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.

Author, year, country, reference	Number and type of population	Cough	Sputum production	Breathlessness or dyspnes	Chest illnesses	Other	Comments
Goldsmith et al., 1962, U.S.A. (95).	3,381 active or retired longshoremen.					Respiratory conditions NS 31.4 (744) Moderate/heavy smokers 43.0 (1,288)	
Coates et al., 1965, U.S.A. (53).	1,342 male and 242 female Detroit post office employees.	1	5-2427.5 (402) (p<0.	NS14.7 sig.) 1-14 .28.2(p<0.001) .001)15-24 .30.7(p<0.001) .001)>25 .34.1(p<0.001)		Cough and chronic phlegm NS 4.0 1-14 5.3 (not sig.) 15-24 17.2 (p<0.001 >25 25.3 (p<0.001	smoking data.)
Deane et al., 1965, U.S.A. (67),	508 tele- phone company workers.					Persistent cough, phlogm, dyspnca NS 4.5 (200) Current cigarette smokers 15.9 (808)	NS includes ex-smokers, pipe, and cigar smokers.
Huhtl, 1965, Finland (126).	553 male and 823 female residents of a Finnish communal region, 40-64 years of age.	Males NS	Males NS	Males NS		Chronic bronchilis Malcs NS 5.7 EX 16.3 1-14 38.0 15-24 41.4 >26 40.0 Females NS 4.5 EX 13.3 1-14 10.4 15-25 >25	Ex-smokers represent those who have atopped smoking for more than 1 month. Dyspnea Grade II only.

Author, year, country, reference	Number and type of population	Cough	:	Sputum production	Breathlessness or dyspnea	Chest illnesses	Other	Comments
Vynder et a)., 1965 U.S.A. (238).	316 male patients in New York City and 316 male patients in California.	Pipe, cigar 33.0 (5 Cigarettes: 1-1045.0 (4 10-2046.0 (8 California NS22.0 (Pipe, cigar 30.0 (5 Cigarettes: 1-1045.0 (10-2074.0 (5 Cigarettes: 10-2074.0	44) 54) 44) 88) 85) 69) 32) (54) (69)					
Freour et al., 1966 France (92).	1,055 randomly chosen males in Bordeaux 30-70 years of age.	4.4		111			Clinical signs of bronchitis and respiratory insufficiency NS25,4 (45) SM54.4 (478)	
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 aye) NS 0.36 All smokers 2.30 Heavy SM 3.34	Heavy smoker— more than 10 ciga- rettes per day.

Author, year, country, reference	Number and type of population	Cough	Sputum production	Breathlessness or dyspnes	Chest illnesses	Other	Comments
Densen	5,313 male	Postal	Postal	Postal			Dyapnes
et al.,	and 7,291	NS 7.0 (903) Pipe, cigar 12.4 (628)	13.1 17.4	19.8 24.8			represented by Grade II
1967, U.S.A.	female postal and transit	Cigarettes	11.4	24.0			only.
(68).	workers.	only27.0(2,587)	28.9	31.7			
		Transit	Transit	Transit			
		NS 6.4(1,012)	9,5	11.7			
		Pipe, cigar 10.5 (765) Cigarettes	14.1	14.2			
		only23.5(8,745)	23.7	21.9			
Higgins	926 white	NS15.4 (162)	NS 31.1	NS 5.0			
et al.,	male resi-	SM47.2 (613)	SM46.2	SM10.7			
1968,	dents of	EX19.3 (144)	EX28.5	EX16,8			
U,S.A. (118).	Marion County, West Virginia, 26-69 years						
	of age.						
Holland	9,786 male	Malea	Females	Males Females			
and	and female	NS 8,8(1,900)	3.2 (3,137)	2.4 2.1			
Ellott,	*chool	SM 6.3(1,098)	6.3 (554)	6.1 8.3			
1968, England	children,	EX 2.9 (1,782)	4.3(1,151)	3.9 4.2			
(121).		<1 cigarette/day,. 1-2		5.8			
(122).		3-4		8.4			
		>5		8.1 18.9			

