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Prevalence of comorbidity in patients with a chronic airway obstruction and controls over the age of 40

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ABSTRACT

The goal of this study is to determine the prevalence of 23 common diseases in subjects with a chronic airway obstruction and in controls. All subjects with a known diagnosis by their general practitioner of asthma or chronic obstructive pulmonary disease (COPD), and who were 40 years and older were selected (*n* = 1145). Subjects who were willing to participate (*n* = 591) and who appeared to have an irreversible airway obstruction (*n* = 290) were included. To recruit controls, a random sample was taken of 676 individuals who were 40 years and older and who were not diagnosed as having asthma or COPD by their general practitioner. Of these 676 individuals 421 were willing to participate. The presence of diseases was determined by using a questionnaire. One hundred and ninety-four subjects (73%) and 229 controls (63%) were shown to be suffering from one or more (other) diseases. In both groups, locomotive diseases, high blood pressure, insomnia and heart disease were most common. Locomotive diseases, insomnia, sinusitis, migraine, depression, stomach or duodenal ulcers and cancer were significantly more common in the subject group than in the control group. For both clinical and research purposes, it is important to consider the presence of diseases in patients with a chronic airway obstruction.

1. INTRODUCTION

Comorbidity may frequently occur in patients with a chronic airway obstruction who are over 40 years old. While this group mainly consists of chronic obstructive pulmonary disease (COPD) patients, most will have a history of heavy smoking. Both smoking and older age are considered risk factors for the occurrence of diseases. In addition, a chronic airway obstruction may in itself be a risk factor for other diseases, as it may result in complications such as heart failure.

Determining the presence of a combination of diseases is important for the clinical practice. First, it influences the quality of life of the patient [1,2], which results in an increased need for health care [3]. Second, diagnosis, treatment and prognosis will be influenced by the occurrence of diseases other than chronic airway obstructions.

Comorbidity is also an important methodological issue in clinical trials and in studies on health-related quality of life. Most of these studies exclude patients with comorbidities. If comorbidity is frequently seen in patients with a chronic airway obstruction, the external validity of these studies may to a large extent be limited. Furthermore, studies in which patients with comorbidity are included and compared with controls may encounter a confounding effect if the comorbidities turn out to be more common among the patient group than among the control group.

For both clinical and research purposes it is thus important to consider the presence of other diseases in patients suffering from a chronic airway obstruction. Nevertheless, it is unclear which diseases should be our main concern as there is only limited information on the frequency and kind of diseases in this patient group. Also, it is unclear which diseases are more common among patients with a chronic airway obstruction than among controls. Only a few diseases have thus far been described in the studies that we found [2,4–6]. Our study therefore determines the prevalence of 23 common diseases in patients with a chronic airway obstruction and in controls.

2. METHODS

2.1. Selection of subjects with a chronic airway obstruction

Twenty-eight general practices from urban and suburban regions in the western part of the Netherlands participated in this study. These practices covered almost 55,000 patients at the time of study. Selection of participants was carried out in three consecutive steps. First, all subjects who were registered with a diagnosis of asthma or COPD in their general practice and who were at least 40 years old were selected at one day in each practice. The 28 practices were visited between October 1996 and June 1997 ($n = 1236$).

Second, the general practitioners were then asked to exclude subjects who met the following criteria: poor cognitive functioning ($n = 35$), a poor mastering of the Dutch language ($n = 29$) and presence of an end-stage disease ($n = 27$). Third, all remaining eligible subjects ($n = 1145$) who were willing to participate underwent a lung function test and filled in a questionnaire between December 1996 and December 1997 ($n = 591$, response is 52%). Lung function data and questionnaire data were obtained on the same day.

Only subjects with a FEV_1/VC-ratio below the reference ratio minus 1.64 X standard deviation before and after inhalation of 400 μg salbutamol were included ($n = 290$). This way only subjects with a chronic obstruction of the airways were selected.

