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Remission of respiratory symptoms by smoking and occupational exposure in a cohort study

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Remission of respiratory symptoms by smoking and occupational exposure in a cohort study. T.M.L. Eagan, A. Gulsvik, G.E. Eide, P.S. Bakke. ©ERS Journals Ltd 2004.
ABSTRACT: Few studies have estimated the remission rates of respiratory symptoms in general populations. No community cohort studies have examined the impact of smoking cessation and previous dust or fumes exposure on the remission of respiratory symptoms.

In the Hordaland County Study, an 11-yr community cohort (1985–1996/1997) from Western Norway, data from 2,819 subjects were used to examine the remission of six respiratory symptoms.

The measured cumulative remission varied from 42.3% for morning cough to 58.4% for chronic cough. Smoking cessation was a significant predictor of remission of the cough symptoms and wheezing, with odds ratios (OR) (95% confidence intervals (CI)) varying from 2.2 (1.3–3.7) for wheezing to 6.2 (3.5–11.2) for morning cough, after adjustment for sex, age, pack-years smoked, previous dust or fumes exposure, and educational level. In those not previously exposed to dust or fumes, the adjusted OR (95% CI) for the remission of morning cough, phlegm cough, dyspnoea grade 2, attacks of dyspnoea and wheezing varied from 1.5 (0.9–2.5) for attacks of dyspnoea to 2.1 (1.1–3.9) for dyspnoea grade 2, as compared to those previously exposed to dust or fumes.

This study suggests a beneficial effect of smoking cessation and an adverse effect of occupational exposure on the remission of respiratory symptoms.
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A frequent observation from clinical practice is the transient nature of respiratory symptoms, both in patients with known obstructive lung disease and in otherwise healthy subjects. Knowledge of the natural history of respiratory symptoms is important when evaluating patients with or without known disease. While several community studies have assessed the incidence of respiratory symptoms [1–7], only two prior studies have examined the remission of respiratory symptoms in general population cohorts [4, 6].

Several community studies have shown a beneficial effect of smoking cessation on the decline in forced expiratory volume in one second (FEV1) [8–13]. However, only one previous cohort study has examined the effect of smoking cessation on respiratory symptoms, although this study compared incidence rates to persistence rates of the symptoms, not remission rates [14].

No community-based data have been found concerning how the remission of respiratory symptoms varies by occupational dust or fumes exposure or educational level. The current authors have previously shown that occupational exposure is an important risk factor for respiratory symptoms in a Norwegian community [15].

In the present study, data were used from the Hordaland County Study, a general population cohort followed for 11 yrs, to estimate the cumulative remission of six respiratory symptoms. Predictors examined were sex, age, smoking habits, previous dust or fumes exposure, and educational level.

Methods

Study population

In 1985, 4,995 randomly sampled subjects, aged 15–70 yrs, were surveyed in the county of Hordaland in Western Norway, with a mailed questionnaire regarding respiratory disease. The response rate was 90%. The sampling procedure and comparisons of responders *versus* nonresponders have been previously described [16]. A follow-up survey was conducted between the autumn of 1996 and spring of 1997 among the sub-sample of 3,786 subjects living in the city of Bergen and the 11 surrounding municipalities. After the exclusion of subjects not responding at baseline (n=416), or those who died within the follow-up period (n=189), 3,181 subjects were eligible for follow-up. A total of 2,819 subjects (89%) replied to a mailed questionnaire. The sampling procedure in 1996/1997 has been previously described in detail [17].

The questionnaires

The wording of the questions on respiratory symptoms is available in *Appendix 1*. The questions have previously been validated against lung function and bronchial reactivity [18], and compared with the British Medical Research Council questionnaire on chronic bronchitis [19]. The definitions of

smoking habits and pack-years have been published previously [7]. In 1985, the subjects were asked whether they had ever worked in a place with much dust or fumes in the air, and this was used as an indicator of previous airborne occupational exposure. In 1996/1997, the subjects were asked about their highest obtained education. By then, the youngest subjects were $\geqslant$26 yrs old and were likely to have reached university level education, if that was their "highest obtained education". Educational level was categorised into three categories: 1) those with up to 9 yrs of schooling (primary), those with 12 yrs of schooling (secondary) and those with a higher degree of education (university). Educational level is a commonly used indicator of socio-economic status [20, 21].