Author, year, country,	Number and type of	Cough	Sputum production	Breathlessness or dyspnea	Chest illnesses	Other	Comments
reference Gandevia 1969 Australia (93).	population 762 male and 1,304 female patients from 13 general practices in all parts of Australia.	Males					Productive cough upon request.
Rimington 1969 England (198).	41,729 male and 22,295 female persons participating in mass miniature radiography servening.					Age-adjusted total prevalence of chronic bronchitis Males NS 6.1 (9,055) EX 9.8 (6,610) Pipe 9.0 (2,921) Cigarettes (23,243) 1- 9 9.1 10-10 15.0 >20 20,6 Females NS 3.4 (12,351) EX 3.8 (959) Pipe 0.0 Cigarettes (8,985) 1- 9 5.1 10-19 10.6 >20 18.5	Cignrette downge gradient significant to p<0.001.
Withelmsen et al., 1969, Sweden (231),	313 males 50-54 years of age randomly sampled from population of Göteborg.					Chronic bronchitis NS 1.0 (88) EX 3.0 (67) 1-14 grams/ day 5.0 (94) >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)

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

Author, year, country, reference	Number and type of population	Cough	Sp	utum produ	etion	Breathlessness or dyspnes	Chest illnesses	Other	Comments
Lambert and	9,975 male and female		ent cough and Males						
Reid, 1970,	responders to a postal	Age 35-45	Ayc 45-55	Age 55-05	Age 65-09				
England (148).	aurvey (4,688 males	NS 7(227) EX 7(303)	6 (200) 11 (358)	11(171) 15(335)	7 (61) 18(148)				
	and 5,287 females	$<20 \dots .15(521)$ 20 \dots .23(191)	22 (488) 28 (204)	30(490) 32(149)	37 (139) 38 (37)				5
	35-69 years of age).	>2027(148)	28 (136) Females	42 (121)	25 (12)				
		NS 3(500) EX 3(127)	4 (637) 8 (128)	5 (925) 7 (94)	6 (21) 7 (41)			•	
		<20 9 (602) 2016 (128)	13 (472) 27 (122)	16(306) 31 (77)	11 (65) 14 (7)				
		>2023 (22)	26 (39)	43 (7)	(1)				
Lefcoe and Wonnacott, 1970.	310 male physicians in London and Ontario,							Age-standardized rates of chronic respiratory disease NS 1.0 (88)	Excluded from ex-amokers are those cigarette
Canada (151),	25-74 years of age.							EX 6.0 (61) SM34.0 (101) Pipe, cigar12,0 (83)	amokera who now amoke pipes or cigar

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

TABLE A2a.—Smoking and chronic obstructive pulmonary disease symptoms'—percent prevalence
(Numbers in parentheses represent total number of individuals in particuar smoking group)

SM = Smokers.

NS = Nonsmokers.

EX = Ex-smokers.

Author, year, country, reference	Number and type of popuation	Cough			Bronchitis		Comments
Cederlot et al., 1966, Sweden (46).	9,319 twin pairs registered in Sweden of 12,889 available.	Observed expected expected	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 (663)	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-amokers 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 bronchopulmonary symptoms is supported.
Cederlof et al., 1969, U.S.A. (45).	4,379 twin pairs (all U.S. veterans) in U.S. National Academy of Sciences Twin Registry (of 9,000 avial- able),	Prevalence Group A: NS 4 1-10 6 11-30 15 >31 27 27 Pipe, cigar 7 7 Group B: MZ DZ	.4 6.4 .3 15.3 .7 27.7 .1 7.1 .NS 2.4	symptoms SM 5.4 9.8	1.8	Group A—as above. Group B—as above. M .8 .1	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 factors.

¹ Data collected by either direct interview, questionnaire, review of medical records and/or medical examination.

TABLE A3.—Smoking and ventilatory function (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	мвс		EFR	-	FEV		vc	Miscellaneous	Comments
Chivers, 1969, England (58).	463 male employees of alkaline industry plant.	6-20	y: 63 	(50)	Height. 66'' 91 (35) 88 (75) 88.5 (9)	68" 108 (31) 101 (112) 92.5 (9)	70'' 101(21) 109(75) 118(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).		25-34 NS 145 (66) EX 143 (31) 1-14 grams .140(193) >15 grams .133 (89)	55-64 101 (29) 89 (62) 87 (157) 80 (186)							FEV 0.75 expressed as mean indirect MBC.
Wilson et al., 1900 U.S.A. (252).	28 male residents of Dallas, Texas, former rural dwellers; matched for body surface, age and height.	,							RV/TLC 14) NS 21 14) SM ¹ 27	