2.2. Selection of the control group

In November 1997, a random selection of 676 individuals was made from patients in 13 general practices who were not registered with a diagnosis of asthma or COPD and who were 40 years of age or older. These 13 practices were part of, and representative of, the 28 practices from which the subjects were selected. The sample was stratified: 178 controls between the age of 40 and 60 were selected and 498 controls of 60 years old or older. This was done because of an over-representation of subjects older than 60 years compared to the control population from which the selection was made. The general practitioners were again asked to exclude controls with poor cognitive functioning ($n = 30$), a poor mastering of the Dutch language ($n = 7$) and with an end-stage disease ($n = 2$) from the total sample of 676 individuals. Additionally, all controls with self-reported asthma or COPD were excluded ($n = 24$). Of the remaining eligible controls, 421 were willing to participate and filled in the questionnaire between April and July 1998 (response was 69%).

2.3. Data collection procedures

To determine the presence of comorbid diseases, all participants were asked to complete a questionnaire on 23 diseases. This questionnaire was developed by Statistics Netherlands and is broadly used in demographic studies in the Netherlands [7]. Diseases included in the questionnaire have a prevalence of more than 2% and are long-lasting by nature. With this questionnaire, participants were asked whether they were suffering from one or more of the 23 listed diseases at that moment. The diseases were described in a way that was easy to understand for the participants; for example, the term “high blood pressure” was used instead of “hypertension.” If participants indicated

that a particular disease was present, they were then asked whether they had used medication and whether they had visited a doctor for this disease in the past 12 months. The following diseases were listed: locomotive diseases (rheumatoid arthritis, arthrosis, slipped disc, disorder of the back for >3 months), hypertension, insomnia, serious heart diseases or myocardial infarction, sinusitis, migraine, depression, dizziness with falling, ulcer stomach/duodenum, cancer, atherosclerosis, thyroid diseases, diabetes, serious intestinal diseases for >3 months, serious skin diseases, gall bladder diseases, stroke, chronic cystitis, kidney stones, thrombosis, epilepsy, liver diseases and renal diseases. In addition, questions on demographic factors (gender, age, education, health insurance, living situation) and smoking were asked.

2.4. Analysis

In the questionnaire all participants were asked about the highest level of education they had received (six levels). The percentages of participants with a high and a low level of education were then calculated. We defined a lower level of education as primary school, lower vocational training and school for lower general secondary education. A high educational level was defined as pre-university education, high vocational training and university. From the data on smoking obtained with the questionnaire, the percentages of smokers, past smokers and never smokers were calculated. A past smoker was defined as someone who had stopped smoking for more than 5 years. A smoker was defined as a current smoker or as someone who had stopped smoking for less than 5 years. The number of diseases (0, ≥ 1 and 0, 1–2, 3–4, ≥ 5) was calculated only for those individuals who had filled in all questions on the presence of diseases.

Chi-square tests were carried out to test whether the prevalence of diseases differed between the subjects and the controls. P-values of less than 0.05 were considered significant. Logistic regression was carried out to adjust for potential confounders. In the logistic regression models the existence of a specific disease or the number (0, ≥ 1) of diseases present was the dependent variable. The independent variable of interest in this study was whether the respondent belonged to the subject group or to the control group. This way we could identify specific diseases that are more often seen in subjects with a chronic airway obstruction. All analyses were carried out using SPSS 8.0.2 for Windows.

3. RESULTS

3.1. Inclusion

Of the 1145 subjects with a known diagnosis of asthma or COPD, 591 were willing to participate (52%). Of these participants in the subject group 290 (49%) were found to have a persistent airway obstruction and were included in the analysis. Subjects without an airway obstruction before or after inhalation of salbutamol were thus excluded. The control group consisted of 421 participants who had filled in and returned the questionnaire. In the subject group the percentage of men among non-participants was 19% lower than among participants, but no difference in age was found. In the control group there were no significant differences in age and gender between non-participants and participants.

3.2. Characteristics of the research groups

In Table 1, the general characteristics of the two groups are presented. In both groups the mean age was 66 years, and one-quarter of the individuals were living alone. The percentages of men, of individuals with a low educational level and of individuals with Dutch National Health Service insurance were significantly higher in the subject group than in the control group. More than half of the patients (51.4%) had a mild airway obstruction (FEV_1 %pred >70%) and 21.7% had a serious airway obstruction (FEV_1 %pred <50%).

