

Longitudinal respiratory studies in older people

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Milne, J S (1978). *Thorax*, 33, 547-554. **Longitudinal respiratory studies in older people.** A random sample of older people in Edinburgh (215 men, 272 women aged 62-90 years) was examined with the MRC questionnaire on respiratory symptoms. The FEV₁ and FVC were recorded. Spirograms were repeated after one and five years and the questions after five years, the sample by then having been reduced to 133 men and 148 women.

After five years 7% of the surviving men and women had developed persistent cough and phlegm. This syndrome had disappeared in 12% of men and 2% of women. Dyspnoea had increased beyond grade 2 in 13% of men and 7% of women and had lessened only in 6% of women.

One-quarter of male and one-seventh of female cigarette smokers had given up smoking, mostly in the first year. Nearly all who stopped were symptomless before and after. In those men who stopped smoking before the study began symptom prevalence was similar to that in those who continued smoking.

Mean values of FEV₁ and FVC declined as age increased, the decline being greater in FVC with resulting rise in FEV₁%. Five-year differences in FEV₁ and FVC were symmetrically distributed with mean differences increasing with age. Mean differences in FEV₁ were 280-350 ml in men and 150-230 ml in women. Prediction equations from the first examinations remained usable for clinical work. Mean values of FEV₁ and FVC at the first examination were smaller in those who died compared with survivors, whether symptoms were present or not. The prevalence of symptoms was greater in those who died.

Several publications report data from population studies of respiratory function (Needham *et al*, 1954; Kory *et al*, 1961; Berglund *et al*, 1963; Ferris *et al*, 1965; Morris *et al*, 1973), but information in these about the elderly tends to be derived from a few subjects in series covering large age ranges. A few papers (Milne and Williamson, 1972(b); Schmidt *et al*, 1973) report studies made exclusively on the elderly. The present paper describes the repetition after one and five years of respiratory function tests in the subjects from one of these studies of the elderly. Details are also given about respiratory symptoms and cigarette smoking at follow-up.

Subjects

The people studied in the first examination were 215 men and 272 women aged 62-90 years who in 1968 formed a simple random sample of the population of 27 000 people in that age range living in

ten city wards in north Edinburgh. The method of sampling with a comparison of respondents and non-respondents has been described elsewhere (Milne *et al*, 1971). After the first examinations in 1968 and 1969 further examinations were made after one (1969/70) and five (1973/4) years. At the five-year examination it was possible to re-examine 113 men and 148 women. Information from these patients only has been used in analysing longitudinal data. During the five years 78 men and 60 women had died which left 24 men and 64 women surviving who for various reasons were not re-examined. Follow-up of the sample has been described in detail elsewhere (Milne and Chopin, 1975).

Methods

Subjects were questioned with the MRC questionnaire on respiratory symptoms (1965) at the first examination (1968/9). The questions were asked

again at the five-year review (1973/4). At the first examination smoking habits were studied in detail (Milne and Williamson, 1972(a)), but at the one-year and five-year reviews subjects were asked only whether they still smoked cigarettes and if so, how many a day. The reproducibility of the questionnaires was tested before the survey began (Milne *et al.*, 1970).

The respiratory function tests were the forced expiratory volume in one second (FEV₁) and the forced vital capacity (FVC) performed on a Vitalograph spirometer. This instrument was reported suitable by Drew and Hughes (1969) for measuring FEV₁ and FVC in population studies of normal subjects and of those with obstructive airways disease. Tests were performed with subjects sitting, and the best of three readings was used in the analysis. Height was measured with a Harpenden stadiometer. Reproducibility of the tests and calibration of the Vitalograph were satisfactory and have been reported elsewhere (Milne and Williamson, 1972(b)). The FEV₁% was calculated as (FEV₁ × 100)/FVC.

Results

SYMPTOM PREVALENCE AND INCIDENCE

Replies to questions from the MRC questionnaire on respiratory symptoms (1965) have been analysed in table 1 in respect of persistent cough and phlegm, chest infections, and dyspnoea at the original and at the five-year examination.

