FEDERAL UNIVERSITY OF PELOTAS
POST-GRADUATE PROGRAM IN EPIDEMIOLOGY

PLATINO STUDY – CHILEAN SURVEY

REPORT

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

PELOTAS, BRAZIL
2004

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 completed in São Paulo, Mexico, Montevideo and Santiago. At the moment the study is under way in Caracas.

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) and in our website (www.platino-alat.org).

This report describes the main results of the Santiago survey, the fourth 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 Santiago de Chile City (Great Santiago City), through a multi-stage cluster sampling (Figure 1).

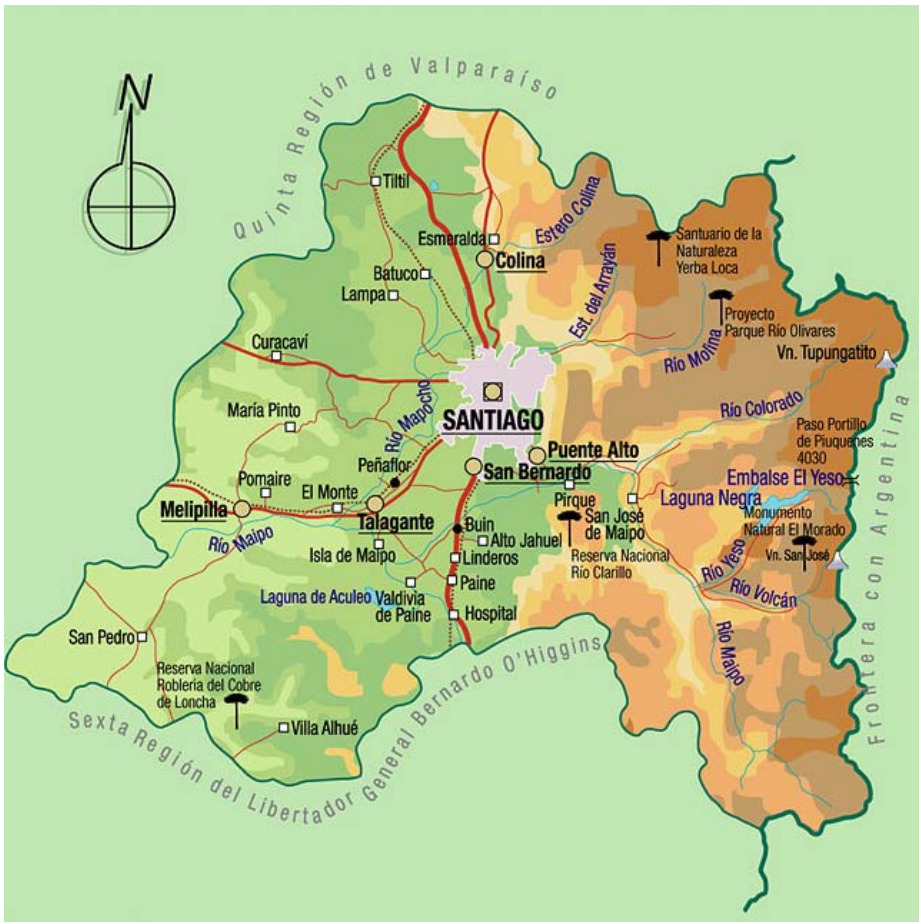


Figure 1. Map of the study area.

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 68 census tracts in the larger metropolitan area of Santiago City, and to select 15 households, on average, from each selected tract. We expected, on average, 1.3 persons aged 40 years or more per household.

For sampling purposes, the metropolitan area was divided into two strata: Santiago municipality and the Greater Santiago area. The latter comprises 34 urban municipalities. This represent 91,4% of the whole population of the Urban Metropolitan Region, and 37% of the Chilean population.

The sample was developed for the Chilean National Census Bureau (INE) using a master sampling frame designed for the Integrated Survey Program of Households (PIDEH). The original sampling frame was based on the 1992 Chilean National Census and is regularly updated.

Selection of census tracts

From this master sample, tracts were stratified within each geographical zone, according their socioeconomic level, taking into acount the following variables: characteristics of the house and the neighborhood, number of bedrooms, schooling, family income, persons per bedroom, family size, and household assets. Three socioeconomic levels were defined: (1) high , (2) intermediate and (3) low (Table 1).

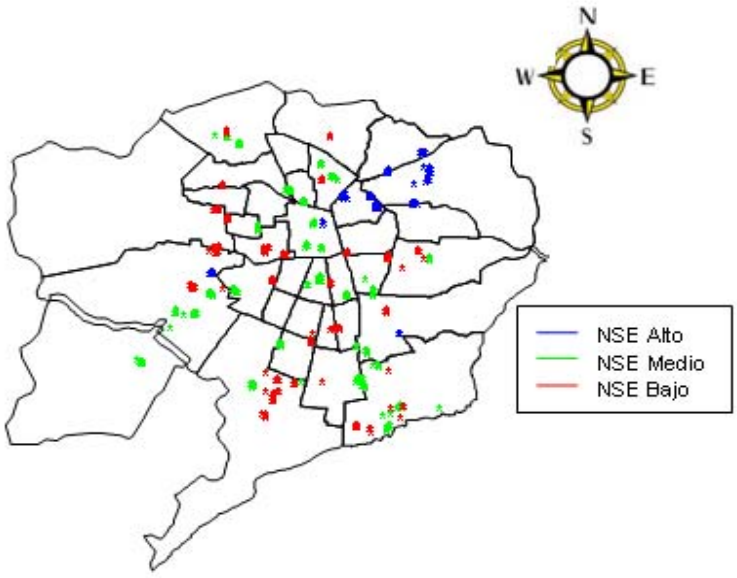
Table 1. Population aged ≥ 40 years and sample sizes

Population		*Sample*		
Socioeconomic Strata	*Number of households*	*Census tracts*	*Selected households*	*Households per tract*
1 (High)	207.584	12	184	15
2 (Medium)	475,763	28	421	15
3 (Low)	467,600	28	414	15
Total	1,150,947	68	1,029	

A systematic sample of 68 census tracts (Table 1) was then obtained with probability proportionate to size, taking into account the number of households in each tract (average of about 200 households per census tract). Collective tracts were previously excluded before the selection.

Figure 2 includes a map of the study area showing the geographical distribution of the tracts included in the sample.

Figure 2. Geographic distribution of selected census tracts according to socioeconomic level. Metropolitan Region of Santiago, Chile (blue = high; green = intermediate; red = low socioeconomic level).



2.2.2. Sampling of the households

Following a similar procedure to that employed in all Platino sites, the number of households in each sampled tract was adjusted for population growth. This entailed applying a correction factor based on the household counts in each tract, updated for the 2003 PIDEH survey.

All adults aged 40 years or more living regularly 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 three months a year in the last two 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 date of the interview.
- ✓ skin color – categorical variable: white, black, Mestizo, 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 Chilean survey, 55 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 three 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. A copy of the questionnaire is presented in Annex 1 and the manual of instructions in Annex 2.

