TABLE A2Smoking and chronic obstructive pulmonary disease symptoms'-percent prevalence (con	(nt_{i})
(Numbers in parentheses represent total number of individuals in particular smoking group)	,

ers in parentneses represent	total number of ind	ividuals in particular smoking	g
SM = Smokers.	NS = Nonsmokers.	$\mathbf{E}\mathbf{X} = \mathbf{E}\mathbf{x}$ -smokers.	

Author, year, country, reference	Number and type of population	Cough		Sputum production	Breathlessness or dyspnea	Chest illnesses	Other	Comment
Wynder	315 male	New York Cit	N					1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
et al., 1965 U.S.A. (238).	patients in New York City and 315 male patients in California.	NS	(44) (54) (44) (88) (85) (69) (32) (54) (91) (69)					
Freour et al., 1966 France (92).	1,055 randomly chosen males in Bordeaux 30-70 years of age.	/40	(69)				Clinical signs of bronchitis and respiratory insufficiency NS	
Haynes, et al., 1966 U.S.A. (108).	179 male preparatory school students 14-19 years of age.						Average number of severe respiratory illnesses per 10 students (adjusted for age) NS	Heavy smoker

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Author, year, country, reference	Number and type of population	Cough	Sputum production	Breathlessness or dyspnea	Chest illnesses	Other	Comments
Densen	5,313 male	Postal	Postal	Postal			
et al.,	and 7,291	NS 7.0 (903)	13.1	19.8			Dyspnea
1967, U.S.A.	female postal and transit	Pipe, cigar 12.4 (628) Cigarettes	17.4	24.8			represented by Grade II
(68).	workers.	only 27.0 (2,687)	28.9	31.7			only.
		Transit	Transit	Transit			
		NS 6.4(1,012)	9,5	11.7			
		Pipe, cigar 10.5 (765) Cigarettes	14.1	14.2			
		only23.5(3,745)	23.7	21.9			
Higgins et al., 1968, U.S.A. (118).	926 white male resi- dents of Marion County, West Virginia, 26-69 years of age.	NS15.4 (162) SM47.2 (513) EX19.3 (144)	NS	NS 5.0 SM10.7 EX16.8			
Holland	9,786 male	Males	Females	Males Females			
and	and female	NS 3.8(1,900)	3.2(3,137)	2.4 2.1			
Elliott,	school	SM 6.3(1,098)	6.3 (554)	6.1 8.3			
1968,	children.	EX 2.9(1,782)	4.3(1,151)	3.9 4.2			
England		<1 cigarette/day		5.8			
(121).		1-2		8.4			
		3-4		8.1			
		>5		18.3			

 TABLE A2.—Smoking and chronic obstructive pulmonary disease symptoms'—percent prevalence (cont.)

 (Numbers in parentheses represent total number of individuals in particular smoking group)

 SM = Smokers.
 NS = Nonsmokers.

 EX = Ex-smokers.

				SM = Sm	lokers.	NS - NON	smokers.	BA -	- Hx-smokers.			
Author, year, country, reference	Number and type of population		Cough		Sputum p	roduction	Breathles or dyspr		Chest illnesses	Other		Comments
Gandevia	762 male and		Males									Productive
1969	1,304 female	NS		(234)								cough upon
Australia	patients	SM	51.3	(528)								request.
(93).	from 13 general		Females									
	practices	\mathbf{NS}		(857)								
	in all parts of	SM	37.4	(447)								
	Australia.											
Rimington	41.729 male									Age-adjusted		Cigarette
1969	and 22,295									prevalence of	-	dosage
England	female persons									chronic bronc	hitis	gradient
(193).	participating									Males		significant
L ===, L ==, 	in mass									NS 5.1		to p<0.001.
	miniature									EX 9.8		
	radiography									Pipe 9.0		
	screening.										23,243)	
	-									1-99.1		
										10-19 15.0		
										>20		
										Females		
										NS 3.4()		
										EX 3.8	(959)	
										Pipe 0.0		
											(8,985)	
										1-9 5.1		
										10-19 10.6		
										>20		
Wilhelmsen	313 males		x x x x							Chronic brond	chitis	
et al.,	50-54 years									NS 1.0	(88)	
1969.	of age randomly									EX 3.0	(67)	
Sweden	sampled from									1-14 grams/		
(281).	population									day 5.0	(94)	
(201).	of Göteborg.									>15 17.0	(64)	

TABLE A2.—Smoking and chronic obstructive pulmonary disease symptoms'-percent prevalence (cont.) (Numbers in parentheses represent total number of individuals in particular smoking group) NS = Nonsmokers. SM = Smokers.

EX = Ex-smokers.

			om = omokers		5 - Nonsmo	Kers. EX	= Ex-smokers.		
Author, year, country, reference	Number and type of population	Cough	S	putum prodi	uction	Breathlessness or dyspnea	Chest illnesses	Other	Comments
Lambert	9,975 male	Persi	istent cough an	d phlegm					
and	and female		Males						
Reid,	responders	Agc	Agc	Age	Agc				
England s (146). (to a postal	35 45	45-55	55-65	65-69				
	survey	NS 7(227)	6(200)	11(171)	7 (61)				
	(4,688 males	EX 7(303)	11 (358)	15(335)	18(148)				
	and 5,287	<2015(521)	22(488)	30(490)	37(139)				
	females	2023(191)	28(204)	32(149)	38 (37)				
	35 69 years	>2027(148)	28(136)	42(121)	25 (12)				
	of age).		Females						
		NS 3(500)		5(925)	6 (21)				
		EX 3(127)	8(128)	7 (94)	7 (41)				
		<20 9(602)	13(472)	16(306)	11 (65)				
		2016(128)	27(122)	31 (77)	14 (7)				
		>2023 (22)	26 (39)	43 (7)	(1)				
lefcoe	310 male			and an and a second				Age-standardized rates	Excluded from
and	physicians							of chronic respiratory	ex-smokers
Wonnacott,	in London							disease	are those
1970,	and Ontario,							NS 1.0 (88)	
Canada	25-74 years							EX 5.0 (61)	cigarette
(151).	of age.								smokers who
								그는 아이는 것은 아이는 것이 같은 것이 없는 것이 없는 것이 없는 것이 없는 것이 없다. 것이 없는 것이 없 않이 없이 없 않이 없이 않이 없는 것이	now smoke
-	losted by sith			-				Pipe, cigar12.0 (33)	pipes or cigar

TABLE A2.-Smoking and chronic obstructive pulmonary disease symptoms'-percent prevalence (cont.) (Numbers in parentheses represent total number of individuals in particular smoking group) SM =: Smokers. NS =: Nonsmokers. EX =: Ex-smokers.

