Risk Factors for Chronic Obstructive Pulmonary Disease in a European Cohort of Young Adults

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Rationale: Few studies have investigated the factors associated with the early inception of chronic obstructive pulmonary disease (COPD). The main risk factor for chronic obstructive pulmonary disease (COPD) is active smoking. As it is generally considered to be a disease of the elderly, there is limited data on the incidence of COPD and its risk factors in young populations.

Scientific Knowledge on the Subject

COPD is characterized by progressive airflow obstruction and the destruction of lung parenchyma. Tobacco smoking is the main cause of COPD and it is also the main determinant of a poor outcome in those who have the disease (2, 3). Other factors may influence the risk of developing COPD. The host factors that seem to play a major role are age (4), a previous history of asthma (5), genes (6), and early respiratory infections (7). Among environmental determinants, occupational exposures (8) and exposure to biomass smoke (9) are primary risk factors. The role of sex, socioeconomic status (10), and body mass index (BMI) on the risk of developing COPD is still open to debate.

The current knowledge about the causes of COPD is generally based on data coming from the elderly population in whom the disease is frequent. However, the risk factors for the early inception of COPD are not well known, because only a few surveys have addressed young populations (11). Furthermore, no studies have investigated to what extent the identification of the risk factors of COPD depends on the criteria used to define the disease.

The aims of the present analysis were: (1) to assess the main risk factors of COPD incidence in an international European
cohort of young adults, and (2) to evaluate whether the identification of the risk factors may depend on the definition used for COPD.

For these purposes, the data from the European Community Respiratory Health Survey (ECRHS) were used. Some of the results of this study have been previously reported in the form of an abstract (12).

METHODS

Design of the Study

The ECRHS I is an international multicenter study on respiratory diseases, performed in 1991 to 1993 on random samples of young adults (20–44 yr) from the general population (13). Each participant was sent a brief screening questionnaire (stage 1), and from those who responded a random sample was selected to undergo a more detailed clinical examination (stage 2). The ECRHS II is a follow-up study of the participants in the ECRHS I stage 2, performed between 1999 and 2002, who underwent the same clinical examination as in the first survey (the full protocol is available at www.ecrhs.org) (14).

Ethical approval was obtained for each center from the appropriate ethics committee and written consent was obtained from each participant.

Subjects and Definitions

A total of 9,511 subjects from 24 centers in 10 European countries participated in the ECRHS I stage 2 (1991–1993: baseline), had valid lung function measurements (prebronchodilator values of FEV₁ and FVC) at baseline according to the American Thoracic Society criterion for reproducibility (15), and did not report having had asthma during lifetime as defined by a positive answer to the question “Have you ever had asthma?” (see Figure E1 in the online supplement). Of these individuals, 6,019 (63.3%) attended the second survey. After excluding the subjects with no valid spirometry and the subjects who reported having asthma during the follow-up, the cohort consisted of 4,636 subjects.

The maximum FEV₁ and FVC from at least two of up to five technically satisfactory maneuvers were considered in each survey. Incident COPD cases were defined according to the following three “modified” (in the sense that post-bronchodilator spirometry was not performed and postbronchodilator lung function measurements were used instead) diagnostic criteria: (1) Global Initiative for Chronic Obstructive Lung Disease (GOLD) (16), if they had a postbronchodilator FEV₁/FVC ratio less than 0.7 at follow-up (but not at baseline); (2) lower limit of normal (LLN) (Quanjer); and (3) LLN (LuftiBus), if they had a prebronchodilator FEV₁/FVC ratio less than or equal to the LLN at follow-up (but not at baseline), where the LLN was computed using the Quanjer and colleagues (17) or the LuftiBus (18) equations, respectively. The latter were used because they represent the most recent reference equations obtained in a large sample of the European population. Moreover, among the published European reference equations, the Quanjer and LuftiBus equations represent the extremes of the expected FEV₁/FVC values (18).

Accordingly, 112 (GOLD), 116 (LLN [Quanjer]), and 205 (LLN [LuftiBus]) subjects with COPD at baseline (“prevalent cases”) were excluded from the corresponding incidence analysis.