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 with their feet placed on top of the 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 identified the midpoint between the last rib and the iliac crest; then the tape was placed around the waist crossing this midpoint. The measurement was read while the tape was held, 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 three-liter 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 (see quality control for spirometry in Annex 3). 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, three experts in spirometry (2 from Mexico and one from Montevideo), the local principal investigator, two Chilean and one Brazilian fieldwork supervisors, a nutritionist, and 16 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 spirometry expert from Montevideo and the Brazilian fieldwork supervisor remained in Santiago for half of the fieldwork period. The following criteria were used to ensure that training was adequate:

- ✓ Anthropometry: the acceptable levels of intra- and inter-observer variability for waist circumference was 1.0 cm and that 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 March 23 to July 31, 2004. The study team included 16 trained interviewers working in pairs (15 nurses and one professional midwife), one local principal investigator, two fieldwork supervisors, one study coordinator, two local spirometry supervisors and a secretary. During the firts half of the survey, technical supervision of fieldwork and spirometric quality control were in charge of professionals from the Brazilian and Uruguayan Platino teams.

All field methods were tested in a pilot study carried out from 16-23 March 2004 in a lower middle-class area in central Santiago, near the study's headquarters.

The logistic of the fieldwork included several steps, begining with an early contact with the selected households in order to provide information about the study and to locate adults within the age range of interest. Special pamphlets were printed and distributed with detailed letters, and a website was created within the official webpage of the Catholic University. Formal approval of police and health authorities was obtained. Mass media support (newspapers, radio and TV) contribute to stimulate the participation of the target population.

During the initial visit, eligible subjects were informed that a study supervisor would contact them in order to arrange the best time for the interview and examination. Because the sampling scheme did not allow replacement of either households or subjects, an intesive regime of visits was planned in order to reduce the rate of refusals. Fieldwork was started I lower and middle income areas of the city, because greater difficulty was foreseen in high-income areas.

Early in the morning, interviewers visited the study headquarters to check the calibration of the equipment and to receive a list of the households to be visited on that day. On that occasion, spirometry results obtained in the previous day were downloaded to the computer.

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 a University 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 5.6 maneuvers pre bronchodilator (BD) and 5.1 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 checked all spirometries daily, and worked with the interviewers to correct any inaccuracies detected. Annex 3 shows results of the regular quality control procedures, which confirmed that average measurement quality was 80% or higher throughout the study period.

Interviews – 10% of the interviews were repeated by the supervisors. Within a week after the interview, a supervisor 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

The protocol was approved by ethical committee of the Research Direction of the Catholic University Medical School. Only subjects who signed the informed consent form took part in the study. The disposable mouthpiece and spacers were given to each interviewed subject. The results of spirometries were sent by mail to each subject and those with abnormal results were referred to health services. A telephone hotline was provided, and two specialists in adult respiratory diseases were available for answering questions by subjects diagnosed by the survey.

2.11. Processing of data

All questionnaires were photocopied and the originals were sent to the Coordinating Centre (CC), while the copy remained in Santiago. In the CC, all questionnaires were revised, open answers were coded and data were entered twice in an 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 Santiago, 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 0% at the household level, 18.2% at the individual questionnaire level, and 0.2% for spirometry. The overall rate of non-response was 18.4%, obtained by multiplying the response rates.

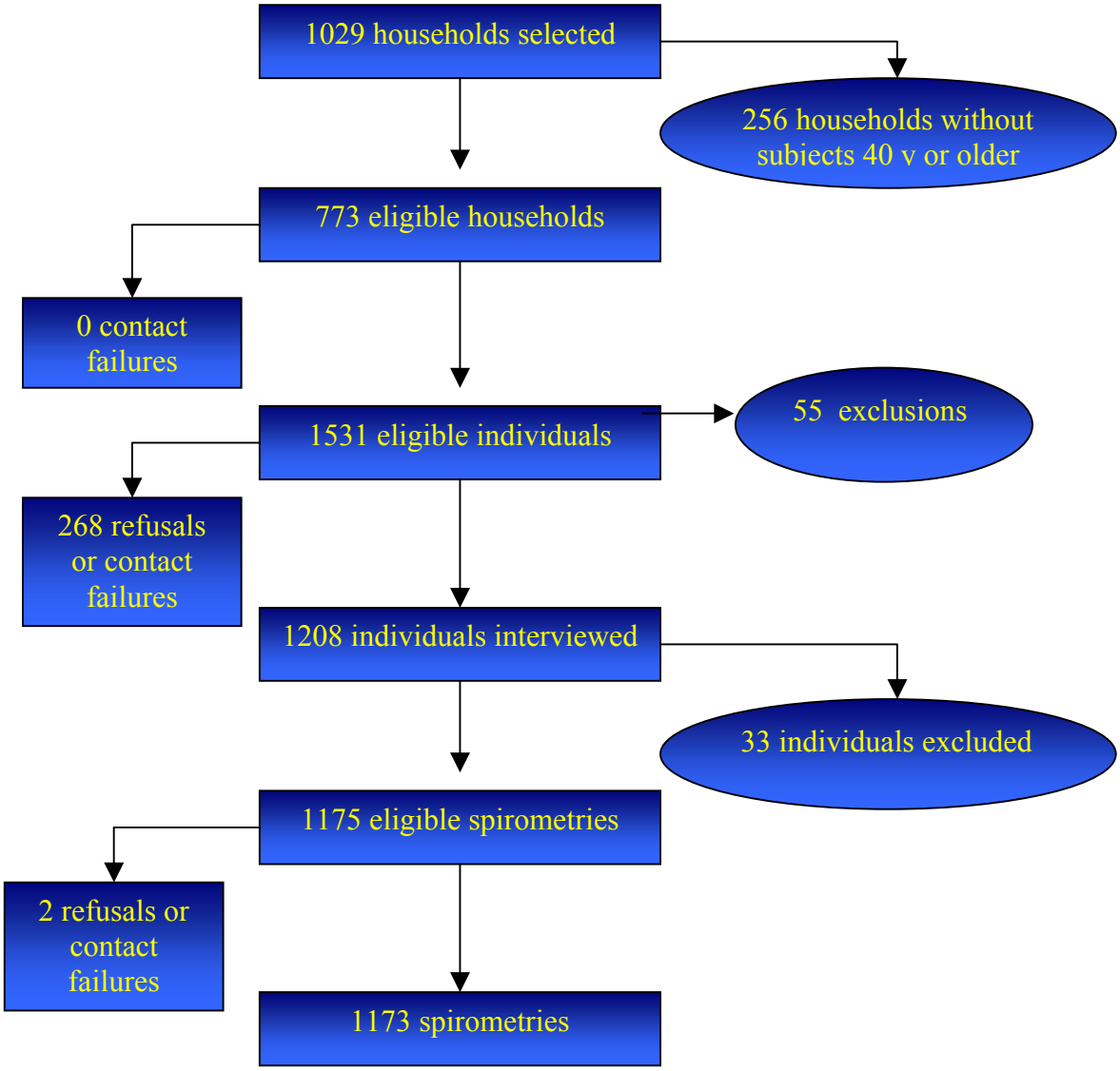


Figure 3. Number of households and individuals included in the different phases of the study.

Even for the 268 non-responders, we tried to obtain information on sex, age and smoking status; 194 (72%) answered these questions. This information was then extrapolated to the 268 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	24.5%
Females	14.1%
Age	
40-49	14.1%
50-59	22.1%
≥ 60	20.4%
Current smoking status	
No	15.9%
Yes	21.0%

3.2. Prevalence of COPD according to different criteria

3.2.1. Spirometric criteria

As discussed in the Methods section, several different spirometric criteria were used to estimate COPD prevalence. Figure 4 shows these estimates and their 95% confidence intervals, which take into account the cluster sample design.