Cigarette-smokers were sought by the question: "Do you smoke cigarettes now?", which was also asked on each occasion. The first two columns

enumerate subjects in whom the symptom was present or absent on both occasions. The third column shows the proportion of subjects whose symptoms developed during the five-year period while the fourth column gives the proportion whose symptoms disappeared during the same period.

Some points from the table need comment. Similar proportions of men (7.1%) and of women (6.3%) developed persistent cough and phlegm during the five years. In the same period the syndrome disappeared in 11.6% of men and 2.1% of women. Only three men and two women became subject to repeated chest infections during the five years, while in two men and one woman this symptom disappeared.

Dyspnoea increased beyond grade 2 during the five years in 13% of men and 7.3% of women. In a similar proportion of women (6.5%) dyspnoea lessened, but this improvement was claimed by only one man.

One-quarter of the men and just over one-seventh of the women who admitted smoking cigarettes at the original examination gave up during the five years. Eleven of 14 men who stopped smoking during the five years gave up after one year, the corresponding figures in women being three of four.

There were no significant age differences in the incidence figures, which were therefore reported separately only by sex.

Stopping smoking during the five years of the study showed little effect on symptoms since 13 of 14 men and all four women who stopped during the period did not have persistent cough and

Table 1 *Respiratory symptoms and cigarette smoking, in a longitudinal study of older men and women, recorded at start of study and at five-year follow-up. (Percentages in parentheses)*

Symptom	Absent both times	Present both times	Present at 5-year exam only	Present at first exam only	No of Subjects
Men					
Persistent cough and phlegm	72 (64.3)	19 (17.0)	8 (7.1)	13 (11.6)	112
Persistent cough and phlegm plus chest infection	103 (92.0)	4 (3.6)	3 (2.7)	2 (1.8)	112
Dyspnoea worse than grade 2	79 (79)	7 (7)	13 (13)	1 (1)	100
Smokes cigarettes	55 (49.1)	42 (37.5)	1 (0.9)	14 (12.5)	112
Women					
Persistent cough and phlegm	123 (86.6)	7 (4.9)	9 (6.3)	3 (2.1)	142
Persistent cough and phlegm plus chest infection	139 (97.9)	0	2 (1.4)	1 (0.7)	142
Dyspnoea worse than grade 2	99 (79.8)	8 (6.5)	9 (7.3)	8 (6.5)	124
Smokes cigarettes	113 (79.6)	24 (16.9)	1 (0.7)	4 (2.8)	142

phlegm on either occasion of being questioned. The effect of stopping smoking earlier was not striking in older men. At the original examination 32 men smoked or had smoked cigarettes and admitted to persistent cough and phlegm. Ten of these men had stopped smoking cigarettes before the study began, but seven of these still had cough and phlegm at the five-year review. The mean time in years at the time of the original examination since stopping smoking was 11.6 (SD 10.0) with a range from one to 30 years. Of the remaining 22 men who continued to smoke, 12 had persistent cough and phlegm at the five-year review.

MEAN VALUES OF RESPIRATORY FUNCTION TESTS AT DIFFERENT STAGES OF THE STUDY

Mean values with 95% confidence limits of FEV₁ and FVC are given for men and for women, each sex being divided into subjects aged less than 70 years and 70 years and over at entry to the study (fig 1). For each age and sex group in the figure there are three means with confidence limits representing (reading from left to right) measurements made at the original examination and after one and five years. Values for FEV₁ are the lower and for FVC the upper groups in the diagram. The figure shows in each group a decline in the mean values as time passes.

The decline in mean values between those from the original examination and those obtained after

five years is steeper in all groups for FVC than for FEV₁. The actual figures in which the five-year difference is expressed as a percentage of the original reading are given in the lower part of figure 1.

Mean values of FEV₁% in the same age and sex groups are given in figure 2. All groups show an increase in the mean value during the five years, which corresponds to the greater reduction of FVC compared with FEV₁ during the five years.