Data analysis

The cumulative remission of any symptom was defined as the proportion of subjects having a symptom at baseline who no longer reported the symptom at follow-up. Logistic regression models were used to estimate the adjusted odds ratios (ORs). The explanatory variables were sex, age, changes in smoking habits, pack-years until follow-up, dust or fumes exposure prior to baseline, and educational level (as reported at follow-up). The outcome variable was the symptom in question and a significance level of $p<0.05$ was chosen. Increasing age correlated with decreasing remission of all symptoms, when age was modelled as a categorical variable with 10-yr-category intervals. Pack-years smoked exhibited a similar relationship. Age and pack-years were thus modelled as continuous variables. Smoking habits were modelled as a five-category variable based on whether the subjects were smoking at baseline and/or follow-up, as follows: never-to-never, non-to-current (consisting both of never-to-current and ex-to-current), current-to-current, current-to-ex, and ex-to-ex. The possible first-order interactions were examined between smoking habits and the co-variables sex, age, educational level, previous dust or fumes exposure and pack-years smoked, respectively. Likewise, all first-order interactions between previous dust or fumes exposure and the other co-variables were examined. Finally, the regression analyses were conducted for each sex separately.

Results

The characteristics of the Hordaland County Study cohort are presented in table 1. There were more female never-smokers than male never-smokers. In addition, male ex- and current-smokers had smoked more pack-years than female smokers. Three times more males than females reported previous occupational dust or fumes exposure in 1985 (table 1). Thus, for the two main exposures, the male subjects were more heavily exposed. The males were also slightly younger than the females, and there were more males with a higher education (table 1).

The baseline prevalences of the six respiratory symptoms are shown in table 2. In general, the symptom prevalence at baseline was higher in subjects with a greater smoking consumption, previous dust or fumes exposure, and lower educational level (table 2).

The 11-yr cumulative remissions of the six symptoms are shown in table 3. The remission was highest for chronic cough and attacks of dyspnoea, and lowest for morning cough. There were no significant differences between the sexes in the remission of any symptom. For dyspnoea grade 2 and the cough symptoms, the remission decreased with increasing age. Current-to-ex smokers had a higher remission than current-to-current smokers of all symptoms, except dyspnoea grade 2. The remission of all symptoms decreased with heavier smoking measured in pack-years, although this was only statistically significant for phlegm cough, chronic cough and dyspnoea grade 2. Subjects with previous dust or fumes exposure had lower remission rates for all symptoms, whereas subjects with a higher degree of education had higher remission rates of all symptoms (table 3).

Table 1. – Characteristics of the Hordaland County Study cohort

	Total	Females	Males
Subjects n	2819	1467	1352
Age in 1985	38.2±15.2	38.9±15.7	37.4±14.6
Smoking habits			
Current-to-current	776 (28.9)	381 (27.6)	395 (30.4)
Non-to-current[#]	135 (5.0)	68 (4.9)	67 (5.2)
Current-to-ex	293 (10.9)	136 (9.8)	157 (12.1)
Ex-to-ex	420 (15.7)	167 (12.1)	253 (19.5)
Never-to-never	1058 (39.5)	631 (45.6)	427 (32.9)
Pack-years until 1996/97[¶]	12.0 (6–21)	9.9 (5–18)	15.0 (8–24)
Dust or fumes exposure in 1985			
Yes	798 (28.3)	191 (13.0)	607 (44.9)
No	2021 (71.7)	1276 (87.0)	745 (55.1)
Educational level in 1996/97			
Primary	501 (17.8)	279 (19.0)	222 (16.4)
Secondary	1536 (54.5)	813 (55.4)	723 (53.5)
University	720 (25.5)	341 (23.2)	379 (28.0)

Data are presented as n (%), median (interquartile range) or as mean±SD. [#]: consists of never-to-current and ex-to-current smokers; [¶]: only among current or ex-smokers.