The potential determinants considered in the analysis (listed in Table 2) are fully described in the online data supplement.

Statistical Analysis

The analysis was performed separately for each COPD criterion (GOLD, LLN [Quanjer], and LLN [LuftiBus]). Incidence rates of COPD were estimated as the ratio between the number of new cases and the number of person-years at risk (per 1,000), which were considered to be equal to the length of the follow-up for each member of the cohort who was COPD-free at baseline. Exact 95% confidence intervals were computed using the Poisson distribution.

The association of each predictor with the incidence of COPD was estimated by the incidence rate ratio (IRR) and the population-attributable fraction (PAF) (19). The IRRs were computed using two-level random-intercept Poisson regression models (20) (level 1 units [subjects] nested into level 2 units [ECRHS centers]) with robust standard errors (obtained by the Huber/White/sandwich estimator of the variance (21)). The models had a dummy indicator of the occurrence of COPD as the dependent variable, a random-intercept term at level 2, and all the predictor variables as fixed effects. The PAFs were computed using the logit routine, after the estimation of Poisson regression models with standard errors adjusted for intracenter correlation, considering only the predictors with statistically significant IRRs at the multivariable analysis.

A sensitivity analysis was performed using STATA software, release 10 (StataCorp, College Station, TX).

RESULTS

Classification and Main Characteristics of the Studied Sample

The median length of the follow-up was 9.0 (range: 6.7–11.4) years among the 4,425 subjects with no airflow obstruction at baseline according to all the three criteria. A total of 122 subjects developed COPD according to at least one of the three diagnostic criteria during the follow-up. The three criteria agreed in classifying 42 subjects as affected by COPD (corresponding to 34.4% of the subjects with COPD according to at least one of the criteria) and 4,303 subjects as individuals with normal lung function (Figure 1). Regardless of the definition used, the subjects with COPD were characterized by a higher percentage of ever smokers (from 72.6 to 80.0%, depending on the definition used for COPD), of individuals with airway hyperresponsiveness (AHR) (from 19.6 to 23.0%), with respiratory infections in childhood (from 14.6 to 17.3%), and with parental asthma (from 16.7 to 17.3%) compared with normal subjects (Table E1). The distribution of age and sex varied considerably according to the diagnostic criteria.

None of the new cases of COPD had a FEV₁ less than 50% predicted, whereas 12.8% (GOLD), 21.3% (LLN [Quanjer]) and 16.7% (LLN [LuftiBus]) had FEV₁ greater than or equal to 50% predicted and less than 80% predicted. With respect to subjects with normal lung function, COPD cases (with any definition) had a poorer lung function both at baseline and at follow-up, and a steeper decline in FEV₁ (Table E2).

Incidence of COPD

The incidence of COPD ranged from 1.85 (LLN [Quanjer]) to 2.88 (GOLD) cases/1,000/yr (Table 1). The GOLD-COPD
incidence was higher in males than in females, even if the difference did not reach statistical significance, whereas the opposite occurred for both the LLN-COPD incidence rates (Figure 2A). A strong positive association was found between age and GOLD COPD incidence ($P < 0.001$), whereas no age trend was observed for the LLN incidence rates (Figure 2B).

**Risk Factors for COPD**

Active smoking at baseline or during the follow-up, AHR, the occurrence of respiratory infections in childhood, and a family history of asthma significantly increased the risk of the occurrence of COPD regardless of the definition used (Table 2). The association of BMI and past smoking with the incidence of COPD varied according to the definition used. In particular, the risk of developing COPD was significantly increased only when the GOLD definition was used for underweight subjects (vs. normal subjects) and for former smokers (vs. nonsmokers). Low socioeconomic class, environmental tobacco smoke (ETS), biomass and occupational exposures, and IgE sensitization were not associated with the incidence of COPD.

**PAF**

Smoking explained the higher percentage of new COPD cases in our cohort (Table 3). In fact, the PAF ranged from 29 to 39%, according to the definition used. AHR, a family history of asthma, and respiratory infection in childhood also accounted for a relevant percentage of incident cases (about 15, 10, and 8%, respectively).