THE ASSOCIATION OF RESPIRATORY FUNCTION TESTS AND SYMPTOMS WITH SURVIVAL

After five years the original sample was divided into those who had survived and those who had died during the period. Mean values with standard errors of FEV₁ and FVC are given in table 2 for those who died and for survivors in men and in women whose age at entry to the study was either less than 70 years or 70 years and more. In corresponding age and sex groups the values in those who died were significantly smaller, except in women aged under 70. There were only 16 deaths in this group, which makes the confidence limits large. The 14 women and two men missing from the table were unable to perform the tests because of intellectual impairment.

Mean values of FEV₁ and FVC were examined in the above age and sex groups of those who died, and survivors with each group were divided into those with and without persistent cough and phlegm. In those who subsequently died mean values were less than in the survivors, whether symptoms were present or not. Lower mean values were present in any age/sex group with symptoms compared with the corresponding group without symptoms. Of 32 differences examined in this way, only two reached statistical significance.

Values of FEV₁% were compared in members of the original sample who died or survived during five years. There being no age effect with this variable, division was by sex only. In men the mean value in those who died (63.3 SE 1.9 N 76) was significantly less than that in survivors (69.9 SE 1.1 N 137). The mean value in women who died (76.9 SE 2.2 N 44) was less than in surviving women (80.6 SE 0.8 N 199) but not significantly so.

Further division of those who died and survivors into those with and without persistent cough and phlegm showed mean values smaller in those who died than in survivors in corresponding groups, but none of the differences was significant.

The prevalence of respiratory symptoms and cigarette smoking, obtained at the original examination, is given for those who died and those who survived the next five years (table 3). In every

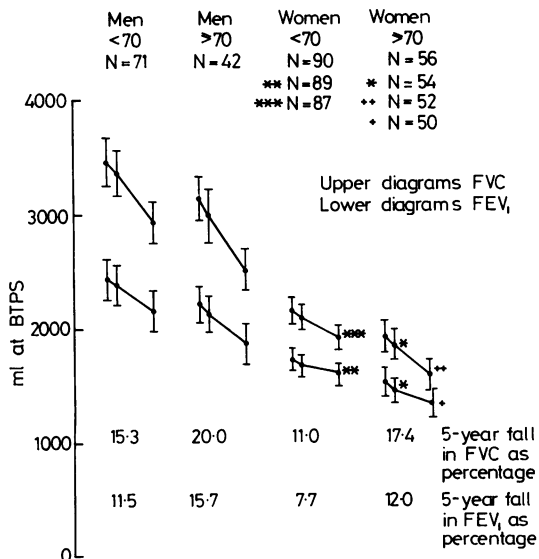


Fig 1 Mean values with 95% confidence limits of FEV₁ and FVC in two age groups of older men and women. Results, from left to right in each group, are from a longitudinal study at zero, one, and five years.

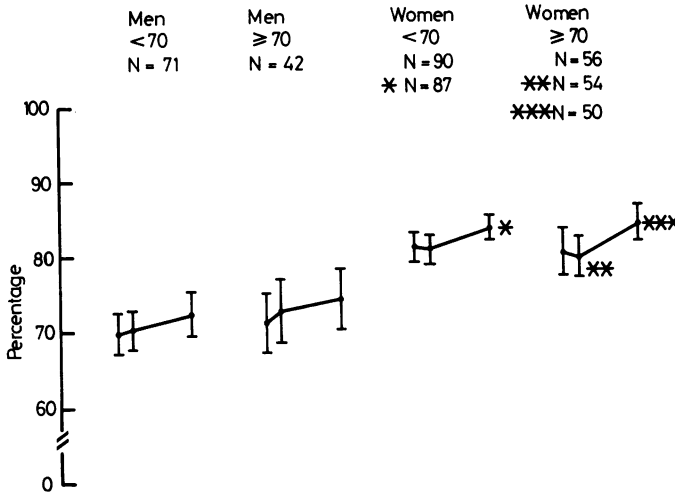


Fig 2 Mean values with 95% confidence limits of FEV₁% in two age groups of older men and women. Results, from left to right in each group, are from a longitudinal study at zero, one, and five years.