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
Ashford et al., 1961, Scotland (11).	4,014 male coal workers at 3 Scottish collieries.			$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	5) 7) 5) 0)		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 (85).	363 male London transport employees.		1-14 grams 53 >15 grams 52	FR 0 (30) 7(156) 8(116) 5 (61)			
Franklin and Lowell, 1961, U.S.A. (87),	213 male factory workers 40-60 years of age.			FEV _{1.0} FEV _{0.25} FEV 0.25 FEV Heavy 2.670 3.011 2.71 Light 2.489 22.666 22.25	0 Light 3,703 (Heavy smoker represents an amount equal to or more than 30 pack years.

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

(Numbers in parenthese 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	٧c	Miscellaneous	Comments
Balchum	1,451 male		MMEFR				Data for: MMEFR
et al., 1962,	employees in		NS 15.5 (38) Pack/year;	7.8 (19)			given as percent 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.		10-13 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 (20)	45.0			<70 percent
			>60 71.0 (24)	62.0			of expected.
Goldemith	3,311 active		MEFR	FEV _{1.0}			Authors concluded
et al.,	or retired		NS313.63(250)	2.99			that cigarette
1962. U.S.A.	longshore-		Pipe, cigar 299.26 (125)	2.80			amoke was found
(95).	men.		EX 295.23(102)	2.84			to have a slight
(93).			Cignrettes/day:				effect on
			120 309.73 (144)	2.89			pulmonury
			20-40 303.44(346)	2.91			function.
			≥40 307.63 (57)	2.90			
Martt, 1962.	73 healthy					$D_L CO$	Smokers defined
U.S.A.	medical per- sonnel with-					NS 33.10(30)	as those smoking
(161).	out signifi-					SM <5 years .228.40 (8)	>20 cigarettes/
(***/.	cantage					5-10 years 328.20(10)	day for varying
	difference					>10 years*24.90(25)	periods.
	between					, , , , , , , , , , , , , , , , , , , ,	
	smokers and						
	nonamokera.						

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.

				TIE = MONIMINOREIS	2m	- Billokers,	$\mathbf{E}\mathbf{v} = \mathbf{E}\mathbf{x}$	Binokers.		
Author, year, country, reference	Number and type of population	MBC		EFR		FEV		vc	Miscellaneous	Commenta
Revotskie et al., 1962, U.S.A. (192),	1,130 male and 1,813 female residents in Framing- ham par- ticipating in the pro- apective atudy.				Cigare 1-1	Males 0,98 (55) ttes/dny; 0 .0.97 (90) 9 .0.91(163)	0.99 (92) 0.93(157)			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 NS 580 SM 1590	(9)				Mean NS Rest36 Exercise: 2 minutes50 4 minutes50 8 minutes	5M 181 141 148
Zwi et al., 1964, U.S.A. (241).	20 medical students or graduate physicians.	187	(10) (10)	MMEFR 4.34 15.09		5.77 5.53			post exercise 39 Authors found a significant different between SM and NS for RV/TLC, compliance, and no elastic resistance.	
Coates et al., 1965, U.S.A. (55).	1,342 male and 242 female post office employees >40 years of age.				45~49 50-54 55-59	FE NS 1 2,99 (186) 2 2,95 (170) 4 12.75 (115) 3 12.64 (64) 4 12.35 (53)	2.64 (42) 2.62 (22) 2.44 (18)	Timed VC NS >25/ 3.89 3.80 3.92 3.80 3.71 3.70 3.54 3.6 3.30 3.3	74 FEV1.0/VC day NS >25/day 5 30.77 0.74 3 30.74 0.70 4 30.74 0.70 1 0.74 0.68	1

