

**FEDERAL UNIVERSITY OF PELOTAS
POST-GRADUATE PROGRAM IN EPIDEMIOLOGY**

PLATINO STUDY – URUGUAYAN 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, Montevideo, 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 Montevideo survey, the third 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 Montevideo and the metropolitan area, 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 4 percent points (see original proposal). To allow for non-response we aimed at obtaining 56 census tracts in Montevideo City, and 12 census tracts from the metropolitan area to select 15 households, on average, from each tract. We expected approximately an average of one person aged 40 years or more per household. In Montevideo this ratio is=1.64.

The metropolitan area was divided into two strata: Montevideo city and its suburban municipalities. 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 strata.

<i>Stratum</i>	<i>Population</i>		<i>Sample (subjects)</i>	<i>Sampling fraction/10,000</i>
	N	%	n	n/N
MONTEVIDEO	2537.4	83.87%	936	1.25
SUBURBIAN	56.6	16.13%	180	1.25
METROPOLITAN REGION (MR)	2594.0	100%	1116	1.25

Population data were obtained from the 1996 National Demographic Census.

2.2.1. Selection of census tracts

For purposes of the annual National Household Surveys (NHS), a frame sample of all census tracts in MONTEVIDEO was prepared by the National Institute of Statistics. This sample is self-weighting, and was used to select the census tracts (CT) for the present survey. This master sample included 2121 census tracts in the Montevideo city and 6611 in the MR (Table 2). Before selecting the CTs, collective tracts (hospitals, army, etc) were excluded. All other tracts in the master sample were then stratified by geographical zone (Montevideo and other municipalities around) and within each zone, they were ranked by mean family income level as measured in the last Household Survey. A systematic sample was then obtained with probability proportionate to size, taking into account the number of households (average 90) in each tract.

Figure 1 - Selection of the 56 census tracts in Montevideo and 12 in the MP stratified by geographical zone and by family income.

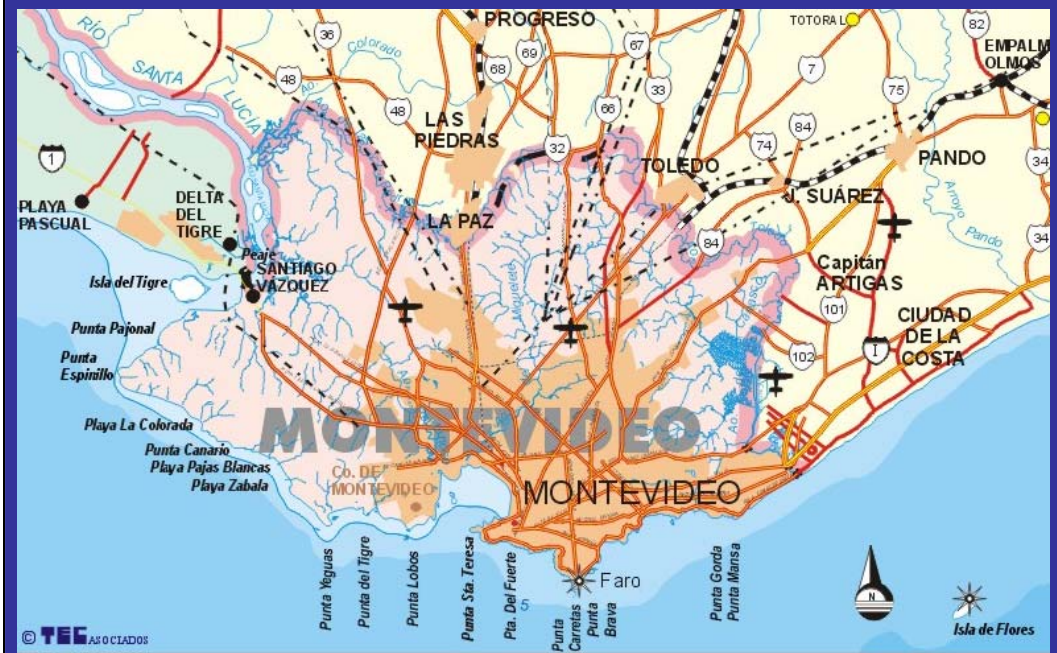


Table 2. Sampling of census tracts by stratum

<i>Stratum</i>	<i>N</i>	<i>B</i>	<i>Census tracts</i> $a = (n/b)$
MONTEVIDEO	936	15	56
SUBURBIAN	180	15	12
METROPOLITAN REGION (MR)	1116	--	68

2.2.2. Sampling of the households

All selected tracts were visited, and all inhabited households in each of these tracts were enumerated in early 2003. These total numbers were divided by the number of households counted in 1996 during the National Census. The ratio of households counted in 2003 over those counted in 1996 represented a correction factor for

population growth. 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 updated 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: $FEV_1/FVC < 70\%$, where FEV_1 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) - $FEV_1/FVC < 70\%$ and $FEV_1 < 80\%$ predicted;
- ✓ European Respiratory Society (ERS, 1993) - $FEV_1/FVC < 88\%$ of predicted in men and $< 89\%$ predicted in women;
- ✓ American Thoracic Society (ATS, 1994) - FEV_1/FVC below 5th percentile and $FEV_1 < 100\%$ 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 Montevideo survey, 34 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. Thirty two 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 Seca[®] stadiometer (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 Seca[®] weight scale (precision 200 g) was used. Subjects were weighted without shoes and wearing light clothes.

2.5.4. Waist circumference. An inextensible Fiberglass[®] tape (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, two fieldwork supervisors, a nutritionist, and 14 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 October, 2003 until January 2004. The study team included 14 interviewers working in pairs (all of whom were technician specialized in pulmonary function test, two field supervisors, one local spirometry supervisors and a secretary.

All field methods were tested in a pilot study carried out in October 2003 in a low-class area in Montevideo city, around the hospital, where Platino Center was placed.

The logistic of the fieldwork included several steps. The first visit to the selected households was carried out by the “scouts” who, in households with subjects aged 40 years or more, delivered an official letter explaining the aim of the study. Eligible subjects were informed that the study supervisors would contact them in order to arrange the best time for the interview and examination.

Daily, the interviewers visited the study headquarters early in the morning to check the calibration of the equipment and to receive a list of the households to be visited. At the same time, spirometry results obtained in the previous day were downloaded.

Each interviewer carried a backpack containing all the equipment. Depending on the distance between the headquarters and the census tract to be visited, interviewers traveled by bus, car or in a rented van.

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 according to this on-the-spot evaluation. During data collection, the spirometries were sent weekly to Mexico by email. The Mexican team analyzed their quality and provided weekly quality control reports with assessments of each individual interviewer. At the same time the local supervisor of the study was also checking the spirometries daily and working with the interviewers to correct any inaccuracies detected by him or by the Montevidean team. Results of the regular quality control procedures, which confirmed that average measurement quality was 80% or higher throughout the study period are in the home page.

Interviews – 10% of the interviews were repeated by the supervisors. Three to four 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 Medicine School and from the Maciel Hospital. 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 hospital.

2.11. Processing of data

All questionnaires were photocopied, and the originals were sent to the Coordinating Centre (CC), while the copy remained in Montevideo. 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 Montevideo, 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 1.6% at the household level, 14.7% at the individual questionnaire level, and 2.9% for spirometry. The overall rate of non-response was 18.1%, obtained by multiplying the response rates.

