Relation of ventilatory impairment and of chronic mucus hypersecretion to mortality from obstructive lung disease and from all causes

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Abstract

The relation of ventilatory impairment and chronic mucus hypersecretion to death from all causes and death from obstructive lung disease (chronic bronchitis, emphysema and asthma) was studied in 13 756 men and women randomly selected from the general population of the City of Copenhagen. During the 10 year follow up 2288 subjects died. In 164 subjects obstructive lung disease was considered to be an underlying or a contributory cause of death (obstructive lung disease related death); in 73 subjects it was considered to be the underlying cause of death (obstructive lung disease death). Forced expiratory volume in one second, expressed as a percentage of the predicted value (FEV_1% pred), and the presence of chronic phlegm were used to characterise ventilatory function and chronic mucus hypersecretion respectively. For mortality analysis the proportional hazards regression model of Cox was used; it included age, sex, pack years, inhalation habit, body mass index, alcohol consumption, and the presence or absence of asthma, heart disease, and diabetes mellitus as confounding factors. By comparison with subjects with an FEV_1 of 80% pred or more, subjects with an FEV_1 below 40% pred had increased risk of dying from all causes (relative risk (RR) = 5·0 for women, 2·7 for men), a higher risk of obstructive lung disease related death (RR = 57 for women, 34 for men), and a higher risk of obstructive lung disease death (RR = 101 for women, 77 for men). Chronic mucus hypersecretion was associated with only a slightly higher risk of death from all causes (RR = 1·1 for women, 1·3 for men). The association between chronic mucus hypersecretion and obstructive lung disease death varied with the level of ventilatory function, being weak in subjects with normal ventilatory function (for an FEV_1 of 80% pred the RR was 1·2), but more pronounced in subjects with reduced ventilatory function (for an FEV_1 of 40% pred the RR was 4·2). A similar though statistically non-significant trend was observed with regard to obstructive lung disease related death. This study shows that impaired lung function is very strongly related to total mortality, obstructive lung disease related mortality, and obstructive lung disease mortality and suggests that chronic mucus hypersecretion, in those with impaired ventilatory function, is also a significant risk factor for death from obstructive lung disease.

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In patients with established chronic obstructive lung disease the degree of lung function impairment correlates well with prognosis and survival.[1–4] During the last decade several epidemiological studies have established that impaired lung function is also a significant predictor of death from all causes in subjects selected from the general population.[5–14] The number of population studies focusing on the ability to predict subsequent death from chronic obstructive lung disease has been small, however, because very large population cohorts are needed to observe a sufficient number of deaths from chronic obstructive lung disease. In a collaborative study collating the results from several different populations Peto *et al*[15] showed that ventilatory impairment, but not chronic mucus hypersecretion, was a very strong predictor of death from chronic obstructive lung disease. These findings supported the previous observations of Fletcher *et al* on the natural history of chronic obstructive lung disease, which were based on longitudinal measurements of pulmonary function,[16] and were recently confirmed by Ebi-Kryston, who analysed the data from the Whitehall study, a prospective study of 18 403 middle aged male civil servants.[17 18] Both the mortality studies were performed in the United Kingdom on men selected on the basis of their occupation.[15 17 18]

Some months ago Speizer *et al* reported in the community based "six cities" study in the United States that ventilatory impairment was the most powerful predictor of death from chronic obstructive lung disease.[19] They observed, however, that phlegm and cough were also significantly related to chronic obstructive lung disease mortality even after adjustment for the level of ventilatory function.[19] This latter finding challenges the idea that recorded symptoms of phlegm and cough are of no use in predicting death from chronic obstructive lung disease after FEV_1 has been taken into account.[15 17 18]

The present analysis was undertaken to investigate whether the previous observations are applicable to a Scandinavian population.