Data collected by either direct interview, questionnaire, review of medical records and/or medical examination.

TABLE A2a.—Smoking and chronic obstructive pulmonary disease symptoms¹-percent prevalence

(Numbers in parentheses represent total number of individuals in particuar smoking group) SM = Smokers. NS = Nonsmokers. EX = Ex-smokers.

- Smokers.	NS = Nonsmokers.	$\mathbf{E}\mathbf{X} = \mathbf{E}\mathbf{x}$ -smokers.
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Author, year, Number and country, type of reference population	l Cough			Bronchitis		Comments
Cederlof 9,319 twin et al., pairs 1966, registered Sweden in Sweden (46). of 12,889 available.	Observed/ expected Group A: cases Males	Hypermorbidity ratio 2.6 2.8 1.9 1.8 2.25 2.57	Observed expected cases 157/50.8 43/11.2 6.6/ 1.1 3.0/ 2.3 4.5/ 1.8 5.5/ 1.8	Hypermorbidity ratio 3.1 3.8 6.0 (274) 1.33 (264) 2.54 (733) 3.0 (653)	Explanation of analyses for respiratory symptom prevalence: Group A analysis—using each firstborn twin as one group in an unmatched relationship to each secondborn twin. Group B analysis—using each twin set as matched pair. All comparisons in Groups A and B are between smoking- discordant pairs.	All ex-smokers included with smokers. MZ—monozygotic pairs DZ—dizygotic pairs Author concludes that since hypermorbidity for smoking persists in smoking-discordant MZ population, a casual relationship of smoking and broncho- pulmonary symptoms is supported.
Cederlof 4,379 twin et al., pairs (all 1969, U.S. veteram U.S.A. in U.S. (45). National Academy of Sciences Twi Registry (of 9,000 avial- able).	$\begin{array}{c} {\rm Group \ A:} \\ {\rm NS} & \dots & 4 \\ 1 - 10 & \dots & 6 \\ 11 - 30 & \dots & 15 \\ > 31 & \dots & 27 \end{array}$.4 6.4 .3 15.3 .7 27.7 .1 7.1 NS	symptoms SM 5.4 9.8	1.6 2.7 8.0 16.8 2.7 <i>NS SM</i> 1.8 4.8 1.6 9.1	3	No ex-smokers included in Group B analysis. The authors conclude that the data indicate a strong probability of a causal connection with smoking. Even these symptoms, however, seem to be influenced by genetic

Data collected by either direct interview, questionnaire, review of medical records and/or medical examination.

Author, year, country, reference	Number and type of population	мвс	EFR		FEV		vc	Miscellaneous	Comments
Chivers, 1959, England (52).	463 male employees of alkaline industry plant.	Cigarettes/day: 0-5 6-20 >20	89(50)	Height. 66'' 91 (35) 88 (75) 88.5 (9)	in-inches 68'' 108 (31) 101 (112) 92.5 (9)	70'' 101(21) 109(75) 113(12)			Mean EFR in liters per minute. Regression analysis of data revealed a significant re- lationship between smoking and de- creasing function.
Higgins et al., 1959, England (116).	occupations (25-34 and 55-64 years	25-34 55-64 NS 145 (56) 101 (29) EX 143 (31) 89 (62) 1-14 grams .140(193) 87(157) >15 grams .133 (89) 80(136)							FEV _{0.75} expressed as mean indirect MBC.
Wilson et al., 1960 U.S.A. (232).	28 male residents of Dallas, Texas, former rural dwellers; matched for body surface, age, and height.					NS . SM .	5.59 (14) NS ² 4.44 (14) SM	<i>RV/TLC</i> 21.1 ² 27.0	1

			110 - 11011011101		moners,	DA - DA-SINO	Acia.		
Author, year, country, reference	Number and type of population	MBC	EFR		FEV		VC	Miscellaneous	Comments
Ashford et al., 1961, Scotland (11).	4,014 male coal workers at 3 Scottish collieries.			21-30 31-40 41-50 51-60	FEV _{1.6} NS 4.09 (103) .3.86 (182) .3.44 (138) .3.04 (110) .2.71 (102) .2.38 (42)	SM 8.96 (280) 8.77 (555) 3.88 (777) 2.96 (755) 2.56 (610) 2.21 (237)			Data represent results after correction for sitting height. SM includes pipe smoker. Data on ex-smoker not included. FEV _{1.0} found significant; lower for SM than NS.
Fletcher and Tinker, 1961, England (<i>85</i>).	363 male London transport employees.		1–14 grams >15 grams	EFR 570 (30) 537 (156) 528 (116) 555 (61)					
Franklin and Lowell, 1961, U.S.A. (87).	213 male factory workers 40-60 years of age.			FEV Heavy 2, Light 12,		2,710 Lig	ht 3,703 (59 vy . ¹ 3,578(104		Heavy smoker represents an amount equal to or more than 30 pack years.

TABLE A3.—Smoking and ventilatory function (cont.) (Numbers in parentheses represent total number of individuals in particular smoking group) NS = Nonsmokers. SM = Smokers. EX = Ex-smokers.

 TABLE A3.—Smoking and ventilatory function (cont.)

 (Numbers in parentheses represent total number of individuals in particular smoking group)

 NS = Nonsmokers.
 SM = Smokers.
 EX = Ex-smokers.

