CHRONIC OBSTRUCTIVE PULMONARY DISEASE

An international survey of chronic obstructive pulmonary disease in young adults according to GOLD stages

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Background: The recently published GOLD guidelines provide a new system for staging chronic obstructive pulmonary disease (COPD) from mild (stage I) to very severe (stage IV) and introduce a stage 0 (chronic cough and phlegm without airflow obstruction) that includes subjects ''at risk'' of developing the disease.
Methods: In order to assess the prevalence of GOLD stages of COPD in high income countries and to evaluate their association with the known risk factors for airflow obstruction, data from the European Community Respiratory Health Survey on more than 18 000 young adults (20–44 years) were analysed.
Results: The overall prevalence was 11.8% (95% CI 11.3 to 12.3) for stage 0, 2.5% (95% CI 2.2 to 2.7) for stage I, and 1.1% (95% CI 1.0 to 1.3) for stages II–III. Moderate to heavy smoking (⩾15 pack years) was significantly associated with both stage 0 (relative risk ratio (RRR) = 4.15; 95% CI 3.55 to 4.84) and stages I+ (RRR = 4.09; 95% CI 3.17 to 5.26), while subjects with stages I+ COPD had a higher likelihood of giving up smoking (RRR = 1.39; 95% CI 1.04 to 1.86) than those with GOLD stage 0 (RRR = 1.05; 95% CI 0.86 to 1.27). Environmental tobacco smoke had the same degree of positive association in both groups. Respiratory infections in childhood and low socioeconomic class were significantly and homogeneously associated with both groups, whereas occupational exposure was significantly associated only with stage 0. All the GOLD stages showed a significantly higher percentage of healthcare resource users than healthy subjects ($p<0.001$), with no difference between stage 0 and COPD.
Conclusions: A considerable percentage of young adults already suffered from COPD. GOLD stage 0 was characterised by the presence of the same risk factors as COPD and by the same high demand for medical assistance.

The recently published Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines provide a new system for staging chronic obstructive pulmonary disease (COPD) from mild (stage I) to very severe (stage IV).[1] As a new approach, the GOLD guidelines have introduced a stage 0 which represents absence of airflow obstruction but presence of chronic symptoms such as cough and phlegm. This stage is meant to include subjects ''at risk'' of developing COPD later in life and to allow intervention while the disease is not yet a health problem. The simple classification of the disease severity into five stages is based on airflow obstruction as measured by spirometry, which is essential for diagnosis and provides a useful description of the severity of COPD.

The GOLD pragmatic approach, which aims at practical implementation of management, can also be useful for case identification and assessment of disease severity in epidemiological studies. In fact, the imprecise and variable definitions of COPD have so far made it hard to quantify the morbidity of this disease and to compare its variation between countries.[2] The specific forced expiratory volume in 1 second (FEV_1) cut off points of the GOLD staging, although not yet clinically validated, could allow an estimation of COPD severity in the general population which might help to optimise the allocation of healthcare resources.

COPD is most often diagnosed in the fifth or sixth decades, but there is already some evidence that it starts much earlier in life.[3–6] Only longitudinal studies of the younger population could allow early detection of the disease; they might highlight the natural history of those in the different GOLD stages and offer assessment of the likelihood of the disease progressing towards more severe stages.

The aim of the present study was to assess the prevalence of COPD severity stages, as defined in the GOLD guidelines, in high income countries and to evaluate whether subjects with stage 0 disease and those with more severe stages share a common pattern of risk factors and use of healthcare resources. Data from the European Community Respiratory Health Survey (ECRHS)[7] were used. This study collected information about health status, lung function, and other factors known or hypothesised to be associated with COPD[3] in more than 18 000 young adults (20–44 years) enrolled between 1991 and 1993 throughout the European Union and elsewhere. The results reported here are from 35 centres in 16 countries. The ongoing ECRHS II study[8] will allow the follow up of these subjects over time and their transition through the GOLD stages.

METHODS

Study design and subjects

The full protocol of the ECRHS has been described elsewhere.[7 9] Briefly, each participating centre selected an area of at least 150 000 inhabitants, defined by pre-existing administrative boundaries, and with an up to date sampling frame. In the first stage of the study, randomly selected samples of at least 1500 people of each sex, aged 20–44 years, were sent a screening questionnaire enquiring about respiratory symptoms, attacks of asthma, use of asthma medications, and hay fever or nasal allergies. In the second stage of the study a random sample of subjects who had completed the screening questionnaire was invited to come for a set of clinical and functional tests, including a standardised clinical interview and an assessment of lung function by spirometry.

