FEDERAL UNIVERSITY OF PELOTAS

POST-GRADUATE PROGRAM IN EPIDEMIOLOGY

PLATINO STUDY – MEXICO SURVEY

REPORT

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1. INTRODUCTION

The prevalence of Chronic Obstructive Pulmonary Disease (COPD) in many developed countries appears to be increasing (Hurd, 2000; Pauwels, 2000; Petty, 2000). There is also some evidence from Latin America that COPD is a growing cause of death, but information on prevalence is scant (Brasil, Datasus). To obtain a detailed picture of the global distribution of this severe condition, it is necessary to know its prevalence in less developed countries. It is possible that, due to the high frequency of smoking - the main risk factor for COPD - in these countries, this disease may represent a major public health problem that has not yet been recognized as such.

The PLATINO study is aimed at measuring COPD prevalence in major cities in Latin America. So far, studies have been launched in São Paulo, Mexico City, Montevideo and Santiago. At least one more city will be included in the near future.

The main objective of the Platino study is to measure COPD prevalence in major Latin American metropolitan areas. The specific objectives are:

- ✓ To measure and compare COPD prevalence using different definitions, including ATS, ERS, GOLD, fixed ratio and symptomatic criteria;
- ✓ To measure the prevalence of known risk factors for COPD including socio-economic status, smoking, type of cigarette smoked, indoor biomass pollution, work exposure, environmental pollution, genetic factors and history of severe respiratory disease in childhood;
- ✓ To describe the distribution of COPD according to age, sex, smoking and the presence of other risk factors;
- ✓ To describe the main clinical symptoms reported by subjects diagnosed with COPD;
- ✓ To assess the sensitivity and specificity of COPD clinical findings, using lung function as the "gold standard";
- ✓ To compare COPD prevalence in Latin America with that reported from other countries (mainly developed ones);
- ✓ To correlate the subject's awareness of suffering from COPD with actual diagnosis;

- ✓ To describe how this disease is being managed in terms of drug therapy, clinical and laboratory investigations, and other relevant aspects;
- ✓ To describe the social and economic consequences of COPD, in terms of work limitations, absenteeism and other relevant issues.

A full description of the rationale and methodology of the study is available in the original study proposal (Platino Project, 2002).

This report describes the main results of the Mexico City survey, the second site where the project has been completed.

2. METHODOLOGY

2.1. Design of the study

A cross sectional design was used in order to provide a representative sample of adults aged ≥ 40 years living in the metropolitan area of Mexico City, through multi-stage cluster sampling.

2.2. Sampling

The sample size calculations required 800 subjects to be able to estimate a prevalence of up to 30% with a margin of error of less than four percent points (see original proposal). To allow for non-response we aimed at obtaining obtaining 68 census tracts in larger metropolitan area of Mexico City, and to select 15 households, on average, from each tract. We expected approximately an average of one person aged 40 years or more per household.

Mexico City metropolitan area was divided into two strata: The Federal District and the surrounding areas from the State of Mexico. Table 1 shows the population of each stratum and the proportion of the sample expected in each area, with the respective sample size.

Table 1. Population aged ≥ 40 years and sample size according to two stratum.

Stratum	*Population*		*Sample (subjects)*	*Sampling fraction/10,000*
	N	**%**	**n**	**n/N**
Federal District	2,411,072	55.9%	570	2,36
State of México	1,902,883	44.1%	450	2,36
METROPOLITAN REGION (MR)	4,313,955	100.0%	1020	2,36

Population data were obtained from the 2000 National Demographic Census.

2.2.1. Selection of census tracts

The Mexico City metropolitan area consisted of 4203 census tracts in 2000, excluding military installations, airports, parks and other non-residential areas. These census tracts were stratified by according to the state (Federal District or State of Mexico) and geographical zone, using cartographical information developed by the Federal District Environment Secretariat (SIG-SIMAT) to monitor outdoor air pollutants in the city. This produced five geographical zones for the Federal District and four for the State of Mexico. Within each of these zones, census tracts were ranked by a socioeconomic status index developed from census data on education, employment and housing conditions. A systematic sample was then obtained with probability proportional to size, taking into account the number of households (average 950) in each tract. Since the number of households per census tracts in Mexico City were on average considerable larger than in São Paulo City and showed greater variability**,** selected census tracts were segmented into areas of about 200-300 households. This was done by only one person using information on area of the blocks composing a census tracts and simple random sampling.

Figure 1 - Selection of the 38 census tracts in the Federal District stratified by geographical zone and by family income.

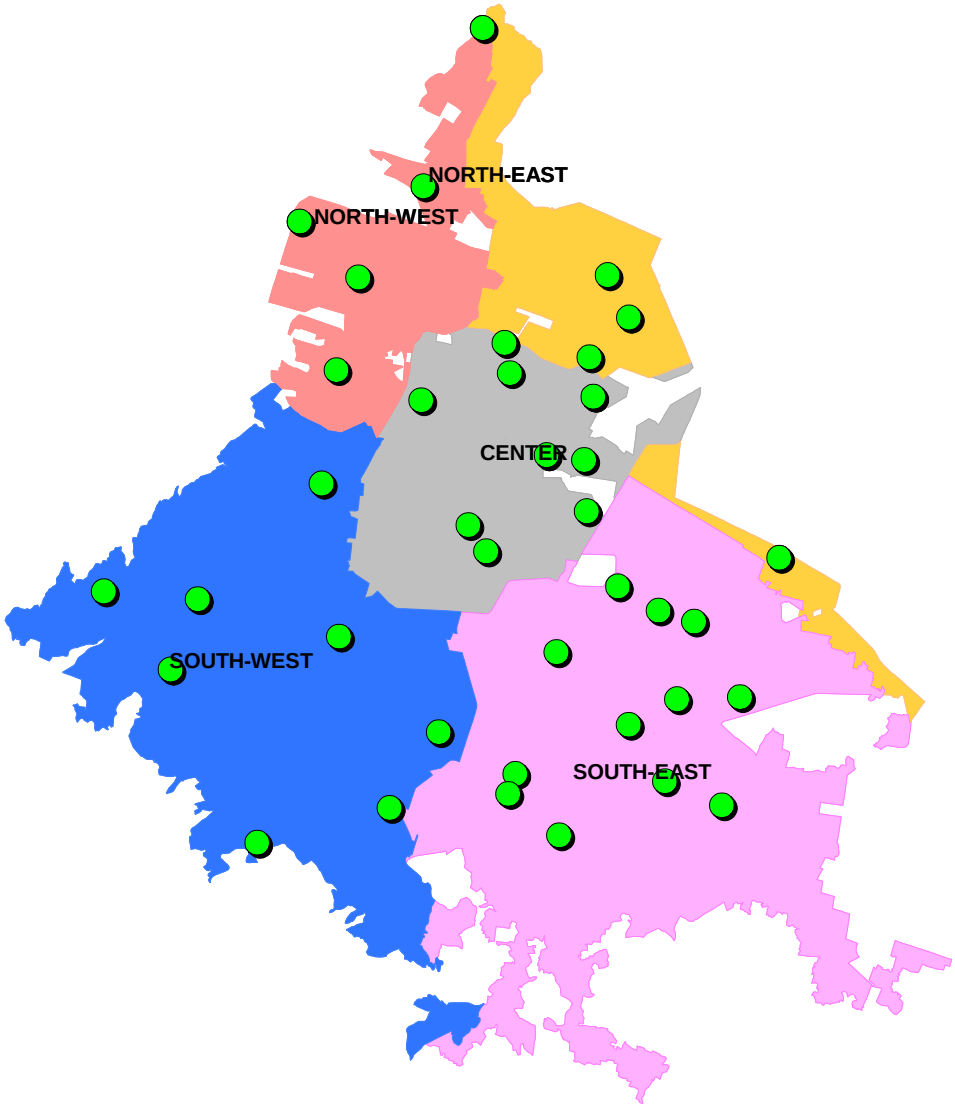

Figure 2 - Selection of the 30 census tracts in the State of Mexico stratified by geographical zone and by family income.

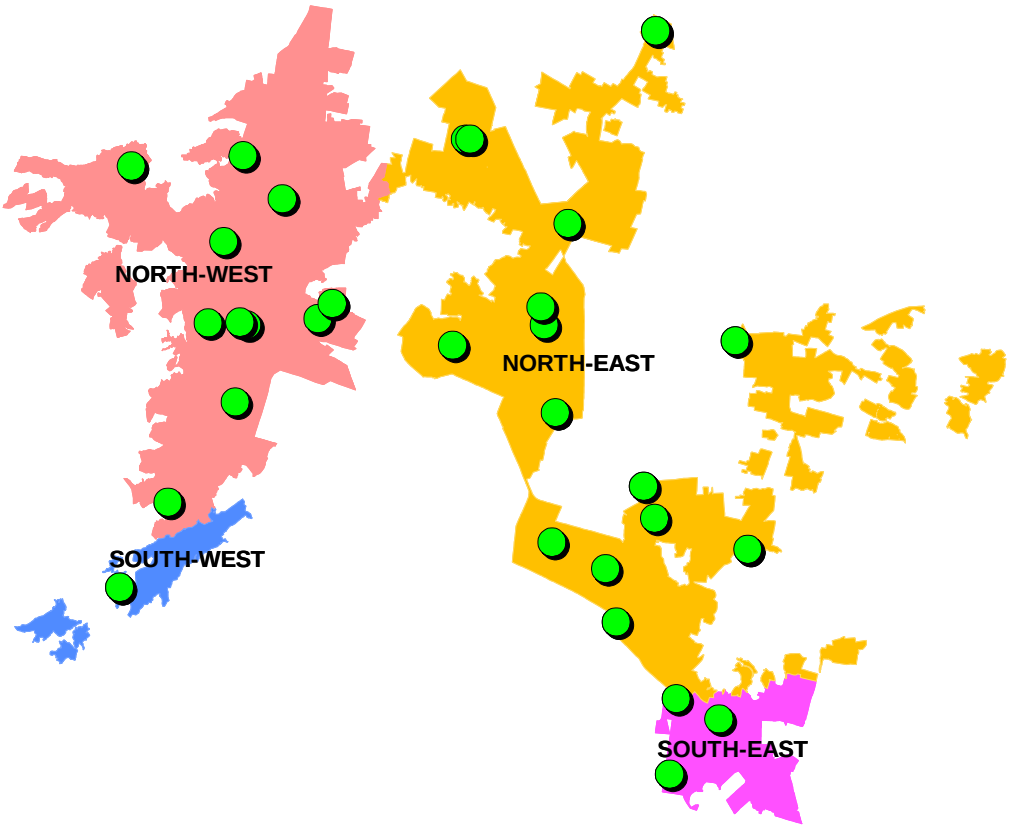

Table 2. Sampling of census tracts by stratum

Stratum	*N*	*B*	*Census tracts* *a = (n/b)*
Federal District	570	15	38
State of Mexico	450	15	30
METROPOLITAN REGION (MR)	***1020***	*--*	***68***

2.2.2. Sampling of the households

All selected tracts or segments were visited, and all inhabited households in each of these tracts were enumerated between May and October 2003, usually two or three weeks before field work in the census tract. Households were systematically selected

from the full updated listing prepared in 2003, by selecting one in every "x" household, where "x" represents the ratio between the total household count and the desired number of households in that tract (Silva, 2002; Kish, 1965). All adults aged 40 years or more living in each of the selected households were included in the study; if there were no adults in this age range in the household, it was not included in the survey and there was no replacement.

