. (*77*) reviewed 571 cases of cancer of the lip. In both studies, a strong association was found between pipe smoking and cancer of the lip. No significant association was found between the use of tobacco in other forms and cancer at this site.

In a study of environmental factors in cancer of the upper alimentary tract, Wynder, et al. (*113*) found an association between pipe smoking, cigarette smoking, and cancer of the lip. There were only 15 cases of cancer of the lip in this study.

Staszewski (*87*) examined the smoking habits of 394 men with carcinoma or precancerous lesions of the lips. An association was found between the smoking of pipes and cigars and cancer of the lip, but this was only of doubtful significance. A significant association was found between the use of cigarettes and cancer of the lip.

Keller (*51*) conducted a study of lip cancers in which he considered a number of factors including histologic types, survival, race, occupations, habits, and associated diseases. A total of 304 patients with primary basal cell or squamous cell carcinoma of the lip and 304 controls from the same hospital matched for age and race were considered in this series. A significant association was found between smoking in all forms and combinations and carcinoma of the lip. It was also found that increasing age and outdoor occupations with exposure to the sun were equally significant factors in the etiology of lip cancer.

In summary, it appears that there are several factors involved in the etiology of cancer of the lip. Among the various forms of tobacco use, pipe smoking either alone or in combination with other forms of smoking seems to be a cause of cancer of the lip. Table 19 summarizes the results of these retrospective studies.

Oral Cancer

The lips, oral cavity, and pharynx are the first tissues exposed to tobacco smoke drawn in through the mouth. Variations in inhalation during the smoking of various tobacco products result in different patterns of distribution of smoke throughout the respiratory tree. However, the oral cavity and adjacent tissues are the sites most consistently exposed to tobacco smoke. For this reason, differences in inhalation should result in less variation in exposure to tobacco smoke for these sites than for the lower trachea and the lung. The inherent carcinogenicity of pipe, cigar, and cigarette smoke is most reliably compared at those tissue sites where dosage and exposure to tobacco smoke are most nearly equal. Data from the epidemiological studies suggest that little difference exists between the smoking of cigarettes, pipes, or cigars and the risk of developing oral cancer.

Hammond and Horn (*40*) examined the association between smoking in various forms and cancer of the combined sites of lip, mouth, pharynx, larynx, and esophagus. The mortality ratios were 5.00 for cigar smokers, 3.50 for pipe smokers, and 5.06 for cigarette smokers compared to nonsmokers. All the deaths from cancer of the lip, oral cavity, and pharynx reported by Doll and Hill (*26*) occurred in smokers. The death rates from cancer at these sites were 0.04 per 1,000 for pipe and cigar smokers, 0.10 per 1,000 for mixed smokers, and 0.05 per 1,000 for cigarette smokers. A fairly detailed analysis of oral cancer was presented by Kahn (*50*) who differentiated between cancer of the oral cavity and cancer of the pharynx. The mortality ratios for oral cancers were 1.00 for those who never smoked, 3.89 for all pipe and cigar smokers, and 4.09 for cigarette smokers. A further breakdown of the pipe and cigar smokers demonstrated a mortality ratio of 4.11 for cigar smokers, 3.12 for pipe smokers, and 4.20 for smokers of pipes and cigars. For cancer of the pharynx, the mortality ratios were 1.00 for those who never smoked, 3.06 for all pipe and cigar smokers, and 12.5 for cigarette smokers. No deaths occurred among those who smoked only cigars. The mortality ratio was 1.98 for pipe smokers and 7.76 for smokers of pipes and cigars. Hammond (*38*) combined cancers of the lip, oral cavity, and pharynx. The pipe and cigar smokers had a mortality ratio of 4.94 and the cigarette smokers a mortality ratio of 9.90 compared to nonsmokers.