For the purpose of the present analysis we considered all the subjects who participated in the second stage of the ECRHS (table 1).

Methods

According to the ECRHS protocol, baseline FEV_1 and forced vital capacity (FVC) were measured in all the subjects who consented. Up to five forced expiratory manoeuvres were performed and the highest FEV_1 and FVC that did not exceed the next highest one by more than 5% were considered for the present analysis. The questions on chronic symptoms and asthma used in the ECRHS were those of the 1976 version of the British Medical Research Council Questionnaire.[10]

Staging was defined according to the GOLD guidelines[1] as follows:

- stage 0 (at risk): presence of chronic symptoms (cough and/or phlegm from the chest, usually in winter and on most days for as long as 3 months each year) at the clinical interview and $FEV_1/FVC \geqslant 70\%$;
- stage I (mild COPD): $FEV_1/FVC < 70\%$ and $FEV_1 \geqslant 80\%$ predicted;[11]
- stage II (moderate COPD): $FEV_1/FVC < 70\%$ and FEV_1 50–80% predicted;
- stage III (severe COPD): $FEV_1/FVC < 70\%$ and FEV_1 30–50% predicted;
- stage IV (very severe COPD): $FEV_1/FVC < 70\%$ and $FEV_1 < 30\%$ predicted.

Subjects in stages I–IV could have or not have chronic symptoms.

Asthma was considered present if a subject replied affirmatively to the question "Have you ever had asthma?". All the subjects who reported asthma without chronic symptoms of cough and/or phlegm were not considered as having COPD. Subjects reporting asthma and chronic symptoms of cough and/or phlegm were considered as having COPD with coexisting asthma.

Subjects were classified according to smoking habits as current smokers, past smokers, and non-smokers. They were considered smokers (current or past) if they stated in the questionnaire that they had smoked at least 20 packs of cigarettes or 360 g of tobacco in a lifetime, or at least one cigarette per day or one cigar a week for 1 year. Current smokers were those who reported currently smoking and were divided into two subgroups according to the pack years smoked in a lifetime (light smokers <15 pack years; moderate to heavy smokers ⩾15 pack years), while a third subgroup comprised people who were currently smoking other tobaccos (cigars, cigarillos or pipe tobacco). Subjects were considered past smokers if they had been smokers (as defined above) and had stopped smoking at least 1 month previously. All the other subjects were considered as non-smokers. Furthermore, non-smokers and past smokers were both divided into two subgroups according to exposure to environmental tobacco smoke (ETS) (exposed if they reported having been exposed for at least 4 hours per day on most days or nights in the previous 12 months; and non-exposed otherwise).

Table 1 Number of subjects randomly selected for the second stage of the European Community Respiratory Health Survey and number (%) of participants

		Subjects selected	Participants	
Country	**Centre**	**N**	**n**	**%**
Spain	Barcelona	534	393	73.6
	Galdakao	576	486	84.4
	Albacete	658	435	66.1
	Oviedo	522	357	68.4
	Huelva	478	271	56.7
France	Bordeaux	2936	544	18.5
	Grenoble	1165	485	41.6
	Montpellier	3736	456	12.2
	Paris	3113	652	20.9
Italy	Pavia	816	312	38.2
	Turin	518	244	47.1
	Verona	504	354	70.2
Switzerland	Basel	1210	853	70.5
Germany	Hamburg	3312	1252	37.8
	Erfurt	1076	731	67.9
Belgium	Antwerp South	800	558	69.7
	Antwerp City	867	564	65.1
The Netherlands	Groningen	599	427	71.3
	Bergen-op-Zoom	638	496	77.7
	Geleen	671	439	65.4
Denmark	Aarhus	652	394	60.4
Sweden	Goteborg	772	682	88.3
	Umea	611	552	90.3
	Uppsala	709	625	88.2
Norway	Bergen	969	969	100.0
Iceland	Reykjavik	672	570	84.8
Ireland	Dublin	599	454	75.8
UK	Cambridge	527	277	52.6
	Ipswich	682	448	65.7
	Norwich	655	473	72.2
USA	Portland	1604	734	45.8
Australia	Melbourne	1644	669	40.7
New Zealand	Wellington	741	481	64.9
	Christchurch	712	459	64.5
	Hawkes Bay	549	316	57.6
Total		36827	18412	50.0

The other risk factors considered in the analysis were self-reported serious respiratory infections before the age of 5 years, a history of occupational exposure to vapours, gas, dust or fumes, and low socioeconomic class (as indicated by having completed full time education before the age of 16 years).