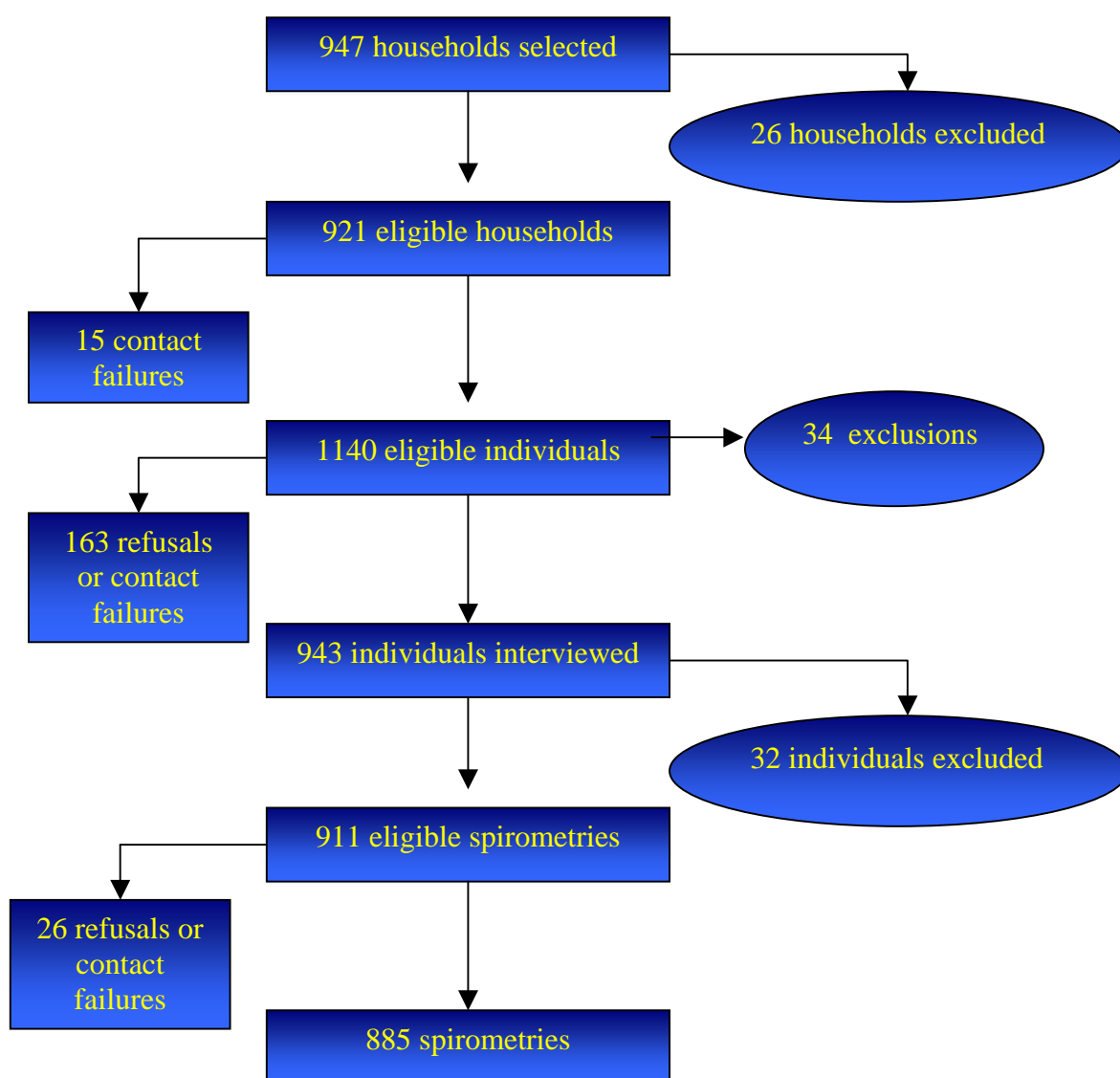


Figure 3. Number of households and individuals included in the different phases of the study.

Even for the 163 non-responders, we tried to obtain information on sex, age and smoking status; 93 (57%) answered these questions. This information was then extrapolated to the 163 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.

<i>Variable</i>	<i>% individual non-response</i>
Sex	
Males	17.7%
Females	12.6%
Age	
40-49	11.1%
50-59	12.7%
≥ 60	17.6%
Current smoking status	
No	14.9%
Yes	14.3%

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.

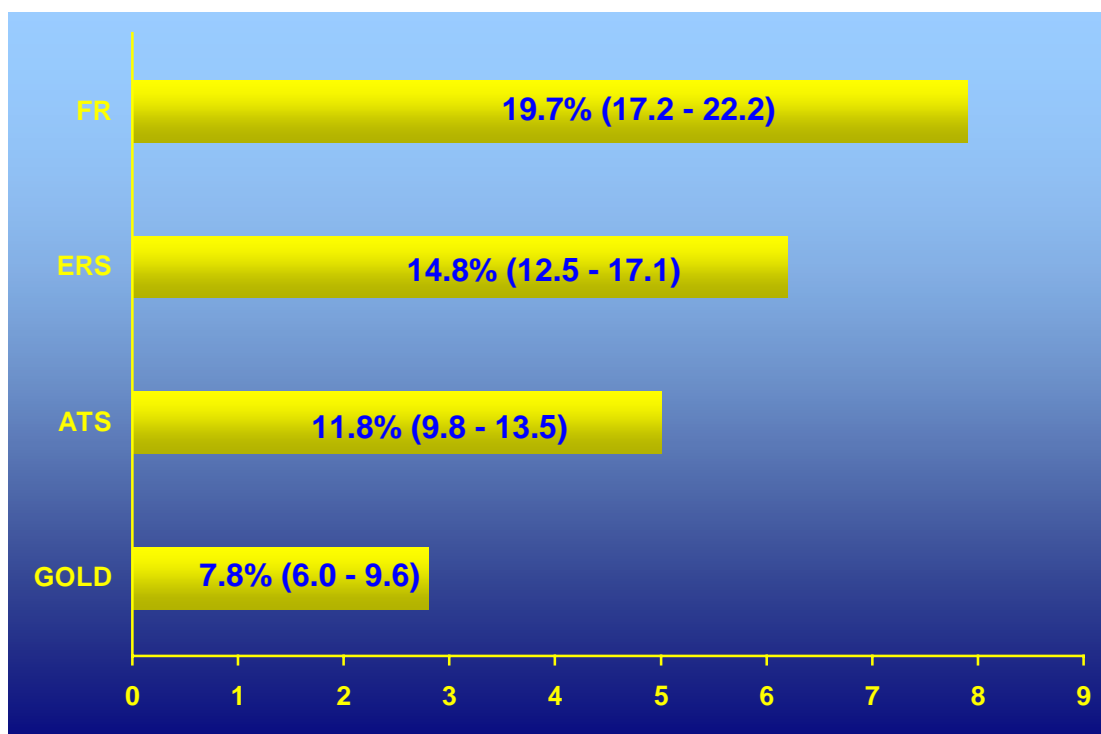


Figure 4. Prevalence of COPD based on different spirometric criteria.

The fixed ratio (FR) criterion showed the highest prevalence, of 19.7%, followed by the ERS (14.8%), ATS94 (11.8%) and GOLD (7.8%) 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 0.87 and 1.02, 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).