Author, year, country, reference	Number and type of population	MBC	EFR	FEV	vc	Miscellaneous	Comments
Balchum	1.451 male		MMEFR				Data for: MMEFR
et al.,	employees		NS 15.5 (38)	7.8(19)			given as percent
1962,	in		Pack/year:				of individuals
U.S.A.	California		<1 15.0 (257)	8.0			with a value of
(24).	light indus-		1-9 10.0 (263)	6.0			<500 L/M;
	try.		10-19 10.0 (303)	12.0			FEV _{1.0}
			20-29 19.0 (236)	24.0			given as percent
			30-39 33.0 (144)	26.0			of individuals
			40-49 38.0 (92)	40.0			with value of
			50-59 55.0 (29)	45.0			<70 percent
			>60 71.0 (24)	62.0			of expected.
Goldsmith	3,311 active		MEFR	FEV _{1.0}			Authors concluded
et al.,	or retired		NS	2.99			that cigarette
1962,	longshore-		Pipe, cigar 299.26(125)	2.80			smoke was found
U.S.A.	men.		EX 295.23(102)	2.84			to have a slight
(95).			Cigarettes/day:				effect on
			≤20 309.73(144)	2.89			pulmonary
			20-40 303.44(346)	2.91			function.
			≧40 307.63 (57)	2.90			
Martt,	73 healthy	÷				D _L CO	Smokers defined
1962,	medical per-					NS 33.10(30)	as those smoking
U.S.A.	sonnel with-					SM <5 years .228.40 (8)	>20 cigarettes/
(161).	out signifi-					5-10 years 328.20(10)	day for varying
	cant age					>10 years 524.90(25)	periods.
	difference						
	between						
	smokers and						
	nonsmokers.						

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				NS =	= Nonsmokers	2	SM =	Smokers.	EX	$= \mathbf{E}\mathbf{x}$ -	smoker	rs.				
Author, year, country, reference	Number and type of population	мвс			EFR			FEV			vo	3	Misce	llaneous		Comments
Revotskie et al., 1962, U.S.A. (192).	1,130 male and 1,813 female residents in Framing- ham par- ticipating in the pro- spective study.						Cigarett 1-10 10-29	Males 0.98 (55)	0.98 0.99 0.93	1						Data presented in terms of ratio of observed to predicted values.
Krumholz et al., 1964, U.S.A. (140).	18 physicians 24-37 years of age.				MEFR 580 1590								Rest Exercise: 2 minute 4 minute 3 minutes post exer	<i>NS</i> 36 s50 s50	¹ n D _L SM ² 31 ³ 41 ¹ 43 ¹ 35	
Zwi et al., 1964, U.S.A. (241).	20 medical students or graduate physicians.	187 193	(10) (10)		MMEFR 4.34 15.09		5.' 15.							ant differ SM and	10n-	
Coates et al., 1965, U.S.A. (53).	1,342 male and 242 female post office employees >40 years of age.					3	55-59	NS 12,99(186) 52.95(170) 12.75(115)	2.85 2.64 2.62 2.44	ig/day (69) (42) (22) (18) (8)	Tim NS 3.89 3.92 3.71 3.54 3.30	red VC >25/day 3.85 3.83 3.74 3.61 3.33	FEV NS 30.77 30.74 20.74 50.74 10.72	.0/VC >25/d 0.74 0.70 0.70 0.68 0.70		

TABLE A3.—Smoking and ventilatory function (cont.) (Numbers in parentheses represent total number of individuals in particular smoking group)

Author, year, country, reference	Number and type of population	d MBC	EFR		FEV		VC		Miscellaneous	s	Comments
Huhti, 1965, Finland (126).	653 male and 823 female residents of a rural region in Finland.	NS EX Cigarettes/day: 1-14 16-24 >25	$\left. \begin{array}{c} PEFR \\ Males \\ 5569 (122) \\ 41 \\ 551 (141) \\ 40 \\ 618 (108) \\ 42 \\ 637 (191) \\ 617 \\ (85) \\ \end{array} \right\} 48 \\ 617 \\ (85) \\ \end{array}$	R† Females 410(709) 403 (30) 481 (77) 483 (7)	$\begin{array}{c} FEV_{1,0}^{\dagger} \\ Male \\ 8.46 \\ 8.46 \\ 3.39 \\ 3.17 \\ 3.09 \\ 3.08 \\ \end{array}$		Forced VC‡ Males Females 4.40 3.19 4.51 3.19 4.40 3.53 4.51 3.59 4.51 3.50	VC‡ emales 3.18 3.19 3.53 3.50			Pipe and cigar smokers not included. † Difference between NS and >25/day is significant for 45-49, 60-64 age groups. ‡ Trend is not statistically
Krumholz et al., 1965, U.S.A. (142).	20 male medical students or graduate physicians.							P SM SM NS NS SM SM	Pulmonary compliance NS 0.241 (10) SM 0.177 (10) Compliance/FRC NS NS 0.043 SM 0.042	oliance 241 (10) 177 (10) 7RC 54 42	significant. Pulmonary compliance Mean body surface S
Rankin et al., 1965, U.S.A. (<i>189</i>).	125 males without a past history of respira- tory disease 20-63 years of age.	NS 118.1 (68) SM ¹ 111.7 (67)		SM SM		FEV.06.		SM	D_L	$\frac{D_L/1}{alveolar}$ $\frac{alveolar}{volume}$ 6.22 $6.4.96$ D	NS includes pipe and cigar smokers and ex-smokers of greater than 1 pack year. D _L values have been corrected for COHb.

 TABLE A3.—Smoking and ventilatory function (cont.)

 (Numbers in parentheses represent total number of individuals in particular smoking group)

 .
 NS = Nonsmokers.

 TABLE A3.—Smoking and ventilatory function (cont.)

 (Numbers in parentheses represent total number of individuals in particular smoking group)

 NS = Nonsmokers.
 SM = Smokers.

 EX = Ex-smokers.

Author, year, country, reference	Number and type of population	MBC	EFR	FE	v	vc	Miscellaneous	Comments
Edelman et al., 1966, U.S.A. (73).	410 male community dwellers 20-103 years of age.	NS 164(152) Current cigarette smokers ⁵ 151(118) EX	7.89 7.86 8.09		<i>FEV</i> _{1.0} 2.83 ³ 2.64 2.80	Vital capacity 4.93 ³ 4.74 4.77		Ex-smokers of cigarettes only. Difference signifi- cant between NS and current cigarette smokers
	age.	Pipe, cigar 167 (47)	8.20		2.91	5.08		at p<0.01.
Peters and Ferris, 1967, U.S.A. (182).	124 male college age students		MEFR NS ² 10.28 Moderate . 10.06 Heavy 9.64 EX 9.48	(54) (29)	FEV1.0 4.63 4.59 4.43 4.74		<i>FEV_{1.0}/VC</i> 287.5 85.3 83.9 83.2	Heavy smoker refers to greater than or equal to 4 pack years. Moderate smoker includes pipe and cigar smokers. Difference between NS and heavy smoker is significant.
Higgins et al., 1968, U.S.A. (118).	926 white male residents of Marion County, West Virginia, 20-69 years of age.			NS EX Cigarette SM 1–14 15–24 >25	3.25(143) 3.48(511) 3.67 (88) 3.57(273)			

 TABLE A3.—Smoking and ventilatory function (cont.)