The use of healthcare resources was evaluated for each subject at the clinical interview by the following questions:

- ''Have you used any medicines (inhaled medicines, pills, capsules or tablets) to help your breathing at any time in the last 12 months?''
- ''Have you ever been seen by a doctor because of breathing problems or because of shortness of breath?''
- ''Have you ever visited a hospital casualty department or emergency room because of breathing problems?''
- ''Have you ever spent a night in hospital because of breathing problems?''

Statistical analysis

A total of 14 855 subjects who answered the questions on chronic symptoms during the clinical interview and who had at least two technically satisfactory measurements of FEV_1 and FVC were analysed.

Data were summarised as prevalence rates (%) with binomial exact 95% confidence intervals. Stage II (moderate COPD) and stage III (severe COPD) were combined as only eight subjects were classified in stage III. The ecological association between the prevalence rates of the GOLD stages was evaluated at the national level by the Spearman rank correlation coefficient (r_S). Meta-analysis was performed using the Mantel-Haenszel method to obtain pooled odds ratios across countries for the association between sex and GOLD stages. Pooled estimates were used when the χ^2 test for heterogeneity did not reveal different patterns in the various countries.

Multinomial regression models[12] were used to assess the association between the GOLD stages (stage 0 and stages I+) and active/passive smoking exposure, respiratory infections in childhood, occupational exposure, socioeconomic status, and sex. The relative risk ratios (RRR) were also adjusted for the effect of the ECRHS country.

The statistical analysis was performed using STATA software, release 7.0 (StataCorp, College Station, TX, USA).

RESULTS

The overall prevalence of subjects with COPD (stages I+) was 3.6% (95% CI 3.3 to 3.9); 2.5% (95% CI 2.2 to 2.7) were in stage I and 1.1% (95% CI 1.0 to 1.3) were in stages II–III, while there were no cases in stage IV. The prevalence of subjects in stage 0 was 11.8% (95% CI 11.3 to 12.3, table 2).

The prevalence of all the stages showed a substantial and statistically significant variation across countries: stage 0 ranged from 7.2% (95% CI 5.2 to 9.7) in Australia to 23.7% (95% CI 21.6 to 26.0) in Spain, stage I from 0.8% (95% CI 0.2 to 1.9) in Iceland to 7.4% (95% CI 5.6 to 9.5) in Switzerland, and stages II–III from 0.4% (95% CI 0.1 to 1.1) in Italy to 3.4% (95% CI 1.6 to 6.1) in Denmark.

In general, the geographical pattern of the prevalence of GOLD stages was not consistent across countries. The prevalence of chronic symptoms without obstruction (stage 0) was not significantly associated with the prevalence of COPD stage I ($r_S = 0.19$, $p = 0.49$; fig 1A), whereas stages I and II–III were only moderately associated ($r_S = 0.54$, $p = 0.03$; fig 1B).

Women had a lower prevalence of both COPD and chronic symptoms without obstruction than men: 2.4% (95% CI 2.1 to 2.8) *v* 4.8% (95% CI 4.3 to 5.3) and 10.9% (95% CI 10.2 to 11.7) *v* 12.6% (95% CI 11.9 to 13.4), respectively. This pattern was consistent within all the countries except Sweden where one centre (Uppsala) had a significantly higher prevalence of women than men in stage 0. The pooled estimate of the odds ratio for women *v* men was 0.85 (95% CI 0.77 to 0.94) for stage 0 and 0.49 (95% CI 0.41 to 0.59) for stages I+.

Among the subjects with airflow obstruction, 32.4% (95% CI 28.4 to 36.6) were symptomatic, 22.3% (95% CI 18.1 to 26.9) being in stage I and 54.5% (95% CI 46.6 to 62.2) in stages II–III. The percentage of subjects with coexisting asthma was not significantly different in stage 0 and in stages I+: 14.1% (95% CI 12.5 to 15.8) *v* 12.5% (95% CI 9.8 to 15.6), respectively.