3.3. Prevalence of diseases in the subject group and the control group

The majority of individuals in each of the two groups reported one or more diseases (73% subjects and 63% controls) (Table 2). If only the diseases are taken into account for which the participant used medication or contacted a doctor in the past 12 months, the prevalence of diseases was 11% lower in the subject group (62%) and 12% lower in the control group (51%). In both cases the prevalence of

diseases (≥ 1) was significantly higher in the subject group than in the control group. In both groups half of the participants had one to two (other) diseases.

A logistic regression analysis was performed to adjust for differences in gender, education and insurance between the subject group and the control group. As the mean age was about the same in both groups (65.8 and 65.9), we did not adjust for age. The adjusted odds ratio was 1.60 (95% CI 1.10–2.33), which indicated that the risk of having a disease was about one and one-half times higher in the subject group. When the analysis for diseases for which subjects used medication or contacted a doctor was performed, the adjusted odds ratio was 1.56 (95% CI 1.10–2.20).

In Table 3 the prevalence of the 23 diseases in both the subject and the control group are shown. In both groups, locomotive diseases, high blood pressure, insomnia and heart disease were most frequently present. There were significant differences in the prevalence of locomotive diseases, insomnia, stomach and duodenal ulcers, migraine, sinusitis, depression, cancer and atherosclerosis between the two groups. The largest difference was 9.9% for sinusitis, the smallest difference was 3.7% for cancer.

Again, logistic regression analyses were carried out to adjust for differences in gender, education and insurance between the subject group and the control group (age was not adjusted for, as the mean age did not differ between the two groups). The adjusted odds ratios in the logistic regression models were significant for locomotive diseases (OR 1.55), insomnia (OR 1.65), stomach and duodenal ulcers (OR 7.33), migraine (OR 3.13), sinusitis (OR 6.08), depression (OR 2.10) and cancer (OR 2.47), indicating a higher risk of the disease in the subject group. While the univariate analysis showed a significant difference in the prevalence of atherosclerosis between the subject group and the control group, this was not the case after adjustment.

3.4. Prevalence of diseases in subgroups of subjects with a chronic airway obstruction

As can be seen in Table 4, the prevalence of one or more diseases increases with age, but is independent of gender, lung function, and smoking history. The same results were obtained for the number of comorbid diseases. The prevalence of locomotive diseases, insomnia and migraine was more common among female subjects (48.1%, 23.3% and 16.3%, respectively) than among male subjects (29.3%, 14.0% and 6.5%, respectively). The opposite was true for heart disease, which was more common among male subjects. Heart disease and high blood pressure occurred significantly more often in subjects older than 70, while the prevalence of sinusitis, migraine and depression was significantly higher in subjects younger than 55. The prevalence of sinusitis and depression were significantly higher in subjects with a mild airway obstruction than in subjects with a moderate-to-severe airway obstruction.

4. DISCUSSION

In this study we determined the prevalence of 23 diseases in a subject group with a chronic airway obstruction and a control group, both over 40 years of age. We found that the majority of subjects was also suffering from one or more other diseases, and that the prevalence of these comorbidities increased with age. The prevalence of comorbidities was 10–12% higher in the subject group than in the control group, depending on the definition used for comorbidity. Diseases that occurred more often in the subject group than in the controls were locomotive diseases, insomnia, sinusitis, migraine, depression, stomach/duodenal ulcers and cancer.

This study focussed on subjects with a chronic airway obstruction, which includes both COPD patients and patients with chronic asthma. The reason for not restricting our study population to COPD patients alone is that there is an important clinical overlap between COPD and asthma in elderly patients. Patients with a chronic airway obstruction who are older than 40 are thus a relevant group for the clinical practice, especially for general practitioners who most often have limited diagnostic facilities. We therefore selected subjects with a registered diagnosis of COPD as well as subjects with a registered diagnosis of asthma for this study. On the basis of lung function data we excluded subjects without an airway obstruction (treated or inactive asthma) and subjects with a reversible airway obstruction (51%) from the subject group.

There were some limitations of this study that need to be mentioned. First, no lung function testing was performed in the control group. It is therefore possible that some controls also had airway disease.