 (Numbers in parentheses represent total number of individuals in particular smoking group)

 NS = Nonsmokers.

 SM = Smokers.

 EX = Ex-smokers.

			$NS \equiv N$	onsmokers.	SM = Smoke	ers, EX	= Ex-smoke	rs.			
Author, year, country, reference	Number and type of population	MBC	EFR	2404077788	FEV		vc		Miscella	aneous	Comments
Sluis- Cremer and Sichel, 1968. South Africa (208).	533 white male factory workers over 35 years of age.		NS Grams/day: 1-14 15-24 >25	35-44 553 (106) 557 (26) 532 (94) †528 (66)	45-54 527(101) 519(17) 446(35) †494(31)	>55 444(27) 410 (7) 401(13) †380(10)	FEV 35-44 45-5 3.70 3.22 3.64 3.33 3.66 2.94 3.54 3.05	14 >55 2 2.76 1 2.24 4 2.28			<pre>1 cigarette == 1 gram. 1 ounce tobacco == 26 grams. 1 cigar = 2 to 5 grams. † Derived slopes found signifi- cantly different from 0.</pre>
Stanescu et al., 1968, Rumania (212).	87 male bus drivers: 27 aged 20-25, 60 aged 40-60, all without respiratory symptoms.				Younger 4,470(14) 4,500(13)			Older 4,290 14,290	Nitrogen Younger 1,53 ¹ 1.47	gradient Older 2.49 \$3.77	
Densen et al., 1969, U.S.A. (69).	5,287 male postal and 7,213 male transit workers in New York City.	- rangi - kan prakeron	NS All cigarette <25 grams/day ≧25 grams/day	· · · · · · · · · · · · · · ·	 	FEV 1.0 Postal White 3.29 (685) 3.11 (2,340) 3.14 (1,292) 3.06 (1,038) Transit White	3.05 2.94 2.95 2.93	(768) (599)			FEV expressed as standardized for specified postal and transit workers at age 45 and at sitting height of 35 inches. Includes mixed
<u></u>			NS All cigarette <25 grams/day ≧25 grams/day .			3.39 (620) 3.11(2,941) 3.15(1,929) 3.02(1,011)	3.08 2.99 3.00	(298) (1,041) (891) (149)			smokers.

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TABLE A3.—Smoking and ventilatory function (cont.) (Numbers in parentheses represent total number of individuals in particular smoking group) NS = Nonsmokers. SM = Smokers. EX = Ex-smokers.

Author, year, country, reference	Number and type of population	MBC	EFR	i	FEV		vc	Miscellaneous	Comments
Rankin et al., 1969, Australia (190).	60 male and 10 female patients with chronic alcoholism 26-66 years of age.				FE ⁴ 97,5 78.4				FEV expressed as percent of predicted value for age, sex, and height.
Wilhelmsen	313 male				PEFR	FEV _{1.0}	VC		1963 values only.
et al.,	residents		10000		525(88)	3.77	4.83		
1969,	of Göteburg				539(67)	3.69	4.77		
Sweden	50-54 years			lay	521 (94)	3.62	4.83		
(231).	of age.		>15 grams/o	lay	492(64)	3.39	4.56		
Lefcoe	310 male		MMI	FR	FE	V 1.0			MMFR has been
and	physicians		NS	4.09 (88)	3.3	9			standardized for
Wonna-	of London,		Cigarette						age and height.
cott,	Ontario.		smokers.	3.64(101)	3.1				
1970,			EX	3.99 (61)	3.3				
Canada			Pipe, cigar	4.17 (33)	3.1	7			
(151).									

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TABLE A3.—Smoking and ventilatory function (cont.) (Numbers in parentheses represent total number of individuals in particular smoking group) EX = Ex-smokers. NS = Nonsmokers. SM = Smokers.

Author, year, country, reference		FEV	Miscellaneous	Comments
Lundman, 1966, Sweden (159).	37 MZ and 62 DZ twin pairs selected from Swedish Twin-Pair Registry.	FEV _{1.0} Significant differences between smoking discordant twin pairs found for: 1. Group A MZ males and females. 2. Group B DZ males. 3. Group A DZ males.	N ₂ washout gradient Significant differences between smoking dis- cordant twin pairs found for: Group B DZ males.	 MZ = monozygotic. DZ = dizygotic. DZ = dizygotic. The author concludes that the degree of ventilation as measured by N_x washout was correlated with cigarette consumption. The FEV_{1.} was significantly lower for smokers and there was a correlation with cigarette consumption. Explanation of analyses for respiratory symptom prevalence: Group A analysis—using each firstborn twin as one group in an unmatched relationship to each secondborn twin. Group B analysis—using each twin set as matched pair. All comparisons in Group A and B are between smoking-discordant pairs.