We have analysed data from the Copenhagen City heart study, a large prospective epidemiological study covering more than 14 000 men and women randomly selected from the general population. The main objective was to explore whether impairment of ventilatory function and chronic mucus hypersecretion were related to mortality from chronic bronchitis, asthma, and emphysema and from all causes.

Methods

POPULATION

The Copenhagen City heart study has been described in detail.[20 21] Briefly, the participants were selected from among 90 000 people living in a defined area around Rigshospitalet, the university hospital of Copenhagen. A sample of 19 698 subjects aged 20 years or more was selected at random after age stratification. The sample fraction was highest (50%) for those aged 40–69 years. The subjects were invited by letter to a health examination on a specific date during the period from 1 March 1976 to 31 March 1978. A total of 14 223 (74% of those invited) attended the examination.

The population sample described in the present paper comprised 13 756 subjects with the complete data required for the analysis. The subjects were followed until the end of 1987. Notification of deaths and cause of death was obtained from the central death register from the National Board of Health. In Denmark a physician, preferably the one who knew the patient best, must complete a death certificate for every death. The death certificate contains the assumed causes of death—always the underlying cause and in many cases also a secondary and a tertiary cause. The underlying cause is defined as the disease or injury that initiated the train of events leading directly to death, whereas the secondary or tertiary cause is a disease (often a disease that follows the underlying cause) that in some way could have 'contributed to death. Denmark still uses the eighth revision of the *International Classification of Diseases*[22] and there is no code describing chronic obstructive airways disease without mention of asthma, bronchitis, or emphysema. In the present paper two cause specific mortality analyses are presented. In the first analysis the end points were deaths where chronic bronchitis, emphysema, or bronchial asthma (that is, codes 490–3) were considered either an immediate or a contributory cause of death. These cases were labelled obstructive lung disease related deaths. The second analysis covered the cases where chronic bronchitis, emphysema, or asthma were considered the underlying (immediate) cause of death, the end points being labelled obstructive lung disease deaths.

The recordings of forced expiratory volume in the first second of expiration (FEV_1) and forced vital capacity (FVC) were made on an electronic spirometer (Monaghan N 403, Littleton, Colorado), which was calibrated daily. As a criterion for correct performance, at least two measurements differing by less than 5% from each other had to be produced. The largest volume was used in the analysis.

Predicted values of FEV_1 were based on spirometric data recorded among the never smokers with a daily consumption of alcohol of less than five drinks who did not suffer from diabetes mellitus, bronchial asthma, or heart disease and had no pulmonary symptoms. The values were obtained by estimating the regression of FEV_1 on age and height. The estimates in ATPS were:

Women:

$FEV_1(ml) = 410 - 27{\cdot}6 \times age\,(y) + 21{\cdot}2 \times height\,(cm)$

Men:

$FEV_1(ml) = 469 - 35{\cdot}2 \times age\,(y) + 32{\cdot}0 \times height\,(cm)$

Chronic mucus hypersecretion was said to be present when cough and sputum had lasted at least three months a year for more than one year. All subjects reported whether they were current smokers, ex-smokers, or never smokers and the duration of smoking. Ex-smokers were defined as former smokers who had stopped smoking more than one year before the examination. Current smokers reported their daily tobacco consumption and the type of tobacco smoked, and whether they inhaled. The total amount of tobacco smoked per day was calculated on the basis of the following equivalents: one plain or filter cigarette = 1 g; one cigar = 5 g; one cheroot or cigarillo = 3 g; one g of pipe tobacco = 1 g. An estimate of lifetime tobacco consumption was calculated as pack years (current tobacco consumption (g/day) × duration of smoking (y)/20). As an indicator of socioeconomic status we used the reported duration of school education. Body mass index was calculated as weight/height^2 (kg/m^2). Alcohol consumption was reported in the questionnaire as the number of drinks per day. The subjects were classified as having heart disease if they reported previous myocardial infarction or current use of heart medication in the questionnaire. Diabetes mellitus and bronchial asthma were registered when subjects gave positive answers to the relevant items in the questionnaire.