TABLE 19.—*Relative risk of lip cancer for men, comparing cigar, pipe, and cigarette smokers with nonsmokers: A summary of retrospective studies*

Author, reference	Number		Relative risk ratio and percentage of cases and controls by type of smoking					
			Nonsmoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Broders (*13*):		Relative risk	1.0	0.8	4.3	.....	0	.....
Cases	537	Percent cases	7	19	41	.....	1	.....
Controls	500	Percent controls	4	16	6	.....	26	.....
Ebenius (*32*):		Relative risk	1.0	.7	4.1	0.5	.....	.....
Cases	439	Percent cases	49	6	41	4	.....	.....
Controls	300	Percent controls	65	12	13	10	.....	.....
Levin, et al. (*60*):		Relative risk	1.0	1.9	2.9	.....	1.4	.....
Cases	143	Percent cases	15	27	48	.....	45	.....
Controls	554	Percent controls	22	20	24	.....	46	.....
Sadowsky, et al. (*77*):		Relative risk	1.0	1.1	4.3	2.6	1.4	0.4
Cases	571	Percent cases	8	2	18	6	44	22
Controls	615	Percent controls	13	3	7	4	53	19
Wynder,[1] et al. (*118*):		Relative risk	0	.8	1.8	.....	1.0	2.2
Cases	14	Percent cases	0	7	29	.....	36	29
Controls	115	Percent controls	24	9	16	.....	36	13
Staszewski (*87*):		Relative risk	1.0	.....	.....	2.1	2.4	.....
Cases	394	Percent cases	7	.....	.....	12	73	.....
Controls	912	Percent controls	13	.....	.....	11	61	.....
Keller: (*51*):		Relative risk	1.0	1.4	4.0		2.6	
Cases	301	Percent cases	7	2	6	1	60	6
Controls	265	Percent controls	17	4	3	0	53	0

[1] Percentage based on less than 20 patients. Ratios: relative to cigarette smokers.

These studies are summarized in table 20. They demonstrate that smokers experience a large and significant risk of developing cancer of the oral cavity compared to nonsmokers. This risk seems to be about the same for all smokers whether an individual uses a pipe, cigar, or cigarette.

A number of retrospective studies have examined the relationship between smoking in various forms and cancer of the oral cavity. The results of these studies are presented in table 21. Some of the variations in relative risk of developing oral cancer observed in the retrospective studies is probably due to the lack of a uniform definition of oral cancer by anatomical site and the various means used in selecting and defining cases and controls. It appears, however, that a significant risk of developing oral cancer exists for smokers compared to nonsmokers and this risk is similar for smokers of pipes, cigars, and cigarettes.

Several epidemiological investigations have demonstrated an association between the combined use of alcohol and tobacco and the development of oral cancer. A few of these studies (*52*, *62*, *63*, *109*) contain data on pipe and cigar smokers. Heavy smoking and heavy drinking are associated with higher rates of oral cancer than are seen with either habit alone.

TABLE 20.—*Mortality ratios for oral cancer in cigar and pipe smokers. A summary of prospective epidemiological studies*

Author, reference	Smoking type					
	Non-smoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Hammond and Horn[1] (*40*)	1.00	5.00	3.50	----	5.06	----
Doll and Hill[2] (*26*, *27*)	0.00	----	----	0.80	1.00	2.00
Hammond (*38*)	1.00	----	----	4.94	[3] 9.90	----
Kahn (*50*):						
Oral [4]	1.00	4.11	3.12	3.89	4.09	----
Pharynx	1.00	----	1.98	3.06	12.54	----

[1] Combines data for oral, larynx, and esophagus.
[2] Ratios: relative to cigarette smokers.
[3] Mortality ratios for ages 45 to 64 only are presented.
[4] Excludes pharynx.