2.3. Variables

2.3.1. Dependent variable

The main outcome of the study was the prevalence of COPD measured by spirometry after bronchodilator use according to the following criterion: FEV1/FVC < 70%, where FEV1 is the forced expiratory volume in the first second, and FVC is forced vital capacity (Viegi, 2000).

Prevalence of COPD was also analyzed according to other criteria:

- ✓ Global Obstructive Lung Disease (GOLD, 2001) - FEV1/FVC<70% and FEV1<80% predicted;
- ✓ European Respiratory Society (ERS, 1993) - FEV1/FVC <88% of predicted in men and < 89% predicted in women;
- ✓ American Thoracic Society (ATS, 1994) - FEV1/FVC below 5th percentile and FEV1<100% predicted;

For the analyses of lung function measurements, the NHANES Mexican-American reference values were used (NHANES, 1994).

Reported symptoms were also evaluated: these included the prevalence of chronic bronchitis (cough with phlegm for at least 3 months a year in the last 2 years); breathlessness due to exercise; and wheezing in the last 12 months (Ciba Foundation Guest Symposium, 1959).

Subjects were also asked if they ever had a medical diagnosis of chronic bronchitis, emphysema or COPD.

2.3.2. Risk factors

The following risk factors were investigated:

- ✓ sex - dichotomous variable: male or female.
- ✓ age - discrete variable: years completed until the interview date.
- ✓ skin color – categorical variable: white, black, mulatto, Asian, Native American
- ✓ educational level - discrete variable: completed years of schooling of the subject.
- ✓ father's education – as above, for the subject's father.
- ✓ occupational exposure to dust: duration of exposure, intensity of contact, frequency of contact and type of work.
- ✓ smoking history – daily amount, age at beginning and stopping, type of cigarette, etc
- ✓ passive smoking – intensity and duration of exposure at home
- ✓ domestic exposure to coal and biomass smoke – exposure to smoke from cooking and heating;
- ✓ hospital admissions – whether or not the subject was hospitalized due to a respiratory illness during childhood;
- ✓ family history of lung disease - chronic bronchitis, emphysema, or COPD.

The subject's anthropometric status (weight, height, and abdominal circumference) was measured using standardized methods and the instruments described below. Body mass index was calculated.

2.4. Exclusion criteria

The general exclusion criteria for the study were mental disease and institutionalization. In the Mexico City survey, no subjects fulfilled these criteria.

Exclusion criteria for spirometry – presence in the last three months of thoracic or abdominal surgery, heart attack, eye surgery (or retinal detachment), hospitalization for any heart problem, current treatment for tuberculosis, self-reported pregnancy or pulse rate above 120 beats/minute. Forty six subjects were excluded due to these criteria.

2.5. Instruments and examinations

2.5.1. Questionnaire - the questionnaire was a composite that included sections of the following questionnaires: ATS/DLD (Ferris, 1978), ECRHS II, Lung Health Study (LHS) and SF-12 were also added to assess overall health status.

2.5.2. Height measurement - A portable stadiometer (Seca® Bodymeter 208, precision 0.1 cm) was used for measuring height. The technique was that recommended by Lohman (Lohman, 1988). Subjects did not wear shoes. They were asked to stand the feet drawing at the bottom of the stadiometer and to keep their heads straight in the Francfort plane while their height was checked.

2.5.3. Weight. An electronic solar cell bathroom scale (Tanita® precision 200 g) was used. Subjects were weighted without shoes and wearing light clothes.

2.5.4. Waist circumference. An inextensible 2 m fiberglass tape (R280 Rotary®, precision 0.1 cm) was used. Firstly the interviewers should identify the middle point between the last rib and the iliac crest; then the tape should be placed around the waist crossing the point already identified; the tape should neither be too tight nor too loose.

2.5.5. Spirometry. A portable, battery operated, ultrasound transit-time based spirometer (Easy-One from NDD) was used. The spirometers had their calibration checked daily with a 3 liters syringe before being used in the field. The spirometers stored up to 400 test results in a memory chip, which was downloaded regularly. The initial evaluation was performed immediately after a short questionnaire established whether the subject was eligible for this procedure (ascertainment of eligibility included measurement of the subject's pulse rate), and after anthropometric examination was completed. Subjects then performed a number of attempts until these resulted in three

ATS acceptable maneuvers, with FVC and FEV1 reproducible to 150 ml. A bronchodilator (salbutamol 200 mcg) was then administered
by inhalation, and the test was repeated 15 minutes later, with the same criteria. All spirometric examinations were carried out with the subject seated, wearing a nose clip and a disposable mouthpiece.

The measurements of weight, height and waist circumference were carried out twice on each subject, and the average value was used.

2.6. Personnel and training

The team for carrying out the training was composed by the main coordinator of the study, two experts in spirometry from Mexico, the local principal investigator, three fieldwork supervisors, a nutritionist, and 6 spirometry technicians and 6 interviewers. Training lasted one week. In addition to the initial training sessions, the local supervisors continued to train interviewers whose performance in the standardization sessions was not optimal, until it became satisfactory. The following criteria were used to ensure that training was adequate:

- ✓ Anthropometry: the intra and inter observed variability accepted for the measurement of waist circumference was 1.0 cm and for height was 0.2 cm (Habicht, 1974).
- ✓ Spirometry: interviewers performed several measurements on different subjects and were then submitted to a formal examination including two complete tests. If they succeeded in these tests they were certified.
- ✓ Questionnaires: after having carried out several interviews with both health and diseased subjects, interviewers had to carry out an interview in the presence of a supervisor and were approved if their performance was satisfactory.

2.7. Logistics of field work

The fieldwork lasted from June to October 2003. From October to December 2003, additional efforts were made to recruit subjects not found beforehand or those

who refused in the first contact. The study team included three scouts, 6 spirometry technicians, 6 interviewers, two field supervisors, two spirometry supervisors and a secretary.

All field methods were tested in a pilot study carried out in June 2003 in a middle-class area in Mexico City, nearby the National Institute of Respiratory Diseases.

The logistic of the fieldwork included several steps. The first visit to the selected area of the city was carried out by the "scouts" who draw a census of inhabited houses in the selected areas. Second, inhabited houses were selected randomly. In selected households with subjects aged 40 years or more, the purpose of the study was explained personally if the subject was available at the moment of the visit and if agreed and technicians were nearby, the tests were done immediately. If it was not possible to do the test immediately an appointment was arranged for the interview and examination. If the subject was not found an official letter explaining the aim of the study was delivered and a telephone number was registered to make further attempts. Appointments were offered for weekdays and weekends, morning, afternoons and evenings, all these at home. It was also offered an appointment to do the testing in a community center, at work, or at the National Institute of Respiratory Diseases to avoid rejection of people not wanting to let strangers in home.

Daily, the interviewers visited the study headquarters early in the morning to receive a list of the households to be visited. At the same time, spirometry results obtained in the previous day were downloaded. Spirometry supervisors were in charge of checking calibration before field work, and download previous tests with the principal investigator.

Each interviewer carried a backpack containing all the equipment. Interviewers were transported to the field work by vans from the Institute, except when the area of work was close to the home of one of the interviewers.

At the end of the study, further attempts were made to reduce refusals. Homes with no answer to personal visits were visited again, and by telephone if was obtained from a neighbor. Contacts were also made with local leaders or organizations to arrange contact with inhabitants. When the telephone number was obtained from a neighbor, a phone call was given by one of the researchers. Testing facilities were given to all subjects as testing at home by appointment was offered, including afternoon or night

and weekend appointments. Appointments at work or at the National Institute of Respiratory Diseases or other agreed places were also offered.

2.8. Quality control

Spirometry – After each test, the automated spirometer provides an evaluation of the quality of readings, based on the repeatability of the three "best" curves (on average each subject performed 6.2 maneuvers pre bronchodilator (BD) and 5.2 post BD). The aim was to obtain a grade "A" test, that is three acceptable tests according to ATS criteria, with FEV1 and FVC reproducible within 150 ml, better than the 200 ml recommended by ATS. The principal investigator analyzed their quality and provided weekly quality control reports with assessments of each individual interviewer. At the same time the local PI of the study was also checking the spirometries daily and working with the interviewers to correct any inaccuracies detected by him or by the Mexican team. Results of the regular quality control procedures, which confirmed the excellent quality throughout the study period, can be obtained at our homepage.

Interviews – 6% of the interviews were repeated by the supervisors. Two to three weeks after the interview, the supervisors contacted the subject interviewed and repeated six questions from the main questionnaire to assess reliability.

Anthropometry – Half way through the fieldwork (end of second month), all the interviewers underwent refresher training in anthropometry, followed by a second round of standardization sessions.

2.10. Ethical considerations

Ethical approval was obtained from the ethical committee of the National Institute of Respiratory Diseases of Mexico City. Only subjects who signed the informed consent participated in the study. The disposable mouthpieces and spacers were given to each subject interviewed and also a T-shirt with the logo of the study. The

results of spirometries were sent to each subject and for those who had COPD or any abnormality in the spirometry was offered the possibility of being seen by a doctor at the National Institute of Respiratory Diseases.

2.11. Processing of data

All questionnaires were photocopied, and the originals were sent to the Coordinating Centre (CC), while the copy remained in Mexico City. In the CC, all questionnaires were revised, open answers were coded and data were entered twice in a Epi-Info database. The spirometry results were sent to Mexico and entered in a STATA database. After spirometry results were cleaned and edited, the database was sent to the CC and linked to the questionnaire database. A full copy of the clean dataset was sent to the study site in Mexico City, and the original database was analyzed in the CC.

2.12. Analysis

Analyses were carried out using the STATA program. These included descriptive analyses of the outcome variables and of risk factor prevalence, bivariate analyses and multivariate analyses. For the multivariate analyses, Poisson regression (Barros, 2003) was used to provide estimates of prevalence ratios and their 95% confidence intervals. Analyses were carried out according to a previously defined conceptual model which took into account the hierarchical relationships between risk factors (Victora, 1997. For example, demographic and social factors were considered as distal determinants while smoking and exposure to pollution were considered as proximate determinants (see Results section). All analyses took into account the cluster sampling procedure. Confounding variables were kept in the model if they had reached a P level of 0.20 or lower in the likelihood ratio test; the 0.05 P level was used for identifying significant risk factors. Tests for linear trend were used when appropriate.

3. RESULTS

3.1. Response rates and number of individuals included

Figure 3 shows the number of households and subjects included in the different phases of the study. Non-response rates were 4.2% at the household level, 26.8% at the individual questionnaire level, and 1.7% for spirometry. The overall rate of non-response was 31.1%, obtained by multiplying the response rates.