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	FI	EV	V	c		Miscellance	ous	Comments
Huhti, 1965, Finland (186).	residents	PEFR† FEV Males Formales Males Males	1.9 [‡] romales 2.42 2.82 2.74 2.82		d VC\$ Females 8.18 8.10 3.53 8.50		:	tipe and cigar anokers not included. Difference between NS and >26/day is significant for 45-49, 60-64 age groups. Trend is not statistically significant.			
Krumhols et al., 1965, U.S.A. (145).	20 male medical atudents or graduate physicians.						-	NS SM	ulmonary co	0.241 (10) 0.177 (10) e/FRC 0.054	
Rankin et al., 1965, U.S.A. (189).	125 males without a past history of respira- tory disease 20-63 year of age.		a para de la companya de la company	NS SM					D _L 31.1 ² 25.9	D _L /alveolar volume 6,22 •4.96	and cigar 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	мвс	EFR	FEV	vc	Miscellaneous	Comments
Edelman et al., 1966, U.S.A. (73).	410 male community dwellers 20-103 years of	NS 164(152) Current cigarette smokers*151(118)	7.89	FEV 1.0 2.83	Vital capacity 4.98		Ex-smokers of cigarettes only. Difference signifi- cant between NS and current
	age.	EX 157 (98) Pipe, cigar 167 (47)	8.09 8.20	2.80 2.91	4.77 5.08		cigarette smokers at p<0.01.
Peters and Ferris, 1967, U.S.A. (182).	124 male college age students,		MEFR NS210.28 (41) Moderate , 10.06 (54) Heavy 9.64 (29) EX 9.48 (10)	FEV 1.0 4.68 4.59 4.43 4.74		FEV _{1.0} /VC ^{287.5} 85.3 83.9 83.2	Heavy smoker refers to greater than or equal to i pack years. Moderate sinoker includes pipe and clgar 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.		Cig 1- 15-	FEV _{1.0}			

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	мвс	EFR	FEV		vc	Miscellaneous	Comments
Sluis- Cremer and Sichel, 1908, South Africa (208).	533 white male factory workers over 35 years of age.		S5-44 NS 553 (106) Grams/day: 1-14 557 (26) 15-24 532 (94) >25 †528 (86)	45-54 527(101) 519 (17) 446 (35) †494 (31)	>55 444(27) 410 (7) 401(13) †380(10)	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		1 cigarette = 1 gram. 1 ounce tobacco = 26 grams. 1 cigar = 2 to 5 grams. † Derived slopes found significantly different from 0.
Stanescu et al., 1968, Rumania (#1#).	87 male bus drivers: 27 aged 20-25, 60 aged 40-60, all without respiratory symptoms.			Younger 4,470 (14) 4,500 (13)	3,310(40)		Nitrogen gradient Younger Older 1,63 2.49 11.47 3.77	
Densen et al., 1969, U.S.A. (69).	5,287 male postal and 7,213 male transit workers in New York City.		NS All cigarette <25 grams/day ≥25 grams/day NS All cigarette		FEV 1.0 Postal White 3.29 (685) 3.11 (2,340) 3.14 (1,292) 3.06 (1,038) Transit White 3.39 (620) 3.11 (2,941)	Non-white 3.05 (204) 2.94 (768) 2.95 (599) 2.93 (161) Non-white 3.08 (288) 2.99 (1.041)		FEV expressed as standardized for specified postal and transit workers at age 45 and at sitting height of 35 inches. Includes mixed smokers.
			<25 grams/day ≥25 grams/day		3.15(1,929) 3.02(1,011)	3.00 (891) 2.96 (149)		

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
Rankin et al., 1969, Australia (190).	60 male and 10 female patients with chronic alcoholism 26-66 years of age.				FE				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		NS		525 (88)	3.77.0	4.83		·
1969.	of Göteburg		EX		539 (67)	3.69	4.77		
Sw∞den	50-54 years		1-14 grams/day		521 (94)	3,62	4.83		
(231).	of age.		>15 grams/day		492 (64)	3.39	4.56		
Lelcoe	310 mule		MMFR		FE	V _{1.0}			MMFR has been
and	physicians		NS 4.09 (88)		3.3	39 ***			standardized for
Wonna-	of London,		Cigarette						age and height.
cott,	Ontario.		smokers. 3.64(101)		3.1				
1976,			EX 3.99 (61)		3.:	38			
Canada (151).			Pipe, cigar 4.17 (33)		3.	17			

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		FEY	Miscellaneous	Comments
Lundman, 1966, Bweden (159),	87 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. The author concludes that the degree of ventilation as measured by Nz washout was correlated with cigarette consumption. The FEV 1.0 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.