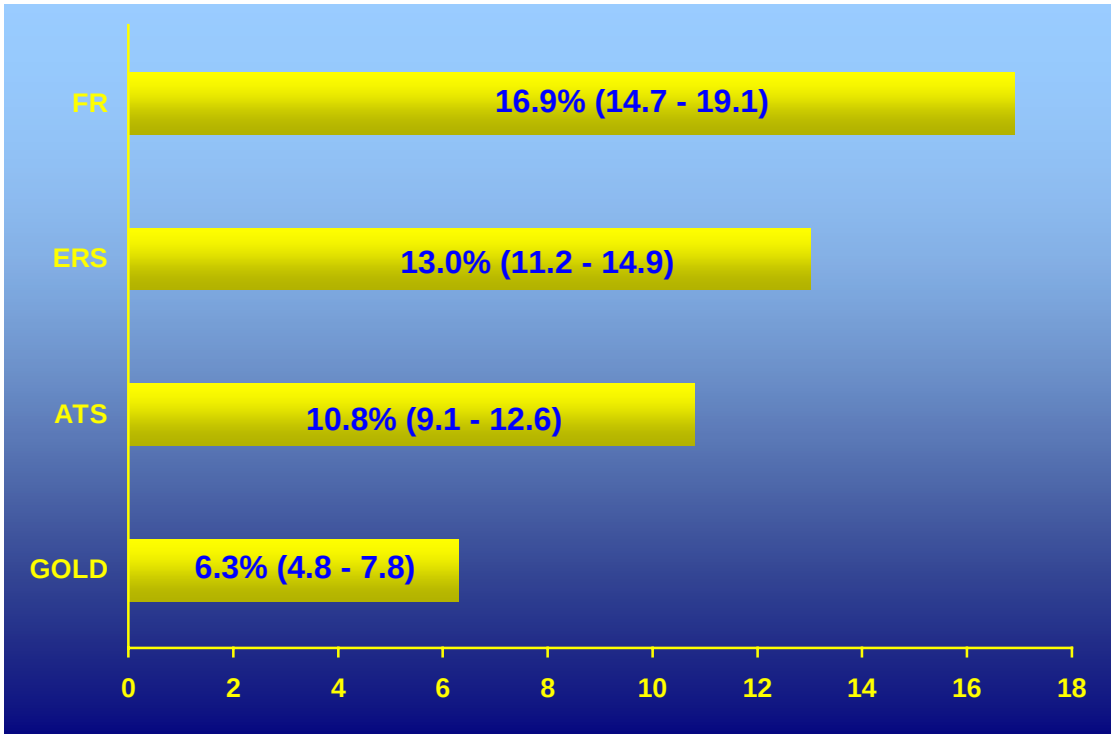


Figure 4. Prevalence of COPD based on different spirometric criteria.

The fixed ratio (FR) criterion showed the highest prevalence, of 16.9%, followed by the ERS (13.0%), ATS94 (10.8%) and GOLD (6.3%) 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 1.04 and 1.17, 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).

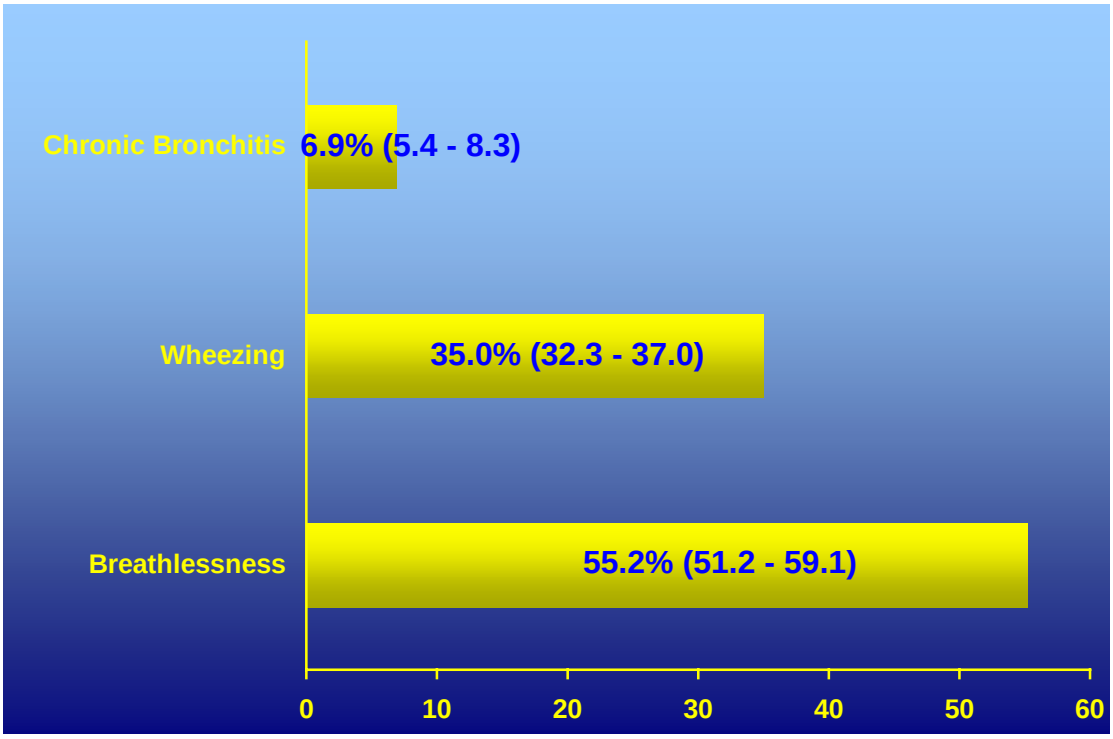


Figure 5. Prevalence of reported respiratory symptoms.

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 6.9%. Breathlessness due to exercise, and wheezing in the last 12 months were reported, respectively, by 55.2% and 35.0% of all subjects (Figure 5).

When 10% of the sample subjects were re-interviewed within one week of the original interview, it was possible to estimate the reliability of the information provided on symptoms. Kappa statistics were equal to 0.45 for cough and 0.59 for sputum, showing that agreement was intermediate.

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 chronic bronchitis, emphysema or COPD was reported by 6.0% of all subjects.