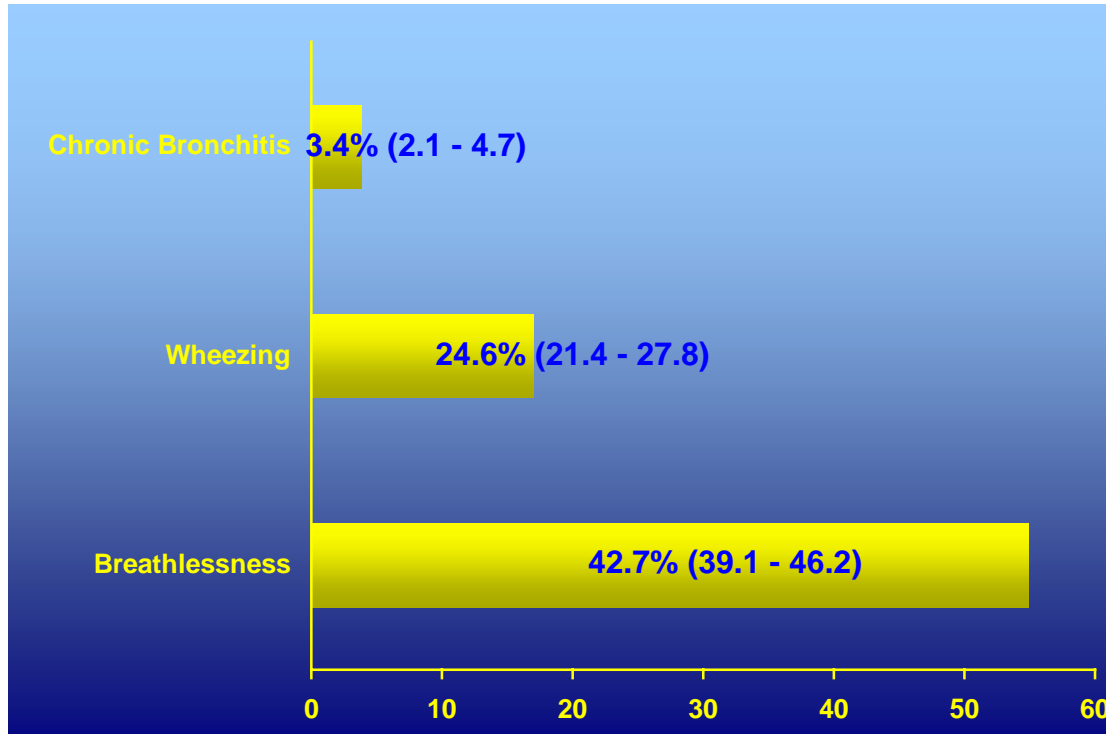


Figure 5. Prevalence of reported respiratory symptoms.

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 3.4%. Breathlessness due to exercise, and wheezing in the last 12 months were reported, respectively, by 42.7% and 24.6% of all subjects (Figure 5).

When 10% 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 0.54 for cough and 0.41 for sputum, showing that agreement was intermediate to poor.

Figure 6 shows the prevalence of reported medical diagnoses of bronchitis, emphysema, asthma and COPD. All conditions, except asthma, were reported by fewer than 5% of those interviewed. A medical diagnosis of either chronic bronchitis, emphysema or COPD was reported by 2.4% of all subjects.

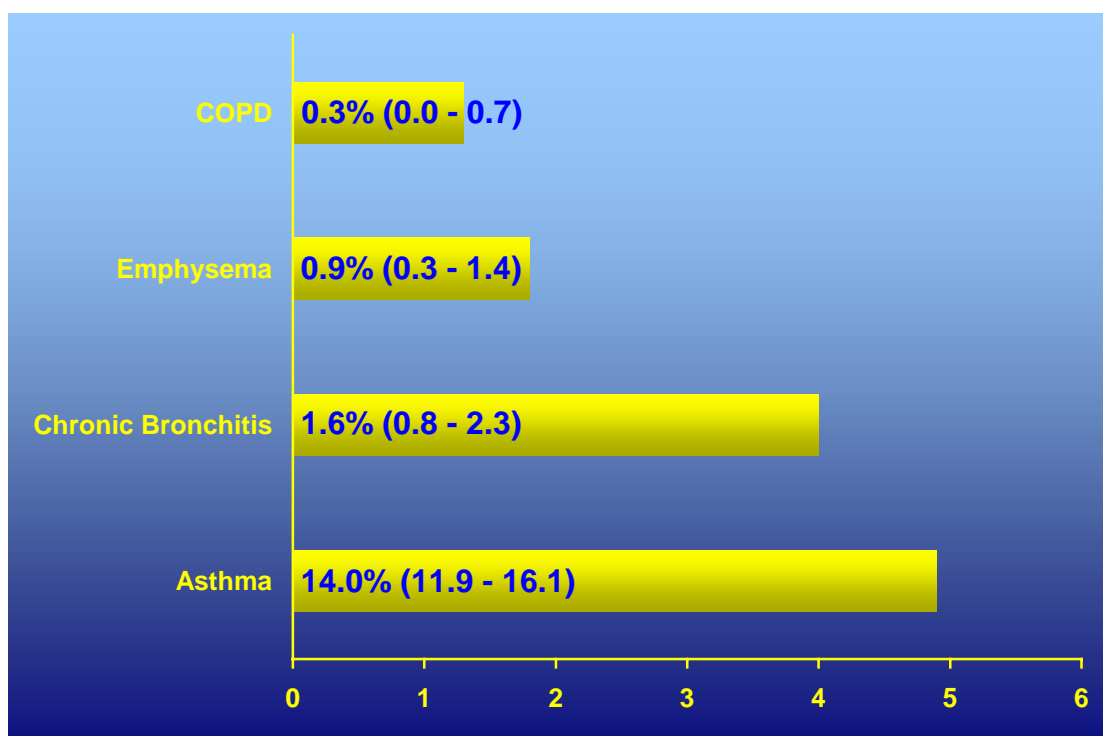


Figure 6. Prevalence of reported medical diagnoses of lung conditions.

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 8.0% and its specificity 97.5%. Positive and negative predictive values were 43.8% and 81.2%, 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).

<i>Prevalence of chronic bronchitis symptoms through questionnaire</i>	<i>Prevalence of COPD (fixed ratio)</i>		<i>Total</i>
	<i>Present</i>	<i>Absent</i>	
Present	14	18	32
Absent	160	691	851
Total	174	709	883

Similar results were obtained when clinical symptoms were compared to the GOLD criterion (Table 6). Sensitivity was 14.5% and specificity 97.3%; positive and negative predictive values were 31.3% and 93.1%, 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).

<i>Prevalence of chronic bronchitis symptoms through questionnaire</i>	<i>Prevalence of COPD (GOLD - NHANES reference)</i>		<i>Total</i>
	<i>Present</i>	<i>Absent</i>	
Present	10	22	32
Absent	59	792	851
Total	69	814	883

These analyses were repeated for self-reported COPD, defined as either chronic bronchitis or breathlessness, or both. Sensitivity increased from 8.0% to 28.5%, but specificity decreased from 97.5% to 73.7% (Table 7). The positive predictive value was 20.9% and the negative predictive value 80.9%.

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.

<i>Prevalence of symptoms of chronic bronchitis and/or breathlessness through questionnaire</i>	<i>Prevalence of COPD (FR criterion)</i>		<i>Total</i>
	<i>Present</i>	<i>Absent</i>	
Present	49	186	235
Absent	123	520	643
Total	172	706	878

For the GOLD criterion, the sensitivity of self-reported COPD was 29.0% and its specificity 73.4% (Table 8). The positive and negative predictive values were respectively 8.5% and 92.4%.

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.

<i>Prevalence of symptoms of chronic bronchitis and/or breathlessness through questionnaire</i>	<i>Prevalence of COPD (GOLD – NHANES reference)</i>		<i>Total</i>
	<i>Present</i>	<i>Absent</i>	
Present	20	215	235
Absent	49	594	643
Total	69	809	878

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 400 subjects who reported breathlessness, 161 (40.3%) presented a change in FEV1 post-bronchodilator use greater or equal than 12% (or 200 ml) 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 sharply reduced.

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. The average age was 60.3 years (SD 12.7). Most subjects classified themselves as having white skin color, followed by mulattoes and blacks.

There were very few Asians and Native Americans. 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 7.9 years (SD 4.5). Almost 40% of the subjects were unable to inform about their fathers' schooling level, and about one fourth reported that their fathers had never attended school.

About 30% of the subjects contacted were smokers, and a further 30% ex-smokers. Current smokers accounted for 33.3% of the men and 24.5% of the women. When 10% of the sample was re-interviewed for quality control, the Kappa statistic for smoking was equal to 0.72, showing high repeatability. Lifetime smoking was also assessed; 41% of all subjects informed having smoked more than 10 pack-years. The prevalence of reported passive smoking in the subject's home in the previous two weeks was 31%.

Almost 40% of all subjects presented values of waist circumference above the recommended cut-off (88 cm for females and 102 cm for males). Overweight and obese subjects ($BMI \geq 25 \text{ kg/m}^2$) comprised almost 70% of the sample. The prevalence of obesity ($BMI \geq 30 \text{ kg/m}^2$) was 29.6% in males and 36.7% in females. Only 2.2% 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 38.6%.