The group of patients with COPD was significantly older and contained a higher percentage of men than did those with stage 0 disease or normal subjects ($p<0.001$, table 3). Compared with healthy individuals, subjects in stage 0 and in stages I+ had a significantly greater prevalence of moderate to heavy smokers, were more exposed to vapours, gas, dust or fumes at work, reported more respiratory infections in childhood, and were in a lower socioeconomic class. The

Table 2 Prevalence (%) with 95% confidence interval of the GOLD severity stages* for the countries participating in the European Community Respiratory Health Survey

	Stage 0 (n = 1751)	Stage I (n = 369)	Stages II–III (n = 168)
Spain	23.7 (21.6 to 26.0)	1.6 (1.0 to 2.4)	1.1 (0.6 to 1.7)
France	9.2 (7.9 to 10.5)	1.0 (0.6 to 1.6)	0.5 (0.3 to 1.0)
Italy	10.4 (8.3 to 12.8)	0.9 (0.4 to 1.9)	0.4 (0.1 to 1.1)
Switzerland	10.4 (8.3 to 12.8)	7.4 (5.6 to 9.5)	2.3 (1.3 to 3.6)
Germany	11.1 (9.6 to 12.7)	2.4 (1.7 to 3.2)	1.3 (0.8 to 2.0)
Belgium	11.7 (9.5 to 14.4)	3.4 (2.2 to 5.1)	2.4 (1.4 to 3.9)
The Netherlands	8.0 (6.6 to 9.6)	2.6 (1.8 to 3.6)	0.9 (0.4 to 1.5)
Denmark	12.5 (8.9 to 16.8)	4.4 (2.4 to 7.4)	3.4 (1.6 to 6.1)
Sweden	11.8 (10.2 to 13.5)	2.3 (1.6 to 3.2)	0.6 (0.3 to 1.1)
Norway	8.4 (6.7 to 10.4)	1.1 (0.5 to 2.1)	1.6 (0.9 to 2.7)
Iceland	11.0 (8.4 to 14.0)	0.8 (0.2 to 1.9)	1.1 (0.4 to 2.5)
Ireland	18.9 (14.6 to 23.8)	4.0 (2.1 to 7.0)	1.3 (0.4 to 3.4)
UK	9.8 (8.0 to 11.8)	2.3 (1.4 to 3.4)	1.0 (0.5 to 1.9)
USA	16.2 (12.6 to 20.3)	4.0 (2.2 to 6.5)	0.8 (0.2 to 2.3)
Australia	7.2 (5.2 to 9.7)	4.3 (2.8 to 6.4)	1.4 (0.6 to 2.8)
New Zealand	10.6 (8.6 to 12.9)	3.7 (2.5 to 5.2)	1.0 (0.5 to 2.0)
Total	11.8 (11.3 to 12.3)	2.5 (2.2 to 2.7)	1.1 (1.0 to 1.3)

*Eight subjects were in stage III and there were no patients in stage IV.