Cancer of the Larynx

The larynx is situated at the upper end of the trachea. Because of its proximity to the oral cavity, the larynx probably has a similar exposure to smoke drawn through the mouth as the buccal cavity and pharynx. Tobacco smoke that is not inhaled may still reach as far as the larynx and upper trachea. Pipe and cigar smokers develop cancer of the larynx at rates comparable to those of cigarette smokers. These

TABLE 21.—*Relative risk of oral cancer for men, comparing cigar, pipe, and cigarette smokers with nonsmokers. A summary of retrospective studies*

Author, reference	Number		Relative risk ratio and percentage of cases and controls by type of smoking					
			Nonsmoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Mills and Porter (*65*):		Relative risk	1.0	----------	----------	7.0	4.1	----------
Cases	124	Percent cases	10	----------	----------	55	36	----------
Controls	185	Percent controls	38	----------	----------	30	32	----------
Sadowsky, et al. (*77*):		Relative risk	1.0	2.0	4.4	----------	1.4	2.1
Cases	1,136	Percent cases	8	4	18	----------	42	28
Controls	615	Percent controls	13	3	7	----------	53	23
Schwartz, et al. (*83*):		Relative risk	1.0	----------	1.6	----------	1.5	----------
Cases	332	Percent cases	16	----------	3	----------	63	----------
Controls	608	Percent controls	23	77	3	----------	58	----------
Wynder, et al. (*109*):		Relative risk	1.0	3.6	6.1	----------	3.0	3.3
Cases	543	Percent cases	3	20	11	----------	57	8
Controls	207	Percent controls	10	13	6	----------	63	8
Wynder, et al. (*113*):		Relative risk	1.0	1.7	.9	----------	1.2	1.4
Cases	115	Percent cases	23	13	12	----------	37	16
Controls	115	Percent controls	26	9	16	----------	36	13

Wynder, et al. (*116*):		Relative risk	1.0	6.0	--------	--------	4.0	----------	
Cases	178	Percent cases	4	33	--------	--------	45	----------	
Controls	220	Percent controls	16	22	--------	--------	45	----------	
Pernu (*73*):		Relative risk	1.0	--------	3.6	--------	2.2	2.9	
Cases	1,400	Percent cases	21	--------	10	--------	59	11	
Controls	713	Percent controls	39	--------	5	--------	50	7	
Staszewski (*87*):		Relative risk	1.0	--------	--------	3.5	3.6	----------	
Cases	383	Percent cases	6	--------	--------	13	72	----------	
Controls	912	Percent controls	17	--------	--------	11	61	----------	
Keller (*52*):		Relative risk	1.0	3.1	3.8	2.2	3.4	----------	
Cases	408	Percent cases	5	7	4	10	69	----------	
Controls	408	Percent controls	14	6	3	13	56	----------	
Martinez (*62*):		Relative risk	1.0	1.7	1.3	--------	1.5	2.3	
Cases	170	Percent cases	8	10	1	--------	39	34	
Controls	510	Percent controls	14	10	2	--------	44	25	
Martinez [1] (*63*):		Relative risk	1.0	2.0	2.8	--------	1.7	2.5	
Cases	346	Percent cases	12	10	15	--------	34	34	
Controls	346	Percent controls	22	9	1	--------	36	25	

[1] This study combines data for oral cancer and cancer of the esophagus.

rates are several times the rates of nonsmokers. The similarity of the mortality ratios of cancer of the larynx for smoking in various forms suggests that the carcinogenic potentials of the smoke from cigars, pipes, and cigarettes are quite alike at this site.

Several of the prospective epidemiological studies include data on deaths from cancer of the larynx for pipe and cigar smokers as well as for cigarette smokers. Hammond and Horn (*40*) combined data for cancer of the larynx with cancer of the esophagus and oral cavity. The mortality ratios compared to nonsmokers were 5.00 for cigar smokers, 3.50 for pipe smokers, and 5.06 for cigarette smokers. There were no deaths from carcinoma of larynx among nonsmokers in the study of British physicians by Doll and Hill (*26*); however, the death rate for cancer of the larynx among pipe and cigar smokers was 0.10 per 1,000 while the death rate for cigarette smokers was 0.05 per 1,000. Kahn (*50*) reported mortality ratios for cancer of the larynx of 10.33 for cigar smokers, 9.44 for pipe and cigar smokers, 7.28 for all pipe and cigar categories combined, and 9.95 for cigarette smokers. No deaths from cancer of the larynx occurred in pipe smokers. Hammond (*38*) reported a mortality ratio of 3.37 for all pipe and cigar smokers and a mortality ratio of 6.09 for cigarette smokers in the age category 45 to 64. These studies are summarized in table 22.