³ Not significant (difference or trend).

p<0.005
p<0.005
p<0.005
p<0.005

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

Symbol	Term	Volume or rate	Definition
MVVMaxii	acity.	Liters	The maximal volume of gas that can be breathed in one minute.
PEFRPeak MEFRMaxir MMEFRMaxir	expiratory flow rate. mal expiratory 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 Force	d expiratory	Liters	Volume expired within a specified time interval. (FEV _{1.0} -volume expired in first second of expiration.)
VCVital		.Liters	Maximal volume of a gas that can be expelled from the lungs by forceful effort following a maximal expiration.
FEV /VC Force	d expiratory ume/vital capacity.	Percent	Volume of forced expiration (in time specified) related to vital capacity,
D _L , Pulmocap	onary diffusing acity.	ml/min/mmHg	The ability of a chosen gas to pass from the alveolus to within the pulmonary capillary.
N ₂ washout Nitro gra	gen washout dient.	Exponential curve.	The stepwise pulmonary alveolar clearance of a gus. (Slope of curve depends upon the uniformity and adequacy of ventilation of all parts of the lung.) It may be done as a single—or multiple—breath procedure.
Comp	liance	.Liters/CMH ₂ 0	Volume change of the lung produced by a unit pressure change.
RVResid	ual volume	.Liters	Volume of gas remaining in the lungs at the end of a maximal expiration.
TLCTotal	lung capacity	. Liters	Volume of gas contained in the lungs at the end of a maximal inspiration
FRCFunc	tional residual pacity,	Liters	Volume of gas remaining in the lungs at the resting expiratory level.
Aleve	olar volume	Liters	Volume of gas contained in pulmonary alveoll.

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 higher in the more polluted region but the prevalence of other respiratory symptoms and mean values were 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 the prevalence of chronic bronchitis as rural males; this difference could not be explained on the basis of smoking habits. (b) No significant urban/rural differences noted for PEFR.³ (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, no 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 (dyspnea, wheezing) and PEFR dysfunction among London 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 prevalence rates among its residents were not accounted for by age differences, but were accounted for after standardization for smoking habits (except that PEFR and FEV _{1.0} dysfunction was more prevalent in New Hampshire, and the authors suggest that this difference reflects 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 correlated 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) SO ₂ 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. (233)	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 over rural 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 increased with air pollution similarly in each smoking group, the absolute differences in morbidity risk increased with increased cigarette consumption, suggesting aynergistic 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 occupational exposure and smoking to chronic obstructive bronchopulmonary disease