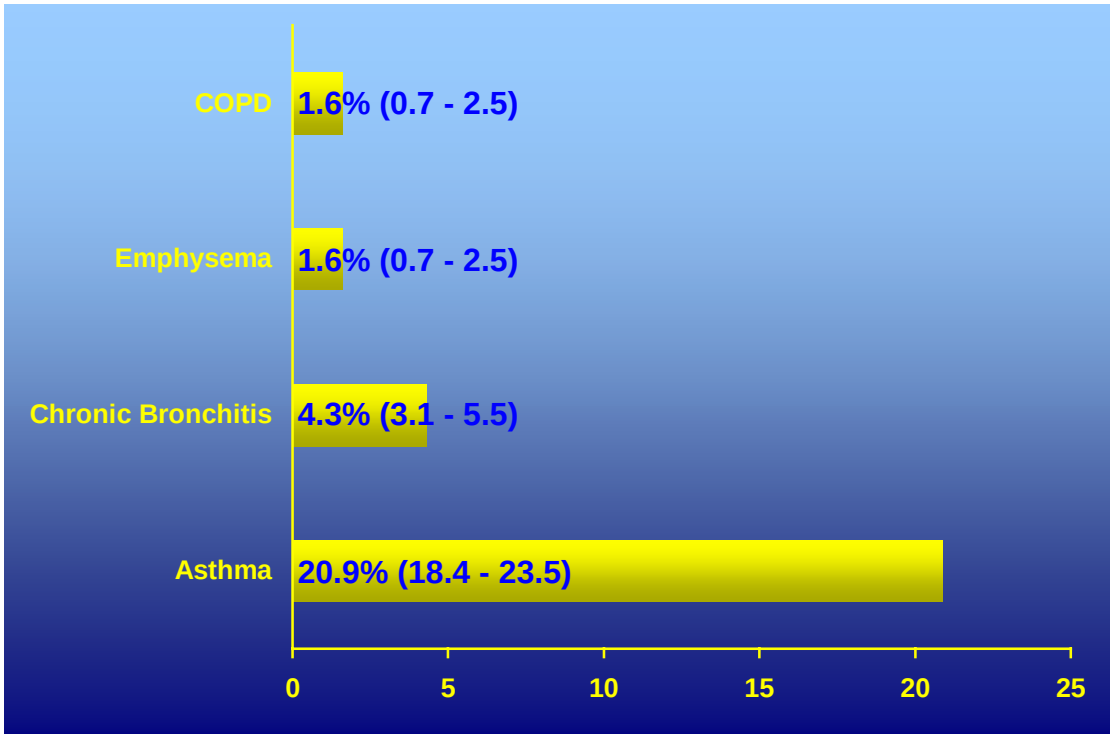


Figure 6. Prevalence of reported medical diagnoses of lung conditions.

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 11.2% and its specificity 93.7%. Positive and negative predictive values were 24.7% and 83.7%, 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	20	61	81
Absent	178	914	1092
Total	198	975	1173

Similar results were obtained when clinical symptoms were compared to the GOLD criterion (Table 6). Sensitivity was 9.6% and specificity 93.3%; positive and negative predictive values were 8.6% and 93.9%, 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	7	74	81
Absent	67	1025	1092
Total	74	1099	1173

These analyses were repeated for self-reported COPD, defined as either chronic bronchitis or breathlessness, or both. Sensitivity increased from 11.2% to 30.6%, but specificity decreased from 93.7% to 61.0% (Table 7). The positive predictive value was 13.2% and the negative predictive value 81.9%.

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.

Prevalence of symptoms of chronic bronchitis and/or breathlessness through questionnaire	*Prevalence of COPD (FR criterion)*		*Total*
	Present	*Absent*	
Present	56	367	423
Absent	127	573	700
Total	183	940	1123

For the GOLD criterion, the sensitivity of self-reported COPD was 27.7% and its specificity 61.7% (Table 8). The positive and negative predictive values were respectively 4.3% and 93.3%.

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	18	405	423
Absent	47	653	700
Total	65	1058	1123

Therefore, diagnoses based on clinical symptoms grossly failed to identify the vast majority of subjects on whom COPD was diagnosed by 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 reduction 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 648 subjects who reported breathlessness, 275 (42.4%) 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.

More than 60% of all subjects were female, as was expected given the greater longevity of women. The average age was 57.0 years (SD 12.0). Most subjects classified themselves as having white skin color, followed by mestizos and Native Americans. There

were very few Asians and blacks. Approximately 1/6 reported a family history (parents, siblings or children) of bronchitis, emphysema or COPD.

Two socioeconomic variables were investigated: schooling of the 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 9.2 years (SD 4.6). More than 40% of the subjects were unable to inform about their fathers' schooling level, and about one fifth reported that their fathers had never attended school.

About 40% of the subjects contacted were smokers, and further 28% ex-smokers. Current smokers accounted for 42.6% of the men and 35.9% of the women. When 10% of the sample was re-interviewed for quality control, the Kappa statistic for smoking was equal to 0.80, showing high repeatability. Lifetime smoking was also assessed; 1/3 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 43%.

More than 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 kg/m^2) comprised almost 3/4 of the sample. The prevalence of obesity (BMI $\geq$ 30 kg/m^2) was 24.5% in males and 37.0% in females. Only 3.2% 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 49%.

Four sources of domestic smoke were studied: coal was used for cooking by 32.8% of all subjects and for heating by 44.3%; the corresponding exposures to biomass (mainly wood) were 42.3% and 36.4%. 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	38.5%
Women	61.5%
Age	
40-49	33.7%
50-59	31.5%
≥ 60	34.8%
Skin color / ethnicity	
White	69.5%
Mestizo	24.5%
Native American	4.3%
Black	1.0%
Asian	0.8%
Family history of CODP, bronchitis or emphysema	
No	83.4%
Yes	16.6%
Schooling level (years)	
0-2	7.2%
3-4	9.9%
5-8	29.9%
≥ 9	53.0%
Schooling of the father	
None	20.2%
Some	39.0%
Does not know	40.8%

a. There were up to 2 missing values in the variables listed in the table, among 1208 subjects.

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

Variable	*Percentage*
Smoking status	
Never smoked	33.3%
Ex-smoker	28.2%
Current smoker	38.5%
Lifetime cigarettes smoked *	
Never smoked	33.7%
≤1 pack-years	6.6%
1.1-10 pack-years	27.3%
>10 pack-years	32.4%
Passive smoking	
No	57.1%
Yes	42.9%
Hospital admission for respiratory illness during childhood	
No	96.8%
Yes	3.2%
Lifetime exposure to dust in workplace	
Never	50.5%
1-9 years	22.5%
≥ 10 years	27.0%
Exposure to coal stove for cooking or heating	
No	45.9%
Yes	54.1%
Exposure to biomass stove for cooking or heating	
No	46.1%
Yes	53.9%
Waist circumference	
Below cut-off	58.3%
Above cut-off (≥88 cm for females or ≥102 for males)	41.7%
Body mass index (kg/m^2)	
<18.5	0.5%
18.5 – 24.9	24.4%
25 – 29.9	42.9%
≥ 30	32.2%

* Different from smoking status due to different number of missing data.

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), but the gender difference using the GOLD criterion was not significant. 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 and COPD, 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 breathlessness also tended to increase with age. No clear age patterns were found for wheezing or chronic bronchitis. In terms of medical diagnoses, only emphysema showed a significant increase with age.

Smoking

The prevalence of COPD was higher among smokers relative to non-smokers for the ATS and ERS criteria. No differences were found for the FR and GOLD criteria in the crude analyses (adjusted analyses are shown below). Wheezing symptoms were also more likely among current smokers. Medical diagnosis of respiratory diseases did not show consistent associations with smoking.

Schooling

The number of years of formal education was inversely associated with the FR, GOLD and ERS spirometric criteria, symptoms of breathlessness, and medical diagnosis of chronic bronchitis and COPD (Table 11).