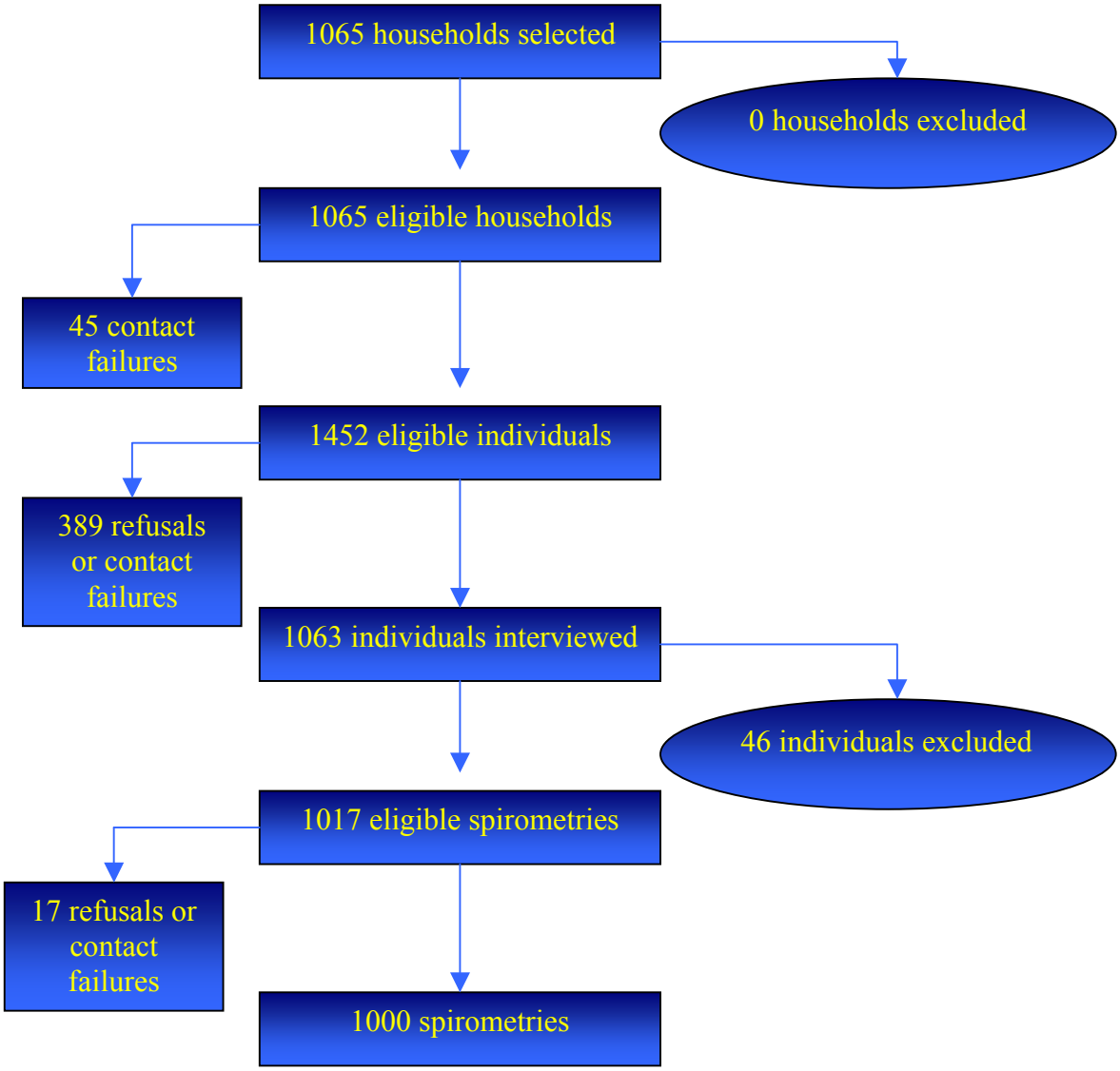

Figure 3. Number of households and individuals included in the different phases of the study.

Even for the 389 non-responders, we tried to obtain information on sex, age and smoking status; 194 (50%) answered these questions. This information was then extrapolated to the 389 non-responders. Table 3 shows the percentage of non-response by sex, age and smoking status.

Table 3. Percentage of non-response by sex, age and smoking status.

Variable	*% individual non-response*
Sex	
Males	35.1%
Females	19.8%
Age	
40-49	27.1%
50-59	23.9%
≥ 60	28.8%
Current smoking status	
No	26.4%
Yes	27.4%

3.2. Prevalence of COPD according to different criteria

3.2.1. Spirometric criteria

As discussed in the Methods section, several different criteria were used to estimate COPD prevalence based on spirometry. Figure 4 shows these estimates and their 95% confidence intervals, which take into account the effect of the clustered sample.

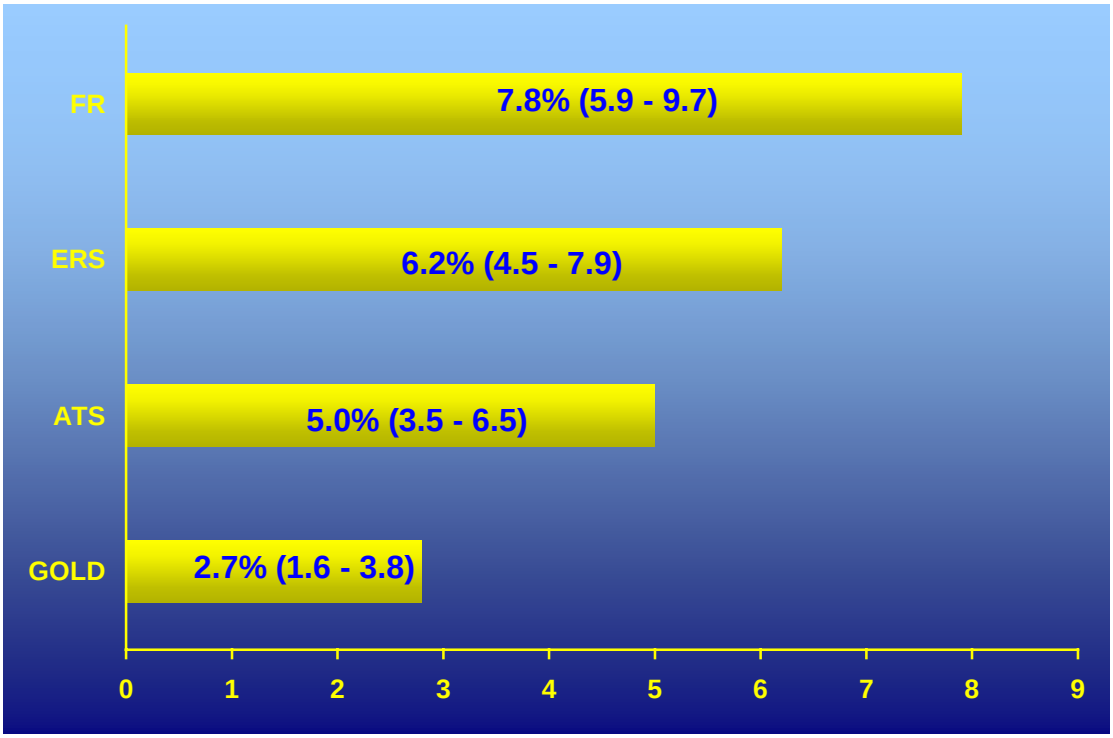

Figure 4. Prevalence of COPD based on different spirometric criteria.

The fixed ratio (FR) criterion showed the highest prevalence, of 7.8%, followed by the ERS (6.2%), ATS94 (5.0%) and GOLD (2.7%) definitions. All criteria, except for the fixed ratio definition, are based on a comparison with a set of standard function curves. The NHANES Mexican-American reference values were used for this purpose.

The design effect (deff) - an estimate of how much the cluster sample affected the variability of the measures – was calculated for the fixed ratio and GOLD estimates. The values obtained were 1.33 and 1.15, respectively. Design effects substantially greater than 1.0 are of concern, but was not the case for these outcome measures. In the sample size calculations for the present study, the design effect had been assumed to be equal to 1.5.

3.2.2 Clinical criteria

Symptoms related to COPD were also studied (Figure 5).

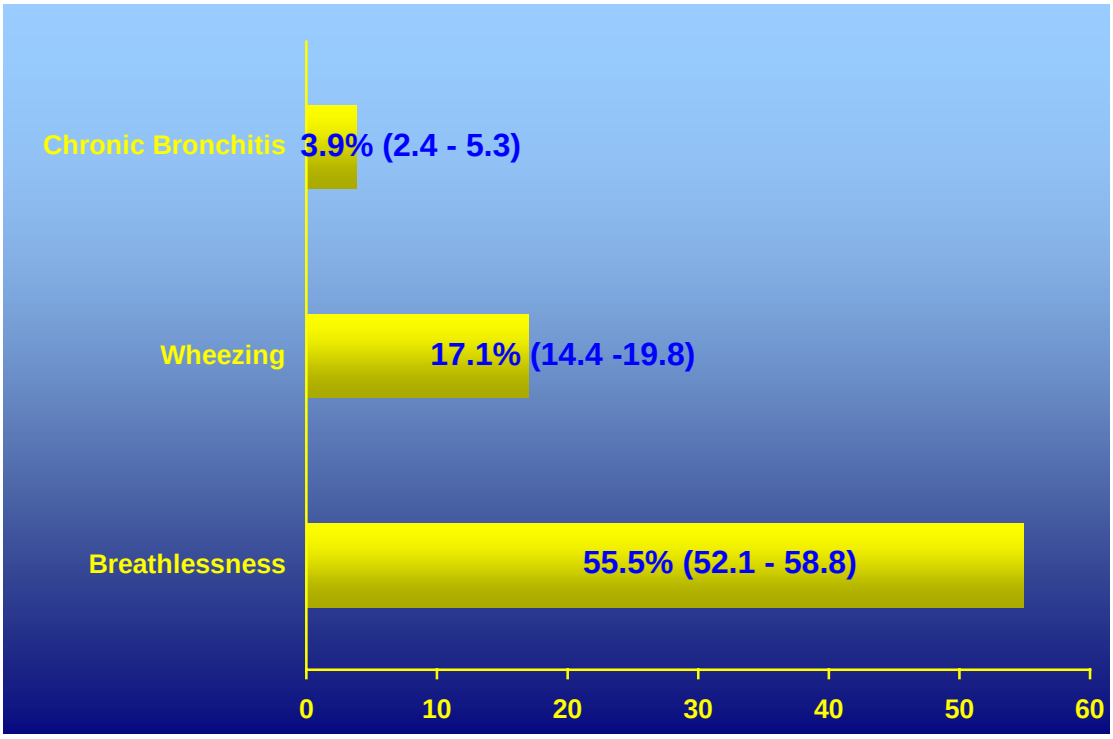

Figure 5. Prevalence of reported respiratory symptoms.

The prevalence of chronic bronchitis according to reported symptoms - cough with phlegm for at least 3 months a year in the last 2 years – was equal to 3.9%. Breathlessness due to exercise, and wheezing in the last 12 months were reported, respectively, by 55.5% and 17.1% of all subjects (Figure 5).

When 5% of the sample subjects were re-interviewed within 2-3 weeks of the original interview, it was possible to estimate the reliability of the information provided on symptoms. Kappa statistics were equal to 0.26 for cough and 0.18 for sputum, showing that agreement was poor.

Figure 6 shows the prevalence of reported medical diagnoses of bronchitis, emphysema, asthma and COPD. All conditions were reported by fewer than 6% of those interviewed. A medical diagnosis of either chronic bronchitis, emphysema or COPD was reported by 5.4% of all subjects.