STATISTICAL ANALYSIS

The analysis is concerned with total mortality, obstructive lung disease related mortality, and obstructive lung disease mortality. We used the Cox proportional hazards model.[23] The regression coefficients were estimated by the maximum likelihood method as suggested by Cox, and the hypothesis of a significant influence of a variable or a first order interaction was assessed by the likelihood ratio test. The two explanatory variables of greatest interest were the FEV_1 as a percentage of the predicted value (FEV_1% pred) and the presence or absence of chronic mucus hypersecretion (yes or no). Other explanatory variables were age, smoking habits, alcohol consumption, body mass index, school education, and the presence or absence of diabetes mellitus, bronchial asthma, and heart disease. The variables with only two outcomes were included as binary variables, whereas variables with more than two outcomes were

sometimes included as continuous variates and sometimes represented by several binary variables, each characterising a specific category.

Initially we used many binary variables for smoking habits, alcohol consumption, and body mass index, taking into account the need to have an adequate number of cases in each category. The categories where the risk appeared to be similar were combined in the final model.

FEV_1% pred was initially included as a continuous variable, especially in the investigation of various interaction terms; but in the final models we used levels that are often used to describe ventilatory function in a clinical setting (≥80, 60–79, 40–59, <40% pred).

The final categories for the other variables were:

Smoking habit
Never-smokers
Ex-smokers 1:
subjects who had smoked for less than 35 years and had stopped smoking before enrolment
Ex-smokers 2:
subjects who had smoked for 35 years or more and had stopped smoking before enrolment
Smokers 1−:
current smokers with less than 35 pack years who did not inhale
Smokers 1+:
current smokers with less than 35 pack years who did inhale
Smokers 2−:
current smokers with 35 pack years or more who did not inhale
Smokers 2+:
current smokers with 35 pack years or more who did inhale.

Alcohol consumption
No daily consumption of alcohol, 1–4 drinks/day, 5 or more drinks/day.

Body mass index
<20 kg/m², 20–29 kg/m², ≥30 kg/m².

School education
<8 years, 8–11 years, >11 years.

Age
A continuous variable.

Sex, chronic mucus hypersecretion, heart disease, bronchial asthma, diabetes
Binary variables.

The level of significance was set at 5%. The results are given in terms of relative risk (RR)—the risk among subjects with a certain characteristic divided by the risk among those without that characteristic.

Table 1 Number of deaths from all causes and from obstructive lung disease (OLD) during the follow up period

Years of follow up	All deaths	OLD related deaths	OLD deaths
−2	275	18	5
3–4	372	19	7
5–6	443	37	16
7–8	482	42	17
9–10	515	30	18
11+	201	18	10
Total	2288	164	73

Table 2 Distribution of the participants and crude death rates according to the study variables