However, in all cases both the general practitioner and the participant in the control group said that there was no diagnosis of asthma or COPD. Moreover, a large community study in the Netherlands had previously shown that patients with an FEV_1 <90% and respiratory symptoms were almost all known to the general practitioner [8]. Only two out of one-thousand individuals turned out to have airway disease that was unknown to their GP according to these criteria. This corresponds to one patient with undetected airway disease in our control group. Still, milder types of airway disease may have been present in the control group. Yet as this study focussed on subjects with a chronic airway obstruction, this probably has been of little importance for our results.

A second limitation of the study may be that a high proportion of eligible subjects dropped out in comparison with the control group. This response may have been influenced by the lung function testing these subjects had to undergo. As a result, individuals with a comparatively worse state of health in the subject group may have dropped out relatively more often than individuals in the control group. This may have caused an underestimation of the prevalence of comorbidity in the subject group. The true differences in prevalence between subject and control group may have been even higher.

A third limitation of the study may be that the results were based on a subjective measure of comorbidity, namely the self-report of patients. Several studies have indicated that patients' self-reports are generally fairly accurate [9– 11]. However, for some diseases agreement between a questionnaire data and medical record data is rather poor, such as in the case of locomotive diseases [9,10]. These diseases may reflect a symptom rather than a physician-diagnosed disease. The data on these diseases should therefore be interpreted as such. Nevertheless, these data are expected to be valid for assessing the symptom rather than the diagnosis, because patients are considered to be the best experts in reporting perceived disease symptoms. Moreover, as misclassification of diseases is probably similar in the subject and the control group, the differences in prevalence between these groups will not have been affected. Similarly, the risk of having a disease represented by the odds ratios will not have been affected.

The high prevalence we found in our study for high blood pressure and heart disease was comparable in the two groups. Although these diseases are important for the clinical practice because of the high prevalence, they seem to be unrelated to chronic airway obstruction. Consistent with the literature, we found that heart diseases were more common among both the elderly and men [1].

The prevalence of locomotive diseases, insomnia, sinusitis, migraine, depression, stomach/duodenal ulcers and cancer was significantly higher in the subject group than in the control group. The high prevalence of locomotive diseases is difficult to explain, but may be related to a lack of physical exercise in the subject group. Stomach or duodenal ulcers and cancer may have been more common in the subject group because most of them (90%) were current or past smokers [12]. The percentage of smokers in the general Dutch population was much lower in 1997, namely 36% for individuals of 45 to 64 years of age and 21% for individuals older than 64 [13]. Although we have no information on smoking history in our control group (a random sample of the general practice population), there is no reason to suggest that their smoking behavior differs from the general Dutch population. The high prevalence of ulcers may also have resulted from the subjects' use of lung medication such as oral corticosteroids [14]. Sinusitis may have been more common in the subject group, as it may be associated with the inflammatory process in the airway system. Insomnia may also have been more common in the subject group as this group might suffer from breathlessness during the night. The higher prevalence of depression we found among subjects has also been mentioned in the literature [6,15].

An unexpected finding was that the prevalence of hypertension, heart disease and stroke, which are also related to smoking, were not higher in the subject group than in the control group. This may be due to the fact that the risk of death due to cardiovascular disease is much higher among subjects with ventilatory impairment than among subjects without ventilatory impairment [16]. As a result, a relatively high proportion of subjects with a chronic airway obstruction who also had cardiovascular disease may have died, subsequently causing a decrease in the prevalence of cardiovascular diseases in subjects with a chronic airway obstruction.

In conclusion, most patients with a chronic airway obstruction, especially older patients, suffer from other diseases and have a higher risk of diseases than controls. Therefore, the effect of other diseases

should be considered when treating a patient with a chronic airway obstruction and when discussing the consequences and prognosis of the disease. Excluding patients with comorbidity in clinical research, which is common practice, may severely limit the external validity. Of course, the extent to which the external validity is limited depends on which patients with which comorbid diseases are excluded. For example, the external validity is severely limited in a study conducted in elderly COPD patients that excludes patients with all kinds of comorbidity, while the external validity is hardly limited in a study conducted in middle-aged COPD patients from which only subjects with heart disease are excluded. Studies including patients with comorbidity should adjust for the potential confounding influence of comorbidity on outcome variables. This is particularly true for diseases that occur more frequently in the subject group than in the control group, such as locomotive diseases, insomnia, sinusitis, migraine, depression, stomach/duodenal ulcer and cancer.