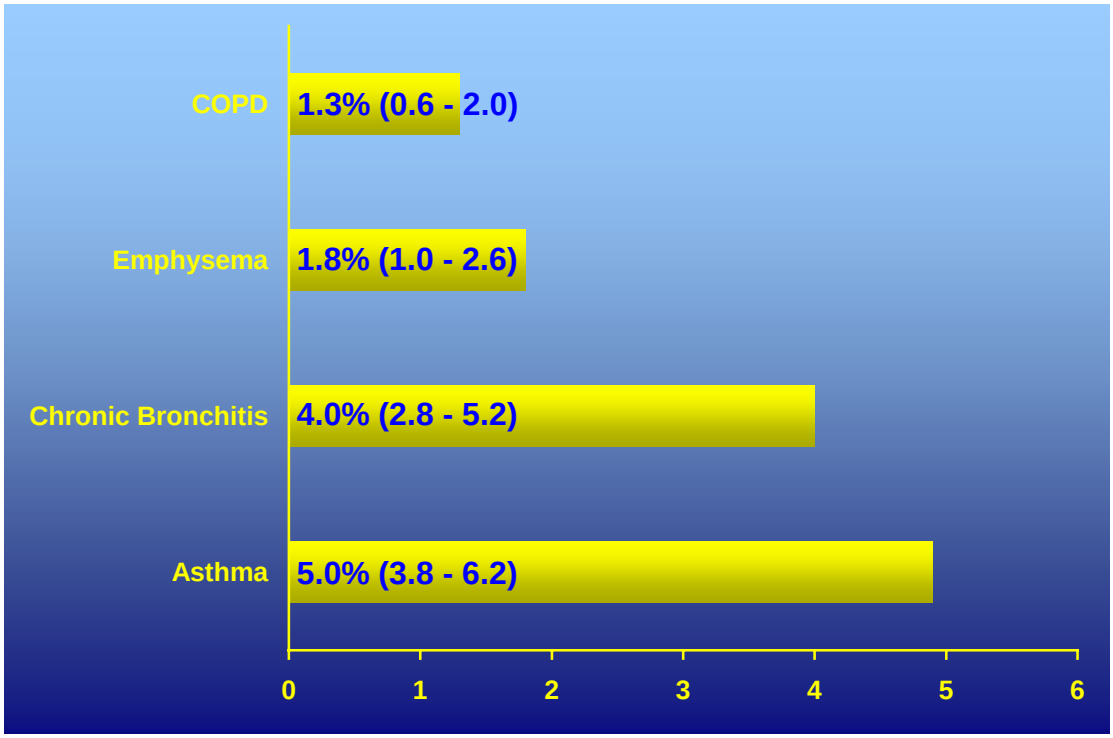

Figure 6. Prevalence of reported medical diagnoses of lung conditions.

3.3. Comparison of clinical and spirometric criteria

The availability of clinical and spirometric results for the same subjects allowed us to compare how these diagnoses relate to one another. Using the FR result as the gold standard, table 5 shows that the sensitivity of clinical bronchitis symptoms was 10.3% and its specificity 96.6%. Positive and negative predictive values were 20.5% and 92.7%, respectively.

Table 5. Comparison of COPD classification (fixed ratio criterion) and symptoms of chronic bronchitis (cough plus sputum for at least 3 months a year, for at least 2 years).

Prevalence of chronic bronchitis symptoms through questionnaire	*Prevalence of COPD (fixed ratio)*		*Total*
	Present	*Absent*	
Present	8	31	39
Absent	70	891	961
Total	78	922	1000

Similar results were obtained when clinical symptoms were compared to the GOLD criterion (Table 6). Sensitivity was 14.8% and specificity 96.4%; positive and negative predictive values were 10.3% and 97.6%, respectively.

Table 6. Comparison of the spirometric COPD classification (GOLD criterion) and the symptoms of chronic bronchitis (cough plus sputum for at least 3 months a year, for at least 2 years).

Prevalence of chronic bronchitis symptoms through questionnaire	*Prevalence of COPD (GOLD - NHANES reference)*		*Total*
	Present	*Absent*	
Present	4	35	39
Absent	23	938	961
Total	27	973	1,000

These analyses were repeated for self-reported COPD, defined as either chronic bronchitis or breathlessness, or both. Sensitivity increased from 10.3% to 45.9%, but specificity decreased from 96.6% to 57.4% (Table 7). The positive predictive value was 8.3% and the negative predictive value 92.7%.

Table 7. Comparison of the spirometric COPD classification (FR criterion) and reported symptoms of chronic bronchitis (cough plus sputum for at least 3 months a year, for at least 2 years) and/or breathlessness.

Prevalence of symptoms of chronic bronchitis and/or breathlessness through questionnaire	*Prevalence of COPD (FR criterion)*		*Total*
	Present	*Absent*	
Present	34	377	411
Absent	40	508	548
Total	74	885	959

For the GOLD criterion, the sensitivity of self-reported COPD was 45.8% and its specificity 57.2% (Table 8). The positive and negative predictive values were respectively 2.7% and 97.6%.

Table 8. Comparison of the spirometric COPD classification (GOLD criterion) and reported symptoms of chronic bronchitis (cough plus sputum for at least 3 months a year, for at least 2 years) and/or breathlessness.

Prevalence of symptoms of chronic bronchitis and/or breathlessness through questionnaire	*Prevalence of COPD (GOLD – NHANES reference)*		*Total*
	Present	*Absent*	
Present	11	400	411
Absent	13	535	548
Total	24	935	959

Therefore, diagnoses based on clinical symptoms evidently failed to identify the vast majority of subjects on whom COPD is present according to spirometry. On the other hand, most subjects with normal spirometry do not report any symptoms. Considering both symptoms of chronic bronchitis and breathlessness, sensitivity increased but specificity decreased. The drop in specificity was partly due to the fact that breathlessness is often reported by asthmatic subjects, who performed well in the spirometry test after the use of bronchodilators.

Of 585 subjects who reported breathlessness, 170 (29.1%) presented a change in FEV1 post-bronchodilator use greater or equal than 12% (or 200 ml) test or had a medical diagnosis of asthma, thus suggesting the presence of asthma. This explains why the specificity of the combined diagnosis (Tables 7 and 8) was reduced sharply.

3.4. Risk factors for COPD

3.4.1. Distribution of the sample according to risk factors

Information was collected on several risk factors for COPD. Table 9 shows the demographic and socioeconomic risk factors, while Table 10 shows all the remaining independent variables.

Almost 60% of all subjects were female, as was expected given the greater longevity of women. Subjects were concentrated in the 40-49 year age group. The average age was 55.5 years (SD 11.9). About half of all subjects classified themselves as having a mixed ethnic background, followed by whites and Indians. Blacks and Asians were rare. Approximately 10% reported a family history (parents, siblings or children) of bronchitis, emphysema or COPD.

Two socioeconomic variables were investigated: schooling of the interviewed subjects and of their fathers, as a proxy for the social class of their family. The average length of schooling of the studied subjects was 7.1 years (SD 5.0). About one in six subjects were unable to inform about their fathers' schooling level, and about one half reported that their fathers had never attended school.

About one in four (25.4%) of the subjects contacted were smokers, and a further fifth (19.0%) were ex-smokers. Current smokers accounted for 38.3% of the men and 16.6% of the women. When 5% of the sample was re-interviewed for quality control, the Kappa statistic for smoking was equal to 0.72, showing a very high degree of repeatability. The lifetime exposure to active smoking was also assessed; 16% of all subjects informed having smoked more that 10 pack-years. The prevalence of reported passive smoking in the subject's home in the previous two weeks was 24.5%.

Almost half of the sample (40.9%) presented values of waist circumference above the proposed cut-off (88 cm for females and 102 cm for males). Overweight and

obese subjects (BMI ≥ 25 kg/m^2) comprised almost four fifths of the sample (79%). The prevalence of obesity was 22.8% in males and 42.4% in females. Only 0.8% of all subjects reported having been admitted to a hospital due to a respiratory illness during childhood. Exposure to dust in the workplace for 10 years or more was reported by 24.4%.

Four sources of domestic smoke were studied: coal was used for cooking by 18.8% of all subjects and for heating by 2.5%; the corresponding exposures to biomass (mainly wood) were 37.0% and 3.6%. Due to the low frequency of exposure to heating fuels, these variables were collapsed into two: exposure to coal and exposure to domestic biomass fuels.

Table 9. Description of the sample according to demographic and socioeconomic variables.

Variable	*Percentage*
Sex	
Men	40.5%
Women	59.5%
Age	
40-49	39.5%
50-59	28.2%
≥ 60	32.3%
Skin color / ethnicity	
Mixed	52.5%
White	25.7%
Indian	17.4%
Black	3.3%
Asian	1.1%
Family history of CODP, bronchitis or emphysema	
No	89.9%
Yes	10.1%
Schooling level (years)	
0-2	19.2%
3-4	11.7%
5-8	32.9%
≥ 9	36.2%
Schooling of the father	
None	54.4%
Some	29.2%
Does not know	16.4%

a. There were up to 5 missing values in the variables listed in the table, among 1074 subjects.

Table 10. Description of the sample according to behavioral, anthropometric and environmental variables.

Variable	*Percentage*
Smoking status	
Never smoked	55.6%
Ex-smoker	19.0%
Current smoker	25.4%
Lifetime cigarettes smoked	
Never smoked	56.3%*
≤1 pack-years	4.8%
1.1-10 pack-years	22.7%
>10 pack-years	16.2%
Passive smoking	
No	75.5%
Yes	24.5%
Hospital admission for respiratory illness during childhood	
No	99.4%
Yes	0.8%
Lifetime exposure to dust in workplace	
Never	55.9%
1-9 years	19.7%
≥ 10 years	24.4%
Exposure to coal stove for cooking or heating	
No	80.6%
Yes	19.4%
Exposure to biomass stove for cooking or heating	
No	62.5%
Yes	37.5%
Waist circumference	
Below cut-off	59.1%
Above cut-off (≥88 cm for females or ≥102 for males)	40.9%
Body mass index (kg/m^2)	
<18.5	0.8%
18.5 – 24.9	20.2%
25 – 29.9	44.5%
≥ 30	34.5%

* For current smoking status there are no missing values, while for lifetime cigarettes smoked there are 4. This explains why the percentage of non-smokers is slightly different from the percentage of subjects with no lifetime exposure.

3.4.2. Crude analyses of main risk factors

Table 11 shows the prevalence of 11 outcomes related to pulmonary conditions, according to the categories of the four main risk factors under study: gender, age, smoking and schooling. All analyses took the clustering of the sample into account.

It is important to bear in mind that, as stated in the original proposal of the study, analyses of risk factors for COPD were planned for the pooled dataset including results from the other participating centers. The statistical power of the comparisons that are reported below is therefore quite low, and some important effects may fail to reach significant levels. For this reason, we have opted to highlight in the next section not only statistically significant results with a $P<0.05$ but also results with P levels from 0.05 to 0.2, because the latter may well become significant when data from all participating sites are pooled in the final analyses. The current results, therefore, must be interpreted with caution.

Gender

Men performed less well than women according to FR, but not in terms of GOLD, ATS or ERS (Table 11). One should bear in mind that the equations used for assessing spirometric results were already stratified by sex.