		No of deaths (% of total deaths)					
	Total	All causes		OLD related		OLD	
Women	7420	826	(11·1)	47	(5·7)	21	(2·5)
Men	6336	1462	(23·1)	117	(8·0)	52	(3·6)
Age (y):							
20–49	5157	238	(4·6)	11	(4·6)	3	(1·2)
50–59	4672	685	(16·3)	42	(6·1)	22	(3·2)
60–69	3107	923	(29·7)	79	(8·6)	32	(3·5)
70+	820	442	(53·9)	32	(7·2)	16	(3·6)
Chronic mucus hypersecretion:							
Absent	12142	1850	(15·2)	82	(4·4)	32	(1·7)
Present	1614	438	(27·1)	82	(18·7)	41	(9·4)
FEV_1 (% pred):							
≥80	10375	1358	(13·1)	55	(2·6)	10	(0·7)
60–79	2547	600	(23·6)	30	(5·0)	13	(2·2)
40–59	647	220	(34·0)	48	(21·8)	23	(10·5)
<40	187	110	(58·8)	51	(46·4)	27	(24·5)
Smoking habit*:							
Never smokers	2784	297	(10·7)	6	(2·0)	4	(1·3)
Ex-smokers 1	1836	208	(11·3)	20	(9·6)	11	(5·3)
Ex-smokers 2	459	175	(38·1)	14	(8·0)	8	(4·6)
Smokers 1−	1671	297	(17·8)	12	(4·0)	5	(1·7)
Smokers 1+	4947	677	(13·7)	59	(8·7)	24	(3·5)
Smokers 2−	553	190	(34·4)	10	(5·3)	3	(1·6)
Smokers 2+	1506	444	(29·5)	43	(9·7)	18	(4·1)
Alcohol (drinks/day):							
0	10145	1491	(14·7)	97	(6·5)	42	(2·8)
1–4	2758	641	(21·0)	46	(8·0)	19	(3·0)
5+	853	219	(25·7)	21	(9·6)	12	(5·5)
Asthma:							
Absent	13458	2207	(16·4)	133	(6·0)	55	(2·5)
Present	298	81	(27·2)	31	(38·3)	18	(22·2)
Heart disease:							
Absent	13150	1973	(15·0)	143	(7·2)	69	(3·5)
Present	606	315	(52·9)	21	(6·7)	4	(1·3)
Diabetes mellitus:							
Absent	13513	2184	(16·2)	161	(7·4)	72	(3·3)
Present	243	104	(42·8)	3	(2·9)	1	(1·0)
Body mass index (kg/m²):							
<20	1069	183	(17·1)	34	(18·6)	17	(9·3)
20–29	9343	1760	(15·9)	116	(6·6)	51	(2·9)
≥30	1239	345	(21·8)	14	(4·1)	5	(1·5)

*For definition of smoking habits see text. OLD—obstructive lung disease.

Results

During the follow up period 2288 subjects died. In 117 men and 47 women obstructive lung disease was registered as either the underlying or a contributory cause of death. In the 91 cases where obstructive lung disease was considered to be a contributory and not the underlying cause, the most common underlying cause was cardiovascular disease (35 cases) and neoplasm (28 cases). In 21 women and 52

Table 3 Estimated relative risk of obstructive lung disease related death in relation to FEV_1 % pred and chronic mucus hypersecretion, and the other explanatory variables

Variable	Relative risk (CI)			
	Women		Men	
FEV_1 (% pred):	***		***	
⩾80	1·0		1·0	
60–79	2·1	(0·8–5·6)	2·8	(1·4–5·3)
40–59	14	(5·8–33)	12	(6·3–21)
<40	57	(21–152)	34	(18–63)
Chronic mucus hypersecretion:			***	
Absent	1·0		1·0	
Present	1·5	(0·7–3·3)	2·8	(1·9–4·9)
Age (per year)	***		***	
	1·1	(1·07–1·15)	1·1	(1·08–1·13)
Asthma:	*		*	
Absent	1·0		1·0	
Present	2·7	(1·1–6·6)	1·9	(1·1–3·2)
Smoking habits:†	**			
Never smokers	1·0		1·0	
Ex-smokers 1	9·0	(2·0–42)	1·3	(0·3–5·3)
Ex-smokers 2	3·6	(0·3–41)	2·5	(0·7–8·8)
Smokers 1 –	2·8	(0·5–15)	1·1	(0·3–4·3)
Smokers 1 +	6·7	(1·5–31)	3·0	(0·9–10)
Smokers 2 –	5·0	(0·4–55)	1·9	(0·5–7·4)
Smokers 2 +	18	(1·3–94)	2·8	(0·8–9·6)
Body mass index (kg/m²):	*		*	
⩾30	1·0		1·0	
20–29	1·7	(0·5–5·8)	1·2	(0·6–2·3)
<20	3·8	(1·3–19)	3·5	(1·5–7·6)

*p < 0·05; **p < 0·01; ***p < 0·001.
†For definition of smoking habits see text.
CI—95% confidence interval.