Table 2 Mean values with standard errors (SE) of FEV₁ and FVC, from first examination, in two age groups of men and of women divided into those who died during and those who survived subsequent five years (ml at BTPS)

Test	Age at entry	Men						Women					
		Survived			Died			Survived			Died		
		Mean	SE	N	Mean	SE	N	Mean	SE	N	Mean	SE	N
FEV	< 70	2397	80	88	1820	129	33	1713	44	119	1551	109	16
	≥ 70	2200	81	49	1719	122	43	1504	49	90	1104	80	33
FVC	< 70	3406	87	88	2880	166	33	2131	54	119	1993	118	16
	≥ 70	3171	96	49	2679	148	43	1895	56	90	1440	91	33

group, except cigarette smoking in women, the prevalence is greater in those who died than in those who survived. This difference reaches statistical significance in men in respect of persistent cough, persistent cough and phlegm with chest illness, and severe dyspnoea and in women in respect of severe dyspnoea only. Other points from the table are the higher prevalences of cough, phlegm, chest illness, and smoking in men and the higher prevalence of severe dyspnoea in women.

DIFFERENCES IN FEV₁, FVC, AND FEV₁% AFTER ONE AND FIVE YEARS

The differences in FEV₁, FVC, and FEV₁% after one and five years were calculated by subtracting, in each subject, the reading of each variable after one or five years from the reading at the first examination. Distributions of the one- and five-year differences, in men and in women, of each of the three variables are displayed in figures 3, 4, and 5. For FEV₁ and FVC the distribution moved further to the right after five years—that is a greater proportion of the sample showed a decrease in FEV₁ or FVC (figs 3 and 4). The distributions show that

the percentage of the sample with a difference in FEV₁ which was greater than zero—that is, which reflected a decrease in FEV₁ as time passed—rose from 66.4% of men and 63.5% of women after one year to 88.5% of men and 81.8% of women after five years. Corresponding percentages for FVC are 61.9% of men and 58.1% of women after one year and 92.0% of men and 86.5% of women after five years.

The distributions of FEV₁% moved to the left as time passed—that is, the value of FEV₁% rose. The percentages of the sample with a difference less than zero—that is, reflecting an increase in FEV₁% as time passed—rose from 53.1% of men and 44.1% of women after one year to 69.9% of men and 67.4% of women after five years (fig 5).

Attempts were made to relate symptoms to five-year differences in respiratory function tests by comparing mean values of five-year differences in FEV₁ and FEV₁% in those who did not admit to cough and phlegm on either occasion with those who admitted these symptoms on at least one occasion. A similar comparison was made between those who smoked or had smoked cigarettes with

Table 3 Prevalence of respiratory symptoms and cigarette smoking at first examination in those who died and those who survived the next five years. (Percentages in parentheses)

Variable under comparison	Dead		Survivors		P
	Absent	Present	Absent	Present	
Men					
Persistent cough	40	36 (47.4)	93	44 (32.1)	< 0.05
Persistent phlegm	38	38 (50)	85	52 (38)	NS
Persistent cough and phlegm	46	30 (39.5)	99	38 (27.7)	NS
Persistent cough and phlegm with chest illness	65	11 (14.5)	130	7 (5.1)	< 0.05
Dyspnoea worse than grade 2	52	19 (26.8)	118	12 (9.2)	< 0.01
Smokes or smoked cigarettes	14	62 (81.6)	29	108 (78.8)	NS
Women					
Persistent cough	47	10 (17.5)	177	34 (16.1)	NS
Persistent phlegm	45	12 (21.1)	181	30 (14.2)	NS
Persistent cough and phlegm	50	7 (12.3)	193	18 (8.5)	NS
Persistent cough and phlegm with chest illness	56	1 (1.8)	210	1 (0.5)	NS
Dyspnoea worse than grade 2	28	16 (36.4)	159	32 (16.8)	< 0.01
Smokes or smoked cigarettes	47	11 (19)	152	59 (28)	NS