**Sensitivity Analysis**

The previous results were confirmed (data not shown) when the main analyses were repeated considering only the subjects who did not report wheezing at baseline (3,835, 3,832, and 3,764 when the incidence of COPD was defined according to the GOLD, LLN [Quanjer], and LLN [LuftiBus] definition, respectively).

**DISCUSSION**

The main results of our study of an international cohort of young adults point out that:

1. Cigarette smoke is the main cause of COPD also in young people.
2. The same host factors that increase the risk of asthma, such as a family history of asthma, the presence of AHR, and the occurrence of respiratory infections in childhood, play an important role in the inception of COPD in young adults.
3. The role of sex, age, former smoking, and BMI largely depends on the criterion used to define COPD.

**Tobacco Smoke Exposure and COPD Incidence in Young Adults**

Tobacco smoke is the major risk factor for COPD (2), and the population-attributable risk of smoking for COPD has been estimated in the range of 50 to 70% (22). The mechanisms responsible for the fact that some smokers develop COPD and others do not are not completely understood (23).

Young adults are a segment of the population in whom COPD may be caused by factors other than smoking, due to the relatively low cumulative exposure to tobacco smoke. In our cohort, however, about three out of four new COPD cases were ever smokers, and the PAF for tobacco smoking was more than double with respect to other potential causes. These findings point out that cigarette smoke is the most important risk factor for COPD also among young adults, and that smoking prevention could reduce the incidence of COPD in the young population by 29 to 39%.

It is believed that COPD occurs after 20 to 25 pack-years of exposure. In our cohort, about half of the incident cases of

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**TABLE 1. NINE-YEAR INCIDENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS DEFINED BY THE THREE SPIROMETRIC CRITERIA**

<table>
<thead>
<tr>
<th></th>
<th>No. of Subjects at Risk</th>
<th>Person-Years</th>
<th>No. of Cases</th>
<th>Incidence Rate (cases/1,000/yr) (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD</td>
<td>4,524</td>
<td>40,625</td>
<td>117</td>
<td>2.88 (2.38, 3.45)</td>
</tr>
<tr>
<td>LLN (Quanjer)</td>
<td>4,520</td>
<td>40,592</td>
<td>75</td>
<td>1.85 (1.45, 2.32)</td>
</tr>
<tr>
<td>LLN (LuftiBus)</td>
<td>4,431</td>
<td>39,774</td>
<td>96</td>
<td>2.41 (1.95, 2.95)</td>
</tr>
</tbody>
</table>

*Definition of abbreviations: CI = confidence interval; GOLD = Global Initiative for Chronic Obstructive Lung Disease; LLN = lower limit of normal.

* Poisson exact 95% CI.
COPD had smoked less than 20 pack-years. Thus, the association observed between smoking and the incidence of COPD is more likely to reflect an early interaction of the tobacco exposure with some genetic or immunologic host characteristics, rather than the effect of the cumulative exposure to cigarette smoke per se. (24)

The risk of developing COPD has been reported to be higher in former smokers than in nonsmokers years after they quit (25). Our data seem to confirm this finding. However, the extent of the risk of developing the disease in this group of young subjects and its statistical significance strongly depended on the criterion used to define the disease. It is likely that these discrepancies reflect differences in specificity and sensitivity of the three definitions used (3, 26).

Factors That Increase the Risk of Asthma Also Increase the Risk of COPD

The Dutch hypothesis (27) postulated that both asthma and COPD share common origins with differences in the phenotypic presentation related to the disease evolution or to the interaction between endogenous and exogenous factors. The results of our analysis clearly show that well-known risk factors for asthma, such as AHR, familiarity, and respiratory infection in childhood, are relevant risk factors also for COPD. The proportion of new cases of COPD due to each of these factors ranges from 8% (respiratory infections) to 15% (AHR).

AHR is a cardinal feature of asthma (28). In agreement with previous studies (29), we found that hyperresponsive subjects without asthma had a fourfold greater risk of developing COPD compared with subjects who were not hyperresponsive. Subjects having at least one parent affected by asthma had a double risk of developing COPD in adulthood, with respect to subjects without any familiar history of asthma. These findings agree with recent studies showing that several genes increase the susceptibility to both asthma and COPD and document the existence of a common genetic background (6, 30, 31).