Four sources of domestic smoke were studied: coal was used for cooking by 24.8% of all subjects and for heating by 8.6%; the corresponding exposures to biomass (mainly wood) were 45.9% and 9.3%. 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.

<i>Variable</i>	<i>Percentage</i>
Sex	
Men	40.3%
Women	59.7%
Age	
40-49	26.3%
50-59	26.2%
≥ 60	47.5%
Skin color / ethnicity	
White	90.5%
Mulatto	6.0%
Black	2.1%
Native Americans	1.0%
Asians	0.4%
Family history of COPD, bronchitis or emphysema	
No	90.2%
Yes	9.8%
Schooling level (years)	
0-2	6.6%
3-4	15.5%
5-8	38.9%
≥ 9	39.0%
Schooling of the father	
None	24.3%
Some	37.4%
Does not know	38.3%

a. There were up to 9 missing values in the variables listed in the table, among 943 subjects.

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

<i>Variable</i>	<i>Percentage</i>
Smoking status	
Never smoked	43.0%
Ex-smoker	29.0%
Current smoker	28.0%
Lifetime cigarettes smoked	
Never smoked	43.0%
≤1 pack-years	2.9%
1.1-10 pack-years	12.7%
>10 pack-years	41.4%
Passive smoking	
No	68.6%
Yes	31.4%
Hospital admission for respiratory illness during childhood	
No	97.8%
Yes	2.2%
Lifetime exposure to dust in workplace	
Never	43.0%
1-9 years	18.4%
≥ 10 years	38.6%
Exposure to coal stove for cooking or heating	
No	86.2%
Yes	13.8%
Exposure to biomass stove for cooking or heating	
No	43.5%
Yes	56.5%
Waist circumference	
Below cut-off	68.1%
Above cut-off (≥88 cm for females or ≥102 for males)	38.9%
Body mass index (kg/m²)	
<18.5	1.8%
18.5 – 24.9	28.1%
25 – 29.9	36.3%
≥ 30	33.8%

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 all spirometric criteria (Table 11). One should bear in mind that the equations used for assessing spirometric results were already stratified by sex.

In terms of symptoms, women were more likely to report breathlessness. Women more often reported a medical diagnosis of asthma. Therefore, males tended to have higher prevalence of spirometric diagnoses, but there were no clear gender differences for conditions with a medical diagnosis, except for asthma, which tended to be more common among women. This difference 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. Reported symptoms of breathlessness also tended to increase with age. No clear age patterns were found for wheezing or chronic bronchitis. In terms of medical diagnoses, only COPD showed a significant increase with age.

Smoking

Table 11 shows that smoking showed associations ($P < 0.05$) with all spirometric outcomes. Prevalence among ex-smokers was higher than current smokers and non-smokers for the GOLD and FR criteria. Current smokers were more likely to be positive according to ATS and ERS criteria. Wheezing symptoms and medical diagnosis of COPD were also more likely among current smokers.

Schooling

The number of years of formal education was inversely associated with the FR spirometric criterion, symptoms of breathlessness, and medical diagnosis of asthma and emphysema (Table 11).

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

	<i>Spirometric criteria</i>				<i>Symptoms</i>			<i>Medical diagnosis</i>			
	<i>FR</i>	<i>GOLD</i>	<i>ATS</i>	<i>ERS</i>	<i>CB</i>	<i>Breathlessness</i>	<i>Wheezing</i>	<i>CB</i>	<i>Emphysema</i>	<i>Asthma</i>	<i>COPD</i>
Sex*	<i>P</i> <0.001	<i>P</i> =0.02	<i>P</i> =0.04	<i>P</i> =0.01	<i>P</i> =0.65	<i>P</i> <0.001	<i>P</i> =0.24	<i>P</i> =0.62	<i>P</i> =0.58	<i>P</i> <0.001	<i>P</i> =0.38
Males	27.2%	10.8%	14.7%	18.6%	3.7%	30.2%	26.8%	1.8%	1.1%	8.4%	0.5%
Females	14.5%	5.7%	9.8%	12.2%	3.2%	51.2%	23.1%	1.4%	0.7%	17.8%	0.2%
Age#	<i>P</i> <0.001	<i>P</i> <0.001	<i>P</i> =0.002	<i>P</i> <0.001	<i>P</i> =0.78	<i>P</i> =0.01	<i>P</i> =0.71	<i>P</i> =0.46	<i>P</i> =0.90	<i>P</i> =0.12	<i>P</i> <0.001
40-49	5.1%	3.0%	6.8%	7.2%	2.8%	34.8%	23.0%	1.6%	0.8%	15.3%	0.0%
50-59	12.7%	7.2%	11.4%	12.2%	4.1%	45.3%	26.3%	2.4%	0.8%	17.0%	0.0%
60-94	35.1%	11.0%	14.9%	20.7%	3.4%	45.6%	24.6%	1.1%	0.9%	11.6%	0.7%
Smoking*	<i>P</i> =0.005	<i>P</i> =0.005	<i>P</i> =0.002	<i>P</i> =0.002	<i>P</i> =0.46	<i>P</i> =0.16	<i>P</i> <0.001	<i>P</i> =0.44	<i>P</i> =0.62	<i>P</i> =0.14	<i>P</i> <0.001
Current	22.5%	9.1%	17.4%	21.0%	4.2%	45.6%	36.0%	1.9%	1.1%	16.7%	0.8%
Past	23.3%	10.9%	11.3%	15.1%	2.2%	37.4%	20.9%	0.7%	1.1%	12.5%	0.4%
Never	15.3%	4.8%	8.4%	10.5%	3.7%	44.5%	19.8%	2.0%	0.5%	16.5%	0.0%
Schooling (years) #	<i>P</i> =0.001	<i>P</i> =0.71	<i>P</i> =0.44	<i>P</i> =0.36	<i>P</i> =0.40	<i>P</i> =0.01	<i>P</i> =0.73	<i>P</i> =0.16	<i>P</i> =0.05	<i>P</i> =0.02	<i>P</i> =0.07
0-2	29.4%	5.9%	9.8%	15.7%	1.6%	50.0%	24.2%	1.6%	0.0%	11.3%	0.0%
3-4	23.5%	6.6%	10.3%	16.2%	2.1%	48.3%	23.3%	0.7%	0.0%	10.3%	0.7%
5-8	21.5%	9.0%	12.5%	15.7%	4.4%	43.8%	24.9%	0.6%	0.8%	12.6%	0.6%
9 or more	15.2%	7.5%	12.1%	13.5%	3.3%	37.8%	25.1%	3.0%	1.4%	17.5%	0.0%
All subjects	19.7%	7.8%	11.8%	14.8%	3.4%	42.7%	24.6%	1.6%	0.9%	14.0%	0.3%
Number in sample	885	885	881	885	941	937	943	943	942	943	941

* 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 87% more likely than women to present with COPD/FR. Individuals aged 60 or over were six times more likely to present COPD/FR than those aged 40-49 years. There were no significant associations with skin color or with family history of COPD, bronchitis or emphysema.

Subjects with up to two years of formal education were 94% more likely to present COPD/FR than those with nine or more years of schooling. Individuals who did not know their fathers' schooling level were more likely to present COPD/FR than other subjects.

Smoking was also associated with COPD/FR ($p=0.005$). Relative to those who never smoked, ex-smokers were 52% more likely to present COPD/FR and current smokers showed an increase of 47%. Individuals with lifetime consumption of cigarettes above 10 pack-years were 78% more likely to present COPD/FR than never smokers. Reported passive smoking in the past two weeks was not significantly associated with the outcome.

No associations were found between COPD/FR and hospital admissions due to respiratory disease in childhood, nor with exposure to domestic biomass smoke. Individuals with more than 10 years exposure to dust at the workplace were 31% more

likely to present the outcome ($p=0.06$) than those who were not exposed, while exposure to biomass stove for cooking or heating was related to a 43% higher risk.

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.

COPD/GOLD was 89% higher in men than women, and about four times higher in older subjects (60 years or more) than in middle-aged adults (40-49 years). No associations were found according to family history of COPD, bronchitis or emphysema, schooling level and paternal schooling. The association with skin color must be interpreted with caution because higher risks were found among Asians, a category that represents only 0.4% of the sample.