Not significant (difference or trend).
 ² p<0.05
 ³ p<0.01
 ⁴ p<0.005
 ⁵ p<0.001

Symbol	Term	Volume or rate	Definition
MVVM	aximal breathing capacity. aximal voluntary ventilation.	Liters	The maximal volume of gas that can be breathed in one minute.
PEFRPe MEFRM MMEFRM	piratory flow rate ak expiratory flow rate. aximal expiratory flow rate. aximal midexpiratory flow rate.	Liters/minute	Rate of flow for a specified portion of a forced expiration (MMEFR-rate of flow measured for middle half of FVC).
FEV _t , Fo	orced expiratory volume.	Liters	Volume expired within a specified time interval. $(FEV_{1,0}-volume expired in first second of expiration.)$
	tal capacity preed vital capacity.	Liters	Maximal volume of a gas that can be expelled from the lungs by forceful effort following a maximal expiration.
FEV ₁ /VCFe	orced expiratory volume/vital capacity.	Percent	Volume of forced expiration (in time specified) related to vital capacity.
D _L P	ulmonary diffusing capacity.	ml/min/mmHg	The ability of a chosen gas to pass from the alveolus to within the pulmonary capillary.
N ₂ washout N	itrogen washout gradient.	Exponential curve.	The stepwise pulmonary alveolar clearance of a gas. (Slope of curve depends upon the uniformity and adequacy of ventilation of all parts of the lung.) It may be done as a singleor multiple-breath procedure.
Co	mpliance	Liters/CMH20	Volume change of the lung produced by a unit pressure change.
			Volume of gas remaining in the lungs at the end of a maximal expiration.
TLC	otal lung capacity	Liters	Volume of gas contained in the lungs at the end of a maximal inspiration.
	unctional residual capacity.	Liters	Volume of gas remaining in the lungs at the resting expiratory level.
A	ieveolar volume	Liters	Volume of gas contained in pulmonary alveoli.

TABLE A4.-Glossary of terms used in tables and text on smoking and ventilatory function

SOURCE: Comroe, J. et al. (56)

 TABLE A6.—Epidemiological studies concerning the relationship of air

 pollution, social class, and smoking to chronic obstructive

 bronchopulmonary disease (COPD)

Author, year, country, reference	Number and type of population	Results
Higgins, 1957, England (112).	301 males and 280 females living in 2 separate districts. (45-64 years of age.)	 Male data only (170): (a) The frequency of recurrent chest illnesses was high er in the more polluted region but the prevalence o other respiratory symptoms and mean values wer similar. (b) Significant difference observed in COPD mortality rate.
College of General Practi- tioners, 1961, England (55).	787 males and 782 females 45-64 years of age from medical doctors' case lists.	 (a) Male urban inhabitants manifested almost twice th prevalence of chronic bronchitis as rural males; thi difference could not be explained on the basis of smoking habits. (b) No significant urban/rural differences noted for PEFR.¹ (c) No significant urban/rural differences noted for COPD symptoms among females.
Ferris and Anderson, 1962, U.S.A. (81).	1,219 males and females living in 3 different areas of a New Hampshire town.	Following adjustment for differences in smoking habits, ne significant differences in chronic bronchitis were observed among the 3 pollution areas.
Mork, 1962, U.S.A. (171).	339 male trapsport employees from London and Norway.	The excess prevalence of serious respiratory symptoms (dy spnea, wheezing) and PEFR dysfunction among Londor Transport employees was only partly eliminated after standardization for smoking, and the author suggests that this is due to differences in air pollution levels.
Schoettlin, 1962, U.S.A. (204).	2,622 males 45-75 years of age.	 (a) No positive correlation found between chronic respiratory illness and city size. (b) A positive correlation was found between chronic respiratory illness and cigarette smoking (particularly duration).
Anderson et al., 1965, Canada (8).	778 residents of Berlin, N.H., and 918 residents of Chilliwack, Canada.	Berlin, New Hampshire, has higher SO_2 and particulate air pollution levels and the higher respiratory disease preva- lence rates among its residents were not accounted for by age differences, but were accounted for after stan- dardization for smoking habits (except that PEFR and FEV _{1.0} dysfunction was more prevalent in New Hamp- shire, and the authors suggest that this difference re- flects air pollution differences).
Holland and Reid, 1965, England (124).	676 male transport employees in London and rural England.	 (a) London employees manifested a greater prevalence of COPD symptoms and PEFR dysfunction than did the rural employees. (b) Smoking habit differences alone were not sufficient to explain this difference in COPD manifestations. (c) Both groups manifested pulmonary dysfunction cor- related with tobacco consumption.
Bates et al., 1966, Canada (27).	216 hospitalized veterans from various areas of Canada (all standardized for age, tobacco consumption, and occupation).	Winnipeg (cleanest of all areas in SO ₂ and industrial dustfall) residents manifested decreased prevalence of chest illnesses, less severe grades of dyspnea, and less sputum volume produced when compared to residents of all other areas.

TABLE A6.—Epidemiological studies concerning the relationship of air
pollution, social class, and smoking to chronic obstructive
bronchopulmonary disease (COPD) (cont.)

Author, year, country, reference	Number and type of population	Results
Ashley, 1969, England (12).	Standardized mortality ratios for males (1958-63) for 53 boroughs with air pollution indexes.	 Positive correlations: (a) Smoke concentration and bronchitis mortality. (b) SO₂ and smoke concentration and bronchitis mortality and social class. (c) Pollution and social class.
Holland et al., 1969, England (122).	10,971 children over 11 years of age in 4 areas.	 Factors affecting prevalence of respiratory symptoms: (a) Smoking—highly significant association. (b) Area of residence (pollution)—significant association except for periods of cough and phlegm lasting more than 3 weeks. (c) Social class, age, sex—no association noted.
Winkelstein and Kantor, 1969, U.S.A. (288).	842 females over 25 years of age in various regions of Buffalo.	 (a) The increased prevalence of respiratory symptoms could not be explained by social class differences. (b) No overall association noted between productive cough and air pollution.
Cooley and Reid, 1970, England (58).	10,887 children 6–10 years of age from con- trasting urban and rural areas.	 Illnesses considered included chronic cough, past bronchitis, blocked nose. (a) Every geographic area showed a clear gradient of increasing illness prevalence with decreasing social class. (b) Social classes I. II, and III showed no urban/rural gradient while IV and V showed a clear excess in frequency of chest illnesses among urban residents.
Lambert and Reid, 1970, England (146).	9,975 males and females responding to questionnaire survey.	 (a) The trend of increasing prevalence of bronchitic symptoms from rural to urban respondents was not negated by adjustment for smoking differences. (b) After adjustment for age and smoking habits, male respondents manifested a clear correlation of persistent cough and phlegm prevalence with increasing air pollution. Correlation was not as striking in females. (c) Although the proportionate rise in symptom prevalence with air pollution similarly in each smoking group, the absolute differences in morbidity risk increased with increased cigarette consumption, suggesting synergistic influences of cigarette smoking and air pollution. (d) In the absence of cigarette smoking, the correlation between the prevalence of persistent cough and phlegm and air pollution was slight.

¹ See Glossary of Terms: Bronchopulmonary table A4.