et al. 1956. England (119). Phillips et al., 1956. U.S.A. (185). Higgins et al., 1959. England (116). Chivers, 1959. England (52). Higgins and Cochrane, 1961. England (115). Brinkman and Coates, 1962. U.S.A. (42). Hyatt et al., 1964. U.S.A. (128).	Number and type of population 185 males (84 nonminers, 101 miners) without pneumoconiosis. 1,274 males factory employees (coke and electrolytic process). 325 males 25-34 years of age and 401 males 65-64 years of age in various occupations. 463 males in non-dusty and dusty occupations (lime and soda	ness, cough, sputum). Miners showed increased prevalence of chronic bronchitis Miners showed decreased MBC.¹ Differences in smoking between the two groups did not account for above differences. None of the industrial environments were associated with an increased prevalence of chronic cough. Cigaretto smoking and age were directly correlated with increased prevalence of chronic cough. 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.
et al. 1956. England (119). Phillips et al., 1956, U.S.A. (185). Higgins et al., 1959, England (116). Chivers, 1959, England (52). Higgins and Cochrane, 1961, England (115). Brinkman and Coates, 1962, U.S.A. (42). Hyatt et al., 1964, U.S.A. (128).	(84 nonminers, 101 miners) without pneumoconiosis. 1,274 males factory employees (coke and electrolytic process). 325 males 25–34 years of age and 401 males 66–64 years of age in various occupations. 463 males in non-dusty and dusty occupations (lime and soda	Miners showed increased prevalence of chronic bronchitis Miners showed decreased MBC. Differences in smoking between the two groups did not account for above differences. 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. 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.
Phillips et al., 1956, U.S.A. (185). Higgins et al., 1959, England (116). Chivers, 1959, England (52). Higgins and Cochrane, 1961, England (115). Brinkman and Costes, 1962, U.S.A. (141). Hyatt et al., 1964, U.S.A. (128).	1,274 males factory employees (coke and electrolytic process). 325 males 25–34 years of age and 401 males 65–64 years of age in various occupa- tions. 463 males in non-dusty and dusty occupations (lime and soda	None of the industrial environments were associated with an increased prevalence of chronic cough. Gigaretto smoking and age were directly correlated with increased prevalence of chronic cough. 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.
et al., 1956, U.S.A. (185). Higgins et al., 1959, England (116). Chivers, 1959, England (52). Higgins and Cochrane, 1961, England (115). Brinkman and Coates, 1962, U.S.A. (42). Hyatt et al., 1964, U.S.A. (128).	factory employees (coke and electrolytic process). 325 males 25–34 years of age and 401 males 65–64 years of age in various occupa- tions. 463 males in non-dusty and dusty occupations (lime and soda	an increased prevalence of chronic cough. Gigarette smoking and age were directly correlated with increased prevalence of chronic cough. 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.
et al., 1959. England (116). Chivers, 1959. England (52). Riggins 3 and Cochrane, 1961. England (115). Brinkman and Coates, 1962. U.S.A. (42). Hyatt 2: et al., 1964. U.S.A. (128).	years of age and 401 males 65-64 years of age in various occupa- tions. 463 males in non-dusty and dusty occupations (lime and soda	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. No significant differences in PEFR 1 between dusty and
1959, England (SI). Higgins 3 and Cochrane, 1961, England (IIS). Brinkman 1 and Coates, 1962, U.S.A. (41). Hyatt 2 et al., 1964, U.S.A. (128).	non-dusty and dusty occupations (lime and soda	•
and Cochrane, 1961, England (115). Brinkman and Coates, 1962, U.S.A. (42). Hyatt et al., 1964, U.S.A. (118).	ash exposure).	Cigarette smoking (especially in those >40 years of age) was associated with decreased PEFR values.
and Coates, 1962, U.S.A. (42). Hyatt 2 et al., 1964, U.S.A. (128).	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.
et al., 1964. U.S.A. (128).	1,317 males 40-65 years of age with various silica exposure bistories.	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.
	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.
1965, Ireland (77).	2,628 male and female flax workers over 35 years of age.	Preparing room workers who manifested byssinosis symptoms 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 between byssinosis symptoms and smoking while male workers did not.
Sluis-Cremer 82 et al., 1967, South Africa (209).	07 - 1 - 1	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.

Table A7.—Epidemiological studies concerning the relationship of occupational exposure and smoking to chronic obstructive bronchopulmonary disease (cont.)

Author, year, country, reference	Number and type of population	Results
et al., 1967,	a 35 years of age.	The dose relationship of cigarettes and COPD I 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. (59).	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 ² values were observed between smokers and nonsmokers. Prevalence of byssinosis symptoms did not show any relationship to length of employment.
Bouhuys et al., 1969, U.S.A. (38).	216 male hemp workers and 247 workers in other industries in 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} ' 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 may obscure such a
Chester et al., 1969, U.S.A. (49).	139 male chlorine plant workers (55 with history of severe exposure).	relationship. Chlorine-exposed group manifested no difference in symptoms and a decreased MBC value when compared with non-exposed group. Smokers in chlorine-exposed group had significantly decreased 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 smoking habits were controlled for.
Tokuhata et al., 1970. U.S.A. (218).	801 male miners	Increased mine exposure was associated with residual vol- ume 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 and COPD symptoms than nonsmokers, regardless of num- ber of years of underground exposure.

¹ See Glossary of Terms in Bronchopulmonary table A4.

Table A10.—Experiments concerning the effect of the chronic inhalation of NO_2 upon 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., 1955 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. (108).	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) Wideapread 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 5½ 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 bysosomal structures. (3) No change in number of ciliated cells.