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<0.001*	*P=0.22*	*P=0.006*	*P=0.001*	*P=0.82*	*P<0.001*	*P=0.25*	*P=0.09*	*P=0.44*	*P<0.001*	*P=0.07*
Males	23.4%	7.5%	14.5%	17.6%	6.7%	42.2%	37.0%	2.8%	1.9%	12.3%	0.9%
Females	12.8%	5.6%	8.5%	10.2%	7.0%	63.3%	33.8%	5.3%	1.4%	26.4%	2.0%
Age#	*P<0.001*	*P<0.001*	*P=0.002*	*P<0.001*	*P=0.41*	*P=0.03*	*P=0.44*	*P=0.10*	*P=0.02*	*P=0.86*	*P=0.67*
40-49	7.1%	2.8%	7.1%	7.6%	7.1%	49.6%	33.9%	3.0%	0.7%	20.2%	1.7%
50-59	13.0%	4.0%	8.8%	13.0%	7.9%	59.7%	40.0%	5.0%	0.8%	22.1%	0.8%
60-94	30.3%	12.0%	16.5%	18.6%	5.7%	56.5%	31.6%	5.0%	3.1%	20.7%	2.1%
Smoking*	*P=0.38*	*P=0.38*	*P=0.05*	*P=0.007*	*P=0.26*	*P=0.11*	*P<0.001*	*P=0.36*	*P=0.23*	*P=0.79*	*P=0.10*
Never	15.9%	5.6%	8.1%	9.9%	5.2%	51.8%	25.1%	4.5%	0.8%	22.1%	0.5%
Former	15.5%	5.7%	9.9%	10.8%	7.3%	53.5%	33.1%	5.3%	2.6%	20.2%	2.1%
Current	18.7%	7.5%	13.9%	17.4%	8.0%	59.2%	45.0%	3.4%	1.5%	20.4%	2.2%
Schooling (years)#	*P=0.001*	*P=0.001*	*P=0.08*	*P=0.05*	*P=0.80*	*P<0.001*	*P=0.27*	*P<0.001*	*P=0.91*	*P=0.67*	*P=0.01*
0-2	33.3%	12.8%	18.0%	19.2%	8.1%	68.7%	41.4%	10.3%	2.3%	21.8%	4.6%
3-4	21.4%	10.3%	12.8%	13.7%	5.0%	62.0%	31.9%	4.2%	1.7%	23.5%	0.0%
5-8	17.7%	7.1%	10.0%	13.7%	6.7%	64.2%	37.4%	6.4%	1.1%	17.2%	3.1%
≥9	13.6%	4.3%	10.1%	11.8%	7.2%	47.1%	33.4%	2.3%	1.7%	22.5%	0.6%
All subjects	16.9%	6.3%	10.8%	13.0%	6.9%	55.2%	35.0%	4.3%	1.6%	20.9%	1.6%
Number in sample	1173	1173	1173	1173	1208	1175	1208	1208	1208	1208	1207

* P-values calculated using the Wald test for heterogeneity

P-values calculated using the Wald test for trend

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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 4.

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 82% more likely than women to present with COPD/FR. Individuals aged 60 or over were four 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. Schooling was negatively associated with COPD/FR. Individuals who did not know their fathers' schooling level were more likely to present COPD/FR than other subjects.

Current smoking status was not associated with COPD/FR, but individuals with lifetime consumption above 10 pack-ears presented a greater likelihood of having COPD/FR. 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 or exposure to dust at the workplace.

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 not significantly higher in men than women. Age was positively associated with COPD/GOLD. No associations were found according to skin color, family history of COPD, bronchitis or emphysema and paternal schooling. The higher the schooling level, the lower the prevalence of COPD/GOLD

Current smoking status was not related to the prevalence of COPD/GOLD, but individuals with lifetime consumption above 10 pack-years were more likely to present COPD/GOLD. All other variables were not significantly related to the prevalence of COPD/GOLD.

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			<0.001*
Men	23.4%	1.82 (1.40; 2.38)	
Women	12.8%	1.00	
Age			<0.001#
40-49	7.1%	1.00	
50-59	13.0%	1.84 (1.28; 2.66)	
≥ 60	30.3%	4.30 (3.05; 6.06)	
Skin color / ethnicity			0.44*
White	17.7%	1.00	
Mestizo	13.6%	0.77 (0.56; 1.05)	
Native American	25.0%	1.41 (0.82; 2.45)	
Black	16.7%	0.94 (0.16; 5.46)	
Asian	11.1%	0.63 (0.09; 4.23)	
Family history of COPD, bronchitis or emphysema			0.93*
No	16.9%	1.00	
Yes	16.6%	0.98 (0.67; 1.44)	
Schooling level			0.001#
0-2	33.3%	2.46 (1.62; 3.74)	
3-4	21.4%	1.58 (1.08; 2.31)	
5-8	17.7%	1.30 (0.94; 1.81)	
≥ 9	13.6%	1.00	
Schooling of the father			0.02*
None	13.6%	1.00	
Some	14.2%	1.05 (0.76; 1.45)	
Does not know	21.1%	1.56 (1.10; 2.20)	

* 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			0.38*
Never smoked	15.9%	1.00	
Ex-smoker	15.5%	0.97 (0.67; 1.42)	
Current smoker	18.7%	1.18 (0.86; 1.62)	
Lifetime cigarettes smoked			0.05#
Never smoked	16.0%	1.00	
≤1 pack-years	11.3%	0.70 (0.33; 1.48)	
1.1-10 pack-years	12.0%	0.75 (0.52; 1.08)	
>10 pack-years	23.0%	1.43 (1.04; 1.97)	
Passive smoking			0.39*
No	17.8%	1.00	
Yes	15.6%	0.87 (0.64; 1.19)	
Hospital admission for respiratory illness during childhood			0.74*
No	16.8%	1.00	
Yes	18.9%	1.13 (0.56; 2.27)	
Lifetime exposure to dust at the workplace			0.30#
Never	16.9%	1.00	
1-9 years	12.4%	0.73 (0.55; 0.98)	
≥ 10 years	20.7%	1.23 (0.91; 1.66)	
Exposure to coal stove for cooking or heating			0.94*
No	16.8%	1.00	
Yes	17.0%	1.01 (0.76; 1.34)	
Exposure to biomass stove for cooking or heating			0.42*
No	15.8%	1.00	
Yes	17.8%	1.12 (0.84; 1.50)	

* 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			0.22*
Men	7.5%	1.35 (0.83; 1.17)	
Women	5.6%	1.00	
Age			<0.001#
40-49	2.8%	1.00	
50-59	4.0%	1.44 (0.74; 2.78)	
≥ 60	12.0%	4.34 (2.48; 7.61)	
Skin color / ethnicity			0.86*
White	6.6%	1.00	
Mestizo	5.6%	0.84 (0.51; 1.39)	
Native American	4.2%	0.63 (0.14; 2.82)	
Black	8.3%	1.26 (0.24; 6.60)	
Asian	11.1%	1.70 (0.23; 12.19)	
Family history of COPD, bronchitis or emphysema			0.20*
No	5.9%	1.00	
Yes	8.3%	1.40 (0.83; 2.35)	
Schooling level			0.001#
0-2	12.8%	2.98 (1.36; 6.52)	
3-4	10.3%	2.38 (1.18; 4.79)	
5-8	7.1%	1.65 (0.89; 3.06)	
≥ 9	4.3%	1.00	
Schooling of the father			0.25*
None	5.9%	1.00	
Some	5.0%	0.85 (0.45; 1.60)	
Do not know	7.7%	1.30 (0.70; 2.42)	

* 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			0.38*
Never smoked	5.5%	1.00	
Ex-smoker	5.7%	1.04 (0.56; 1.94)	
Current smoker	7.5%	1.37 (0.82; 2.30)	
Lifetime cigarettes smoked			0.06#
Never smoked	5.4%	1.00	
≤1 pack-years	3.8%	0.69 (0.22; 2.17)	
1.1-10 pack-years	3.4%	0.62 (0.32; 1.20)	
>10 pack-years	10.0%	1.85 (1.07; 3.19)	
Passive smoking			0.35*
No	5.8%	1.00	
Yes	7.0%	1.21 (0.81; 1.81)	
Hospital admission for respiratory illness during childhood			0.10*
No	6.1%	1.00	
Yes	13.5%	2.22 (0.84; 5.86)	
Lifetime exposure to dust at the workplace			0.99#
Never	7.0%	1.00	
1-9 years	3.4%	0.48 (0.24; 0.97)	
≥ 10 years	7.5%	1.08 (0.66; 1.75)	
Exposure to coal stove for heating			0.22*
No	5.4%	1.00	
Yes	7.2%	1.33 (0.83; 2.13)	
Exposure to biomass stove for heating			0.49*
No	6.8%	1.00	
Yes	5.9%	0.86 (0.56; 1.32)	

* Wald test for heterogeneity # Wald test for trend

3.4.4. Multivariable analyses

The multivariable analyses took into account four hierarchical 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, 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 lifetime exposure, because its association with the outcomes was stronger in the crude analyses. Paternal schooling was also not included in these analyses because of the high number of missing data.