Table 4 Estimated relative risk of death from obstructive lung disease in relation to FEV_1 % pred and chronic mucus hypersecretion and the other explanatory variables

Variable	Relative risk (CI)			
	Women		Men	
FEV_1 (% pred):	***		***	
⩾80	1·0		1·0	
60–79	3·2	(0·4–23)	5·7	(1·9–17)
40–59	31	(6·0–164)	24	(8·5–69)
<40	101	(16–633)	77	(27–220)
Chronic mucus hypersecretion:	*		**	
Absent	1·0		1·0	
Present	4·0	(1·3–13)	2·7	(1·4–4·9)
Age (per year)	***		***	
	1·1	(1·05–1·18)	1·1	(1·05–1·11)
Asthma:	*			
Absent	1·0		1·0	
Present	3·6	(1·0–13)	1·8	(0·8–3·8)
Smoking habits:†			*	
Never smokers	1·0		1·0	
Ex-smokers	4·7	(0·5–42)	1·5	(0·4–7·4)
Smokers 1	2·1	(0·2–19)	1·7	(0·3–7·2)
Smokers 2	6·1	(0·6–64)	2·6	(1·4–4·9)
Body mass index (kg/m²):	*		**	
⩾25	1·0		1·0	
<25	4·0	(1·1–14)	2·7	(1·4–4·9)

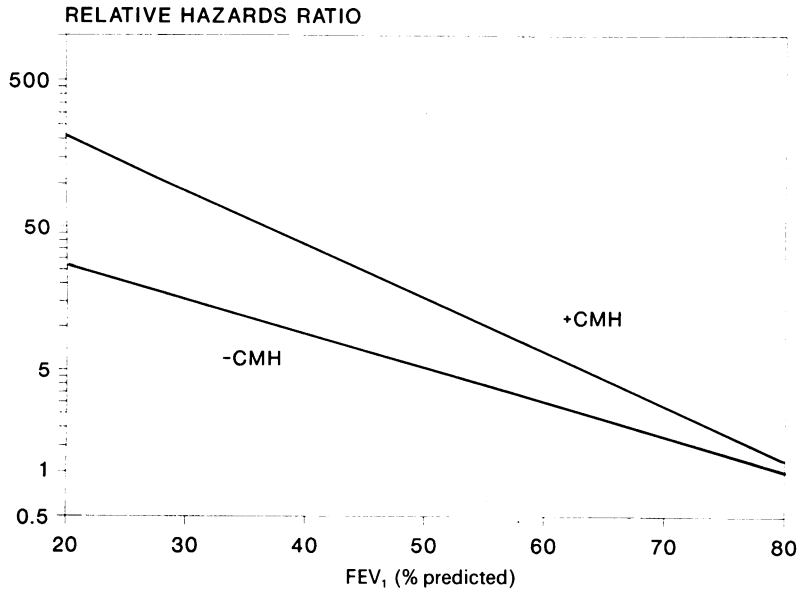
*p < 0·05; **p < 0·01; ***p < 0·001.
†Smokers 1: current smokers with less than 35 pack years; smokers 2: current smokers with 35 pack years or more.
CI—95% confidence interval.

men obstructive lung disease was considered as the underlying cause of death. The distribution of deaths during the follow up period is shown in table 1.

The distribution of the participants and crude death rates according to the study variables are given in table 2. The unadjusted incidence of death from all causes increased with age, lung function impairment, chronic mucus hypersecretion, smoking, and alcohol consumption. Mortality was higher in men than women and in subjects with bronchial asthma, diabetes mellitus, and heart disease than in those without these conditions. Subjects with a body mass index of 20–29 kg/m² had a slightly lower unadjusted mortality than those with both lower and higher values. Similar trends were observed with regard to obstructive lung disease related mortality and obstructive lung disease mortality except for the lack of an association between diabetes and heart disease and death and the fact that both obstructive lung disease related and obstructive lung disease deaths were more common in subjects in the lowest body mass index category (table 2).