Several retrospective studies have examined the smoking habits of patients with cancer of the larynx and appropriately matched controls. The small number of pipe and cigar smokers in each study results in relative risk ratios that are quite unstable; however, it appears that pipe and cigar smokers experience a risk of developing cancer of the larynx that is similar to the risk observed among cigarette smokers (table 18).

TABLE 22.—*Mortality ratios for cancer of the larynx in cigar and pipe smokers. A summary of prospective epidemiological studies*

Author, reference	Smoking type					
	Non-smoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Hammond and Horn [1] (*40*)	1.00	5.00	3.50	----	5.06	----
Doll and Hill [2] (*26, 27*)	0.00	----	----	2.00	1.00	0.60
Hammond (*38*)	1.00	----	----	3.37	[3] 6.09	----
Kahn (*50*)	1.00	10.33	----	7.28	9.95	----

[1] Combines data for oral, larynx, and esophagus.
[2] Ratios: relative to cigarette smokers.
[3] Only mortality ratios for ages 45 to 64 are presented.

Wynder, et al. (*108*, *113*) distinguished between intrinsic and extrinsic larynx cancers. For smokers the relative risk of developing cancer of the intrinsic larynx was similar to the relative risk of lung cancer whereas the relative risk of developing extrinsic larynx cancer was more like the relative risk of cancer of the upper digestive tract.

Histologic changes of the larynx in relation to smoking in various forms were described by Auerbach, et al. (*5*). Microscopic sections of the larynx from 942 subjects were examined for the presence of atypical nuclei and proliferation of cell rows. Sections were taken from four separate areas of the larynx in each case. Among those who smoked cigars and pipes but not cigarettes, only 1 percent had no atypical cells and more than 75 percent of the subjects had lesions with 50 to 69 percent atypical cells. Four of the cigar and pipe smokers had carcinoma in situ and in one of these four cases early invasion was seen in three of the sections. Of those who never smoked regularly, 75 percent had no atypical cells. The cigar and pipe smokers had a similar percentage of cells with atypical nuclei as cigarette smokers who smoked one to two packs per day. With respect to the proliferation of cell rows in the basal layer of the true vocal cord, the least proportion of cases with eight or more cell rows was found in men who never smoked, and the greatest proportion was found in heavy cigarette smokers. Pipe and cigar smokers had a distribution of cell rows that was comparable to that of cigarette smokers who consumed about a pack a day.

Several retrospective studies have reported an association between the combined use of tobacco and alcohol and cancer of the larynx. A study by Wynder, et al. (*108*) included some information on pipe and cigar smoking in relation to drinking habits and the development of cancer of the larynx, but because of the limited number of pipe and cigar smoking subjects this relationship could not be adequately determined.

Cancer of the Esophagus

The esophagus is not directly exposed to tobacco smoke drawn into the mouth; however, the esophagus does have contact with that portion of tobacco smoke that is condensed on the mucous membranes of the mouth and pharynx and then swallowed. The esophagus is also exposed to a portion of tobacco smoke that is deposited in the mucus cleared from the lung by the ciliary mechanism or by coughing. Variations in inhalation of a tobacco product may not appreciably alter the exposure the esophagus receives from smoke dissolved in mucus and saliva. This suggestion receives support from the prospective and retrospective epidemiological studies which demonstrate similar mortality rates for cancer of the esophagus in smokers of cigars, pipes, and cigarettes.