The adjusted ORs for the remission of the six symptoms are presented in table 4. After adjustment of the variables included in the table, males had approximately twice the chance for remission of dyspnoea grade 2 when compared to females. Higher age was significantly associated with a decrease in remission for the cough symptoms and dyspnoea grade 2. The odds of remission of morning cough were approximately six times higher in those who had given up smoking as compared to persistent smokers, after adjustment for sex, age, pack-years, previous dust or fumes exposure, and educational level. The odds of remission among current-to-ex smokers were significantly higher than current-to-current smokers for all cough symptoms and wheezing. For all symptoms except wheezing, a higher smoking consumption was associated with a lower remission, however, this was not statistically significant.

The association between previous dust or fumes exposure and a decrease in remission was strengthened after adjustment, whereas educational level failed to be significantly associated with remission, except for the remission of chronic cough among those with a university level education.

There was a significant interaction between age and changes in smoking habits for the remission of dyspnoea grade 2. Increasing age predicted a lower chance for remission of dyspnoea grade 2 in all smoking categories, except current-to-current smokers. The OR (with 95% confidence interval (CI)) for the effect of a 10-yr increase in age, in current-to-current smokers, on the remission of dyspnoea grade 2 was 1.1 (0.7–1.6). For the other smoking categories, the ORs for the effect of age on the remission of dyspnoea grade 2 varied between 0.3 (0.1–1.2) among non-to-current smokers to 0.6 (0.4–0.8) among never-to-never smokers. There were no overt differences in the adjusted ORs for remission of any of the symptoms when the analyses were conducted for each sex separately.

Table 2. – The prevalence of respiratory symptoms (%) at baseline in 1985 for the Hordaland County Study

	Subjects n	Morning cough	Phlegm cough	Chronic cough	Dyspnoea grade 2	Attacks of dyspnoea	Wheezing
Sex							
Females	1467	18.2	17.2	8.0	11.8	13.0	18.5
Males	1352	23.7	25.0	11.2	8.1	11.3	22.0
Age in 1985							
15–29	980	19.2	21.7	9.9	6.0	10.9	22.2
30–49	1114	20.4	20.8	9.1	9.3	12.1	18.0
50–70	725	23.7	20.1	10.5	16.4	13.9	20.7
Smoking habits							
Current-to-current	776	37.2	32.9	17.3	11.0	17.4	36.5
Non-to-current	135	16.3	17.8	7.4	8.9	15.6	18.5
Current-to-ex	293	30.7	28.7	14.3	17.1	13.0	31.1
Ex-to-ex	420	9.3	13.8	13.8	9.1	11.2	11.9
Never-to-never	1058	11.8	14.2	6.1	8.2	8.4	9.5
Pack-yrs smoked							
1–10	656	14.9	19.4	6.6	5.8	10.8	18.0
11–19	496	29.0	25.0	12.5	11.9	14.1	31.7
⩾20	431	43.4	36.2	20.9	18.3	20.4	38.5
Dust or fumes exposure in 1985							
Yes	798	27.9	30.2	14.2	12.7	15.3	28.6
No	2021	18.0	17.3	8.0	9.0	10.9	16.9
Educational level in 1996/97							
Primary	501	25.6	23.0	11.6	15.6	12.6	23.8
Secondary	1536	22.2	21.4	10.0	9.6	13.5	21.2
University	720	15.1	18.5	7.8	6.7	8.8	15.1
Total	2819	21.1	20.7	10.0	11.2	12.2	20.6

Table 3. – The 11-yrs cumulative remission (%)[#] of six respiratory symptoms in the Hordaland County Study