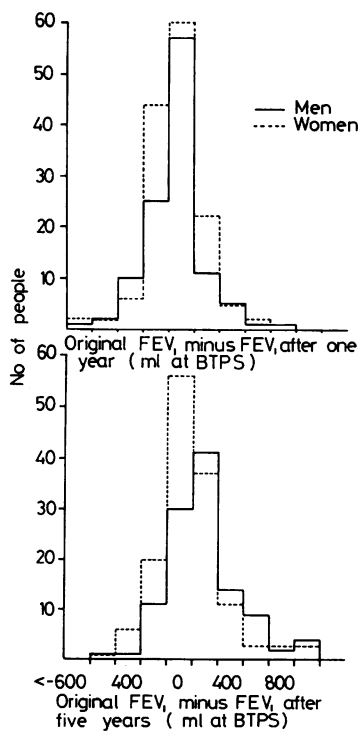


Fig 3 Distributions of one-year and five-year differences in FEV₁ in older men and women.

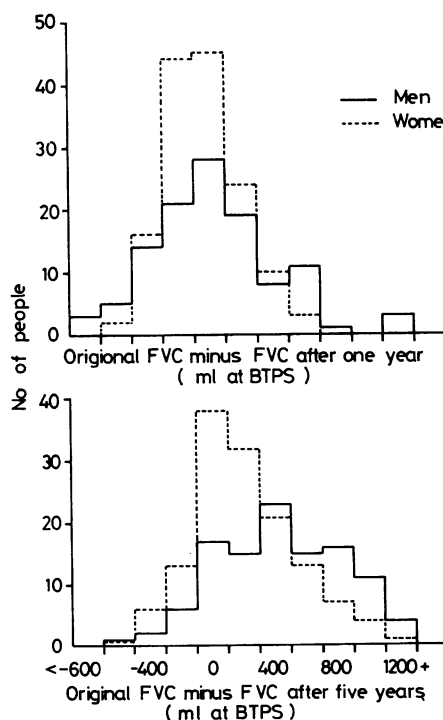


Fig 4 Distributions of one-year and five-year differences in FVC in older men and women.

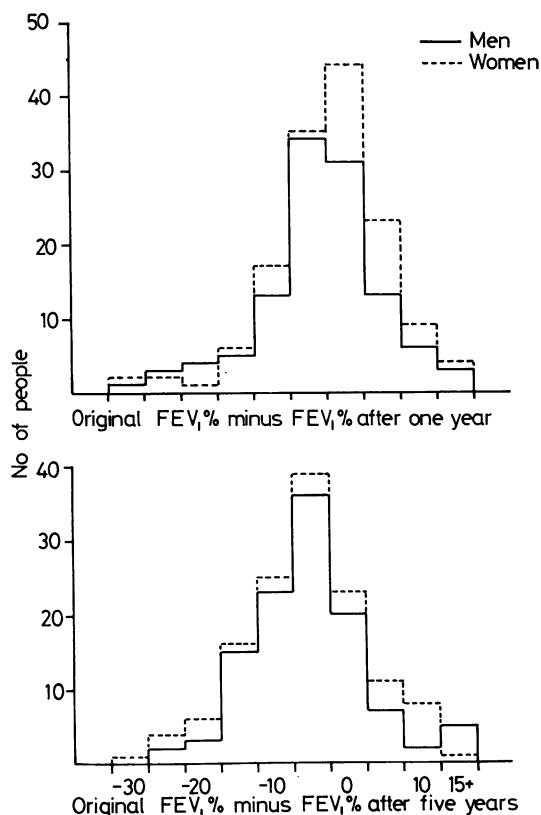


Fig 5 Distributions of one-year and five-year differences in $FEV_1\%$ in older men and women.

those who had not. None of these differences in either sex was statistically significant.