Estimated relative risks for obstructive lung disease related mortality are given in table 3. In neither sex was the presence or absence of heart disease or diabetes, alcohol consumption, or the length of school education significantly related to mortality. The risk increased with decreasing FEV_1% pred and body mass index, with increasing age, and with the presence of bronchial asthma. Chronic mucus hypersecretion was significantly associated with obstructive lung disease death in men only, whereas lifetime tobacco consumption was related to mortality only in women.

The analysis of the obstructive lung disease mortality is shown in table 4. Among women there were no deaths from obstructive lung disease among the non-inhalers or those with the highest body mass indices. The grouping according to smoking habits and body mass index was therefore slightly modified. In both sexes FEV_1% pred and presence or absence of chronic mucus hypersecretion were significantly related to mortality. The analysis of first order interaction terms showed a significant interaction ($p = 0·02$) between the effects of FEV_1 and chronic mucus hypersecretion on obstructive lung disease mortality. This interaction indicates that chronic mucus hypersecretion was associated with only a slightly increased risk of obstructive lung disease death in subjects with a high FEV_1% pred, while the risk increased substantially with low values. The figure illustrates this interaction by showing the estimated relative risks for obstructive lung disease mortality obtained from a regression model with FEV_1% pred as a continuous variable. The remaining independent variables were the same as in table 4. The plot of relative risks for subjects with and without chronic mucus hypersecretion indicates that the relative effect of chronic mucus hypersecretion on obstructive lung disease mortality is small among subjects with a high FEV_1% pred (for an FEV_1% pred of 80 the RR is 1·2), but much higher among subjects with a low FEV_1% pred (for an FEV_1 % pred of 40 the RR is 4·2). Table 5 shows the raw data on which this interaction is based by giving the number of deaths from obstructive lung disease and the unadjusted observed rates of obstructive lung disease deaths per 100 000 person years according to the presence or absence of chronic mucus hypersecretion and the level of FEV_1% pred.



Estimated relative risk of death from obstructive lung disease according to the presence of chronic mucus hypersecretion (CMH) and the level of FEV_1. Derived from a Cox regression model including FEV_1% predicted and chronic mucus hypersecretion as the independent variables of interest and age, sex, asthma, smoking habits, and body mass index as explanatory variables. FEV_1% predicted was included as a continuous variable. The risk among subjects with an FEV_1% predicted of 80% and no chronic mucus hypersecretion was set to 1.

The results of the regression analysis of total mortality are given in table 6. The association of FEV_1 impairment with deaths from all causes was highly significant for both sexes, but much lower than the association with obstructive lung disease related and obstructive lung disease deaths. Chronic mucus hypersecretion was significantly associated with deaths from all causes only in men, the relative risk being much lower than that for obstructive lung disease deaths. A long duration of smoking and inhalation, heart disease or diabetes, a very high or very low body mass index, and both abstinence from alcohol and a high alcohol consumption were associated with a significantly higher risk of death (all causes), whereas asthma was not. There was no significant interaction between the effects of chronic mucus hypersecretion and FEV_1% pred with regard to total mortality.

Discussion

The results of the present study confirm the very strong relation between reduced FEV_1 and increased mortality, both from all causes and especially from obstructive lung disease. In addition, in line with the findings of Speizer *et al*[19] we report a statistically significant relation between chronic mucus hypersecretion and obstructive lung disease mortality. The latter association, although much weaker than that between low FEV_1 and death from obstructive lung disease, is not negligible among subjects with impaired ventilatory function.