TABLE 23.—*Relative risk of cancer of the larynx for men, comparing cigar, pipe, and cigarette smokers with nonsmokers. A summary of retrospective studies*

Author, reference	Number	Relative risk ratio and percentage of cases and controls by type of smoking						
			Nonsmoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Schrek, et al. (*81*):								
Cases	73	Relative risk	1.0	0	1.1	---	2.3	---
Controls	522	Percent cases	14	0	7	---	80	---
		Percent controls	24	10	11	---	59	---
Sadowsky, et al. (*77*):								
Cases	273	Relative risk	1.0	2.2	2.3	---	3.7	4.1
Controls	615	Percent cases	4	2	5	---	60	29
		Percent controls	13	3	7	---	53	23
Wynder, et al. (*108*):								
Cases	209	Relative risk	1.0	15.5	27.7	11.1	24.6	---
Controls	209	Percent cases	.5	8	5	1	86	---
		Percent controls	11	10	4	2	74	---
Wynder, et al. (*113*):								
Cases	60	Relative risk	1.0	9.7	4.5	---	6.3	6.3
Controls	271	Percent cases	5	17	15	---	47	17
		Percent controls	24	9	16	---	36	13
Wynder, et al. (*116*):								
Cases	142	Relative risk	1.0	14.5	16.0	---	22.0	16.0
Controls	220	Percent cases	1	20	1	---	62	16
		Percent controls	16	22	1	---	45	16

Pernu (*73*):		Relative risk	1.0		4.5		8.7	3.2		
Cases	546	Percent cases	7		4		78	4		
Controls	713	Percent controls	30		5		50	7		
Staszewski (*87*):		Relative risk	1.0			5.9	50.2			
Cases	207	Percent cases	.5			2	88			
Controls	912	Percent controls	17			11	61			
Svoboda (*90*):		Relative risk	1.0		2.6		10.0			
Cases	205	Percent cases	3		3		95			
Controls	320	Percent controls	22		7		71			
Stell (*88*):		Relative risk	1.0			1.3	2.4			
Cases	190	Percent cases	11			8	79			
Controls	190	Percent controls	17			10	50			

In the prospective epidemiological studies, cigar, pipe, and cigarette smokers all had similar mortality ratios from cancer of the esophagus. Hammond and Horn (*40*) combined the categories of carcinoma of the esophagus, larynx, pharynx, oral cavity, and lip and described mortality ratios of 5.00 for cigar smokers, 3.50 for pipe smokers, and 5.06 for cigarette smokers. Doll and Hill (*26*) reported an esophageal cancer mortality ratio of 2.0 for pipe and cigar smokers, 4.8 for mixed smokers, and 1.5 for cigarette smokers. Kahn (*50*) reported the following mortality ratios for smoking in various forms compared to nonsmokers: cigar only, 5.33; pipe only, 1.99; pipe and cigar, 4.17; all pipes and cigars combined, 4.05; and cigarettes only, 6.17. The results of these prospective studies are summarized in table 24.

Several retrospective investigations have also examined the association between smoking in various forms and cancer of the esophagus. These studies have been summarized in table 25. The evidence suggests that cigar, pipe, and cigarette smokers develop cancer of the esophagus at rates substantially higher than those seen in nonsmokers, and that little difference exists between these rates observed in smokers of pipes and cigars and cigarettes.

Histologic changes in the esophagus in relation to smoking in various forms were investigated by Auerbach, et al. (*7*), who looked for atypical nuclei, disintegrating nuclei, hyperplasia, and hyperactive esophageal glands. A total of 12,598 sections were made from tissues obtained from 1,268 subjects. For each of the parameters investigated, pipe and cigar smokers demonstrated significantly more abnormal histologic changes than nonsmokers; however, these changes were not as severe or as frequent as those seen in cigarette smokers.

Several retrospective studies conducted in the United States and other countries have examined the synergistic roles of tobacco use and heavy alcohol intake on the development of cancer of the esophagus. Four of these investigations contain data on pipe and cigar smoking (*12, 62, 63, 107*). It appears that smoking in any form in combination with heavy drinking results in especially high rates of cancer of the esophagus.