The occurrence of respiratory infection early in life is one of the strongest risk factors for the development of asthma (32). Our results showed that also the risk of developing COPD is doubled in subjects who had respiratory infections in their childhood. Respiratory infections in infancy are largely due to viruses (33). Virus infections may lead to permanent changes in the respiratory tract, such as nasal polyps and scarring of the cilia (34). Viral infections in childhood are also associated with an increased risk of respiratory symptoms and asthma in adulthood (35, 36). Thus, the interaction between endogenous factors such as viral infections and environmental factors such as cigarette smoke may lead to a greater risk of COPD (37, 38). In line with this hypothesis, we found that the occurrence of respiratory infections in childhood was associated with an increased risk of COPD (Table 2).

Definition of abbreviations: AHR = airway hyperresponsiveness; BMI = body mass index; CI = confidence interval; ETS = environmental tobacco smoke; GOLD = Global Initiative for Chronic Obstructive Lung Disease; IRR = incidence rate ratio; LLN = lower limit of normal; PAF = population-attributable fraction.

For a detailed description of the covariates, see the online data supplement.

* P < 0.05.
† P < 0.001.

### Table 2. Mutually Adjusted Incidence Rate Ratios for the Association Between Each Potential Predictor and the Incidence of Chronic Obstructive Pulmonary Disease as Defined by the Three Spirometric Criteria

<table>
<thead>
<tr>
<th>Predictor</th>
<th>GOLD (95% CI)</th>
<th>LLN (Quanjer) (95% CI)</th>
<th>LLN (LuftiBus) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>0.53 (0.32, 0.86)*</td>
<td>0.95 (0.52, 1.75)</td>
<td>1.68 (0.99, 2.86)</td>
</tr>
<tr>
<td>Age (&gt; 35 vs. &lt; 35 yr)</td>
<td>2.24 (1.48, 3.39)*</td>
<td>1.25 (0.65, 2.39)</td>
<td>0.92 (0.53, 1.60)</td>
</tr>
<tr>
<td>BMI (vs. normal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>3.55 (1.59, 7.93)*</td>
<td>2.53 (0.72, 7.64)</td>
<td>1.14 (0.31, 4.22)</td>
</tr>
<tr>
<td>Overweight/obese</td>
<td>0.62 (0.42, 0.91)*</td>
<td>0.78 (0.30, 2.00)</td>
<td>1.03 (0.55, 1.94)</td>
</tr>
<tr>
<td>Low socioeconomic class</td>
<td>1.02 (0.56, 1.83)</td>
<td>0.63 (0.27, 1.50)</td>
<td>0.83 (0.45, 1.54)</td>
</tr>
<tr>
<td>Smoking habits (vs. nonsmoker)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quitter/sustained quitter</td>
<td>2.08 (1.34, 3.21)*</td>
<td>1.69 (0.92, 3.10)</td>
<td>1.30 (0.81, 2.09)</td>
</tr>
<tr>
<td>Persistent smoker/new smoker/restarter</td>
<td>2.61 (1.62, 4.20)*</td>
<td>2.42 (1.35, 4.33)*</td>
<td>2.43 (1.25, 4.73)*</td>
</tr>
<tr>
<td>ETS</td>
<td>1.08 (0.71, 1.66)</td>
<td>1.09 (0.68, 1.76)</td>
<td>1.10 (0.62, 1.93)</td>
</tr>
<tr>
<td>Biomass exposure</td>
<td>1.17 (0.69, 1.97)</td>
<td>1.25 (0.57, 2.74)</td>
<td>0.95 (0.53, 1.70)</td>
</tr>
<tr>
<td>Occupational exposures</td>
<td>1.01 (0.69, 1.47)</td>
<td>1.02 (0.59, 1.77)</td>
<td>1.19 (0.86, 1.66)</td>
</tr>
<tr>
<td>AHR</td>
<td>3.97 (2.07, 7.65)*</td>
<td>3.89 (1.78, 8.33)*</td>
<td>3.39 (1.72, 6.70)*</td>
</tr>
<tr>
<td>IgE sensitization</td>
<td>0.69 (0.44, 1.10)</td>
<td>0.86 (0.46, 1.60)</td>
<td>1.11 (0.68, 1.79)</td>
</tr>
<tr>
<td>Respiratory infections in childhood</td>
<td>1.88 (1.02, 3.46)*</td>
<td>1.97 (0.86, 4.54)</td>
<td>2.23 (1.64, 3.04)*</td>
</tr>
<tr>
<td>Family history of asthma</td>
<td>1.95 (1.25, 3.04)*</td>
<td>2.24 (1.12, 4.48)*</td>
<td>2.09 (1.26, 3.47)*</td>
</tr>
</tbody>
</table>