	Morning cough	Phlegm cough	Chronic cough	Dyspnoea grade 2	Attacks of dyspnoea	Wheezing
Sex						
Females	40.5	51.4	57.6	41.0	54.7	44.9
Males	43.8	48.8	59.0	50.5	58.8	47.5
Age in 1985						
15–29	49.5*	59.2*	69.1*	69.5*	57.9	46.8
30–49	42.3	46.6	55.5	47.1	59.3	44.3
50–70	34.3	41.2	48.7	30.3	51.5	48.0
Smoking habits						
Current-to-current	33.9*	39.6*	53.7	50.6	54.1	40.3*
Non-to-current	36.4	50.0	50.0	66.7	66.7	36.0
Current-to-ex	72.2	56.0	73.8	38.0	65.8	57.1
Ex-to-ex	35.9	56.9	46.2	44.7	53.2	54.0
Never-to-never	41.6	61.3	65.6	41.4	56.2	45.0
Pack-yrs smoked						
1–10	53.1	61.3*	74.4*	71.1*	60.6	45.0
11–19	42.4	57.5	54.8	45.8	54.3	48.3
⩾20	36.4	48.4	50.0	38.0	56.8	42.7
Dust or fumes exposure in 1985						
Yes	35.9*	43.2*	55.8	39.6	50.8	41.2*
No	46.2	54.6	60.3	47.5	59.7	49.6
Educational level in 1996/97						
Primary	37.5*	47.8	43.1*	39.7*	47.6*	44.5
Secondary	40.5	48.0	57.5	41.2	55.3	44.0
University	54.1	58.7	75.0	62.5	69.8	50.5
Total	42.3	49.9	58.4	44.7	56.6	46.2

[#]: the number of subjects eligible for remission varies with each symptom, but can be obtained from table 2, where the baseline prevalence is given as a percentage of n. *: within-group differences in cumulative remission $p<0.05$ (Chi-squared test).

Discussion

The 11-yr cumulative remission varied from 42 to 58% for the six respiratory symptoms. There was a beneficial effect of smoking cessation on the remission of cough, attacks of dyspnoea and wheezing. This is the first study to show that previous dust or fumes exposure has a negative impact on the remission of respiratory symptoms in a general population sample.

First, there are some methodological considerations. A

Table 4. – The adjusted odds ratios for the remission of six respiratory symptoms in the Hordaland County Study

	Morning cough	Phlegm cough	Chronic cough	Dyspnoea grade 2	Attacks of dyspnoea	Wheezing
Subjects n	547	551	253	260	317	529
Sex						
Females	1	1	1	1	1	1
Males	1.2 (0.8–1.9)	1.0 (0.7–1.5)	1.2 (0.7–2.2)	2.0 (1.01–3.8)	1.4 (0.8–2.5)	1.1 (0.8–1.7)
Age per 10-yr increase	0.8 (0.7–0.97)	0.8 (0.7–0.9)	0.8 (0.6–0.99)	0.6 (0.5–0.8)	1.0 (0.8–1.2)	0.9 (0.8–1.02)
Smoking habits						
Current-to-current	1	1	1	1	1	1
Non-to-current	0.8 (0.3–2.1)	1.3 (0.5–3.1)	0.6 (0.2–2.4)	2.1 (0.5–8.5)	1.2 (0.4–3.5)	0.8 (0.4–2.0)
Current-to-ex	6.2 (3.5–11.2)	2.6 (1.5–4.5)	3.4 (1.4–8.4)	0.9 (0.4–2.1)	1.4 (0.6–3.1)	2.2 (1.3–3.7)
Ex-to-ex	1.0 (0.5–2.4)	2.5 (1.3–5.0)	0.5 (1.0–2.0)	1.5 (0.5–4.0	0.7 (0.3–1.6)	2.1 (1.03–4.2)
Never-to-never	1.0 (0.5–2.0)	2.3 (1.3–4.3)	1.0 (0.4–2.6)	0.9 (0.3–2.6)	0.8 (0.4–1.8)	1.5 (0.8–2.8)
Pack-years per 10 yrs increase	0.9 (0.7–1.1)	0.9 (0.8–1.1)	0.8 (0.6–1.01)	0.8 (0.6–1.1)	0.9 (0.7–2.4)	1.1 (0.9–1.3)
Dust or fumes exposure in 1985						
Yes	1	1	1	1	1	1
No	1.7 (1.1–2.5)	1.5 (1.02–2.2)	1.1 (0.6–2.0)	2.1 (1.1–3.9)	1.5 (0.9–2.5)	1.6 (1.1–2.3)
Educational level in 1996/97						
Primary	1	1	1	1	1	1
Secondary	1.0 (0.6–1.6)	0.8 (0.5–1.3)	1.6 (0.8–3.1)	0.7 (0.4–1.3)	1.3 (0.7–2.4)	0.8 (0.5–1.3)
University	1.5 (0.8–2.8)	0.9 (0.5–1.5)	3.0 (1.3–7.2)	0.9 (0.4–2.3)	2.2 (0.97–5.1)	1.1 (0.6–1.9)