For each of the three variables (FEV_1 , FVC, $FEV_1\%$) the effect of age was examined in men and in women by the linear regression of the five-year difference on age at entry to the study. The equations showed that the differences with time in

FEV_1 and FVC increased significantly with increasing age at entry, but no age effects were found in respect of differences in $FEV_1\%$. Mean values of one-year and five-year differences are therefore displayed in table 4 in two age groups of men and women for FEV_1 and FVC and in all men and all women for $FEV_1\%$.

In both men and women mean values of differences in FEV_1 and FVC are larger in the older subjects (table 4). Seven of the ten means of one-year differences differ significantly from zero. The mean values of five-year differences are all significantly different from zero ($P < 0.001$).

COMPARISON OF PREDICTION EQUATIONS FROM THE ORIGINAL EXAMINATION AND FROM THE EXAMINATION OF FIVE-YEAR SURVIVORS
Prediction equations for FEV_1 and FVC were calculated, using age and height as the independent variables, in men and women without persistent cough and phlegm examined at the five-year review. The results are compared with the prediction equations from the original study in table 5. The differences between the regression coefficients are not statistically significant. The coefficient of regression on age of FEV_1 in men has become significant during the five years. The last column in the table shows values of FEV_1 and FVC calculated from the regressions for a subject aged 80 years with standing height of 1600 mm. Although calculated values in five-year survivors are smaller than such values in corresponding groups of the original study, the sizes of the standard errors of estimate suggest that the prediction equations from the original study (Milne and Williamson, 1972(b)) might still be valid for clinical work.

Discussion

This longitudinal study has shown the decline, as

Table 4 Mean values with SE of one-year differences and of five-year differences in FEV_1 , FVC, and $FEV_1\%$ in older men and women (volumes ml BTPS)

Sex and age		One-year difference			Five-year difference		
at entry	Variable	Mean	SE	N	Mean	SE	N
Men	< 70	54^*	27	71	280^{***}	35	71
	≥ 70	89^*	38	42	347^{***}	55	42
Women	< 70	47^*	19	89	150^{***}	28	88
	≥ 70	94^{**}	32	54	229^{***}	42	52
Men	< 70	102^{NS}	53	71	531^{***}	49	71
	≥ 70	156^*	60	42	627^{***}	75	42
Women	< 70	58^*	25	90	251^{***}	33	86
	≥ 70	104^{**}	31	54	379^{***}	54	50
All men	$FEV_1\%$	-0.90^{NS}	0.80	113	-2.79^{***}	0.74	113
All women		0.50^{NS}	0.71	143	-3.03^{***}	0.83	136

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; NS not significant.

Table 5 Prediction equations for FEV₁ and FVC, based on age and height, calculated from data from original examination and from examination of five-year survivors

	Sex and age range	Test	Const	Prediction equation			SE	R	N	SE about regression	Calculated value in subject aged 80, height 1.6 m
				Regr Coeff (Age)	SE	Regr Coeff (Height)					
Original study (1968/9)	Men 62-90	FEV	-3412.5	-14.10 ^{NS}	8.28	3.987***	0.756	0.43	142	643	1839
		FVC	-5009.0	-18.35*	8.95	5.681***	0.817	0.53	142	696	2613
	Women 62-90	FEV	-91.97	-26.57***	4.96	2.307***	0.441	0.50	226	427	1474
		FVC	-841.1	-26.97***	5.84	3.062***	0.519	0.50	226	485	1901
Five-year review (1973/4)	Men 67-95	FEV	-1108.3	-30.34**	11.15	3.322***	0.920	0.48	84	597	1780
		FVC	-486.6	-44.36***	10.81	3.994***	0.892	0.60	84	579	2355
	Women 67-95	FEV	1035.4	-30.33***	7.12	1.760*	0.678	0.46	118	403	1425
		FVC	643.3	-34.17***	7.74	2.381**	0.737	0.50	118	438	1719

NS=not significant; *P < 0.05; **P < 0.01; ***P < 0.001.

age increased, in values for respiratory function tests described by Fletcher and Peto (1977).