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TABLES

Table 1
Characteristics of subjects and controls

Characteristic	Subjects[a] (n=290)	Controls (n=421)	P-value χ^2-test/t-test
Male	186 (64.1)	172 (41.1)	<0.001
Age	65.8 (10.9)	65.9 (12.5)	ns
Low education level	242 (86.1)	314 (79.5)	0.03
DNHS[b] insurance	231 (79.9)	284 (67.9)	<0.001
Living alone	75 (25.9)	107 (25.8)	ns
FEV_1 >70% predicted	149 (51.4)	—	—
FEV_1 50–70 predicted	78 (26.9)	—	
FEV_1 <50% predicted	63 (21.7)	—	
FEV_1 reversibility ≤12%	217 (74.8)	—	—

Data are expressed as numbers (%) or mean (SD).
[a]FEV_1/VC before and after salbutamol <predicted −1.64 × SD.
[b]Dutch National Health Service.

Table 2
Prevalence of comorbidity in subjects and controls

	All diseases					Diseases for which participants used medication or contacted a doctor				
	Subjects (n=265)		Controls (n=364)		Adjusted[b] odds ratio	Subjects (n=265)		Controls (n=364)		Adjusted[b] odds odds ratio
Number of diseases	n	(%)	n	(%)	OR (95% CI)	n	(%)	n	(%)	OR (95% CI)
0	71	(26.8)	135	(37.1)	1.60 (1.10–2.33)	100	(37.7)	180	(49.5)	1.56 (1.10–2.20)
≥1	194	(73.2)	229	(62.9)		165	(62.3)	184	(50.5)	
0	71		135		—	100		180		—
1–2	134	(50.6)	189	(51.9)		135	(50.9)	162	(44.5)	
3–4	42	(15.8)	32	(8.8)		21	(7.9)	16	(4.4)	
≥5	18	(6.8)	8	(2.2)		9	(3.4)	6	(1.6)	

[a]The number of diseases was only calculated for participants who filled in the complete questionnaire on diseases.
[b]The control group is the reference group, odds ratios are adjusted for gender, education and insurance.

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Table 3
Prevalence of specific diseases in subjects and controls and results of logistic regression

	Subjects (n=290)			Controls (n=421)			Adjusted odds ratios[a]	
Diseases	n	(%)	Ranking	n	(%)	Ranking	OR	(95% CI)
Locomotive diseases	104	(36.1)*	1	116	(28.6)	1	1.55	(1.09–2.20)
High blood pressure	65	(22.7)	2	87	(21.4)	2		
Insomnia	50	(17.3)*	3	46	(11.3)	3	1.65	(1.04–2.62)
Heart disease	38	(13.1)	4	45	(11.0)	4		
Sinusitis	36	(12.4)*	5	10	(2.5)	14	6.08	(2.87–12.89)
Migraine	29	(10.0)*	6	17	(4.2)	9	3.13	(1.60–6.13)
Depression	25	(8.7)*	7	18	(4.4)	8	2.10	(1.07–4.11)
Dizziness	21	(7.3)	9	20	(4.9)	6		
Ulcer stomach/duodenum	21	(7.2)*	8	6	(1.5)	20	7.33	(2.41–22.25)
Cancer	18	(6.2)*	10	10	(2.5)	15	2.47	(1.06–5.78)
Atherosclerosis	16	(5.5)*	11	7	(1.7)	17		
Thyroid diseases	14	(4.9)	12	19	(4.7)	7		
Diabetes	13	(4.5)	13	29	(7.1)	5		
Intestinal diseases	12	(4.2)	14	12	(2.9)	12		
Skin diseases	12	(4.2)	15	10	(2.5)	16		
Gall bladder diseases	11	(3.8)	16	7	(1.7)	18		
Stroke	9	(3.1)	17	15	(3.7)	10		
Chronic cystitis	9	(3.1)	18	7	(1.7)	19		
Kidney stones	8	(2.8)	19	12	(2.9)	13		
Thrombosis	7	(2.4)	20	13	(3.2)	11		
Epilepsy	4	(1.4)	21	4	(1.0)	21		
Liver diseases	1	(0.3)	22	2	(0.5)	22		
Renal diseases	1	(0.3)	23	1	(0.2)	23		

[a]The control group is the reference group, only significant odds ratios are given, odds ratios are adjusted for gender, education and insurance.
*P-value <0.05 (χ^2-test, subject/control × disease present/absent).