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

Author, year, country, reference	System	Method 1	Results
Mendenhal and Shreeve, 1937, U.S.A. (164).	In vitro; Calf trachea	Cigarette smoke by direct application or in solution.	Controls—ciliary activity depressed approximately 4 percent. Experimental—ciliary activity depressed approximately 40 percent.
Rakieten et al., 1942, U.S.A. (188).	In vitro: (a) rabbit and rat trachael rings. (b) human nasal mucous membrane	I. Nicotine in Locke-Ringers solution. II. Gigarette smok 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 (187).	In vitro: Rabbit trachea	Nicotine in Locke's solution.	Nicotine at 10-3 g./cc had no effect on ciliary activity.
Hilding, 1956, U.S.A. (120).	In vitro: Cow traches	Cigarette smoke (direct exposure).	All trachess showed depressed or absent ciliary activity.
Krueger and Smith, 1958, U.S.A. (199).	In vivo: Rabbit traches	Cigarette smoke.	Cigarette smoke decreased ciliary activity by approximately 200 beats/minute.
Daihamn, 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 rabbit trachest epithelium.	Cigarette smoke.	Decreased ciliary activity noted on exposure to cigarette smoke: (a) Repetitive exposure was associated with persistence of response over longer periods 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 tracheal epithelium obtained during snesthesia.	in solution.	Ciliary activity was fully inhibited within 6-28 minutes of exposure depending upon concentration of smoke in solution.

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 2nd 5th puff, Acid (phenolic) fraction solution—immediaciliastasis. Whole extract fraction solution—no ciliastasis. 1 percent phenol solution—immediate ciliastasis.
Dalhamn and Rylander, 1964, Sweden (61).	In vivo: Cat trachea.	Cigarette smoke.	Unfiltered cigarettes—ciliastasis in 3/5 carafter 5 cigarettes. Filtered cigarettes—no ciliastasis after 8 cigarettes (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 ciliastasia after 12-2 hours of exposure.
Dalhamn and Rylander, 1965, Sweden (62).	In viro: Cattrachea,	Cigarette smoke.	The longer the time interval between expo sures, the more puffs were required to caus ciliastasis.
Wynder et al. 1965, U.S.A. (235).	In rivo: Fresh water mussel ciliated epithelium	Various compounds in solution.	Formic, acetic, propionic, benzoic acids al more ciliatoxic than phenol. Oxalic acid less ciliatoxic than phenol. Formaldebyde, acrolein more ciliatoxic than phenol.
Carson et al., 1966, U.S.A. (44).	In vito: Cat traches.	Cigarette smoke.	Percent decrease in ciliary activity Control 6 Unfiltered smoke 53 Cellulose acetate filter 46 Carbon cellulose acetate filter 30
Dalhamn, 1966. Sweden (60).	In vivo: Cat traches.	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
Sensler and Battista, 1966, U.S.A. (155).	In rivo: Rabbit trachea, cat trachea, dog trachea, monkey trachea. rat trachea.	and components in Tyrode's	Rabbit traches—Total smoke condensate of 3 cigarettes, gas phase condensate of 7 cigarettes caused similar ciliastasis. Other species—All found sensitive to ciliastatic components of cigarette smoke. Bulk of activity noted in gas phase (HCH, formaldehyde, acrolein).

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, 1967, Sweden (61).	In vivo: Cat trachea.	Cellulone 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 traches.	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 traches.	Whole and filtered cigarette smoke exposed or unexposed 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 cilisted 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).
Battlata and Kensler, 1970, U.S.A. (29).	In vivo: Hen traches.	Cigarette smoke.	The authors observed that: (1) Whole smoke acutely depressed ciliary activity in 4-6 puffs. (2) Gas phase was only slightly less depressant than whole smoke. (3) Chronic exposure (1 cigarette/day for 32 days) to smoke resulted in no apparent permanent defect in ciliary activity (although mucous production was significantly 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 cigarette and cigar smoke.	Average number of puffs required to arrest ciliary activity Cigarette smoke
Kennedy and Elliott, 1970, U.S.A. (154).	In vivo: Protozoan (ciliated).	Mainstream cigarette smoke.	Electron microscopic observations: (1) After 7 minutes exposure—alteration of mitochondrial structure. (2) After 42 minutes exposure—destruction of internal mitochondrial membrane structure. (3) Gas phase alone, while ciliatoxic, did cause mitochondrial swelling but no disruption of membrane structure.

³ Unless otherwise stated, method entailed the direct observation of ciliary activity using markers.