Smokers were 88% more likely to present COPD/GOLD than non-smokers, whereas ex-smokers showed an increased risk of 125%. Individuals with lifetime cigarette consumption above 10 pack-years were 2.6 times more likely to present COPD/GOLD than never smokers. Exposure to dust at the workplace for more than 10 years was associated with 89% increased risk of COPD/FR, relative to those who were not exposed. The following variables were not related to COPD/GOLD: exposure to biomass or coal stove for cooking or heating, hospital admissions due to respiratory problems in childhood, and passive smoking.

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

<i>Variable</i>	<i>% COPD Fixed Ratio Criteria</i>	<i>PR (CI95%)</i>	<i>P-value</i>
Sex			<0.001*
Men	27.2%	1.87 (1.45; 2.42)	
Women	14.5%	1.00	
Age			<0.001#
40-49	5.1%	1.00	
50-59	12.7%	2.50 (1.36; 4.60)	
≥ 60	32.1%	6.34 (3.62; 11.13)	
Skin color / ethnicity			0.08*
White	20.3%	1.00	
Mulatto	11.5%	0.57 (0.27; 1.20)	
Black	11.1%	0.55 (0.17; 1.75)	
Native Americans	33.3%	2.46 (0.91; 6.66)	
Asians	50.0%	1.64 (0.62; 4.33)	
Family history of COPD, bronchitis or emphysema			0.11*
No	20.5%	1.00	
Yes	11.6%	0.57 (0.29; 1.13)	
Schooling level			0.001#
0-2	29.4%	1.94 (1.21; 3.11)	
3-4	23.5%	1.55 (1.08; 2.23)	
5-8	21.5%	1.41 (1.04; 1.92)	
≥ 9	15.2%	1.00	
Schooling of the father			0.03*
None	13.6%	1.00	
Some	19.6%	1.45 (0.98; 2.13)	
Does not know	23.8%	1.76 (1.17; 2.63)	

* Wald test for heterogeneity

Wald test for trend

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

<i>Variable</i>	<i>% COPD Fixed Ratio Criteria</i>	<i>PR (CI95%)</i>	<i>P-value</i>
Smoking status			0.005*
Never smoked	15.3%	1.00	
Ex-smoker	23.3%	1.52 (1.16; 1.99)	
Current smoker	22.5%	1.47 (1.06; 2.05)	
Lifetime cigarettes smoked			<0.001#
Never smoked	15.3%	1.00	
≤1 pack-years	11.1%	0.73 (0.24; 2.17)	
1.1-10 pack-years	12.1%	0.79 (0.45; 1.39)	
>10 pack-years	27.2%	1.78 (1.38; 2.29)	
Passive smoking			0.11*
No	21.1%	1.00	
Yes	16.6%	0.79 (0.59; 1.06)	
Hospital admission for respiratory illness during childhood			0.69*
No	19.7%	1.00	
Yes	15.8%	0.80 (0.27; 2.40)	
Lifetime exposure to dust at the workplace			0.06#
Never	17.5%	1.00	
1-9 years	17.9%	1.02 (0.70; 1.49)	
≥ 10 years	22.9%	1.31 (0.99; 1.73)	
Exposure to coal stove for cooking or heating			0.04*
No	18.6%	1.00	
Yes	26.7%	1.43 (1.01; 2.03)	
Exposure to biomass stove for cooking or heating			0.71*
No	19.1%	1.00	
Yes	20.1%	1.06 (0.78; 1.43)	

* Wald test for heterogeneity

Wald test for trend

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

<i>Variable</i>	<i>% COPD Gold Criteria</i>	<i>PR (CI95%)</i>	<i>P-value</i>
Sex			0.02*
Men	10.8%	1.89 (1.12; 3.19)	
Women	5.7%	1.00	
Age			<0.001#
40-49	3.0%	1.00	
50-59	7.2%	2.43 (1.05; 5.60)	
≥ 60	11.0%	3.71 (1.69; 8.14)	
Skin color / ethnicity			0.001*
White	7.9%	1.00	
Mulatto	3.9%	0.48 (0.13; 1.86)	
Black	5.6%	0.70 (0.12; 4.10)	
Native Americans	11.1%	1.40 (0.20; 9.71)	
Asians	50.0%	6.29 (2.36; 16.79)	
Family history of COPD, bronchitis or emphysema			0.79*
No	7.8%	1.00	
Yes	7.0%	0.90 (0.39; 2.06)	
Schooling level			0.71#
0-2	5.9%	0.79 (0.27; 2.32)	
3-4	6.6%	0.89 (0.45; 1.76)	
5-8	9.0%	1.21 (0.70; 2.07)	
≥ 9	7.5%	1.00	
Schooling of the father			0.79*
None	7.5%	1.00	
Some	8.6%	1.15 (0.71; 1.88)	
Do not know	7.2%	0.97 (0.50; 1.86)	

* Wald test for heterogeneity

Wald test for trend

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

<i>Variable</i>	<i>% COPD Gold Criteria</i>	<i>PR (CI95%)</i>	<i>P-value</i>
Smoking status			0.005*
Never smoked	4.8%	1.00	
Ex-smoker	10.9%	2.25 (1.37; 3.69)	
Current smoker	9.1%	1.88 (1.07; 3.31)	
Lifetime cigarettes smoked			<0.001#
Never smoked	4.8%	1.00	
≤1 pack-years	0.0%	Non-calculable	
1.1-10 pack-years	4.3%	0.89 (0.37; 2.14)	
>10 pack-years	12.5%	2.59 (1.63; 4.11)	
Passive smoking			0.33*
No	8.4%	1.00	
Yes	6.5%	0.77 (0.46; 1.31)	
Hospital admission for respiratory illness during childhood			0.63*
No	7.6%	1.00	
Yes	10.5%	1.38 (0.36; 5.24)	
Lifetime exposure to dust at the workplace			0.004#
Never	5.3%	1.00	
1-9 years	8.9%	1.68 (0.92; 3.08)	
≥ 10 years	10.0%	1.89 (1.21; 2.93)	
Exposure to coal stove for heating			0.29*
No	7.5%	1.00	
Yes	10.0%	1.34 (0.77; 2.33)	
Exposure to biomass stove for heating			0.87*
No	8.0%	1.00	
Yes	7.7%	0.96 (0.58; 1.58)	

* 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 COPD. 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, and 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 include both 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 missing data.