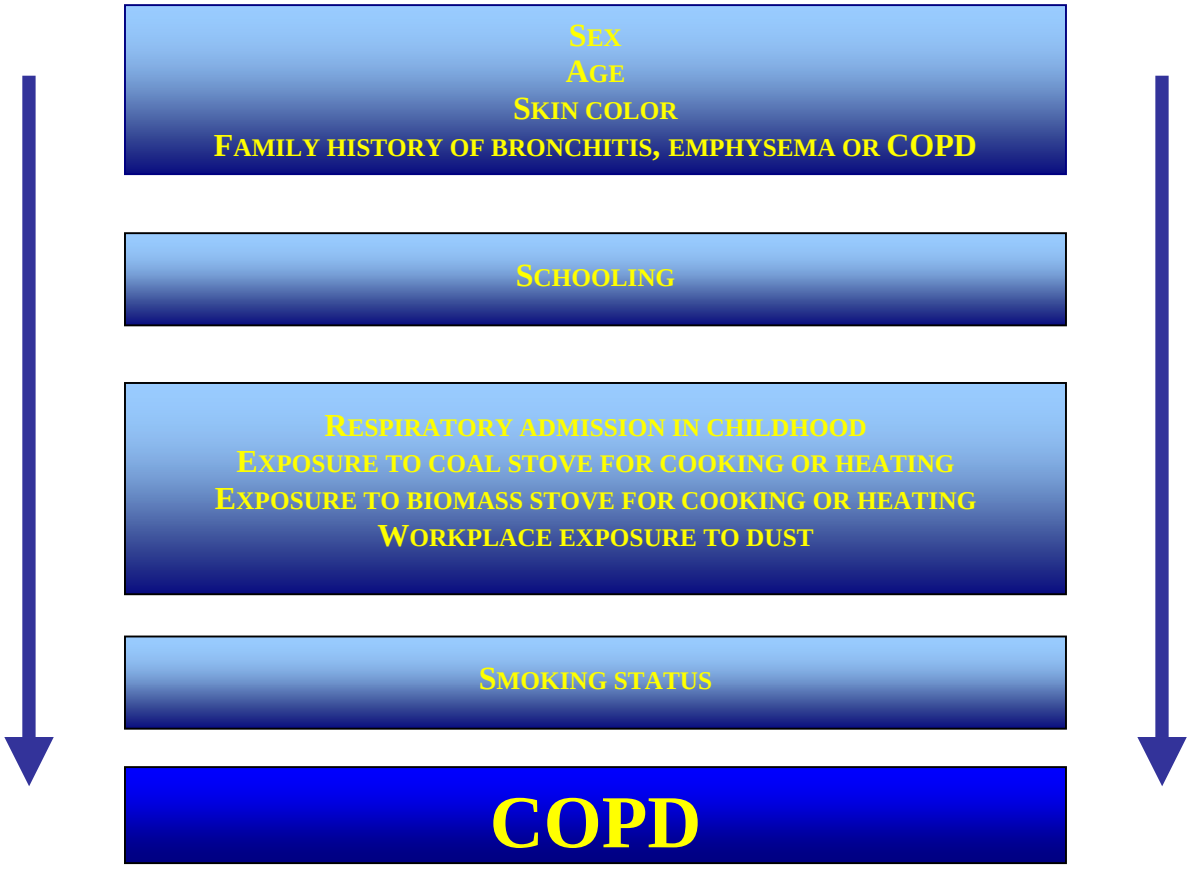

Figure 7. Conceptual framework for guiding the multivariable analyses.

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

FR criterion

Table 16 shows the results of the COPD/FR outcome. Male sex and higher age were associated with higher COPD/FR prevalence. Skin color and family history of respiratory disease were not related to the prevalence of COPD/FR.

In the second level of analyses, schooling was negatively associated with COPD/FR. History of respiratory admission, exposure to coal or biomass smoke and exposure to dust at the workplace were not significantly related to COPD/FR.

Individuals with lifetime cigarette consumption above 10 pack-years were 51% more likely to present COPD/FR than never smokers.

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

Level¨	*Variable*	*PR (CI95%)*	*P-value*
1	**Sex**		<0.001*
	Men	1.89 (1.47; 2.44)	
	Women	1.00	
1	**Age**		<0.001#
	40-49	1.00	
	50-59	1.84 (1.29; 2.64)	
	≥ 60	4.39 (3.13; 6.17)	
1	**Skin color / ethnicity**		0.78*
	White	1.00	
	Mestizo	0.87 (0.63; 1.20)	
	Native American	1.27 (0.78; 2.07)	
	Black	0.62 (0.11; 3.45)	
	Asian	0.79 (0.14; 4.52)	
1	**Family history of COPD, bronchitis or emphysema**		0.68*
	No	1.00	
	Yes	1.08 (0.74; 1.58)	
2	**Schooling level**		0.06#
	0-2	1.63 (1.07; 2.47)	
	3-4	1.13 (0.78; 1.64)	
	5-8	1.09 (0.79; 1.49)	
	≥ 9	1.00	
3	**Hospital admission for respiratory illness during childhood**		0.80*
	No	1.00	
	Yes	1.09 (0.57; 2.08)	
3	**Lifetime exposure to dust at the work-place**		0.82#
	Never	1.00	
	1-9 years	0.81 (0.61; 1.10)	
	≥ 10 years	1.05 (0.77; 1.43)	
3	**Exposure to coal stove for heating or cooking**		0.40*
	No	1.00	
	Yes	0.90 (0.70; 2.15)	
3	**Exposure to biomass stove for heating or cooking**		0.63*
	No	1.00	
	Yes	0.93 (0.70; 1.24)	
4	**Lifetime cigarettes smoked**		0.01#
	Never smoked	1.00	
	≤1 pack-years	0.90 (0.45; 1.80)	
	1.1-10 pack-years	1.01 (0.72; 1.43)	
	>10 pack-years	1.51 (1.12; 2.04)	

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

GOLD criterion

Table 17 shows the results of the multivariable analyses for the COPD/GOLD outcome. Men had a higher risk than women, but the difference was not statistically significant. 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. No associations were found with a family history of respiratory diseases or skin color.

In the second level of the multivariable analyses, schooling was inversely associated with COPD/GOLD.

COPD/GOLD was not associated with coal smoke exposure, hospital admissions due to respiratory symptoms during childhood or workplace exposure to dust. Exposure to biomass smoke was associated with a lower likelihood of COPD/GOLD. Individuals with lifetime cigarette consumption above 10 pack-years presented a 128% greater likelihood of having COPD/GOLD.

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.