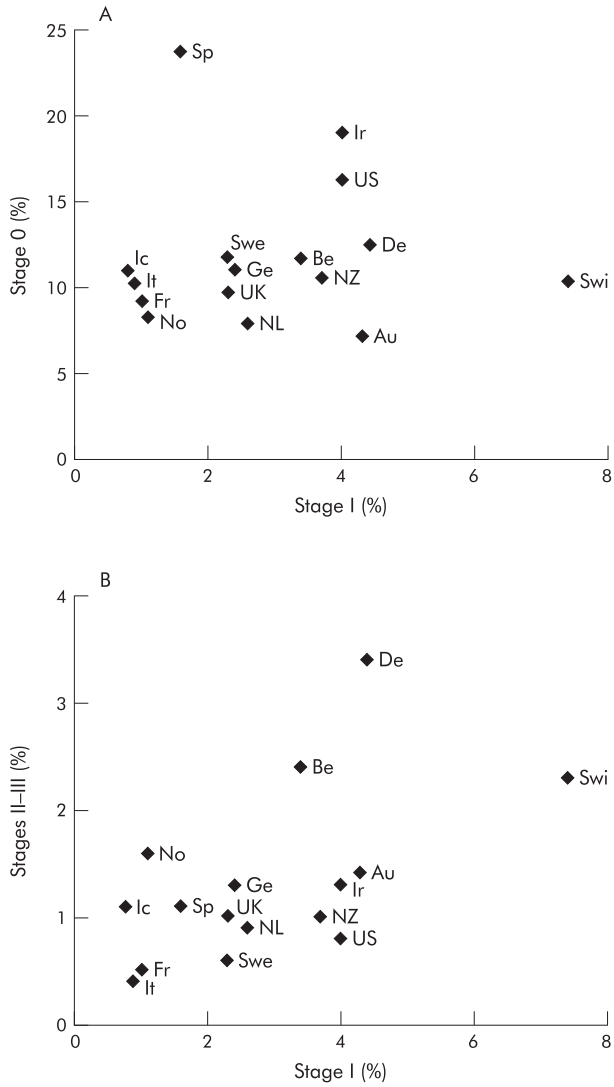

Figure 1 Scatterplots of the prevalences (%) of COPD stage I and (A) chronic symptoms without airflow obstruction (stage 0) and (B) COPD stages II–III. Each symbol represents the pair of values for a single country. Au, Australia; Be, Belgium; De, Denmark; Fr, France; Ge, Germany; Ic, Iceland; Ir, Ireland; It, Italy; NL, The Netherlands; NZ, New Zealand; No, Norway; Sp, Spain; Swe, Sweden; Swi, Switzerland; UK, United Kingdom; US, United States.

crude RRRs were positively associated with stage 0 and stages I+ for all the risk factors considered.

Following multivariate analysis, almost all the risk factors considered were significantly associated with both stage 0 and stages I+ (table 4). The strength of the association showed some variation between stages: subjects in stage 0 had a higher risk of being light (<15 pack years) or moderate to heavy smokers (≥15 pack years), while subjects in stages I+ had a higher likelihood of being past or moderate to heavy smokers and of smoking other tobaccos than did the healthy subjects. ETS (evaluated in non-smokers and past smokers) was moderately and homogeneously associated with both stage 0 and COPD. Respiratory infections in childhood and low socioeconomic class were significantly and homogeneously associated with both stage 0 and stages I+, whereas occupational exposure was significantly associated only with stage 0. After adjusting for all the risk factors, women had the same likelihood of having only chronic symptoms as men, while their likelihood of having airflow obstruction was significantly lower. When the same analysis was repeated excluding all the subjects with coexisting asthma classified in the GOLD stages, the pattern of associations was consistent with the main analysis (data not shown).

Compared with the group of healthy subjects, all the GOLD stages, including stage 0, were characterised by a significantly higher percentage of people who had visited a doctor (32.6% *v* 18.4%, p<0.001), had taken medication (24.1% *v* 14.0%, p<0.001), had attended an emergency department (ED) at least once and/or had had at least one hospital admission (10.8% *v* 5.1%, p<0.001) because of respiratory problems. Subjects in stage 0 and in stages I+ had a very similar use of healthcare resources. When all the subjects with coexisting asthma classified in the GOLD stages were excluded from the analysis, the percentage of healthcare resource users decreased by about one third in all the groups, whereas the relative pattern of consumption did not change (data not shown).

DISCUSSION

The results of our analysis show that in young adults (1) a considerable percentage of subjects already suffered from COPD and an even higher percentage of them reported chronic symptoms (stage 0); (2) the severity of the disease was still mild to moderate, with a wide variation among and within countries; (3) stage 0 and stages I+ of the GOLD classification of COPD identify groups of subjects that shared a common pattern of the individual risk factors and had a high use of healthcare resources because of respiratory problems.

To our knowledge, this is the first international study of almost 18 000 subjects that gives an estimate of the prevalence of COPD according to the GOLD definition and that focuses on the young adult population (aged 20–44 years). Based on this definition, our results support evidence that the disease develops earlier than is usually believed. This should be taken into account when planning future widespread programmes for early detection of the disease and preventive measures.[13]

The mean percentage of subjects with GOLD stage 0 was 11.8%, ranging from 7.2% in Australia to 23.7% in Spain. As expected with this young age group, the percentage of subjects with stages I+ disease was much lower than that of subjects with stage 0 disease, and no subject was found in the most severe stage (stage IV). However, despite their young age, the percentage of subjects with stages I+ disease was relevant (3.6%), with some countries showing a prevalence of more than 5% (Switzerland, Belgium, Denmark, Ireland and Australia).