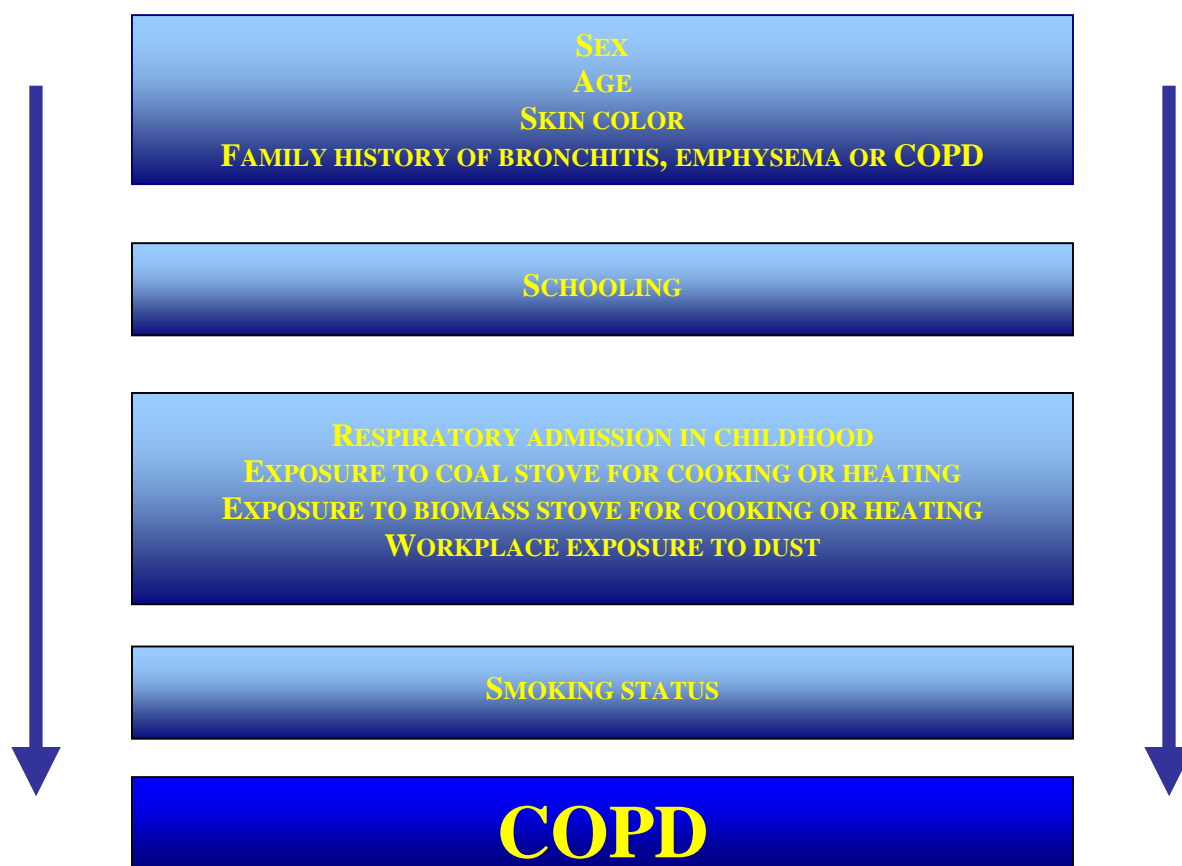


Figure 7. Conceptual framework for guiding the multivariable analyses.

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. Male sex and higher age were associated with higher COPD/FR prevalence. Asian individuals presented higher risk for COPD, but the small number of cases must be considered. 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 or biomass smoke and exposure to dust at the workplace were not significantly related to COPD/FR. Smoking showed a strong dose-response association with COPD/FR.

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

Level ^{**}	Variable	PR (CI95%)	P-value
1	Sex		<0.001*
	Men	1.98 (1.56; 2.51)	
	Women	1.00	
1	Age		<0.001#
	40-49	1.00	
	50-59	2.42 (1.31; 4.50)	
	≥ 60	6.39 (3.65; 11.18)	
1	Skin color / ethnicity		0.05*
	White	1.00	
	Mulatto	0.67 (0.32; 1.43)	
	Black	0.87 (0.27; 2.84)	
	Native Americans	1.55 (0.71; 3.37)	
	Asians	2.68 (1.29; 5.58)	
1	Family history of COPD, bronchitis or emphysema		0.45*
	No	1.00	
	Yes	0.78 (0.41; 1.49)	
2	Schooling level		0.93#
	0-2	1.08 (0.69; 1.68)	
	3-4	0.92 (0.64; 1.32)	
	5-8	1.08 (0.81; 1.42)	
	≥ 9	1.00	
3	Hospital admission for respiratory illness during childhood		0.83*
	No	1.00	
	Yes	1.13 (0.35; 3.60)	
3	Lifetime exposure to dust at the work-place		0.51#
	Never	1.00	
	1-9 years	0.99 (0.69; 1.43)	
	≥ 10 years	1.10 (0.81; 1.50)	
3	Exposure to coal stove for heating or cooking		0.54*
	No	1.00	
	Yes	1.10 (0.80; 1.52)	
3	Exposure to biomass stove for heating or cooking		0.53*
	No	1.00	
	Yes	0.92 (0.70; 1.20)	
4	Smoking status		<0.001#
	Never smoked	1.00	
	Ex-smoker	1.27 (0.96; 1.70)	
	Current smoker	1.89 (1.38; 2.58)	

* 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 twice the risk of women. Age was positively associated with the outcome, with a near four-fold increase for those aged 60 years or more relative to the 40-49 year age group. Asian skin color was associated with a higher risk of COPD/GOLD. No associations were found with a family history of respiratory diseases.

In the second level of the multivariable analyses, schooling was not associated with COPD/GOLD.

COPD/GOLD was not associated with coal or biomass smoke, nor with hospital admissions due to respiratory symptoms during childhood. On the other hand, both workplace exposure to dust and smoking were associated with a increased risk.

These results were quite similar to 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.

<i>Level*</i>	<i>Variable</i>	<i>PR (CI95%)</i>	<i>P-value</i>
1	Sex		0.007*
	Men	2.01 (1.22; 3.30)	
	Women	1.00	
1	Age		<0.001#
	40-49	1.00	
	50-59	2.30 (0.97; 5.44)	
	≥ 60	3.69 (1.65; 8.23)	
1	Skin color / ethnicity		<0.001*
	White	1.00	
	Mulatto	0.54 (0.14; 2.02)	
	Black	1.00 (0.16; 6.09)	
	Native Americans	1.27 (0.22; 7.30)	
	Asians	6.78 (2.76; 16.64)	
1	Family history of COPD, bronchitis or emphysema		0.69*
	No	1.00	
	Yes	1.19 (0.51; 2.77)	
2	Schooling level		0.07#
	0-2	0.50 (0.17; 1.49)	
	3-4	0.58 (0.30; 1.11)	
	5-8	0.94 (0.54; 1.65)	
	≥ 9	1.00	
3	Lifetime exposure to dust at the work-place		0.04#
	Never	1.00	
	1-9 years	1.80 (0.91; 3.55)	
	≥ 10 years	1.66 (1.02; 2.68)	
3	Hospital admission for respiratory illness during childhood		0.38*
	No	1.00	
	Yes	1.84 (0.46; 7.33)	
3	Exposure to biomass stove for heating or cooking		0.62*
	No	1.00	
	Yes	0.89 (0.55; 1.43)	
3	Exposure to coal stove for heating or cooking		0.60*
	No	1.00	
	Yes	1.15 (0.67; 2.00)	
4	Smoking status		0.006#
	Never smoked	1.00	
	Ex-smoker	1.95 (1.11; 3.43)	
	Current smoker	2.24 (1.25; 3.99)	

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

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 0.83) for subjects below the cut-off point, it was 2.15 (SD 0.52) for those above. The same trend was observed for forced vital capacity (FVC), with averages of 3.75 (SD 1.03) and 2.74 (SD 0.57) for subjects below or above the cut-off points, respectively ($P<0.001$). Thus, central adiposity was inversely related to lung function.

The association between BMI and COPD is summarized in Figure 8. According to both criteria, the prevalence of COPD was higher in the low-BMI group ($<18.5\text{kg/m}^2$) and a decreased trend was observed in the remaining categories. However, this trend was less clear for the GOLD criterion.

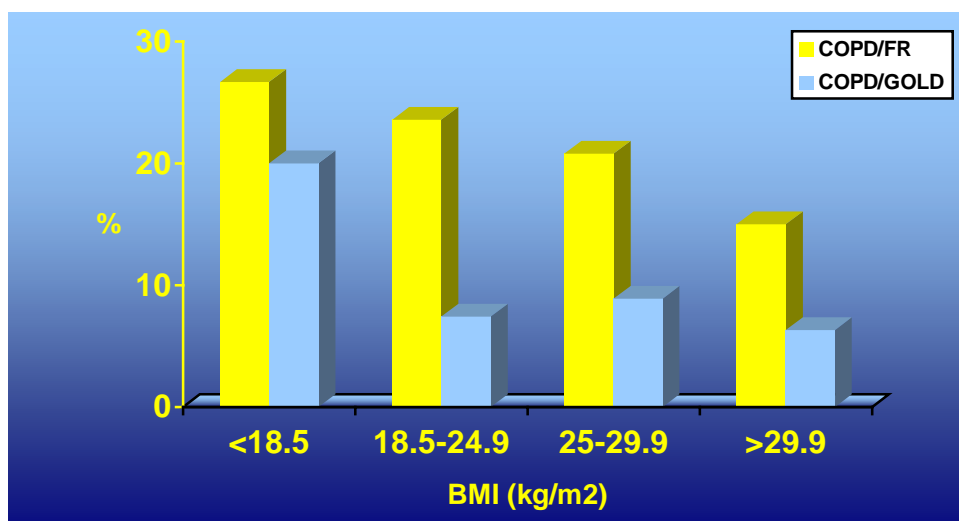


Figure 8. Relationship between COPD (FR and GOLD criteria) and body mass index (BMI).