In terms of symptoms, men were slightly more likely (4.4% versus 3.5%) to fulfill the criteria for chronic bronchitis but the difference was far from being significant ($P=0.51$). Women, on the other hand, were significantly more likely to report breathlessness and wheezing. Conditions requiring a medical diagnosis tended to be more often reported by women, particularly asthma. COPD, chronic bronchitis and emphysema were seldom reported. These differences may be explained by the variability in care-seeking patterns by gender.

Age

As expected, prevalence of spirometric conditions increased with age (Table 11), despite the fact that the reference curves already took age into account. No clear age patterns were found for symptoms. In terms of medical diagnoses, only asthma failed to show a significant increase with age.

Smoking

Table 11 shows that smoking showed some degree of association (P<0.20) with all spirometric outcomes, except ERS. Prevalence among ex-smokers was consistently higher than current smokers and non-smokers. Smokers were also more likely to report wheezing symptoms (P=0.02) but not breathlessness or chronic bronchitis. Ex-smokers presented higher prevalence of emphysema and COPD, but this may be explained by care seeking patterns or the confounding effect of age.

Schooling

The number of years of formal education was inversely associated with the FR spirometric criterion and with breathlessness (Table 11), and possibly (P=0.17) with reported wheezing, but not with any of the other indicators studied.

Table 11. Prevalence of selected pulmonary outcomes according to proposed risk factors.

	Spirometric criteria				*Symptoms*			*Medical diagnosis*			
	FR	***GOLD***	***ATS***	***ERS***	***CB***	***Breathlessness***	***Wheezing***	***CB***	***Emphysema***	***Asthma***	***COPD***
Sex*	*P=0.003*	*P=0.14*	*P=0.20*	*P=0.35*	*P=0.51*	*P<0.001*	*P=0.03*	*P=0.10*	*P=0.89*	*P=0.06*	*P=0.48*
Males	11.0%	3.4%	6.1%	7.1%	4.4%	42.3%	13.7%	2.8%	1.9%	3.3%	1.6%
Females	5.6%	2.2%	4.2%	5.6%	3.5%	64.4%	19.5%	4.9%	1.8%	6.2%	1.1%
Age#	*P<0.001*	*P=0.01*	*P=0.03*	*P=0.001*	*P=0.39*	*P=0.09*	*P=0.31*	*P=0.03*	*P=0.001*	*P=0.13*	*P=0.006*
40-49	2.2%	1.5%	3.7%	3.7%	3.1%	52.9%	19.3%	2.9%	0.2%	3.3%	0.5%
50-59	4.6%	1.8%	3.5%	4.2%	4.7%	54.5%	15.0%	3.3%	2.0%	6.7%	0.7%
60-94	18.4%	5.3%	8.2%	11.5%	4.1%	59.5%	16.3%	6.1%	3.5%	5.5%	2.9%
Smoking*	*P=0.04*	*P=0.17*	*P=0.17*	*P=0.32*	*P=0.05*	*P=0.02*	*P=0.05*	*P=0.16*	*P=0.002*	*P=0.49*	*P=0.04*
Never	6.2%	2.0%	4.0%	5.4%	2.9%	57.3%	15.4%	4.6%	1.2%	4.7%	0.9%
Past	12.3%	4.3%	6.4%	7.5%	6.9%	59.5%	16.3%	5.5%	5.0%	6.4%	3.0%
Current	8.1%	3.1%	6.1%	6.9%	3.7%	48.3%	21.5%	1.9%	0.7%	4.4%	1.1%
Schooling (years)#	*P=0.02*	*P=0.14*	*P=0.58*	*P=0.28*	*P=0.58*	*P=0.003*	*P=0.17*	*P=0.64*	*P=0.78*	*P=0.58*	*P=0.69*
0-2	11.3%	4.3%	5.9%	7.5%	3.4%	61.2%	19.1%	4.4%	2.0%	5.9%	1.0%
3-4	12.1%	2.6%	3.5%	7.8%	3.2%	63.9%	19.4%	3.2%	1.6%	5.7%	2.4%
5-8	6.1%	2.1%	5.5%	5.5%	4.0%	55.8%	16.3%	2.9%	2.0%	4.0%	0.6%
9 or more	6.0%	2.2%	4.3%	5.7%	4.2%	49.4%	15.8%	5.2%	1.6%	4.9%	1.8%
All subjects	7.8%	2.7%	5.0%	6.2%	3.9%	55.5%	17.1%	4.1%	1.8%	5.0%	1.3%
Number in sample	1,000	1,000	1,000	1,000	1,063	1,055	1,063	1,063	1,059	1,063	1,062

* P-values calculated using the Wald test for heterogeneity

P-values calculated using the Wald test for trend

3.4.3. Additional crude analyses

The analyses shown in the preceding sections demonstrated that reported symptoms and medical diagnoses were not reliable and failed to show associations with well-known determinants of poor lung function. Thus, the detailed analyses of other risk factors were restricted to two spirometric outcomes: GOLD and FR. The GOLD criteria are used because they are the most frequently employed in the international literature, and FR has the advantage of not requiring the use of reference curves. Results according to the ATS and ERS criteria are shown in Annex 1.

FR criteria

Table 12 shows the unadjusted prevalence of COPD according to FR criteria (COPD/FR), as well as the corresponding prevalence ratios and confidence intervals, for the demographic and socioeconomic risk factors. Table 13 shows the same information for the behavioral and environmental risk factors.

Men were twice more likely than women to present with COPD/FR (P=0.003). Individuals aged 60 or over were eight times more likely to present with COPD/FR than those aged 40-49 years. Mixed ethnicity was associated with a decreased risk of COPD/FR. There was no association between a family history of bronchitis, emphysema or COPD with COPD/FR.

Subjects with up to four years of formal education were twice as likely to present COPD/FR as those with nine or more years of schooling. Schooling of the father, on the other hand, was not significantly associated with COPD/FR.

Smoking was also associated with COPD/FR (p=0.04). Ex-smokers had twice the risk of non-smokers, and current smokers showed an increase of 30%. A strong dose-response association was also found with lifetime consumption of cigarettes. Reported passive smoking in the past two weeks was not significantly associated with the outcome.

No associations were found between COPD/FR and the following variables: hospital admissions due to respiratory disease in childhood, reported exposure to dust in the workplace, exposure to coal smoke in the home and exposure to domestic biomass smoke.

GOLD criteria

The unadjusted analyses of risk factors for COPD using the GOLD criteria (COPD/GOLD) are presented in Tables 14 and 15. Most results were very similar to those obtained with COPD/FR, although P levels in Tables 14 and 15 tended to be higher than those in Tables 12 and 13 because prevalence of COPD/GOLD is lower than that of COPD/FR and therefore statistical power is reduced.

Overall, the risk factors for COPD/FR and COPD/GOLD were the same in the crude analysis, but the relationship between schooling level and COPD/GOLD was not significant (p=0.14).

Table 12. Crude analysis between COPD (fixed ratio criteria) and the demographic and socioeconomic independent variables

Variable	*% COPD Fixed Ratio Criteria*	*PR (CI95%)*	*P-value*
Sex			0.003*
Men	11.0%	1.97 (1.27; 3.05)	
Women	5.6%	1.00	
Age			<0.001#
40-49	2.2%	1.00	
50-59	4.6%	2.07 (0.78; 5.51)	
≥ 60	18.4%	8.39 (3.77; 18.70)	
Skin color / ethnicity			0.04*
White	12.7%	1.00	
Mixed	5.3%	0.42 (0.24; 0.74)	
Black	14.3%	1.13 (0.41; 3.10)	
Indians	7.0%	0.55 (0.26; 1.15)	
Asian	10.0%	0.79 (0.12; 5.37)	
Family history of COPD, bronchitis or emphysema			0.41*
No	8.0%	1.00	
Yes	5.9%	0.74 (0.36; 1.52)	
Schooling level			0.02#
0-2	11.3%	1.89 (0.99; 3.61)	
3-4	12.1%	2.02 (1.08; 3.80)	
5-8	6.1%	1.02 (0.60; 1.74)	
≥ 9	6.0%	1.00	
Schooling of the father			0.61*
None	7.2%	1.00	
Some	8.1%	1.11 (0.66; 1.89)	
Does not know	9.3%	1.28 (0.78; 2.09)	

* Wald test for heterogeneity # Wald test for trend

Table 13. Crude analysis between COPD (fixed ratio criteria) and the behavioral and environmental independent variables.

Variable	*% COPD Fixed Ratio Criteria*	*PR (CI95%)*	*P-value*
Smoking status			0.04*
Never smoked	6.2%	1.00	
Ex-smoker	12.3%	1.99 (1.17; 3.40)	
Current smoker	8.0%	1.30 (0.80; 2.12)	
Lifetime cigarettes smoked			0.003#
Never smoked	6.1%	1.00	
≤1 pack-years	7.8%	1.28 (0.48; 3.41)	
1.1-10 pack-years	6.6%	1.08 (0.60; 1.94)	
>10 pack-years	15.5%	2.54 (1.60; 4.04)	
Passive smoking			0.13*
No	8.7%	1.00	
Yes	5.2%	0.60 (0.30; 1.17)	
Hospital admission for respiratory illness during childhood			0.61*
No	7.8%	1.00	
Yes	12.5%	1.61 (0.25; 10.21)	
Lifetime exposure to dust at the workplace			0.33#
Never	7.2%	1.00	
1-9 years	6.9%	0.96 (0.50; 1.83)	
≥ 10 years	9.9%	1.37 (0.77; 2.45)	
Exposure to coal stove for cooking or heating			0.94*
No	7.9%	1.00	
Yes	7.7%	0.98 (0.59; 1.62)	
Exposure to biomass stove for cooking or heating			0.95*
No	7.9%	1.00	
Yes	7.8%	0.99 (0.66; 1.48)	

* Wald test for heterogeneity # Wald test for trend

Table 14. Crude analysis between COPD (GOLD criteria) and the demographic and socioeconomic independent variables.

Variable	*% COPD Gold Criteria*	*PR (CI95%)*	*P-value*
Sex			0.14*
Men	3.4%	1.56 (0.86; 2.82)	
Women	2.2%	1.00	
Age			0.01#
40-49	1.5%	1.00	
50-59	1.8%	1.19 (0.28; 5.17)	
≥ 60	5.3%	3.60 (1.31; 9.91)	
Skin color / ethnicity			0.05*
White	5.5%	1.00	
Mulatto	1.3%	0.24 (0.09; 0.66)	
Black	5.7%	1.03 (0.24; 4.38)	
Indians	2.3%	0.42 (0.13; 1.35)	
Asian	0.0%	Non-calculable	
Family history of COPD, bronchitis or emphysema			0.64*
No	2.8%	1.00	
Yes	2.0%	0.71 (0.17; 3.00)	
Schooling level			0.14#
0-2	4.3%	1.98 (0.81; 4.86)	
3-4	2.6%	1.19 (0.30; 4.68)	
5-8	2.1%	0.98 (0.38; 2.55)	
≥ 9	2.2%	1.00	
Schooling of the father			0.52*
None	2.4%	1.00	
Some	3.7%	1.53 (0.66; 3.56)	
Do not know	1.9%	0.77 (0.24; 2.51)	

* Wald test for heterogeneity # Wald test for trend

Table 15. Crude analysis between COPD (GOLD criteria) and the behavioral and environmental independent variables.