TABLE A7.—Epidemiological studies concerning the relationship of occupationalexposure and smoking to chronic obstructive bronchopulmonary disease

Author, year, country, reference	Number and type of population	Results
Higgins et al. 1956, England (119).	185 males (84 nonminers, 101 miners) without pneumo- coniosis.	Miners showed increased symptom prevalence (breathless- ness, cough, sputum). Miners showed increased prevalence of chronic bronchitis Miners showed decreased MBC. ¹ Differences in smoking between the two groups did not ac- count for above differences.
Phillips et al., 1956, U.S.A. (185).	1,274 males factory employees (coke and electrolytic process).	None of the industrial environments were associated with an increased prevalence of chronic cough. Cigarette smoking and age were directly correlated with increased prevalence of chronic cough.
Higgins et al., 1959, England (116).	325 males 25–34 years of age and 401 males 55–64 years of age in various occupa- tions.	 Miners as compared to workers in non-dusty occupations: 25-34 years of age-significantly increased prevalence of chronic bronchitis and MBC abnormalities. 55-64 years of age-less significantly increased prevalence of chronic bronchitis and MBC abnormalities than in 25-34 years of age group. No smoking information available.
Chivers, 1959, England (52).	463 males in non-dusty and dusty occupations (lime and soda ash exposure).	No significant differences in PEFR ¹ between dusty and non-dusty groups. Cigarette smoking (especially in those >40 years of age) was associated with decreased PEFR values.
Higgins and Cochrane, 1961, England (115).	300 male miners and 300 male nonminers 35–64 years of age.	Miners showed increased prevalence of symptoms and de- creased MBC values which remained even after standard- ization for smoking habits. Total dust exposure was not directly correlated with these findings. Wives of miners showed similar symptom and test changes as compared with wives of nonminers.
Brinkman and Coates, 1962, U.S.A. (42).	1,317 males 40-65 years of age with various silica exposure histories.	Increased silica exposure was associated with an increased prevalence of chronic bronchitis. Highest prevalence of chronic bronchitis was noted in the non-exposed group; and this group was noted to have the highest number of smokers and highest consumption.
Hyatt et al., 1964, U.S.A. (128).	267 male miners and ex-miners 45-55 years of age.	Increased history of underground work was associated with an increased bronchopulmonary symptom prevalence and decreased pulmonary function values. The impairment of pulmonary function associated with underground work was separate from effect of smoking; but smoking and underground work did show additive effects.
Elwood et al., 1965, Ireland (77).	2,528 male and female flax workers over 35 years of age.	Preparing room workers who manifested byssinosis symp- toms also showed an increased prevalence of chronic bronchitis independent of age or smoking when compared with non-preparing room workers. Female workers manifested a significant association be- tween byssinosis symptoms and smoking while male work- ers did not.
Sluis-Cremer et al., 1967, South Afric (209).	827 miners and nonminers over 35 years of age. a	Those smokers exposed to gold mine dust manifested more symptoms of COPD ¹ than did non-dust exposed smokers, while prevalence of symptoms, among nonsmokers, was similar for the two groups.

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TABLE A7.—Epidemiological studies concerning the release provide the state of	ationship of oc c upational ulmonary disease (cont.)

Author, ye ar , country, reference	Number and type of population	Results				
et al., 1967, nonminers over		The dose relationship of cigarettes and COPD ¹ symptoms was much more noticeable among those exposed to dust. The authors stressed the synergistic actions of cigarette smoking and dust exposure.				
Bouhuys et al., 1969, U.S.A. (39).	455 male cotton textile workers (214 exposed to dust in carding and spinning rooms, 241 not exposed).	Those exposed to dust manifested a significantly greater prevalence of byssinosis symptoms than nonexposed. Smokers manifested a significantly greater prevalence of byssinosis symptoms than nonsmokers. No significant differences in Monday morning FEV ¹ values were observed between smokers and nonsmokers. Prevalence of byssinosis symptoms did not show any re- lationship to length of employment.				
Bouhuys 216 male hemp et al., workers and 247 1969, workers in other U.S.A. industries in (38). same region, 20-69 years of age.		 Hemp workers (especially the older ones) were noted to have different smoking habits from control group-fewer heavy smokers, more light smokers, more ex-smokers due to doctor's orders. Aged 20-49 — a. No difference in FEV_{1.0}¹ values between controls and hemp workers in any smoking category. b. No difference in FEV_{1.0} values between men in different smoking categories. Aged 50-69 — a. Hemp workers manifested decreased FEV_{1.0} values in all smoking groups except for heaviest smokers. Ex-smokers had lowest FEV_{1.0} values. b. Those smoking most had lower FEV_{1.0} values as compared with light and non-smokers. The authors conclude that: There appears to be no synergism between smoking and hemp exposure as to effect on FEV_{1.0} although the selection process whereby those with symptoms have a greater tendency to stop smoking most based. 				
Chester et al., 1969, U.S.A. (49).	139 male chlorine plant workers (55 with history of severe ex- posure).	Chlorine-exposed group manifested no difference in symp- toms and a decreased MBC value when compared with non-exposed group. Smokers in chlorine-exposed group had significantly de creased MBC and FEV values as compared with non- smokers in non-exposed group.				
Greenberg et al., 1970, England (97).	121 workers in washing powder factory (48 found to be sensitized to product, 73 not).	Sensitized group manifested lower FEV _{1.0} /FVC ¹ values as compared with nonsensitized group even after smok ing habits were controlled for.				
Tokuhata et al., 1970, U.S.A. (218).	801 male miners	 Increased mine exposure was associated with residual volume and FEV abnormalities even after adjustments for age and smoking. A systematic exposure-impairment relationship was noted only among smokers while relatively few nonsmokers showed COPD impairment. Smoking miners manifested more X-ray alterations an COPD symptoms than nonsmokers, regardless of number of years of underground exposure. 				

¹See Glossary of Terms in Bronchopulmonary table A4.