Data are presented as odds ratio (95% confidence interval).

reporting error occurs when a subject replies "yes" when he or she should have replied "no" (over-reporting), or vice versa (under-reporting). In a longitudinal study, a possible reporting error in the outcome of interest can affect the estimates of the crude incidence or remission rates [22]. To what degree the crude incidence or remission is affected is dependent on the degree of reporting error and the prevalence of the outcome at baseline. The estimates of the remission are particularly vulnerable to a misclassification of the outcome, due to the inclusion of only symptomatic subjects at baseline. In the event of even a small over-reporting of symptoms, a relatively large over-estimation of the crude remission rate is possible (see Appendix 2). Furthermore, it has been shown that a non-differential measurement error in the outcome leads to an underestimation of the OR and a widening of the CI in an ordinary logistic regression analysis [23]. When the extent of misclassification is known, a method exists for correcting the estimates [23]. However, a recently published paper has shown that this conservative effect on the OR may not always be true for longitudinal studies [24], in which case there is currently no established method for correction of the estimates.

It is not known whether or not there is an actual reporting error in the present study. Ideally, validation of the outcome against an objective measure would provide an estimate of a possible misclassification. However, it is intrinsically difficult to produce an objective validation of morning cough, for example, in a large general population sample. Another approach would be to assess the repeatability of the answers to the questionnaire. This is also difficult in a study of respiratory symptoms, as one needs to ask the question while the symptom is still likely to be present, while not so close in time that the subject remembers their former reply. At least one study has been conducted on the repeatability on a questionnaire on respiratory symptoms in a general population from Western Norway [18]. Although repeatability was high, and in accordance with repeatability found in a study using the IUATLD Bronchial Symptom Questionnaire [25], there was almost certainly some misclassification in the outcome. Although the present authors believe under-reporting is more likely than over-reporting in a general population, cumulative remission rates are likely to be overestimated and there is some uncertainty regarding the precision of the estimated ORs.

Secondly, the 189 subjects who died before the follow-up study had a higher prevalence of all symptoms, except attacks of dyspnoea, at the baseline survey in 1985, as compared to those who survived. These 189 subjects were less likely to have a remission of their symptoms and this could also have lead to an overestimation of the remission.

Thirdly, the exact wording of the question regarding wheezing was changed from baseline to follow-up. Whereas the initial question asked about wheezing-ever, the follow-up is limited to wheezing within the last 12 months. This might lead to over-estimating the cumulative remission of wheezing.

Finally, the present study does not have data on the history of occupational exposure within follow-up for the sample. This is unfortunate, as it would be of interest to know whether reducing occupational exposure within the follow-up would increase the remission.

Two previous cohort studies have examined cumulative remission rates of several respiratory symptoms [4, 6]. In the Tucson, Arizona and Krakow, Poland cohorts, the follow-up lasted 12.2 and 13 yrs, respectively [4]. In general, the estimated annual remission rates from the current study are comparable to both the Tucson and the Krakow cohorts for chronic cough, phlegm cough, dyspnoea, attacks of dyspnoea and wheezing. In the Tucson/Krakow cohorts, the ORs for remission decreased with higher age for chronic cough and for dyspnoea, but not for wheezing and attacks of dyspnoea, and for phlegm cough only in smokers [4]. The present study confirms the effect of higher age on decreasing remission of the cough symptoms and dyspnoea, and not on attacks of dyspnoea and possibly wheezing. However, in the present study, the effect of age on the remission of phlegm cough was not dependent on smoking habits. The study of the Tucson/Krakow cohorts examined only the effect of current-to-current smokers *versus* never-to-never smokers on the remission, finding a lesser chance for remission of dyspnoea among male persistent smokers and of chronic cough among persistent smokers in both sexes [4].