Variable	*% COPD Gold Criteria*	*PR (CI95%)*	*P-value*
Smoking status			0.17*
Never smoked	2.0%	1.00	
Ex-smoker	4.3%	2.14 (0.95; 4.84)	
Current smoker	3.1%	1.53 (0.65; 3.61)	
Lifetime cigarettes smoked			0.07#
Never smoked	2.0%	1.00	
≤1 pack-years	0.0%	Non-calculable	
1.1-10 pack-years	3.5%	1.77 (0.76; 4.16)	
>10 pack-years	5.0%	2.51 (1.13; 5.57)	
Passive smoking			0.11*
No	3.2%	1.00	
Yes	1.2%	0.37 (0.11; 1.25)	
Hospital admission for respiratory illness during childhood			0.12*
No	2.6%	1.00	
Yes	12.5%	4.77 (0.67; 33.72)	
Lifetime exposure to dust at the workplace			0.92#
Never	2.5%	1.00	
1-9 years	3.5%	1.36 (0.54; 3.44)	
≥ 10 years	2.5%	0.98 (0.39; 2.49)	
Exposure to coal stove for heating			0.91*
No	2.7%	1.00	
Yes	2.6%	0.94 (0.29; 3.07)	
Exposure to biomass stove for heating			0.96*
No	2.7%	1.00	
Yes	2.7%	0.98 (0.48; 2.00)	

* Wald test for heterogeneity # Wald test for trend

3.4.4. Multivariable analyses

The multivariable analyses took into account four levels of determination of the outcome (Victora, 1997) (Figure 7). The most distal level included sex, age, skin color and a family history of bronchitis, emphysema or COPD, which are biological characteristics that may influence other determinants of CODP. The second level includes schooling, which is mostly determined in childhood and adolescence. The third level incorporates exposures that refer to the subjects' earlier life: hospital admissions, exposure to dust in the workplace, exposure to domestic smoke. The current exposure is smoking (level 4).

Due to the high level of collinearity between smoking status (non, ex, current smoker) and lifetime exposure (pack-years), it was not possible to have all these variables in the model and thus we opted for retaining smoking status. Paternal schooling was also not included in these analyses because of the high number of unknown answers.

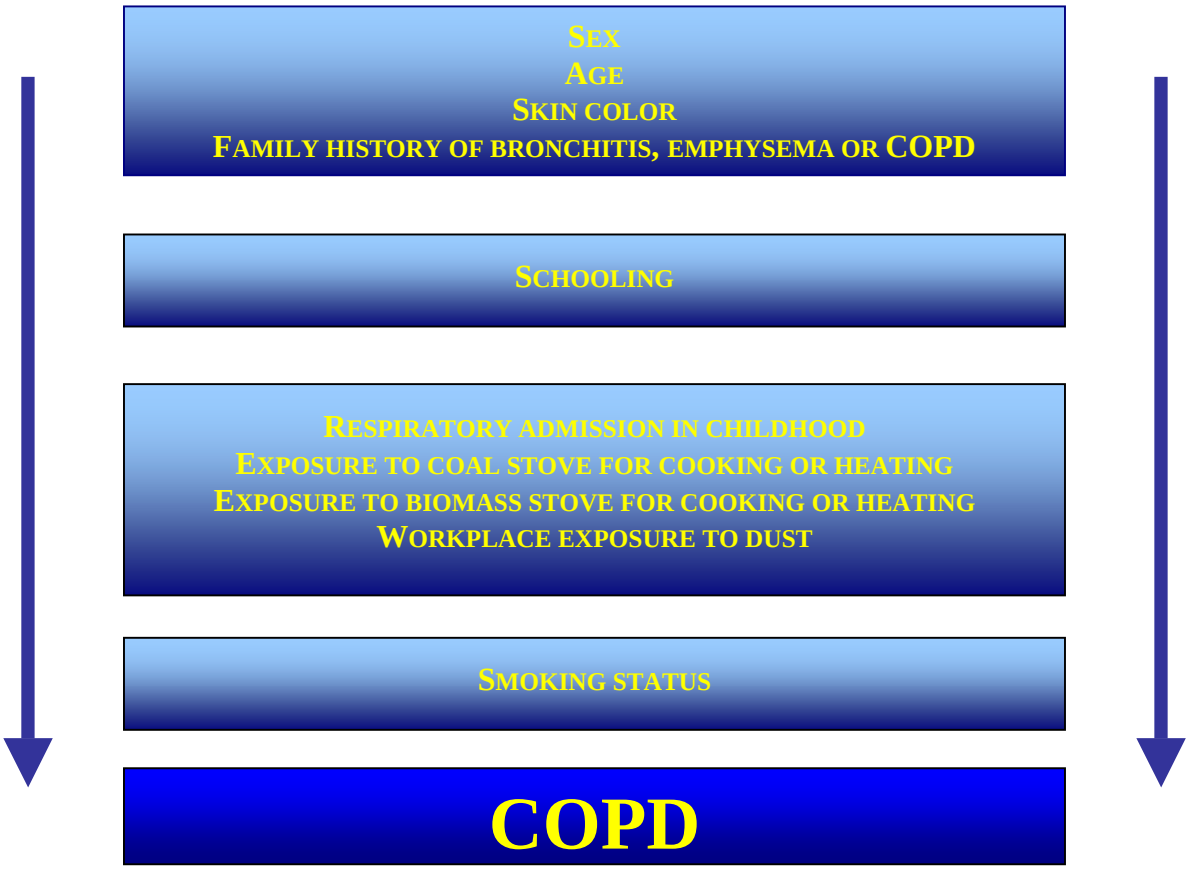

Figure 7. Conceptual framework for guiding the multivariable analyses.

These analyses are presented separately for the FR and GOLD criteria.

FR criteria

Table 16 shows the results of the COPD/FR outcome. The effects of sex, age, skin color and family history were very similar to those obtained in the unadjusted analyses. Therefore, male sex and higher age were associated with higher COPD/FR prevalence. The association with family history had a P level greater than 0.20, and this variable was excluded from the model because it could not confound the effect of other exposures.

In the second level of analyses, schooling was not related to COPD/FR. The crude association of schooling with COPD was being confounded by age, because older subjects had both lower schooling and poorer lung function.

History of respiratory admission, exposure to coal smoke and exposure to dust at the workplace were not significantly related to COPD/FR. Surprisingly, exposure to biomass stove for cooking or heating was a protective factor for COPD/FR. This result is difficult to interpret.

The relationship between COPD/FR and smoking was different from the crude analysis. In the adjusted analysis, smokers were more likely to present COPD/FR, followed by ex-smokers. The higher risk of ex-smokers in the crude analyses was probably due in part to the fact that ex-smokers were older (average 59.9 years) than smokers (average 51.8 years) and non-smokers (average 56.5 years).

Table 16. Adjusted analysis between COPD (fixed ratio criteria) and the independent variables.

Level¨	*Variable*	*PR (CI95%)*	*P-value*
1	**Sex**		0.005*
	Men	1.88 (1.21; 2.90)	
	Women	1.00	
1	**Age**		<0.001#
	40-49	1.00	
	50-59	2.02 (0.76; 5.37)	
	≥ 60	7.56 (3.38; 16.90)	
1	**Skin color / ethnicity**		0.10*
	White	1.00	
	Mixed	0.49 (0.29; 0.81)	
	Black	1.06 (0.42; 2.69)	
	Indian	0.64 (0.31; 1.33)	
	Asian	0.82 (0.12; 5.42)	
1	**Family history of COPD, bronchitis or emphysema**		0.99*
	No	1.00	
	Yes	1.00 (0.48; 2.08)	
2	**Schooling level**		0.69#
	0-2	0.80 (0.42; 1.53)	
	3-4	1.02 (0.61; 1.69)	
	5-8	0.73 (0.45; 1.19)	
	≥ 9	1.00	
3	**Hospital admission for respiratory illness during childhood**		0.18*
	No	1.00	
	Yes	3.00 (0.59; 15.32)	
3	**Lifetime exposure to dust at the work-place**		0.66#
	Never	1.00	
	1-9 years	1.27 (0.69; 2.33)	
	≥ 10 years	1.11 (0.64; 1.91)	
3	**Exposure to coal stove for heating or cooking**		0.59*
	No	1.00	
	Yes	0.86 (0.50; 1.49)	
3	**Exposure to biomass stove for heating or cooking**		0.04*
	No	1.00	
	Yes	0.67 (0.45; 0.99)	
4	**Smoking status**		0.11#
	Never smoked	1.00	
	Ex-smoker	1.31 (0.74; 2.31)	
	Current smoker	1.47 (0.90; 2.41)	

* Wald test for heterogeneity # Wald test for trend ¨ Level of the variable in the hierarchical model

GOLD criteria

Table 17 shows the results of the multivariable analyses for the COPD/GOLD outcome. Men had a 54% higher prevalence, but the difference was not quite significant (P=0.16). Age was positively associated with the outcome, with a 209% increase for those aged 60 years or more. Mixed skin color was related to a decreased risk of COPD/GOLD. No associations were found with the family history of respiratory diseases.

In the second level of analyses, schooling was not associated with COPD/GOLD. The crude effect of schooling was being confounded by age, as for COPD/FR.

COPD/GOLD was not associated with coal or biomass smoke and exposure to dust at the workplace, but it was possibly associated (P=0.12) to hospital admissions due to respiratory symptoms during childhood, with a prevalence ratio of about 6. .

Again, the multivariable analysis approximated the risks of ex- and current smokers, but the trend was not significant (p=0.12).

These results were quite comparable with those observed in the multivariable analyses of COPD/FR, as shown by the prevalence ratios in Tables 16 and 17. P levels for GOLD tended to be less significant because prevalence and therefore statistical power were smaller.

Table 17. Adjusted analysis between COPD (GOLD criteria) and the independent variables.