TABLE A10.—Experiments concerning the effect of the chronic inhalation of NO2upon the tracheobronchial tree and pulmonary parenchyma of animals

Author, year, country, reference	Animal	Results
Freeman and Haydon, 1964 U.S.A. (90).	Sprague-Dawley rats.	 25 p.p.m.: (a) after 37-41 days—moderate hypertrophy and hyperplasia of bronchial and bronchiolar epithelium. (b) after 146-157 days—(1) Advanced hypertrophy and hyperplasia of bronchial and bronchiolar epithelium, (2) Increased lung volume. (3) Proliferation of connective tissue.
Haydon et al., 1965 U.S.A. (107).	Sprague-Dawley rats.	 12.5 p.p.m. to death: (a) Hypertrophy and occasional metaplasia of bronchial and bronchiolar epithelium. (b) Increase in number of actively secreting goblet cells.
Haydon et al., 1967 U.S.A. (106).	Albino rabbits.	 8-12 p.p.m. for 4 months: (a) Abnormal dilatation of peripheral air spaces. (b) Decreased density of alveolar walls. (c) Hypertrophy and hyperplasia of bronchial epithelium (especially terminal bronchiolar). (d) Increase in size of alveolar ducts. (e) Increased elastic tissue staining. (f) Increased alveolar size.
Freeman et al., 1968, U.S.A. (91).	Sprague-Dawley rats.	 0.8 p.p.m2 p.p.m. for entire lifespan: (a) Alveolar distention. (b) Reduction in number of cilia. (c) Epithelial inactivity ("dormancy").
Freeman et al., 1968, U.S.A. (89).	Sprague-Dawley rats.	 18 p.p.m. (a) 5 days-terminal bronchiolar epithelial hypertrophy. (b) 4 weeks-(1) Widespread bronchiolar epithelial hypertrophy. (2) Non-necrotizing emphysema.
Blair et al., 1969, U.S.A. (32).	Female Swiss Albino mice.	 0.5 p.p.m.: (a) 6 hours/day for 3 months—pneumonitis. (b) 24 hours/day for 3 months—(1) Respiratory bronchiolar obstruction. (2) Alveolar expansion and bronchiolar inflammation consistent with early focal emphysema.
Kleinerman, 1970, U.S.A. (136).	Male Syrian Golden hamsters.	 100 p.p.m. for 5¹₂ hours: (a) thymidine autoradiography—intense burst of proliferation of epithelium returning to normal in 4 days (more persistent distally). (b) electron microscope-(1) Decreased number of secretory cells + secretory granules. (2) Increased number of lysosomal structures. (3) No change in number of ciliated cells.

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Author, year, country, reference	System	Method ¹	Results
Mendenhall and Shreeve, 1937, U.S.A. (164).	In vitro: Calf trachea	Cigarette smoke by direct appli- cation or in solution.	Controls—ciliary activity depressed approxi- mately 4 percent. Experimental—ciliary activity depressed ap- proximately 40 percent.
Rakieten et al., 1942, U.S.A. (188).	In vitro: (a) rabbit and rat trachael rings. (b) human nasal mucous membrane	 Nicotine in Locke-Ringers solution. Cigarette smoke in solution. 	 I. Ciliary activity depressed only upon exposure to 100 mg, percent solution. II. Ciliary activity depressed after 15-20 minutes exposure depending on concentration of smoke in solution.
Kordik et al., 1952, England (137).	In vitro: Rabbit trachea	Nicotine in Locke's solution.	Nicotine at 10-5 g./cc had no effect on ciliary activity.
Hilding, 1956, U.S.A. (120).	In vitro: Cow trachea	Cigarette smoke (direct exposure).	All tracheas showed depressed or absent ciliary activity.
Krueger and Smith, 1958, U.S.A. (189).	In vivo: Rabbit trachea	Cigarette smoke.	Cigarette smoke decreased ciliary activity by approximately 200 beats/minute.
Dalhamn, 1959, Sweden (59).	In vivo: I. Rat trachea In vitro: II. Rabbit trachea III. Human ciliated mucosa	Cigarette smoke.	 I. 7/10 showed cessation of ciliary activity after one exposure. II. 6/10 showed cessation of ciliary activity after one exposure. III. 6/7 showed cessation of ciliary activity after one cigarette exposure.
Falk et al., 1959 U.S.A. (80).	In vitro: Rat and rabbi tracheal epithelium.	Cigarette smoke. t	 Decreased ciliary activity noted on exposure to cigarette smoke: (a) Repetitive exposure was associated with persistence of response over longer period of time. (b) "Tar"-rich cigarette was more inhibitory than "tar"-poor. (c) Filtered smoke was less inhibitory than unfiltered.
Ballenger, 1960, U.S.A. (25).	In vitro: Human bronchial and trachea epithelium obtained during anesthesia.	Cigarette smoke in solution. I	Ciliary activity was fully inhibited within 5-24 minutes of exposure depending upon concen tration of smoke in solution.

 TABLE A13.—Experiments concerning the effect of cigarette smoke or its constituents upon ciliary function

 TABLE A13.—Experiments concerning the effect of cigarette smoke or its constituents upon ciliary function (cont.)

Author, year, country, reference	System	Method 1	Results				
Wynder et al., 1963, U.S.A. (236).	In vivo: Fresh water mussel ciliated epithelium.	Cigarette smoke; and its fractions in solution.	Unfiltered cigarette smoke—ciliastasis by 2r 5th puff. Acid (phenolic) fraction solution—immedia ciliastasis. Whole extract fraction solution—no ciliastasis. Neutral fraction solution—no ciliastasis. 1 percent phenol solution—immediate cilias sis.				
Dalhamn and Rylander, 1964, Sweden (61).	In vivo: Cat trachea.	Cigarette smoke.	Unfiltered cigarettes—ciliastasis in 3/5 cats after 5 cigarettes. Filtered cigarettes—no ciliastasis after 8 ciga- rettes (5 cats). Controls—no ciliastasis (5 cats).				
Ballenger et al., 1965, U.S.A. (26).	In vitro: Human ciliated tracheal epithelium obtained during. anesthesia.	Nicotine in solution.	Initial stimulation of activity followed by de- cline and complete ciliastasis after 12-24 hours of exposure.				
Dalhamn and Rylander, 1965, Sweden (62).	In vivo: Cat trachea.	Cigarette smoke.	The longer the time interval between expo- sures, the more puffs were required to cause ciliastasis.				
Wynder et al., 1965, U.S.A. (285).	In vivo: Fresh water mussel ciliated epithelium	Various compounds in solution.	Formic, acetic, propionic, benzoic acids all more ciliatoxic than phenol. Oxalic acid less ciliatoxic than phenol. Formaldehyde, acrolein more ciliatoxic than phenol.				
Carson et al., 1966, U.S.A. (44).	In vivo: Cat trachea.	Cigarette smoke.	Percent decrease in ciliary activity Control 0 Unfiltered smoke 53 Cellulose acetate filter 45 Carbon cellulose acetate filter 30				
Dalbamn, 1966, Sweden (60).	In vivo: Cat trachea.	Cigarette smoke.	Mean number of puffs required to produce ciliastisis No filter 91 Charcoal filter 170 Commercial cellulose acetate filter 194 Charcoal and acetate filter 512 Cambridge filter 600				
Kensler and Battista, 1966, U.S.A. (185).	In vivo: Rabbit trachea, cat trachea, dog trachea, monkey trachea. rat trachea.		Rabbit trachea—Total smoke condensate of 3 cigarettes, gas phase condensate of 7 ciga- rettes caused similar ciliastasis. Other species—All found sensitive to ciliastatic components of cigarette smoke. Bulk of ac- tivity noted in gas phase (HCH, formalde- hyde, acrolein).				