Table 5 Unadjusted observed rate of obstructive lung disease deaths (per 100 000 person years) and the number of deaths from obstructive lung disease (n) according to FEV_1 % pred and chronic mucus hypersecretion (CMH)

FEV_1 (% pred)	No CMH (rate (n))	CMH (rate (n))
≥80	1 (7)	3 (3)
60–79	40 (9)	102 (4)
40–59	23 (10)	79 (13)
<40	82 (6)	310 (21)

An association between chronic mucus hypersecretion and mortality has been reported in several studies where the level of ventilatory function was not included in the analysis.[2 5-7 24] Only a few previous studies have shown a significant relation between chronic mucus hypersecretion and death from all causes after inclusion of the FEV_1.[12 15 25 26] In the Cracow study this relation was significant only in women,[12] and in our study only in men. The very low relative risk was very close to that found by Peto *et al*[15] and by Annesi and Kauffmann.[26]

The association found between chronic mucus hypersecretion and death from obstructive lung disease in the present study contrasts with the previous British findings.[15 17 18] Since the longitudinal studies of Fletcher *et al*[16] and Kauffmann *et al*[27] chronic mucus hypersecretion has no longer been thought to have a causal role in obstructive impairment of lung function; yet it is believed to predispose to airway infections.[16 28] In a recent prospective study Vestbo *et al* found a significant relation between mucus hypersecretion and admission to hospital on account of chronic obstructive lung disease after including FEV_1 in the analysis.[29] As airway infection in patients with impaired lung function is the most common precipitating cause of fatal respiratory failure, and as most deaths from chronic obstructive lung disease take place in hospital, it is surprising that no significant link between chronic mucus hypersecretion and death from respiratory disease and specifically chronic obstructive lung disease has been reported in the two previous population studies.[15 17 18] In the present analysis we looked carefully for a possible interaction between the effects of impaired FEV_1 and chronic mucus hypersecretion on obstructive lung disease mortality. Such an interaction was indeed present, suggesting that chronic mucus hypersecretion has an appreciable influence on the risk of death from obstructive lung disease only in those with already impaired ventilatory function. This observation is in accordance with the role of chronic mucus hypersecretion as a factor predisposing to respiratory infections, and with the recent suggestions of Fletcher and Pride.[30]

Although we think that the hypothesis that chronic mucus hypersecretion affects obstructive lung disease mortality by promoting respiratory infection is biologically plausible, we cannot exclude the possibility that the statistically significant association between chronic mucus hypersecretion and death from obstructive lung disease was spurious and due to residual confounding by some unmeasured aspect of smoking.

There are several possibilities for explaining the discrepancies between our findings and the results of the two previous British studies. Firstly, our study is community based and differs from the previous ones with regard to

Table 6 Estimated relative risk of death from all causes in relation to FEV_1 % pred and chronic mucus hypersecretion and the other explanatory variables

Variable	Relative risk (CI)			
	Women		Men	
FEV_1 (% pred):	***		***	
≥80	1·0		1·0	
60–79	1·6	(1·4–1·9)	1·3	(1·2–1·5)
40–59	2·5	(2·0–3·2)	1·5	(1·2–1·8)
<40	5·0	(3·3–7·6)	2·7	(2·1–3·5)
Chronic mucus hypersecretion:			***	
Absent	1·0		1·0	
Present	1·1	(0·9–1·3)	1·3	(1·1–1·4)
Age (y)	***		***	
	1·1	(1·09–1·18)	1·1	(1·08–1·12)
Smoking habits:†	***		***	
Never smokers	1·0		1·0	
Ex-smokers 1	1·3	(1·0–1·7)	0·8	(0·6–1·1)
Ex-smokers 2	1·3	(0·8–2·1)	1·2	(0·9–1·6)
Smokers 1−	1·4	(1·1 –1·7)	1·1	(0·9–1·5)
Smokers 1+	2·2	(1·7–2·7)	1·6	(1·3–2·0)
Smokers 2−	1·7	(1·2–2·6)	1·3	(1·0–1·7)
Smokers 2+	3·4	(2·5–4·7)	1·7	(1·3–2·1)
Body index (kg/m²):	**		*	
≥30	1·3	(1·1–1·6)	1·2	(1·0–1·4)
20–29	1·0		1·0	
<20	1·5	(1·2–1·9)	1·3	(1·0–1·7)
Heart disease:	***		***	
Absent	1·0		1·0	
Present	2·2	(1·7–2·9)	2·1	(1·8–2·4)
Diabetes mellitus:	***		***	
Absent	1·0		1·0	
Present	2·6	(1·8–3·8)	1·7	(1·3–2·6)
Alcohol (drinks/day):	*		*	
0	1·4	(1·1–1·8)	1·1	(0·9–1·2)
1–4	1·0		1·0	
≥5	1·4	(0·7–3·0)	1·2	(1·0–1·5)