Level¨	*Variable*	*PR (CI95%)*	*P-value*
1	**Sex**		0.16*
	Men	1.54 (0.84; 2.81)	
	Women	1.00	
1	**Age**		0.03#
	40-49	1.00	
	50-59	1.14 (0.26; 4.92)	
	≥ 60	3.09 (1.09; 8.78)	
1	**Skin color / ethnicity**		<0.001*
	White	1.00	
	Mulatto	0.26 (0.09; 0.73)	
	Black	0.99 (0.24; 4.07)	
	Indian	0.46 (0.14; 1.50)	
	Asian**	-	
1	**Family history of COPD, bronchitis or emphysema**		0.80*
	No	1.00	
	Yes	0.83 (0.18; 3.69)	
2	**Schooling level**		0.86#
	0-2	1.08 (0.37; 3.20)	
	3-4	0.75 (0.21; 2.69)	
	5-8	0.77 (0.32; 1.86)	
	≥ 9	1.00	
3	**Lifetime exposure to dust at the work-place**		0.84#
	Never	1.00	
	1-9 years	1.63 (0.66; 4.04)	
	≥ 10 years	0.85 (0.38; 1.91)	
3	**Hospital admission for respiratory illness during childhood**		0.12*
	No	1.00	
	Yes	6.14 (0.62; 60.54)	
3	**Exposure to biomass stove for heating or cooking**		0.39*
	No	1.00	
	Yes	0.72 (0.34; 1.52)	
3	**Exposure to coal stove for heating or cooking**		0.84*
	No	1.00	
	Yes	0.85 (0.25; 2.85)	
4	**Smoking status**		0.12#
	Never smoked	1.00	
	Ex-smoker	1.69 (0.78; 3.66)	
	Current smoker	1.86 (0.82; 4.23)	

* Wald test for heterogeneity # Wald test for trend ¨ Level of the variable in the hierarchical model

** Due to the fact that no Asians presented COPD/GOLD, the PR is not calculable

3.4.5. COPD and anthropometry

Subjects whose waist circumference was above the cut-off points (88 cm for females and 102 cm for males) showed significant lower (P<0.001) forced expiratory volume (FEV1) values than those with normal waist circumferences. While the average FEV1 was 2.84 (SD 0.77) for subjects below the cut-off point, it was 2.23 (SD 0.52) for those above. The same trend was observed for forced vital capacity (FVC), with averages of 3.58 (SD 0.89) and 2.72 (SD 0.59) for subjects below or above the cut-off points, respectively (P<0.001). However, when waist circumference was treated as a continuous variable, no significant associations were found with FEV1, FVC or FEV1/FVC ratio, indicating possible non-linearity.

The association between BMI and COPD is summarized in Figure 8. According to the FR criterion, the prevalence of COPD was higher in the low-BMI group (<18.5kg/m^2) and a decreased trend was observed in the remaining categories. According to the GOLD criterion, results are difficult to interpret, because the low BMI group presented no cases of COPD/GOLD.

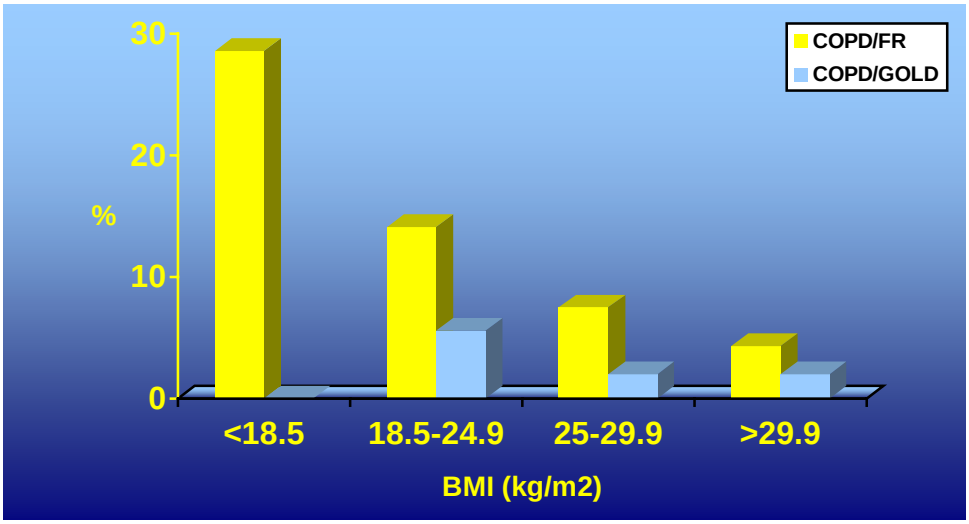

Figure 8. Relationship between COPD (FR and GOLD criteria) and body mass index (BMI).

3.5. Additional analyses

3.5.1. Co-morbidity

Table 18 shows the lifetime prevalence of medical diagnoses for some key conditions. Hypertension and "gastritis" were reported by over 30% of all subjects. Diabetes and heart problems were reported by 10-15%, and other conditions were less frequently reported. Given the subjective nature of this information, these variables should be interpreted with due caution.

One variable from this subset was chosen for the repeatability analyses. Lifetime history of a diagnosis of tuberculosis, when checked by a supervisor on a later occasion, resulted in a kappa coefficient of 1.0, showing perfect agreement between the original interview and the re-interview. The kappa statistic was not calculated for the other conditions.

Table 18. Lifetime prevalence of selected medical diagnoses.

Condition	*Prevalence*
Gastritis	33.6%
Hypertension	31.2%
Diabetes	15.2%
Heart problem	10.5%
Stroke	1.7%
Tuberculosis	1.0%
Lung cancer	0.2%

Table 19 shows the associations between these reported diagnoses and COPD. Except for a significant association between tuberculosis and the GOLD result, all other associations were non-significant.

Table 19. Prevalence of COPD according to co-morbidity.

Condition	*COPD (FR criteria)*		*COPD (GOLD criteria)*	
	Prevalence	*P*	*Prevalence*	*P*
Heart problem		0.84		0.29
Yes	8.3%		1.0%	
No	7.7%		2.9%	
Hypertension		0.89		0.72
Yes	7.6%		3.0%	
No	7.9%		2.6%	
Diabetes		0.26		0.59
Yes	10.1%		3.4%	
No	7.4%		2.6%	
Lung cancer		-		-
Yes	0.0%		0.0%	
No	7.8%		2.7%	
Stroke		0.99		-
Yes	7.7%		0.0%	
No	7.8%		2.7%	
Tuberculosis		0.20		0.001
Yes	18.2%		18.2%	
No	7.7%		2.5%	
Gastritis		0.49		0.11
Yes	8.6%		3.9%	
No	7.4%		2.1%	

3.5.2. Etiologic fractions

Information on the adjusted prevalence ratios (Tables 16 and 17) and on the frequency of different exposures (Tables 9 and 10), allowed us to estimate the etiologic fraction, or population attributable risk of COPD due to different exposures. This expresses the proportion of COPD cases in the community that would be prevented if the exposure was completely eradicated.

According to COPD/FR, the attributable risk for smoking is 10.7%, while it is 19.7% according to COPD/GOLD. Therefore, about one in 5-10 COPD cases would be prevented by smoking control.

We have also calculated attributable risks of hospital admissions due to respiratory disease in childhood. The attributable were 13.8% and 29.1% for COPD/FR and COPD/GOLD, respectively.

3.5.3. Role of smoking in the gender differential in COPD

Male sex was associated with a higher risk of COPD with borderline significance, according to all spirometric criteria used. These associations were reduced after controlling for smoking status. The male/female prevalence ratio was 1.97 for COPD/FR, but when we control for smoking, the value is 1.94. For the COPD/GOLD indicator, the value decreased from 1.56 to 1.40. This shows that part of the excess in COPD among males (particularly for COPD/GOLD) is due to the fact that they smoke more often.

3.6. Medical management

Overall, 7.3% of the individuals reported having used medicines for lung or respiratory problems in the previous 12 months (Table 20). The prevalence rates for COPD/FR positive and negative were, respectively, 14.1% and 6.3% (P=0.009). The most frequently used drugs were bronchodilators, mucolytics, xanthynes and jarobes (Table 20). Among broncodilator users, the majority used it via spray, which is recommended. Most subjects reported using this drug only for symptomatic relief, which is inadequate.

Although influenza immunization is recommended for all COPD patients, only 14.1% of those who were COPD/FR positive reported being vaccinated in the previous year, compared to 9.6% of the remainder (P=0.20).

Subjects were asked if they had ever been submitted to spirometry. The lifetime frequency was 6.9%. Subjects with a diagnosis of COPD/FR presented a lifetime frequency of spirometry twice as high (12.8%) as those without a diagnosis (6.1%). No trends were observed according to educational level.

Table 20. Drugs used for respiratory problems in the past 12 months.

Drug	*N*	*Percentage*
Bronchodilator	32	27.4%
Mucolytics	18	15.4%
Xanthynes	8	6.8%
Jarobes	8	6.8%
Inhaled steroids	5	4.3%
Anti-histaminic	3	2.6%
Others	43	36.7%
Total	117	100%

3.7. Consequences of COPD

Table 21 compares COPD/FR positive and negative subjects in relation to several indicators of quality of life.

Table 21. Association between COPD/FR status and quality of life indicators.

Quality of life indicator	*Prevalence according to COPD/FR status*		*P*
	Positive	*Negative*	
Difficulty in carrying out moderate physical activities	30.0%	17.4%	0.005
Difficulty in carrying out intense physical activities	40.0%	23.9%	0.001
Any limitation due to physical health in the past year	21.3%	19.7%	0.73
Any limitation in the workplace due to physical health	21.3%	18.6%	0.56
Any limitation due to mental health in the past year	13.8%	20.5%	0.15
Any limitation in the workplace due to mental health	8.8%	16.7%	0.07

An additional question inquired whether lung disease affected daily activities in the past year. Of COPD/FR positive subjects, 10.0% answered affirmatively, while 5.9% of the remainder did so (P=0.15).

3.8. Economic impact of COPD

Formal employment in the previous 12 months was reported by 51.3% individuals (42.5% among COPD/FR positive and 53.6% among the negative; P=0.06). This difference disappeared, however, after adjustment for age, because both COPD and unemployment were more common among older subjects.

Among the individuals who did not work in the previous year, 2.3% reported that this was due to lung disease.

Approximately one in ten individuals (9.9%) reported having limited leisure activities due to health problems. The percentages were 8.8% and 8.6% among COPD/FR positive and negative subjects, respectively (P=0.96).

4. DISCUSSION

This is the final report from the second site to complete the PLATINO study. An earlier report summarized the main findings of the São Paulo (Brazil) survey (Menezes, 2003). The present results have to be interpreted with caution because, for most comparisons being made, the required sample size will only be reached after data from all five centers become available in the near future. A full discussion of the implications of the study will be prepared after data collection in all sites is completed.

4.1 Discussion of methodological issues

The non-response rates in Mexico - 31.1% - was considerably higher than that of 15.3% observed in São Paulo. These rates take into account refusals both at the household level – where access to the household was not obtained – and at individual level – when there was access to the household but one or more residents were not interviewed. For the latter, information on non-response by sex is available, and it was more frequent among men (35.1%) than women (19.8%). Fortunately, response rates did not vary according to age or to smoking status.

Several strategies were used in an attempt to reduce non-response. These included repeated visits by different field workers and supervisors, at different times of day and different days of the week. According to the field team, an overwhelming concern about physical security is the reason for a large proportion of all refusals.

On the other hand, the study demonstrated that the spirometric examinations were acceptable to over 98% of those who accepted to be interviewed. Other positive aspects of the study included the strong quality control and standardization protocols.

4.2. Discussion of main results

Prevalence estimates for COPD varied markedly according to the criteria used. When the study was designed it was agreed that the COPD/FR criterion would be used as the main outcome of the study. This showed that 7.8% of all subjects were affected, that is, about one in every 13 individuals. As expected, when the GOLD criteria were used, prevalence was markedly lower (2.7%) because these criteria are more specific. Given that non-response was greater among men than women, the above results may be underestimated, because men have higher prevalence of COPD. If 50% of the sample was made up by men, then COPD/FR prevalence would increase to 8.8% and COPD/GOLD to 2.9%. Because non-response rates did not vary by age or smoking status, there is no need to correct prevalence levels for these variables.

These prevalence levels were markedly lower than those observed in the São Paulo study, of 15.8% and 6.0%, respectively. Further research is needed to understand these important differences.