The estimated annual remission rates in the cohort study from the Netherlands were two to three times higher for all symptoms as compared with both the Tucson/Krakow cohorts and the present study [6]. However, the follow-up in the Dutch study lasted 3 yrs and a comparison of estimated

annual remission between studies with varying lengths of follow-up may not be valid.

The cough symptoms can be interpreted as markers of inflammatory processes, reacting to irritant stimuli. The beneficial effect of smoking cessation on the remission of the cough symptoms is presumably due to the removal of the irritant(s). Dyspnoea on exertion can be caused by disease in the small airways and impairment of gas exchange [26]. The fact that smoking cessation did not have a beneficial effect on the remission of dyspnoea grade 2 could indicate irreversible damage. This is in accordance with studies on lung function in smokers, where ex-smokers did not regain their lost FEV_1 after smoking cessation [8, 9, 11, 12].

Attacks of dyspnoea and wheezing are indicators of intermittent airways obstruction. The finding of a beneficial effect of smoking cessation on the remission of wheezing and possibly attacks of dyspnoea could implicate a beneficial effect also on the remission of asthma.

Several cross-sectional community-based studies have observed a higher prevalence of respiratory symptoms in subjects with occupational airborne exposure as compared to those without occupational exposure [27–32]. Theoretically, this may be due to increased incidence or reduced remission of respiratory symptoms in exposed *versus* unexposed subjects. The present authors have previously shown the former to be the case [15]. This is the first study to show that there is an actual negative effect of previous dust or fumes exposure on the remission of respiratory symptoms.

Educational level did not significantly affect the remission of the symptoms, with the possible exceptions of a beneficial effect of a university level education on the remission of chronic cough and attacks of dyspnoea. The authors are not aware of previous studies on remission of respiratory symptoms adjusting for educational level or other measures of socio-economic status.

In conclusion, this study confirms the beneficial effect of smoking cessation to the remission of several respiratory symptoms. In addition, this is the first study to show a decreased remission of respiratory symptoms among subjects with prior occupational exposure, after adjustment for sex, age, smoking habits and educational level.

Appendix 1

The wording of the questions in 1985 and 1996/1997 regarding respiratory symptoms were similar, except for the questions on wheezing.

1985

Do you usually cough or clear your throat in the morning? [yes, no]

Do you usually have phlegm when coughing? [yes, no]

Do you have a cough for $\geqslant 3$ months altogether during a year? [yes, no]

Are you breathless when you climb two flights of stairs at an ordinary pace? [yes, no] (dyspnoea grade 2)

Do you sometimes experience attacks of breathlessness? [yes, no]

Do you ever have wheezing in your chest? [yes, no]

1996/1997

Have you had wheezing in your chest in the last 12 months? [yes, no]

Appendix 2

Consider a cohort study with a sample size of 1,000 and two time points. The baseline prevalence of the symptom in question is 15%, the true cumulative incidence 20% and the true cumulative remission 10% (table 5).

Table 5. – True findings from a hypothetical study

	Follow-up		
	No	Yes	Sum
Baseline			
No	680	170	850
Yes	15	135	150
Sum	695	305	1000

Given that 3% of subjects will over-report (*i.e.* say they have a symptom when in fact they do not) and 5% of the subjects will under-report (say they do not have a symptom when in fact they do), at both baseline and follow-up, table 6 would be obtained.

Table 6. – Observed findings in the study in the presence of a reporting error

	Follow-up		
	No	Yes	Sum
Baseline			
No	649.1	182.88	832
Yes	40.28	127.72	168
Sum	689.4	310.6	1000

In which case a cumulative incidence would be estimated as follows:

$$(182.88/832) \times 100 = 22\% \quad (1)$$

and the cumulative remission would be estimated as follows:

$$(40.28/168) \times 100 = 24\% \quad (2)$$

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