Level¨	*Variable*	*PR (CI95%)*	*P-value*
1	**Sex**		0.15*
	Men	1.42 (0.88; 2.27)	
	Women	1.00	
1	**Age**		<0.001#
	40-49	1.00	
	50-59	1.44 (0.75; 2.77)	
	≥ 60	4.47 (2.56; 6.79)	
1	**Skin color / ethnicity**		0.87*
	White	1.00	
	Mestizo	0.99 (0.59; 1.66)	
	Native American	0.61 (0.14; 2.67)	
	Black	0.81 (0.15; 4.35)	
	Asian	2.09 (0.36; 12.00)	
1	**Family history of COPD, bronchitis or emphysema**		0.11*
	No	1.00	
	Yes	1.51 (0.90; 2.53)	
2	**Schooling level**		0.07#
	0-2	1.93 (0.80; 4.63)	
	3-4	1.72 (0.85; 3.50)	
	5-8	1.34 (0.71; 2.53)	
	≥ 9	1.00	
3	**Lifetime exposure to dust at the work-place**		0.80#
	Never	1.00	
	1-9 years	0.53 (0.28; 1.02)	
	≥ 10 years	0.98 (0.61; 1.59)	
3	**Hospital admission for respiratory illness during childhood**		0.20*
	No	1.00	
	Yes	1.75 (0.73; 4.19)	
3	**Exposure to biomass stove for heating or cooking**		0.04*
	No	1.00	
	Yes	0.65 (0.43; 0.98)	
3	**Exposure to coal stove for heating or cooking**		0.31*
	No	1.00	
	Yes	1.25 (0.81; 1.94)	
4	**Lifetime cigarettes smoked**		0.02#
	Never smoked	1.00	
	≤1 pack-years	0.98 (0.31; 3.09)	
	1.1-10 pack-years	0.94 (0.47; 1.88)	
	>10 pack-years	2.28 (1.25; 4.14)	

* 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 2.85 (SD 0.81) for subjects below the cut-off point, it was 2.48 (SD 0.69) for those above. The same trend was observed for forced vital capacity (FVC), with averages of 3.74 (SD 0.99) and 3.21 (SD 0.84) 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 (<18.5kg/m^2) and a decreased trend was observed in the remaining categories. However, this trend was less clear for the GOLD criterion.

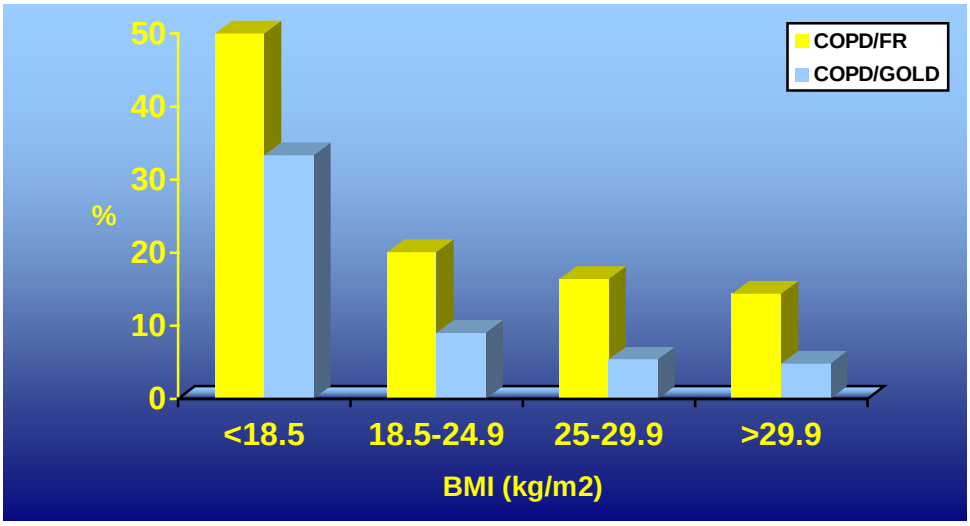

Figure 8. Relationship between COPD (FR and GOLD criteria) and body mass index (BMI).

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 8-16%, 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 0.74, showing good 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*
Hypertension	37.9%
Gastritis	34.5%
Heart problem	16.8%
Diabetes	8.7%
Stroke	4.4%
Tuberculosis	5.9%
Lung cancer	0.0%

Table 19 shows the associations between these reported diagnoses and COPD. History of tuberculosis was related to a higher risk of COPD/FR. Other diseases were not associated with COPD in these cross-sectional analyses.

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

Condition	*COPD (FR criteria)*		*COPD (GOLD criteria)*	
	Prevalence	*P*	*Prevalence*	*P*
Heart problem		0.66		0.38
Yes	18.0%		7.7%	
No	16.7%		6.0%	
Hypertension		0.22		0.20
Yes	18.6%		7.5%	
No	15.9%		5.6%	
Diabetes		0.63		0.59
Yes	15.2%		6.1%	
No	17.0%		5.4%	
Stroke		0.70		0.34
Yes	18.9%		9.4%	
No	16.8%		6.2%	
Tuberculosis		<0.001		<0.001
Yes	34.3%		21.4%	
No	21.4%		5.4%	
Gastritis		0.31		0.26
Yes	15.4%		5.2%	
No	17.7%		6.9%	

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 cigarette consumption above 10 pack-years is 14.2%, while it is 29.3% according to COPD/GOLD. Therefore, about one in 3-6 COPD cases would be prevented if all current smokers quit their addiction. If, in addition to this, all ex-smokers had never smoked – that is, the complete elimination of smoking from this sample – 15% of all COPD/FR and 38% of all COPD/GOLD cases would have been prevented.

3.5.3. Role of smoking in the gender differential in COPD

Male sex was associated with a higher risk of COPD, according to all spirometric criteria used. However, these associations were somewhat reduced after controlling for smoking status. The male/female prevalence ratio was 1.89 for

COPD/FR, but when we control for smoking, the value is 1.73. For the COPD/GOLD indicator, the value decreased from 1.42 to 1.16. 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, 29.1% of all subjects (351 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 individuals were, respectively, 35.9% and 27.9% (P=0.03). The most frequently used drug was Salbutamol followed by Ambroxol and Amoxicillin (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 half (52.0%) of those who were COPD/FR positive reported being vaccinated in the previous year, compared to 31.5% of the remainder (P<0.001).

Subjects were asked if they had ever been submitted to spirometry. The lifetime frequency was 17.9%. Subjects with a diagnosis of COPD/FR presented a lifetime frequency of spirometry twice as high (28.8%) as those without a diagnosis (15.4%).

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

Drug	*N*
Salbutamol	153
Ambroxol (Bromhexin)	63
Amoxicillin	56
Acetaminophen	34
Acetaminophen + Ephedrine	31
Ibuprofen	15

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	27.3%	21.3%	0.003
Difficulty in carrying out intense physical activities	52.0%	47.0%	0.28
Any limitation due to physical health in the past year	28.3%	25.1%	0.35
Any limitation in the workplace due to physical health	28.8%	25.1%	0.28
Any limitation due to mental health in the past year	32.3%	34.7%	0.53
Any limitation in the workplace due to mental health	23.7%	27.3%	0.30

3.8. Economic impact of COPD

Formal employment in the previous 12 months was reported by 58.8% individuals (43.4% among COPD/FR positive and 62.2% 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 individuals who did not work in the previous year, 1.0% reported that this was due to lung disease.

Approximately one in nine individuals (11.8%) reported having limited leisure activities due to health problems. The percentages were 13.1% and 10.5% among COPD/FR positive and negative subjects, respectively (P=0.27).

4. DISCUSSION

This is the final report from the fourth site to complete the PLATINO study. Previous reports described the surveys carried out in São Paulo (Menezes, Platino survey report - Brazilian sample, 2003), Mexico City (Menezes, Platino survey report - Mexican sample, 2004) and Montevideo (Menezes, Platino survey report – Montevideo 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, must 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 are pooled. 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 less than 1% 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 16.9% of all subjects were affected, that is, about one in every six individuals.