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 10-20%, 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.

<i>Condition</i>	<i>Prevalence</i>
Hypertension	36.1%
Gastritis	30.2%
Heart problem	16.1%
Diabetes	7.8%
Stroke	1.9%
Tuberculosis	1.1%
Lung cancer	0.4%

Table 19 shows the associations between these reported diagnoses and COPD. Individuals with history of lung cancer were more likely to present COPD. History of stroke and tuberculosis was related to a higher risk of COPD/FR. Diabetes was related to a decreased risk of COPD/FR.

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

<i>Condition</i>	<i>COPD (FR criteria)</i>		<i>COPD (GOLD criteria)</i>	
	<i>Prevalence</i>	<i>P</i>	<i>Prevalence</i>	<i>P</i>
Heart problem		0.20		0.39
Yes	23.7%		9.6%	
No	18.9%		7.5%	
Hypertension		0.69		0.09
Yes	20.4%		9.9%	
No	19.3%		6.7%	
Diabetes		0.04		0.28
Yes	10.3%		4.4%	
No	20.4%		8.1%	
Lung cancer		<0.001		<0.001
Yes	100.0%		75.0%	
No	19.3%		7.5%	
Stroke		0.02		0.13
Yes	41.2%		17.7%	
No	19.2%		7.6%	
Tuberculosis		0.06		0.71
Yes	44.4%		11.1%	
No	19.4%		7.8%	
Gastritis		0.35		0.21
Yes	21.6%		6.1%	
No	18.8%		8.5%	

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 19.9%, while it is 25.8% according to COPD/GOLD. Therefore, about one in 4-5 COPD cases would be prevented by smoking control.

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. However, these associations

were greatly reduced after controlling for smoking status. The male/female prevalence ratio was 1.98 for COPD/FR, but when we control for smoking, the value is 1.68. For the COPD/GOLD indicator, the value decreased from 2.01 to 1.64. This shows that part of the excess in COPD among males is due to the fact that they smoke more often.

3.6. Medical management

Overall, 9.8% of the individuals (92 subjects) 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, 21.3% and 7.0% (P=0.01). The most frequently used drugs were bronchodilators, associations of bronchodilators and inhaled steroids, systemic steroids and inhaled steroids (Table 20). Most subjects reported using bronchodilators via inhaler, but only for symptomatic relief, which is inadequate.

Although influenza immunization is recommended for all COPD patients, only 23.6% of those who were COPD/FR positive reported being vaccinated in the previous year, compared to 14.8% of the remainder (P=0.005).

Subjects were asked if they had ever been submitted to spirometry. The lifetime frequency was 14.6%. Subjects with a diagnosis of COPD/FR presented a lifetime frequency of spirometry twice as high (23.6%) as those without a diagnosis (12.7%).

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

<i>Drug</i>	<i>N</i>	<i>Percentage</i>
Bronchodilators	40	33.6%
Bronchodilator plus inhaled steroids	34	28.6%
Systemic steroids	10	8.4%
Inhaled steroids	9	7.6%
Mucolytic drugs	4	3.4%
Syrups	4	3.4%
Xanthines	2	1.7%
Others	16	13.4%
Total	119	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.

<i>Quality of life indicator</i>	<i>Prevalence according to COPD/FR status</i>		<i>P</i>
	<i>Positive</i>	<i>Negative</i>	
Difficulty in carrying out moderate physical activities	28.7%	22.4%	0.08
Difficulty in carrying out intense physical activities	29.9%	22.5%	0.04
Any limitation due to physical health in the past year	26.6%	18.0%	0.01
Any limitation in the workplace due to physical health	25.3%	17.6%	0.02
Any limitation due to mental health in the past year	24.7%	30.0%	0.17
Any limitation in the workplace due to mental health	22.1%	16.7%	0.12

3.8. Economic impact of COPD

Formal employment in the previous 12 months was reported by 50.8% individuals (36.8% among COPD/FR positive and 55.7% among the negative; $P < 0.001$). 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, 0.7% reported that this was due to lung disease.

Approximately one in ten individuals (11.9%) reported having limited leisure activities due to health problems. The percentages were 8.6% and 11.0% among COPD/FR positive and negative subjects, respectively ($P = 0.36$).

4. DISCUSSION

This is the final report from the third site to complete the PLATINO study. Previous reports described the surveys carried out in São Paulo (Menezes, report Platino survey - Brazilian sample, 2003) and in Mexico City (Menezes, report Platino survey - Mexican sample, 2004).

The results presented here have a high level of precision for estimating the prevalence rates of COPD and of risk factors. The analyses of associations between exposures and disease, however, have to be interpreted with caution because, for most comparisons being made, the required sample size will only be reached after data from the four other centers become available in the near future. Therefore, the present Discussion section will be limited to an outline of the main results. Associations that were not significant in this report may well become so when data from the other centers are incorporated.

4.1. Discussion of methodological issues

The positive aspects of the study include the relatively high response rate of 82%. Given the size of the study area and the understandable reluctance of the population to welcome strangers, the response rate is excellent. Response rates were somewhat lower among men and among older individuals. Response rates among smokers and non-smokers were similar.

The study demonstrated that the spirometric examinations were acceptable to a vast majority of the sample, and only 3% of those eligible failed to undergo the exam. Other positive aspects 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 19.7% of all subjects were affected, that is, about one in every five individuals.

As expected, when the GOLD criteria were used, prevalence was markedly lower (7.8%) because these criteria are more specific. Also as expected, clinical symptoms showed wide variability and low validity. Medical diagnoses related to COPD (either chronic bronchitis, emphysema or COPD diagnoses) were reported by 2.4% of all subjects.

As mentioned, 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, older age, Asian ethnic background and smoking were significantly associated with COPD. No other significant associations were detected. 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 most subjects with COPD take medication only when they have symptoms which is inappropriate. Preventive interventions are also inadequate; only one in four of the diseased, for example, were immunized against influenza in the previous year. Finally, diagnostic procedures were poor; the percentages of COPD/FR subjects who ever underwent spirometry was around 24%.

We have also shown that presence of COPD affected some, but not all types of daily activities. The lack of a major effect may be due to the fact that the Montevideo population includes a high proportion of elderly individuals, who suffer from a number of chronic conditions, not only COPD.

4.3. Conclusions

The Montevideo survey confirmed that the PLATINO protocol is able to recruit a representative sample of a large metropolitan area with a high response rate. Standardization and quality control procedures ensured that data quality was appropriate. The data collection, analyses and report preparation were conducted in a timely fashion.

Finally, we would like to thank the support provided by ALAT and BI, as well as the continued participation of the PLATINO Steering Committee.

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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.