Women had a lower prevalence of both chronic symptoms (stage 0) and COPD than men, which agrees with the findings of previous studies.[14–17] The sex difference in the prevalence was consistent across and within countries (except Sweden), and the men/women ratio increased significantly in the most severe stages. While the sex difference in chronic symptoms was entirely explained by the different distribution in exposure to the considered risk factors (as shown in the multivariate analysis), the significantly higher risk of having COPD for men may be due either to the fact that they were more exposed to other hazards (occupational, lifestyle, etc) not considered in the present analysis or to their greater susceptibility than women.

COPD can coexist with asthma even if the inflammation characteristic of the disease is distinct from that of asthma.[18] In our sample we found that 13.7% of the subjects classified in stages 0+ reported coexisting asthma. In these patients an overlap between asthma and COPD may have been present, but we could not exclude the possibility that chronic cough and phlegm were purely expressions of asthma. Unfortunately, because of the lack of information on diurnal

Table 3 Main characteristics of the subjects considered in the analysis according to the GOLD severity stages, and crude relative risk ratios (RRR)* with 95% confidence intervals for the association between each risk factor and the GOLD severity stage

	No respiratory disorders (n = 12567) %	Stage 0 (n = 1751)		Stages I+ (n = 537)	
		%	RRR (95% CI)	%	RRR (95% CI)
Active/passive smoking exposure:					
Non-smokers and ETS−†	37.9	21.4	1.00	24.0	1.00
Past smokers and ETS−	17.3	10.2	1.05 (0.87 to 1.27)	15.6	1.42 (1.07 to 1.89)
Non-smokers and ETS+	7.5	5.4	1.29 (1.02 to 1.64)	5.0	1.06 (0.69 to 1.62)
Past smokers and ETS+	4.4	3.1	1.23 (0.91 to 1.67)	4.0	1.45 (0.91 to 2.33)
Smokers (<15 pack years)	19.9	28.5	2.55 (2.20 to 2.94)	14.4	1.15 (0.86 to 1.53)
Smokers (⩾15 pack years)	11.5	30.1	4.65 (4.01 to 5.38)	33.5	4.58 (3.62 to 5.81)
Smokers (other tobaccos)‡	1.5	1.3	1.47 (0.93 to 2.31)	3.5	3.50 (2.09 to 5.86)
Presence of respiratory infections before the age of 5 years	8.9	12.2	1.47 (1.26 to 1.72)	14.1	1.71 (1.32 to 2.20)
Presence of occupational exposure to vapours, gas, dust or fumes in a lifetime	41.6	54.4	1.67 (1.51 to 1.85)	52.3	1.54 (1.29 to 1.83)
Low socioeconomic class	19.5	29.0	1.68 (1.50 to 1.89)	28.0	1.60 (1.30 to 1.97)
Females	51.1	46.3		33.7	
Mean (SD) age (years)	33.6 (7.2)	33.2 (7.1)		36.8 (6.5)	
Mean (SD) FEV_1 % predicted	106.6 (13.1)	103.9 (13.1)		86.6 (15.1)	

*Calculated by multinomial regression models (reference population: subjects with neither chronic symptoms nor airflow obstruction).
†ETS+/−: subjects exposed/not exposed to environmental tobacco smoke.
‡Cigars, cigarillos or pipe tobacco.

variation in symptoms or on airway hyperresponsiveness or on inflammation, a more precise diagnosis was not achievable.

In our study the lack of relationship between stages 0 and I and the weak relationship between stage I and stages II–III suggest that the progression from less to more severe stages is not a straight process affecting all patients. Likewise, many patients in stages I+ did not report chronic symptoms, either because they did not have them or because they did not recognise them.[4 19 20] These findings apparently agree with the results of the retrospective cohort study by Vestbo *et al*,[21] which made the authors conclude that GOLD stage 0 is of little help in identifying subjects at risk for COPD, while cigarette smoking itself remains the best predictor. However, the cross sectional nature of our data compels caution in interpreting the findings and cannot contribute to evaluation of the prognostic value of stage 0. In our opinion, this crucial point regarding aspects of global health policy requires truly prospective studies such as the ongoing ECRHS II. Our data can only spotlight the impressively high prevalence of subjects in stage 0, which represents an important health problem, as confirmed by the high use of healthcare resources found in these subjects.[22]