TABLE 24.—*Mortality ratios for cancer of the esophagus in cigar and pipe smokers. A summary of prospective epidemiological studies*

Author, reference	Smoking type					
	Non-smoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Hammond and Horn [1] (*40*)	1.00	5.00	3.50	----	5.06	----
Doll and Hill (*26, 27*)	1.00	----	----	2.00	1.50	4.80
Hammond (*38*)	1.00	----	----	3.97	[2] 4.17	----
Kahn (*50*)	1.00	5.33	1.99	4.05	6.17	----

[1] Combines data for oral, larynx, and esophagus.
[2] Mortality ratio for ages 45 to 64.

TABLE 25.—*Relative risk of cancer of the esophagus for men, comparing cigar, pipe, and cigarette smokers with nonsmokers. A summary of retrospective studies*

Author, reference	Number	Relative risk ratio and percentage of cases and controls by type of smoking					
		Nonsmoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Sadowsky, et al. (*77*):							
Cases	104	Relative risk	1.0	4.8	3.8	5.1	3.8	3.3
Controls	615	Percent cases	4	5	8	6	60	18
		Percent controls	13	3	7	4	53	19
Wynder, et al. (*113*):								
Cases	39	Relative risk	1.0	3.1	2.1	----------	2.6	.4
Controls	115	Percent cases	13	15	18	----------	51	3
		Percent controls	24	9	16	----------	36	13
Pernu (*78*):								
Cases	202	Relative risk	1.0	----------	3.0	----------	2.7	5.9
Controls	713	Percent cases	17	----------	7	----------	59	18
		Percent controls	39	----------	5	----------	50	7
Schwartz, et al. (*84*):								
Cases	249	Relative risk	1.0	----------	2.6	----------	11.7	8.6
Controls	249	Percent cases	2	----------	2	----------	88	7
		Percent controls	18	----------	7	----------	67	7
Wynder and Bross (*107*):								
Cases	150	Relative risk	1.0	3.6	9.0	6.0	2.8	3.7
Controls	150	Percent cases	5	19	9	4	51	11
		Percent controls	15	16	3	2	55	9

TABLE 25—*Relative risk of cancer of the esophagus for men, comparing cigar, pipe, and cigarette smokers with nonsmokers. A summary of retrospective studies.*—Continued

Author reference	Number		Relative risk ratio and percentage of cases and controls by type of smoking					
			Nonsmoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Bradshaw and Schonland (*12*):		Relative risk	1.0	----------	4.8	--------	2.3	----------
Cases	117	Percent cases	15	----------	41	--------	63	----------
Controls	366	Percent controls	32	----------	18	--------	58	----------
Martinez (*62*):		Relative risk	1.0	2.0	--------	--------	1.5	2.2
Cases	120	Percent cases	8	9	--------	--------	31	43
Controls	360	Percent controls	14	8	--------	--------	34	34
Martinez [1] (*63*):		Relative risk	1.0	2.0	2.8	--------	1.7	2.5
Cases	346	Percent cases	21	10	15	--------	34	34
Controls	346	Percent controls	22	9	1	--------	36	25

[1] This study combines data for oral cancer and cancer of the esophagus.

Lung Cancer

Abundant evidence has accumulated from epidemiological, experimental, and autopsy studies establishing that cigarette smoking is the major cause of lung cancer. Several prospective epidemiological studies have demonstrated higher lung cancer mortality ratios for pipe and cigar smokers than for nonsmokers, but the risk of developing lung cancer for pipe and cigar smokers is less than for cigarette smokers. Table 26 presents a summary of these prospective studies. Dose-response relationships such as those that helped demonstrate the nature of the association between cigarette use and lung cancer could not be as thoroughly studied for pipe and cigar smokers because of the relatively few smokers in these categories. Although the number of deaths were few, Doll and Hill (*26*) reported increased death rates from lung cancer for pipe and cigar smokers with increasing tobacco consumption (table 27). Kahn (*50*) also demonstrated a dose-response relationship for lung cancer by the amount smoked (table 28).