<i>Variable</i>	<i>% COPD ATS Criteria</i>	<i>PR (CI95%)</i>	<i>p-value</i>
Sex			0.04*
Men	14.7%	1.50 (1.03; 2.19)	
Women	9.8%	1.00	
Age			0.002#
40-49	6.8%	1.00	
50-59	11.4%	1.68 (0.90; 3.12)	
≥ 60	14.9%	2.19 (1.30; 3.67)	
Skin color / ethnicity			0.06*
White	11.7%	1.00	
Mulatto	11.5%	0.99 (0.48; 2.06)	
Black	11.8%	1.01 (0.32; 3.19)	
Indians	22.5%	1.91 (0.53; 6.86)	
Asian	50.0%	4.29 (1.58; 11.64)	
Family history of COPD, bronchitis or emphysema			0.99*
No	11.7%	1.00	
Yes	11.8%	1.00 (0.49; 2.04)	
Schooling level			0.44#
0-2	9.8%	1.00	
3-4	10.3%	1.05 (0.45; 2.44)	
5-8	12.5%	1.28 (0.51; 3.22)	
≥ 9	12.1%	1.23 (0.56; 2.73)	
Schooling of the father			0.51*
None	9.9%	1.00	
Some	12.5%	1.27 (0.84; 1.91)	
Do not know	12.4%	1.26 (0.74; 2.14)	
Smoking status			<0.001#
Never smoked	8.4%	1.00	
Ex-smoker	11.3%	1.36 (0.92; 2.00)	
Current smoker	17.4%	2.08 (1.41; 3.07)	
Lifetime cigarettes smoked			<0.001#
Never smoked	8.4%	1.00	
≤1 pack-years	3.7%	0.44 (0.06; 3.42)	
1.1-10 pack-years	3.5%	0.42 (0.16; 1.08)	
>10 pack-years	18.5%	2.22 (1.57; 3.14)	
Passive smoking			0.64*
No	12.1%	1.00	
Yes	11.2%	0.92 (0.67; 1.28)	
Hospital admission for respiratory illness during childhood			0.21*
No	11.5%	1.00	
Yes	21.1%	1.83 (0.70; 4.77)	
Lifetime exposure to dust at the workplace			0.20#
Never	10.4%	1.00	
1-9 years	12.6%	1.21 (0.74; 1.98)	
≥ 10 years	13.0%	1.26 (0.88; 1.79)	
Exposure to coal stove for cooking or heating			0.38*
No	11.4%	1.00	
Yes	14.3%	1.25 (0.76; 2.07)	
Exposure to biomass stove for cooking or heating			0.78*
No	11.4%	1.00	
Yes	12.1%	1.06 (0.70; 1.60)	

* Wald test for heterogeneity

Wald test for trend

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

<i>Variable</i>	<i>% COPD ERS Criteria</i>	<i>PR (CI95%)</i>	<i>p-value</i>
Sex			0.01*
Men	18.6%	1.52 (1.11; 2.09)	
Women	12.2%	1.00	
Age			<0.001#
40-49	7.2%	1.00	
50-59	12.2%	1.71 (0.93; 3.14)	
≥ 60	20.7%	2.88 (1.73; 4.80)	
Skin color / ethnicity			0.12*
White	14.8%	1.00	
Mulatto	15.4%	1.04 (0.59; 1.85)	
Black	11.1%	0.75 (0.24; 2.34)	
Indians	22.2%	1.51 (0.42; 5.36)	
Asian	50.0%	3.39 (1.29; 8.88)	
Family history of COPD, bronchitis or emphysema			0.45*
No	15.1%	1.00	
Yes	11.6%	0.77 (0.39; 1.53)	
Schooling level			0.36#
0-2	15.7%	1.00	
3-4	16.2%	1.03 (0.47; 2.25)	
5-8	15.7%	1.00 (0.48; 2.08)	
≥ 9	13.5%	0.86 (0.44; 1.68)	
Schooling of the father			0.07*
None	10.3%	1.00	
Some	15.1%	1.47 (0.99; 2.19)	
Do not know	17.5%	1.70 (1.07; 2.70)	
Smoking status			<0.001*
Never smoked	10.5%	1.00	
Ex-smoker	15.1%	1.45 (1.00; 2.09)	
Current smoker	21.0%	2.00 (0.39; 2.89)	
Lifetime cigarettes smoked			<0.001#
Never smoked	10.5%	1.00	
≤1 pack-years	11.1%	1.06 (0.34; 2.29)	
1.1-10 pack-years	5.2%	0.49 (0.23; 1.06)	
>10 pack-years	22.6%	2.16 (1.55; 3.00)	
Passive smoking			0.36*
No	15.5%	1.00	
Yes	13.4%	0.86 (0.62; 1.19)	
Hospital admission for respiratory illness during childhood			0.44*
No	14.6%	1.00	
Yes	21.1%	1.45 (0.56; 3.70)	
Lifetime exposure to dust at the workplace			0.06#
Never	12.7%	1.00	
1-9 years	13.7%	1.08 (0.67; 1.73)	
≥ 10 years	17.7%	1.39 (0.99; 1.94)	
Exposure to coal stove for cooking or heating			0.26*
No	14.3%	1.00	
Yes	18.3%	1.29 (0.83; 2.00)	
Exposure to biomass stove for cooking or heating			0.53*
No	13.9%	1.00	
Yes	15.5%	1.12 (0.79; 1.57)	

* Wald test for heterogeneity

Wald test for trend

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

<i>Level*</i>	<i>Variable</i>	<i>PR (CI95%)</i>	<i>p-value</i>
1	Sex		0.02*
	Men	1.55 (1.07; 2.25)	
	Women	1.00	
1	Age		0.001#
	40-49	1.00	
	50-59	1.62 (0.86; 3.03)	
	≥ 60	2.21 (1.32; 3.68)	
1	Skin color / ethnicity		0.04*
	White	1.00	
	Mulatto	1.07 (0.52; 2.20)	
	Black	1.26 (0.39; 4.07)	
	Indians	1.79 (0.51; 6.36)	
	Asian	4.37 (1.74; 10.94)	
1	Family history of COPD, bronchitis or emphysema		0.58*
	No	1.00	
	Yes	1.22 (0.60; 2.47)	
2	Schooling level		0.04#
	0-2	1.00	
	3-4	1.11 (0.48; 2.57)	
	5-8	1.56 (0.62; 3.95)	
	≥ 9	1.77 (0.77; 4.06)	
3	Hospital admission for respiratory illness during childhood		0.14*
	No	1.00	
	Yes	2.09 (0.78; 5.61)	
3	Lifetime exposure to dust at the workplace		0.55#
	Never	1.00	
	1-9 years	1.19 (0.70; 2.03)	
	≥ 10 years	1.12 (0.77; 1.63)	
3	Exposure to biomass stove for heating or cooking		0.99*
	No	1.00	
	Yes	1.00 (0.67; 1.51)	
3	Exposure to coal stove for heating or cooking		0.66*
	No	1.00	
	Yes	1.12 (0.68; 1.84)	
4	Smoking status		<0.001*
	Never smoked	1.00	
	Ex-smoker	1.30 (0.86; 1.96)	
	Current smoker	2.47 (1.65; 3.69)	

* 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.

<i>Level***</i>	<i>Variable</i>	<i>PR (CI95%)</i>	<i>p-value</i>
1	Sex		0.004*
	Men	1.57 (1.16; 2.14)	
	Women	1.00	
1	Age		<0.001#
	40-49	1.00	
	50-59	1.70 (0.92; 3.15)	
	≥ 60	2.97 (1.78; 4.94)	
1	Skin color / ethnicity		0.06*
	White	1.00	
	Mulatto	1.16 (0.62; 2.15)	
	Black	1.00 (0.32; 3.17)	
	Indians	1.43 (0.41; 4.92)	
	Asian	3.43 (1.52; 7.72)	
1	Family history of COPD, bronchitis or emphysema		0.90*
	No	1.00	
	Yes	0.96 (0.49; 1.89)	
2	Schooling level		0.30#
	0-2	1.00	
	3-4	1.09 (0.52; 2.31)	
	5-8	1.27 (0.60; 2.66)	
	≥ 9	1.32 (0.65; 2.68)	
3	Hospital admission for respiratory illness during childhood		0.26*
	No	1.00	
	Yes	1.78 (0.65; 4.87)	
3	Lifetime exposure to dust at the workplace		0.21#
	Never	1.00	
	1-9 years	1.09 (0.65; 1.82)	
	≥ 10 years	1.26 (0.87; 1.80)	
3	Exposure to biomass stove for heating or cooking		0.90*
	No	1.00	
	Yes	1.02 (0.73; 1.42)	
3	Exposure to coal stove for heating or cooking		0.81*
	No	1.00	
	Yes	1.05 (0.68; 1.62)	
4	Smoking status		<0.001*
	Never smoked	1.00	
	Ex-smoker	1.36 (0.92; 2.02)	
	Current smoker	1.45 (0.69; 3.54)	

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