On the other hand, subjects in stage 0 shared the same risk factors as patients with COPD. Active smoking was strongly associated with both stage 0 and stages I+ COPD. The overall pattern of the association between smoking exposure and the GOLD stages strongly suggests that patients with more severe disease had given up smoking or had changed type of tobacco. Respiratory infections in childhood and low social class showed the same degree of association with both stage 0 and stages I+, as did ETS exposure which was moderately and positively associated with both stage 0 and stages I+ in non- and past smokers. At variance, after adjusting for the other risk factors, occupational exposure was associated with stage 0 but not with COPD, probably because more susceptible subjects were not employed in the most dangerous jobs (healthy worker effect) or because the question we used was not properly stated.

Table 4 Mutually adjusted relative risk ratios (RRRs)* (with 95% confidence intervals) for the association between the GOLD severity stages and active/passive smoking exposure, respiratory infections before the age of 5 years, occupational exposure to vapours, gas, dust or fumes in a lifetime, socioeconomic class, and sex

	RRR (95% CI)		Comparison between RRRs†
	Stage 0	Stages I+	
Active/passive smoking exposure (*v* non-smoker and ETS−)‡			
Past smoker and ETS−	1.05 (0.86 to 1.27)	1.39 (1.04 to 1.86)	0.10§
Non-smoker and ETS+	1.18 (0.92 to 1.51)	1.16 (0.75 to 1.80)	0.77¶
Past smoker and ETS+	1.15 (0.84 to 1.56)	1.41 (0.86 to 2.29)	
Smoker (<15 pack years)	2.38 (2.05 to 2.77)	1.22 (0.90 to 1.65)	<0.001††
Smoker (⩾15 pack years)	4.15 (3.55 to 4.84)	4.09 (3.17 to 5.26)	
Smoker (other tobaccos)**	1.45 (0.91 to 2.31)	3.25 (1.91 to 5.53)	
Respiratory infections (present *v* absent)	1.47 (1.25 to 1.74)	1.62 (1.24 to 2.12)	0.53
Occupational exposure (present *v* absent)	1.47 (1.31 to 1.65)	1.08 (0.88 to 1.31)	0.006
Socioeconomic class (low *v* high)	1.22 (1.07 to 1.40)	1.34 (1.05 to 1.71)	0.51
Sex (female *v* male)	1.00 (0.89 to 1.12)	0.55 (0.45 to 0.67)	<0.001

*Also adjusted for the effect of the ECRHS countries (reference population: subjects with neither chronic symptoms nor airflow obstruction).
†p values obtained by the Wald test.
‡ETS+/−: presence/absence of exposure to environmental tobacco smoke.
§p value for comparison between the adjusted RRRs for past smoking.
¶p value for comparison between the adjusted RRRs for exposure to environmental tobacco smoke.
**Cigars, cigarillos. or pipe tobacco.
††p value for comparison between the adjusted RRRs for current smoking.

Subjects with stage 0 and stages I+ disease used more healthcare resources because of respiratory problems than did healthy people. Those with stage 0 disease had the same utilisation of healthcare resources as individuals with stages I+ disease, even when the subjects with coexisting asthma were not considered, suggesting that the presence of chronic symptoms of cough and/or phlegm was the main reason for using healthcare services by patients of this age group with mild to moderately severe COPD.

One potential problem in interpreting our results is that there was a large variation in response rates across countries. A low response rate may lead to considerable overestimation or underestimation of the actual prevalence if participation in the survey is related to the presence of symptoms.[23] However, previous studies have shown that the effect of non-response was negligible in the second stage of ECRHS.[24 25] A further limitation that should be taken into account when considering the prevalence estimates at national level is that the centres were not selected to be representative of their countries and that, in some countries, only one centre was present.

In conclusion, COPD is an important health problem even in young adults, both because of the high prevalence of the disease and the frequent use of healthcare resources. Our study shows that GOLD stage 0 identifies a particular group of subjects exposed to the same risk factors as those with COPD and characterised by requiring medical assistance for respiratory problems as frequently as do COPD patients.

The ongoing follow up of these subjects in ECRHS II[8] will highlight the natural history of individuals in the different GOLD stages and will offer the possibility of assessing the likelihood of those in stage 0 progressing to more severe stages.