Results regarding clinical symptoms showed wide variability and low validity. Medical diagnoses related to COPD (either chronic bronchitis, emphysema or COPD diagnoses) were reported by 5.4% of all subjects, a result that is very similar to the Brazilian finding of 5.3%.

The analyses of risk factors were affected by the low statistical power of the study, which was designed as a collaborative study for which final analyses will await data from other sites. Our preliminary analyses showed that male sex and older age were associated with COPD/FR; while smoking showed a possible (but not significant) association. A paradoxical finding was that exposure to biomass stoves was associated with a significant reduction in risk, although this only became apparent after adjustment for age. A comparison of our results with the medical literature will be carried out after the final analyses.

COPD was also associated with anthropometric variables (BMI and abdominal circumference), but this association must be interpreted with caution due to the possibility of reverse causality, that is, that pulmonary illness may have led to weight loss.

Regarding case-management, important problems were identified. Most subjects with COPD do not take medication that could substantially improve their condition, and those who take such medication often do it inappropriately, both in terms of the route of administration and of its frequency. Preventive interventions are also inadequate; only one in seven of the diseased, for example, received flu vaccination in the previous year. Finally, diagnostic procedures were poor; only 12% of those with COPD/FR had ever done spirometric examinations. And only about one in ten COPD/FR subjects reported having a medical diagnosis of COPD.

We have also shown that presence of COPD has important consequences on the daily activities and quality of life of those affected.

4.3. Conclusions

The Mexican survey showed that the study protocol was adequate, although response rates were lower than one might desire, due to reasons that were beyond the control of the investigators. Standardization and quality control procedures ensured that data quality was appropriate.

The experience gained in Mexico City, in addition to that already obtained in the São Paulo survey, was being used to improve the implementation of the study in Montevideo and Santiago, the next sites in the study.

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ANNEX 1. TABLES OF COPD PREVALENCE ACCORDING ATS AND ERS CRITERIA

Table 22. Crude analysis between COPD (ATS criteria) and the independent variables.

Variable	*% COPD ATS Criteria*	*PR (CI95%)*	*p-value*
Sex			0.11*
Men	13.1%	1.33 (0.94; 1.87)	
Women	9.9%	1.00	
Age			0.02#
40-49	8.9%	1.00	
50-59	11.7%	1.32 (0.86; 2.01)	
≥ 60	14.3%	1.62 (1.09; 2.39)	
Skin color / ethnicity			0.3*
White	10.6%	1.00	
Mulatto	9.8%	0.92 (0.62; 1.38)	
Black	16.5%	1.55 (0.95; 2.54)	
Native Brazilians	17.4%	1.64 (0.66; 4.06)	
Asian	18.2%	1.71 (0.62; 4.72)	
Family history of COPD, bronchitis or emphysema			0.6*
No	11.6%	1.00	
Yes	9.9%	0.86 (0.49; 1.50)	
Schooling level			0.03#
0-2	15.8%	1.75 (1.02; 3.01)	
3-4	11.2%	1.25 (0.76; 2.05)	
5-8	9.5%	1.05 (0.56; 1.98)	
≥ 9	9.0%	1.00	
Schooling of the father			0.7*
None	11.4%	1.00	
Some	10.0%	0.88 (0.58; 1.32)	
Do not know	12.6%	1.10 (0.70; 1.75)	
Smoking status			<0.001#
Never smoked	6.9%	1.00	
Ex-smoker	9.5%	1.39 (0.86; 2.24)	
Current smoker	21.5%	3.14 (1.99; 4.96)	
Lifetime cigarettes smoked			<0.001#
Never smoked	6.9%	1.00	
≤1 pack-years	7.8%	1.14 (0.62; 2.09)	
1.1-10 pack-years	12.1%	1.76 (1.02; 3.03)	
>10 pack-years	23.7%	3.46 (2.18; 5.49)	
Passive smoking			0.08*
No	10.3%	1.00	
Yes	13.8%	1.35 (0.97; 1.89)	
Hospital admission for respiratory illness during childhood			0.9*
No	11.4%	1.00	
Yes	10.3%	0.91 (0.30; 2.80)	
Lifetime exposure to dust at the workplace			0.05#
Never	9.1%	1.00	
1-9 years	12.6%	1.37 (0.86; 2.19)	
≥ 10 years	13.5%	1.47 (0.99; 2.19)	
Exposure to coal stove for cooking or heating			0.03*
No	10.4%	1.00	
Yes	16.6%	1.59 (1.05; 2.42)	
Exposure to biomass stove for cooking or heating			0.7*
No	11.0%	1.00	
Yes	11.7%	1.06 (0.74; 1.53)	

* Wald test for heterogeneity # Wald test for trend

Table 23. Crude analysis between COPD (ERS criteria) and the independent variables

Variable	*% COPD ERS Criteria*	*PR (CI95%)*	*p-value*
Sex			1.0*
Men	14.3%	1.01 (0.73; 1.40)	
Women	14.2%	1.00	
Age			<0.001#
40-49	9.9%	1.00	
50-59	15.3%	1.54 (1.11; 2.14)	
≥ 60	19.1%	1.93 (1.38; 2.70)	
Skin color / ethnicity			0.3*
White	14.4%	1.00	
Mulatto	11.3%	0.92 (0.62; 1.38)	
Black	18.6%	0.79 (0.54; 1.15)	
Native Brazilians	21.7%	1.51 (0.67; 3.38)	
Asian	18.2%	1.26 (0.46; 3.46)	
Family history of COPD, bronchitis or emphysema			0.8*
No	14.4%	1.00	
Yes	13.5%	0.94 (0.57; 1.54)	
Schooling level			0.07#
0-2	17.6%	1.56 (0.93; 2.62)	
3-4	15.0%	1.33 (0.83; 2.13)	
5-8	13.1%	1.16 (0.66; 2.05)	
≥ 9	11.3%	1.00	
Schooling of the father			0.6*
None	14.3%	1.00	
Some	12.4%	0.87 (0.59; 1.28)	
Do not know	16.0%	1.12 (0.76; 1.66)	
Smoking status			0.004#
Never smoked	11.7%	1.00	
Ex-smoker	12.0%	1.02 (0.68; 1.53)	
Current smoker	21.5%	1.83 (1.26; 2.68)	
Lifetime cigarettes smoked			0.003#
Never smoked	11.7%	1.00	
≤1 pack-years	10.4%	0.89 (0.53; 1.47)	
1.1-10 pack-years	14.6%	1.24 (0.78; 1.99)	
>10 pack-years	23.2%	1.97 (1.34; 2.91)	
Passive smoking			0.08*
No	12.9%	1.00	
Yes	17.3%	1.34 (0.96; 1.86)	
Hospital admission for respiratory illness during childhood			0.6*
No	14.4%	1.00	
Yes	10.3%	0.72 (0.23; 2.23)	
Lifetime exposure to dust at the workplace			0.12#
Never	12.7%	1.00	
1-9 years	13.9%	1.09 (0.71; 1.68)	
≥ 10 years	16.7%	1.31 (0.93; 1.83)	
Exposure to coal stove for cooking or heating			0.03*
No	13.2%	1.00	
Yes	20.0%	1.51 (1.04; 2.20)	
Exposure to biomass stove for cooking or heating			0.7*
No	14.7%	1.00	
Yes	13.8%	0.94 (0.69; 1.30)	

* Wald test for heterogeneity # Wald test for trend

Table 24. Adjusted analysis between COPD (ATS criteria) and the independent variables.

Level¨	*Variable*	*PR (CI95%)*	*p-value*
1	**Sex**		0.09*
	Men	1.34 (0.95; 1.89)	
	Women	1.00	
1	**Age**		0.02#
	40-49	1.00	
	50-59	1.31 (0.86; 2.00)	
	≥ 60	1.63 (1.10; 2.41)	
1	**Skin color / ethnicity**		0.2*
	White	1.00	
	Mulatto	0.96 (0.64; 1.44)	
	Black	1.60 (0.98; 2.61)	
	Native Brazilians	1.64 (0.65; 4.05)	
	Asian	1.74 (0.68; 4.44)	
1	**Family history of COPD, bronchitis or emphysema**		0.6*
	No	1.00	
	Yes	0.87 (0.50; 1.52)	
2	**Schooling level**		0.12#
	0-2	1.55 (0.88; 2.71)	
	3-4	1.12 (0.67; 1.89)	
	5-8	1.02 (0.55; 1.90)	
	≥ 9	1.00	
3	**Hospital admission for respiratory illness during childhood**		0.9*
	No	1.00	
	Yes	1.09 (0.35; 3.35)	
3	**Lifetime exposure to dust at the workplace**		0.08#
	Never	1.00	
	1-9 years	1.48 (0.92; 2.37)	
	≥ 10 years	1.40 (0.95; 2.07)	
3	**Exposure to biomass stove for heating or cooking**		0.6*
	No	1.00	
	Yes	0.92 (0.65; 1.31)	
3	**Exposure to coal stove for heating or cooking**		0.03*
	No	1.00	
	Yes	1.61 (1.05; 2.47)	
4	**Smoking status**		<0.001#
	Never smoked	1.00	
	Ex-smoker	1.41 (0.87; 2.27)	
	Current smoker	3.54 (2.21; 5.66)	

* Wald test for heterogeneity # Wald test for trend ¨ Level of the variable in the hierarchical model

Table 25. Adjusted analysis between COPD (ERS criteria) and the independent variables.

*Level****	*Variable*	*PR (CI95%)*	*p-value*
1	**Sex**		0.9*
	Men	1.03 (0.74; 1.44)	
	Women	1.00	
1	**Age**		<0.001#
	40-49	1.00	
	50-59	1.54 (1.11; 2.14)	
	≥ 60	1.93 (1.37; 2.70)	
1	**Skin color / ethnicity**		0.3*
	White	1.00	
	Mulatto	0.82 (0.56; 1.20)	
	Black	1.33 (0.86; 2.04)	
	Native Brazilians	1.47 (0.68; 3.16)	
	Asian	1.21 (0.48; 3.05)	
1	**Family history of COPD, bronchitis or emphysema**		0.8*
	No	1.00	
	Yes	0.94 (0.57; 1.54)	
2	**Schooling level**		0.4#
	0-2	1.28 (0.75; 2.16)	
	3-4	1.12 (0.69; 1.82)	
	5-8	1.10 (0.63; 1.93)	
	≥ 9	1.00	
3	**Hospital admission for respiratory illness during childhood**		0.8*
	No	1.00	
	Yes	0.86 (0.27; 2.73)	
3	**Lifetime exposure to dust at the workplace**		0.10#
	Never	1.00	
	1-9 years	1.20 (0.78; 1.85)	
	≥ 10 years	1.32 (0.95; 1.82)	
3	**Exposure to biomass stove for heating or cooking**		0.3*
	No	1.00	
	Yes	0.85 (0.62; 1.17)	
3	**Exposure to coal stove for heating or cooking**		0.10*
	No	1.00	
	Yes	1.39 (0.94; 2.06)	
4	**Smoking status**		0.001#
	Never smoked	1.00	
	Ex-smoker	1.06 (0.72; 1.57)	
	Current smoker	2.11 (1.45; 3.08)	

* Wald test for heterogeneity ** Wald test for trend *** Level of the variable in the hierarchical model