*p < 0·05; **p < 0·01; ***p < 0·001.
†For definition of smoking habits see text.
CI—95% confidence interval.

the sex, age, and employment status of the participants. Secondly, there are several problems with establishing the cause of death. With elderly people who have been suffering from multiple disorders diagnosing the cause of death presents considerable difficulties, and death certification is known to vary between countries and with time.[31 32] Finally, the number of deaths from obstructive lung disease or chronic obstructive lung disease in any of these studies is not very large and further studies are therefore needed. To increase the number of endpoints we initially included in the analysis both the deaths where obstructive lung disease was considered the underlying cause and those where it was a contributory cause (obstructive lung disease related deaths). Further analysis showed that the results based on the "true" obstructive lung disease deaths were very similar. If this is true of other large studies, more data could be provided by analysing data on obstructive lung disease related deaths in other populations where the number of true obstructive lung disease deaths is too small for useful analysis.

We recently reported that chronic mucus hypersecretion as well as FEV_1 impairment is a significant though relatively weak predictor of death from lung cancer (RR = 1·5).[33] This finding, in conjunction with the present finding of an association between chronic mucus hypersecretion and death from obstructive lung disease, is in agreement with the view of Annesi and Kauffmann that, although chronic mucus hypersecretion is less important than ventilatory impairment, it should not be regarded as a negligible health problem.[26]

As in previous studies, men had a higher mortality than women, both from all causes and from obstructive lung disease. As only one previous analysis of mortality from chronic obstructive lung disease included women,[19] we paid special attention to the possible differences between the sexes. We found no systematic differences, though the increase in relative risk for both total and pulmonary deaths with decreasing FEV_1 seemed to be steeper in women than in men.

Our finding of a significant association between all cause mortality and alcohol consumption, body mass index, heart disease, and diabetes is in agreement with findings in previous epidemiological surveys.[7 12 34–37] Whereas subjects both with a very high and with a very low body mass index had an increased relative risk for death from all causes, only those with a very low body mass index had an increased relative risk for death from obstructive lung disease. This is consistent with the often reported emaciation that occurs in patients with advanced obstructive airways disease and with the fact that weight loss in patients with chronic obstructive lung disease is associated with increased subsequent mortality.[38 39] Low body mass index was significantly associated with higher mortality during the whole observation period, suggesting that it has a role as a predictor of death from obstructive lung disease not only in the immediate future but also in the long term.

Previous studies on mortality in patients with bronchial asthma have given different results, probably owing to selection of patients.[40–43] The unadjusted incidence of deaths, both from all causes and from obstructive lung disease, in subjects with asthma was higher than in the non-asthmatic subjects (table 2). After adjustment for the other explanatory variables, however, of which lung function was the most important, this relation remained significant for obstructive lung disease mortality but not for total mortality.

In conclusion, the present study confirms that impaired ventilatory lung function is strongly related to death from obstructive lung disease and from all causes. In contrast to some previous findings, our results suggest that chronic mucus hypersecretion is an additional risk factor for death from obstructive lung disease in patients with impaired ventilatory function.

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