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REFERENCES

1 **National Institute of Health, National Heart Lung and Blood Institute (NHLBI)**. *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease*. Based on April 1998 NHLBI/WHO Workshop, April 2001 (updated 2003).
2 **Snider GL**. Nosology for our day: its application to chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2003;**167**:678–83.
3 **Cerveri I**, Accordini S, Verlato G, *et al*. for the European Community Respiratory Health Survey (ECRHS) Study Group. Variations in the prevalence across countries of chronic bronchitis and smoking habits in young adults. *Eur Respir J* 2001;**18**:85–92.
4 **Coultas DB**, Mapel D, Gagnon R, *et al*. The health impact of undiagnosed airflow obstruction in a national sample of United States adults. *Am J Respir Crit Care Med* 2001;**164**:372–7.
5 **Sobradillo Pena V**, Miravitlles M, Gabriel R, *et al*. Geographic variations in prevalence and underdiagnosis of COPD: results of the IBERPOC multicentre epidemiological study. *Chest* 2000;**118**:981–9.
6 **Calverley PM**. COPD: early detection and intervention. *Chest* 2000;**117**:365–71S.
7 **Burney PGJ**, Luczynska C, Chinn S, *et al*. for the European Community Respiratory Health Survey. The European Community Respiratory Health Survey. *Eur Respir J* 1994;**7**:954–60.
8 **Anon**. The European Community Respiratory Health Survey II. *Eur Respir J* 2002;**20**:1071–9.
9 **The European Community Respiratory Health Survey**. *Medicine and health*. EC Directorate General XIII. L-2920. Luxembourg: Office for Official Publications, 1994.
10 **Medical Research Council**. *Respiratory symptoms questionnaire*. London: The Council, 1976.
11 **Quanjer PH**, Tammeling GJ, Cotes JE, *et al*. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J* 1993;**16**(Suppl):5–40.
12 **Hosmer WH**, Lemeshow S. *Applied logistic regression*. New York: John Wiley & Sons, 1989.
13 **Cerveri I**, Accordini S, Corsico A, *et al*. for ISAYA Study Group. Chronic cough and phlegm in young adults. *Eur Respir J* 2003;**22**:413–7.
14 **Feinleib M**, Rosenberg HM, Collins JG, *et al*. Trends in COPD morbidity and mortality in the United States. *Am Rev Respir Dis* 1989;**140**(3 Pt 2):S9–18.
15 **Buist AS**, Vollmer WM. Smoking and other risk factors. In: Murray JF, Nadel JA, eds. *Textbook of respiratory medicine*. Philadelphia: WB Saunders, 1994:1959–87.
16 **Thom TJ**. International comparisons in COPD mortality. *Am Rev Respir Dis* 1989;**140**(3 Pt 2):S27–34.
17 **Xu X**, Weiss ST, Rijcken B, *et al*. Smoking, changes in smoking habits, and rate of decline in FEV_1: new insight into gender differences. *Eur Respir J* 1994;**7**:1056–61.
18 **Fabbri LM**, Romagnoli M, Corbetta L, *et al*. Differences in airway inflammation in patients with fixed airflow obstruction due to asthma or chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2003;**167**:418–24.
19 **Rennard S**, Decramer M, Calverley PM, *et al*. Impact of COPD in North America and Europe in 2000: subjects' perspective of Confronting COPD International Survey. *Eur Respir J* 2002;**20**:793–4.
20 **Becklake MR**, Kauffmann F. Gender differences in airway behaviour over the human life span. *Thorax* 2000;**55**:629.
21 **Vestbo J**, Lange P. Can GOLD stage 0 provide information of prognostic value in chronic obstructive pulmonary disease? *Am J Respir Crit Care Med* 2002;**166**:329–32.
22 **Cerveri I**, Corsico A, Zoia MC. GOLD stage 0. *Am J Respir Crit Care Med* 2003;**167**:936.
23 **de Marco R**, Verlato G, Zanolin E, *et al*. Nonresponse bias in EC Respiratory Health Survey in Italy. *Eur Respir J* 1994;**7**:2139–45.
24 **Janson C**, Chinn S, Jarvis D, *et al*. Physician-diagnosed asthma and drug utilization in the European Community Respiratory Health Survey. *Eur Respir J* 1997;**10**:1795–802.
25 **Burney P**, Malmberg E, Chinn S, *et al*. The distribution of total and specific serum IgE in the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1997;**99**:314–22.