Author, year, country, reference	System	Method ¹	Results
Dalhamn and Rylander, 1967, Sweden (63).	In vivo: Cat trachea.	Cellulose acetate- filter cigarettes with varying amounts of "tar" but simi- lar gas phases.	Increased amounts of tar were associated with decreased number of puffs required to inhibit ciliary activity.
Dalhamn and Rylander, 1968, Sweden (64).	In vivo: Cat trachea.	Unfiltered and Cambridge-filter cigarettes.	Whole smoke found to be markedly more toxic to ciliary activity than volatile (gas) phase at lower dosages (puff volume). This differ- ence diminishes with increasing puff volume.
Kaminski et al., 1968, U.S.A. (133).	In vivo: Cat trachea.	Whole and filtered cigarette smoke exposed or unex- posed to "wet chamber" made to stimulate oral mucosa and saliva.	Wet chamber adsorption significantly reduced the ciliastatic activity of whole smoke, but did not affect the ciliastatic activity of smoke previously filtered by Cambridge or charcoal filters.
Krahl and Bulmash, 1969, U.S.A. (138).	In vivo: Common mollusk ciliated epithelium.	Cigarette smoke dissolved in sea water.	Significant ciliastasis, reversible.
Battista and Kensler, 1970, U.S.A. (28).	In vitro: Chicken tracheal epithelium.	Cigarette smoke or HCN in Tyrode's solution.	 The authors observed that: (1) The more diluted smoke required more puffs to cause ciliastasis. (2) Activated charcoal filtered smoke was less ciliastatic than cellulose acetate filtered smoke and also contained less HCN and acrolein. (3) HCN alone was ciliastatic but recovery was more rapid than after cigarette smoke alone. They conclude that the gas phase components are more related to ciliastasis (as particulate matter is not significantly decreased by charcoal filtration while HCN and acrolein are)
Battista and Kensler, 1970, U.S.A. (29).	In vivo: Hen trachea.	Cigarette smoke.	 The authors observed that: (1) Whole smoke acutely depressed ciliary activity in 4-6 puffs. (2) Gas phase was only slightly less depress sant than whole smoke. (3) Chronic exposure (1 cigarette/day for 32 days) to smoke resulted in no apparent permanent defect in ciliary activity (all though mucous production was signific cantly increased).

 TABLE A13.—Experiments concerning the effect of cigarette smoke or its constituents upon ciliary function (cont.)

Author, year, country, reference	System Method ¹		Results			
Dalhamn and Rylander, 1970, Sweden (65).	In vivo: Cat trachea.	Unfiltered eigarette and eigar smoke.	Average number of puffs required to arrest ciliary activity Cigarette smoke 73 Cigar smoke 114 The authors note that cigar smoke is of different pH and that it contains more iso prene, acetone, toluene, and acetonitrile.			
Kennedy and Elliott, 1970, U.S.A. (184).	In vivo: Protozoan (ciliated).	Mainstream cigarette smoke.	 Electron microscopic observations: (1) After 7 minutes exposure—alteration o mitochondrial structure. (2) After 42 minutes exposure—destruction of internal mitochondrial membrane structure. (3) Gas phase alone, while ciliatoxic, dis cause mitochondrial swelling but no dis ruption of membrane structure. 			

 TABLE A13.—Experiments concerning the effect of cigarette smoke or its
 constituents upon ciliary function (cont.)

¹ Unless otherwise stated, method entailed the direct observation of ciliary activity using markers.

Author, year, country, reference	System	Method	Results Exposure to cigarette smoke was associated with decreased surface tension in lung extra Surface tension of rats (lung extracts) exposed to cigarette smoke was decreased					
Miller and Bondurant, 1962, U.S.A. (165)	Rat lung extracts	Cigarette smoke: (1) Applied to extract. (2) Exposure of rats.						
Cook	40 subjects undergoing		Surface tension values of surfactant					
and Webb 1966, U.S.A.	bronchoscopy: 14 normal 7 nonsmokers with		values of	20 percent area	100 percent area	Stability index (reflects surfactant activity)	† Values significantly different from values of normals	
(57)	pulmonary disease 19 smokers with and without pulmonary		Normal Pulmonary	6.5	60.0	1.61	at $p < 0.02$ level.	
	discase.		patients Chronic smokers	†17.0 15.7	†50.0 51.0	1.00 1.04		
Giammona 1967, U.S.A. (94)	In vitro: Surfactant material induced from dogs and rats. In vivo: Dogs, cats, and guinea pigs.	Exposed to cigarette smoke for 3 hours/day for up to 3 weeks.	tension. In vivo: Dogs and cats (ex	posed for sed for 3 v	1 week)—no si weeks)—signific	ant decrease in maximal		
Webb, et al. 1967, U.S.A. (224)	Bronchial washing, from dog lungs.	Direct exposure to cigarette smoke.	Control Smoke	Surface Number 11 10	tension values o 20 percent area 7.1 18.7 { (1		Stability index 1,60 0.84	

TABLE A14 Experiments concerning the effect of cigarette smoke on pulmonary surfactant as	and surface	tension
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