### Table 3. Mutually Adjusted Population-Attributable Fractions for the Association Between Each Potential Predictor and the Incidence of Chronic Obstructive Pulmonary Disease as Defined by the Three Spirometric Criteria

<table>
<thead>
<tr>
<th>Predictor</th>
<th>GOLD (95% CI)</th>
<th>LLN (Quanjer) (95% CI)</th>
<th>LLN (LuftiBus) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (BMI &lt; 18.5 kg/m²)</td>
<td>0.04 (0.00, 0.07)</td>
<td>0.04 (0.00, 0.11)</td>
<td>0.01 (0.00, 0.05)</td>
</tr>
<tr>
<td>Ever smoking</td>
<td>0.39 (0.15, 0.56)</td>
<td>0.38 (0.12, 0.56)</td>
<td>0.29 (0.01, 0.50)</td>
</tr>
<tr>
<td>AHR</td>
<td>0.15 (0.06, 0.22)</td>
<td>0.17 (0.04, 0.29)</td>
<td>0.15 (0.03, 0.25)</td>
</tr>
<tr>
<td>Respiratory infections in childhood</td>
<td>0.06 (0.00, 0.13)</td>
<td>0.09 (0.00, 0.20)</td>
<td>0.08 (0.03, 0.12)</td>
</tr>
<tr>
<td>Family history of asthma</td>
<td>0.09 (0.02, 0.16)</td>
<td>0.11 (0.00, 0.22)</td>
<td>0.10 (0.01, 0.19)</td>
</tr>
</tbody>
</table>

Definition of abbreviations: AHR = airway hyperresponsiveness; BMI = body mass index; CI = confidence interval; GOLD = Global Initiative for Chronic Obstructive Lung Disease; IRR = incidence rate ratio; LLN = lower limit of normal; PAF = population-attributable fraction.

Also adjusted for sex and age. 0.00: negative values truncated to zero.

* 95% CI calculated on log(1 - PAF) scale.
the airways (34). Some viruses may persist as a latent infection in the airways (35), increasing the susceptibility to COPD.

Are Sex, Age, and BMI Associated with the Risk of Developing COPD in Young Adults?

Our findings indicate that the answer to this question depends on the definition. When the GOLD COPD criterion was used, male, underweight, and older subjects had a significantly increased risk of developing COPD. When a sex-age-based definition was used (LLN criteria), the age, sex, and BMI associations with COPD lost their statistical significance, and sex and age even showed a reverse association.

COPD prevalence is higher in subjects older than 40 years of age compared with those younger than 40 years, regardless of the diagnostic criteria used (16). However, an increasing pattern of prevalence with age does not imply a similar trend in incidence. Unfortunately, very few studies on COPD incidence are available. All longitudinal studies in northern Europe found that incidence of COPD increased with age, but almost all of them used the GOLD as a diagnostic criterion, and the age range investigated was much wider than ours (36–40).

The role of sex in determining COPD risk remains unclear (16). In the past, most studies showed that COPD prevalence and mortality were greater among men than women. More recent studies showed that the sex difference in COPD prevalence tends to disappear (41, 42). Regarding COPD incidence, most (36–38) but not all (39) studies found a higher risk in men than in women. Our results suggest that part of the contrasting findings in literature may be due to methodological differences.

An association between COPD prevalence and low BMI has been reported in several studies (43), but it is not clear whether a low BMI precedes or follows the onset of the disease. Our longitudinal study points out that subjects with BMI less than 18.5 kg/m² had a threefold risk of developing the disease compared with subjects with a normal weight. However, the association was weaker when LLN diagnostic criteria were used.