Table 4
Prevalence of ⩾1 disease and of the most common diseases in subgroups of subjects with a chronic airway obstruction

	Male (n=186)		Female (n=104)		FEV_1 <50% pred (n=63)		FEV_1 50–70% (n=78)		FEV_1 >70% pred (n=149)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
⩾1 disease[a]	123	(72.4)	71	(74.7)	41	(70.7)	52	(75.4)	101	(73.2)
Locomotive diseases	54	(29.3)*	50	(48.1)	17	(27.0)	29	(37.7)	58	(39.2)
High blood pressure	38	(20.8)	27	(26.2)	9	(14.8)	21	(27.3)	35	(23.6)
Insomnia	26	(14.0)*	24	(23.3)	12	(19.4)	9	(11.5)	29	(19.5)
Heart disease	30	(16.2)*	8	(7.7)	9	(14.3)	13	(16.9)	16	(10.7)
Sinusitis	19	(10.2)	17	(16.3)	6	(9.5)*	4	(5.1)	26	(17.4)
Migraine	12	(6.5)*	17	(16.3)	4	(6.3)	6	(7.7)	19	(12.8)
Depression	12	(6.5)	13	(12.6)	1	(1.6)*	5	(6.5)	19	(12.8)
Dizziness	13	(7.1)	8	(7.7)	1	(1.6)	7	(9.0)	13	(8.8)
Ulcer stomach/duodenum	13	(7.0)	8	(7.7)	5	(7.9)	6	(7.7)	10	(6.7)
Cancer	13	(7.0)	5	(4.8)	4	(6.3)	7	(9.0)	7	(4.7)
Atherosclerosis	10	(5.4)	6	(5.8)	1	(1.6)	5	(6.4)	10	(6.8)

	40–55 yrs. (n=50)		55–70 yrs. (n=118)		>70 yrs. (n=118)		Never smokers (n=27)		Past smokers[b] (n=103)		Smokers[b] (n=159)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
⩾ disease[a]	29	(60.4)*	73	(69.5)	89	(82.4)	15	(62.5)	73	(77.7)	105	(71.9)
Locomotive diseases	13	(26.0)	44	(37.6)	45	(38.5)	6	(22.2)	38	(37.6)	59	(37.1)
High blood pressure	3	(6.0)*	27	(23.5)	34	(29.1)	7	(25.9)	29	(28.2)	29	(18.7)
Insomnia	12	(24.0)	21	(17.9)	17	(14.4)	5	(18.5)	13	(12.6)	31	(19.6)
Heart disease	1	(2.0)*	16	(13.7)	21	(17.8)	1	(3.7)	17	(16.5)	20	(12.7)
Sinusitis	12	(24.0)*	11	(9.3)	12	(10.2)	3	(11.1)	14	(13.6)	18	(11.3)
Migraine	11	(22.0)*	9	(7.6)	9	(7.7)	7	(25.9)*	6	(5.9)	16	(10.1)
Depression	10	(20.0)*	8	(6.8)	6	(5.1)	2	(7.4)	8	(7.8)	15	(9.5)
Dizziness	5	(10.0)*	3	(2.6)	13	(11.1)	0		7	(6.9)	14	(8.9)
Ulcer stomach/duodenum	3	(6.0)	9	(7.6)	9	(7.6)	1	(3.7)	15	(4.9)	15	(9.4)
Cancer	1	(2.0)	4	(3.4)	11	(9.3)	0		8	(7.8)	10	(6.3)
Atherosclerosis	2	(4.1)	5	(4.2)	9	(7.6)	0	(0.0)	3	(2.9)	13	(8.2)

*P-value < 0.05 (χ^2-test, disease present/absent × e.g. male/female).
[a]⩾1 diseases was only calculated for subjects who filled in the complete questionnaire on diseases.
[b]Past smokers were defined as individuals who had stopped smoking for more than 5 years; smokers were defined as current smokers or as individuals who had stopped smoking for less than 5 years.

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