A few of the retrospective studies contained enough smokers to allow an examination of dose-response relationships for pipe and cigar smoking and lung cancer (*1*, *61*, *74*, *77*). An increased risk of developing lung cancer was demonstrated with the increased use of pipes and cigars as measured by amount smoked and inhalation. The retrospective investigation of Abelin and Gsell (*1*) is of particular interest. The smoking habits of 118 male patients with cancer of the lung from a rural area of Switzerland were compared with those reported in a survey of all male inhabitants of a town in the same region. About 20 percent of the population of this area were regular cigar smokers, the most popular cigar being the Stümpen, a small Swiss-made machine-manufactured cigar cut at both ends with an average weight of 4.5 g. In this investigation, cigar smokers experienced a risk of developing lung cancer that was similar to the risk of cigarette smokers. A dose-response relationship was demonstrated for inhalation and amount smoked. These data suggest that the heavy smoking of certain cigars may result in a risk of lung cancer that is similar to that experienced by cigarette smokers.

Several pathologists have reported histologic changes in the bronchial epithelium in relation to smoking in various forms. Knudtson (*57*) examined the bronchial mucosa of 150 lungs removed at autopsy and correlated the histologic changes noted with the history of smoking, age, occupation, and residence. Specimens obtained from the six cigar and pipe smokers demonstrated basal cell hyperplasia; however, there was no squamous or atypical proliferative metaplasia as is frequently seen in the heavy cigarette smokers.

Sanderud (*78*) examined histologic sections from the bronchial tree of 100 male autopsy cases for the presence of squamous epithelial

metaplasia. In this study, 39 percent of the population were nonsmokers, 20 percent were pipe smokers, and 38 percent smoked cigarettes. A total of 80 percent of the pipe smokers and cigarette smokers demonstrated squamous metaplasia of the bronchial tree, whereas only 54 percent of the nonsmokers had this abnormality.

Auerbach, et al. (*6*) examined 36,340 histologic sections obtained from 1,522 white adults for various epithelial lesions including: presence or absence of ciliated cells, thickness or number of cell rows, atypical nuclei, and the proportion of cells of various types. The pathologic findings in the bronchial epithelium of pipe and cigar smokers are compared to those found in nonsmokers and cigarette smokers (table 25). Pipe and cigar smokers had abnormalities that were intermediate between those of nonsmokers and cigarette smokers, although cigar smokers had pathologic changes that in some categories approached the changes seen in cigarette smokers.

TABLE 26.—*Mortality ratios for lung cancer deaths in male cigar and pipe smokers. A summary of prospective studies*

Author, reference	Type of smoking					
	Non-smoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Hammond and Horn (*40*)	1.00	3.35	8.50	----	23.12	19.71
Doll and Hill (*26, 27*)	1.00	----	----	6.14	13.29	7.43
Best (*9*)	1.00	2.94	4.35	----	14.91	----
Hammond (*38*)	1.00	1.85	2.24	1.97	9.20	7.39
Kahn (*50*)	1.00	1.59	1.84	1.67	12.14	----

TABLE 27.—*Lung cancer death rates for cigar and pipe smokers by amount smoked—Doll and Hill*

Smoking type	Death rate per 100	Number of deaths
Nonsmoker	0.07	3
Cigar and pipe:		
1 to 14 g. per day	.42	12
15 to 24 g. per day	.45	6
>24 g. per day	.96	3
Cigarette only	.96	143

Source: Doll, R., Hill, A. B. (*25*).

TABLE 28.—*Lung cancer mortality ratios for cigar and pipe smokers by amount smoked—Kahn*

Smoking type	Mortality ratio	Number of deaths
Nonsmoker	1.00	78
Cigar smokers:		
<5 cigars per day	1.14	12
5 to 8 cigars per day	2.64	11
>8 cigars per day	2.07	2
Pipe smokers:		
<5 pipefuls per day	.77	2
5 to 19 pipefuls per day	2.20	12
>19 pipefuls per day	2.47	3
Cigar and pipe:		
8 or less cigars, 19 or less pipefuls	1.62	18
>8 cigars, >19 pipefuls	2.19	2

Source: Kahn, H. A. (*50*).