To sum up, we have shown that the role of age, sex, and low BMI on the development of COPD differs according to the definition of the disease. The discrepancy in the relative risk estimates when different diagnostic criteria are used is hard to interpret. The LLN criterion might lack specificity in young populations, leading to the underestimation of the associations between the disease and risk factors. On the contrary, the GOLD criterion may produce false-positive associations in the age range (20–54 yr) studied because it does not consider the physiological decline in FEV₁/FVC. Whatever the truth is, we may empirically conclude that, because of the contrasting results, aging, sex, and low BMI play only a minor role in the early development of COPD.

Environmental Exposure, Socioeconomic Class, and the Risk of Developing COPD

Previous studies (8, 9) found an association between ETS, occupational and biomass exposures, socioeconomic class, and the incidence of COPD. However, we were not able to confirm these findings. The young age of our cohort could have implied a relatively low cumulative exposure to environmental factors. Furthermore, these factors have been measured using simple questions during a clinical interview, and exposures could have thus been misclassified. Moreover, due to the relatively low number of subjects with COPD in young adults, the power of our study might not have been enough to detect small effects (e.g., ETS).

Air pollution was not considered among the environmental determinants because we had previously shown that cross-community background monitor data do not accurately characterize the individual exposure (44).

COPD Incidence and the Performance of Different Diagnostic Criteria

As expected, in our study, COPD incidence (as measured according to the GOLD criterion) was slightly lower than the incidence measured in other older populations in Europe (36, 38, 40).

The agreement between the GOLD and the two LLN definitions in identifying subjects affected by COPD was relatively poor. In fact, only 34.4% were simultaneously diagnosed as having COPD by all three criteria. The variation between the two LLN definitions was similar to the variation found between the GOLD and the LLN (LuftiBus). Despite their differences, all the definitions agreed in identifying the risk factors that have a major impact on the population. When the diagnostic criteria disagreed, the estimates of the strength of the association between potential risk factors and the incidence of COPD showed a wide variation not only between the GOLD and the LLN criteria but also within the two LLN criteria. This finding points out that the choice of the reference equations for calculating the LLN may introduce a relevant source of variation and suggests the need for a definition of COPD that is not exclusively based on spirometric tests (26).

Limitations and Strengths of the Study

The main limitation of our study is the use of prebronchodilator spirometric values for defining COPD. As a consequence, subjects with asthma with fully reversible obstruction could have been falsely classified as having COPD. To minimize this potential bias, all the subjects who reported asthma at baseline or during the follow-up were excluded. Moreover, when the main analyses were restricted to the subgroup of individuals who did not report current wheezing at baseline, the associations between the incidence of COPD and the main risk factors were confirmed. Due to the lack of post-bronchodilator measurements, we cannot rule out that some cases of undiagnosed asthma with transient airflow obstruction at the end of the follow-up could have been erroneously classified as COPD. However, as the probability for a subject with asthma to report neither the label of asthma nor wheezing in the last year is very low, it is extremely likely that the misclassification bias, if present, could have affected our results only to a minor extent.

Other limitations are the relatively small number of subjects with incident COPD (which is a consequence of the young age of the population studied), which did not make it possible to evaluate sex-stratified associations, as well as the lack of information on other chronic lung conditions. As in other longitudinal studies, the participation rate was low in some centers, and hence a potential selection bias could be present. However, our findings were confirmed when the four centers with the lowest participation rate (< 50%) were excluded (data not shown). The main strengths are the population-based prospective nature of our study and its highly standardized multicenter international framework.

Conclusions

COPD is a considerable problem for young adults and the most important risk factor for developing COPD is cigarette smoke. Smoking prevention should be given the highest priority to reduce the occurrence of the disease. AHR, a family history of
asthma, and respiratory infections in childhood are other important determinants of the occurrence of the disease. The variation in incidence estimates and in the identification of risk factors due to different diagnostic criteria of COPD suggests the need for an epidemiological definition of the disease that is not exclusively based on spirometry.

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References