Prediction equations based on data from the five-year review did not differ significantly from the original equations (table 5). The exception was the coefficient of regression of FEV₁ on age in men, which was significant at the five-year but not at the original examination. The prediction equations of Schmidt *et al* (1973) produce values greater than those recorded in the first examination in the present study, but the size of the standard errors of estimate in the present study (table 5) means the differences are less than at first sight.

A study from Sweden (Wilhelmsen *et al*, 1969) reported five-year differences of 330 ml in vital capacity and 230 ml in FEV₁ in men aged 50 at entry to their study. These differences are smaller than those in older men in the present study, which has, however, shown that the differences increase with increasing age at entry. Other studies in industry (Higgins *et al*, 1968, Howard, 1970) have reported differences in FEV_{0.75} after five years. These results are not directly comparable with those from the present study but are of the same order of size. Cotes (1968) quotes a mean loss of FEV₁ with age in men of 300 ml per decade. The symmetrical distribution of differences in FEV₁ over six months in the study of Fletcher and Peto (1977) caused these authors to think that sudden large irreversible falls in FEV₁ were rare. The distributions of one- and five-year differences in the present study were also symmetrical.

In the present study the decline in FEV₁ and FVC increased with increasing age. This finding

is in agreement with the work of Fletcher and Peto. Howard (1970) reported a similar age effect on FEV₁ and FVC changes and that FVC fell more in a given time than FEV₁. He thought this was due to the greater size of FVC compared with FEV₁ and noted little change in FEV₁%. The present study showed a similar greater fall with a corresponding increase in FEV₁%, which was statistically significant and of the order of 3% (table 4).

Howard thought that the variation in the rate of decline of FEV₁ in individuals meant that the normal population without symptoms included subjects in whom the FEV₁ was declining rapidly. Hence the "normal" regression coefficient in prevalence studies could be too high. Recent work by Fletcher and Peto has shown that FEV₁ declines more rapidly as time passes in cigarette smokers than in non-smokers and that such smokers need not have symptoms. Higgins and Oldham (1962) found, in men aged 20-69 years, that the decline did not vary with age.

A ten-year follow-up of civil servants with chronic bronchitis (Oswald *et al*, 1967) showed that dyspnoea was the symptom that best estimated prognosis. The death rate in that study rose as the degree of dyspnoea at the original examination increased. The severer grades of dyspnoea were the symptom most likely to be associated with death in the present study.

Changes in symptom prevalence over a period are difficult to explain. Sharp *et al* (1973) in a seven-year longitudinal study of middle-aged men, in which the MRC questionnaire on respiratory

symptoms was used, found that symptom prevalence recorded at the start declined during the period of study. The original proportions of those with cough and phlegm and of those who smoked cigarettes fell during the seven years. This was true of cough and phlegm in men more than in women in the present study, while the proportion who smoked declined in both sexes. Dyspnoea worse than grade 2 tended to disappear in a greater proportion of women compared with men (table 1).

With respect to incidence of symptoms in men during the period of study, Sharp *et al* found that 6.6% of their men developed cough and phlegm and 16.5% developed dyspnoea during seven years, the corresponding figures during five years in the present study being 7.1% and 13%.

Many subjects in the present study who appear as non-smokers at the first and at the five-year examinations (30 of 55 men and 13 of 113 women in table 1) had once smoked cigarettes but stopped before the study began. The relatively small numbers who stopped during the study (14 men, 4 women) made it difficult to assess the effect of stopping. Fletcher and Peto in their eight-year longitudinal study of working men in London were able to separate the effect of smoking in increasing the rate of decline of FEV₁ with age from its effect in producing the syndrome of persistent cough and phlegm. The design of the present study and the possibly inaccurate information gathered about when smoking had ceased before the study began made it impossible to use the present study to describe such separation.

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