As expected, when the GOLD criteria were used, prevalence was markedly lower (6.3%) 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 6.0% 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 adjusted analyses showed that male sex, older age, low schooling level and lifetime smoking were significantly associated with COPD as assessed through the fixed ratio criteria. 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 half of the diseased, for example, were immunized against influenza in the previous year. Finally, diagnostic procedures were poor; the percentage of COPD/FR subjects who ever underwent spirometry was 29%.

We have also shown that presence of COPD affected the subjects' ability to carry out physical activities, but the disease had little effect on most other indicators of quality of life. Further analyses will be carried out with data from all sites, not only considering each quality of life variable on its own, but also assessing the impact of COPD on composite indicators of quality of life.

4.3. Conclusions

The Santiago survey confirmed results from other sites showing 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: 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			0.006*
Men	14.5%	1.71 (1.17; 2.51)	
Women	8.5%	1.00	
Age			0.02#
40-49	7.1%	1.00	
50-59	8.8%	1.24 (0.81; 1.90)	
≥ 60	16.5%	2.35 (1.53; 3.60)	
Skin color / ethnicity			0.85*
White	11.3%	1.00	
Mulatto	9.8%	0.86 (0.58; 1.28)	
Black	8.3%	0.74 (0.13; 4.23)	
Indians	10.4%	0.92 (0.41; 2.10)	
Asian	11.1%	0.98 (0.19; 5.16)	
Family history of COPD, bronchitis or emphysema			0.12*
No	10.1%	1.00	
Yes	14.5%	1.43 (0.90; 2.27)	
Schooling level			0.08#
0-2	18.0%	1.79 (0.97; 3.28)	
3-4	12.8%	1.28 (0.79; 2.07)	
5-8	10.0%	0.99 (0.67; 1.46)	
≥ 9	10.1%	1.00	
Schooling of the father			0.31*
None	8.9%	1.00	
Some	10.0%	1.13 (0.69; 1.85)	
Do not know	12.5%	1.41 (0.85; 2.32)	
Smoking status			0.04*
Never smoked	8.1%	1.00	
Ex-smoker	9.9%	1.22 (0.80; 1.87)	
Current smoker	13.9%	1.72 (1.13; 2.62)	
Lifetime cigarettes smoked			0.001#
Never smoked	8.3%	1.00	
≤1 pack-years	5.0%	0.60 (0.22; 1.68)	
1.1-10 pack-years	7.7%	0.93 (0.60; 1.44)	
>10 pack-years	17.2%	2.07 (1.37; 3.14)	
Passive smoking			0.57*
No	10.4%	1.00	
Yes	11.4%	1.10 (0.80; 1.50)	
Hospital admission for respiratory illness during childhood			0.24*
No	10.7%	1.00	
Yes	16.2%	1.52 (0.75; 3.10)	
Lifetime exposure to dust at the workplace			0.01*
Never	10.7%	1.00	
1-9 years	7.1%	0.66 (0.45; 0.98)	
≥ 10 years	14.1%	1.31 (0.90; 1.93)	
Exposure to coal stove for cooking or heating			0.51*
No	10.2%	1.00	
Yes	11.5%	1.13 (0.79; 1.61)	
Exposure to biomass stove for cooking or heating			0.61*
No	10.3%	1.00	
Yes	11.3%	1.09 (0.78; 1.54)	

* Wald test for heterogeneity # Wald test for trend

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

Variable	*% COPD ERS Criteria*	*PR (CI95%)*	*p-value*
Sex			0.001*
Men	17.6%	1.74 (1.28; 2.35)	
Women	10.2%	1.00	
Age			<0.001#
40-49	7.6%	1.00	
50-59	13.0%	1.72 (1.19; 2.48)	
≥ 60	18.6%	2.45 (1.64; 3.67)	
Skin color / ethnicity			0.75*
White	13.5%	1.00	
Mulatto	11.5%	0.85 (0.60; 1.21)	
Black	8.3%	0.62 (0.10; 3.63)	
Indians	16.7%	1.23 (0.64; 3.40)	
Asian	11.1%	0.82 (0.15; 4.43)	
Family history of COPD, bronchitis or emphysema			0.53*
No	12.7%	1.00	
Yes	14.5%	1.14 (0.75; 1.75)	
Schooling level			0.05#
0-2	19.2%	1.63 (0.99; 2.68)	
3-4	13.7%	1.16 (0.70; 1.91)	
5-8	13.7%	1.16 (0.80; 1.68)	
≥ 9	11.8%	1.00	
Schooling of the father			0.23*
None	11.0%	1.00	
Some	12.1%	1.09 (0.69; 1.73)	
Do not know	15.0%	1.36 (0.87; 2.15)	
Smoking status			0.007*
Never smoked	9.9%	1.00	
Ex-smoker	10.8%	1.09 (0.71; 1.67)	
Current smoker	17.4%	1.76 (1.22; 2.54)	
Lifetime cigarettes smoked			<0.001#
Never smoked	10.1%	1.00	
≤1 pack-years	6.3%	0.62 (0.23; 1.67)	
1.1-10 pack-years	9.5%	0.95 (0.62; 1.44)	
>10 pack-years	20.3%	2.02 (1.40; 2.90)	
Passive smoking			0.76*
No	12.8%	1.00	
Yes	13.4%	1.05 (0.77; 1.43)	
Hospital admission for respiratory illness during childhood			0.52*
No	12.9%	1.00	
Yes	16.2%	1.25 (0.63; 2.51)	
Lifetime exposure to dust at the workplace			0.10#
Never	12.4%	1.00	
1-9 years	9.4%	0.75 (0.50; 1.14)	
≥ 10 years	17.2%	1.39 (1.00; 1.93)	
Exposure to coal stove for cooking or heating			0.97*
No	13.1%	1.00	
Yes	13.0%	0.99 (0.72; 1.37)	
Exposure to biomass stove for cooking or heating			0.45*
No	12.2%	1.00	
Yes	13.8%	1.14 (0.81; 1.59)	

* Wald test for heterogeneity # Wald test for trend

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

Level¨	*Variable*	*PR (CI95%)*	*p-value*
1	**Sex**		0.003*
	Men	1.78 (1.22; 2.29)	
	Women	1.00	
1	**Age**		<0.001#
	40-49	1.00	
	50-59	1.35 (0.82; 1.89)	
	≥ 60	2.43 (1.53; 3.71)	
1	**Skin color / ethnicity**		0.23*
	White	1.00	
	Mulatto	0.91 (0.61; 1.36)	
	Black	0.55 (0.09; 3.22)	
	Indians	0.93 (0.42; 2.65)	
	Asian	1.13 (0.20; 6.51)	
1	**Family history of COPD, bronchitis or emphysema**		0.07*
	No	1.00	
	Yes	1.54 (0.97; 2.45)	
2	**Schooling level**		0.36#
	0-2	1.46 (0.79; 2.71)	
	3-4	1.10 (0.66; 1.83)	
	5-8	0.88 (0.59; 1.31)	
	≥ 9	1.00	
3	**Hospital admission for respiratory illness during childhood**		0.33*
	No	1.00	
	Yes	1.45 (0.69; 3.05)	
3	**Lifetime exposure to dust at the workplace**		0.64#
	Never	1.00	
	1-9 years	0.66 (0.43; 1.00)	
	≥ 10 years	1.13 (0.77; 1.67)	
3	**Exposure to biomass stove for heating or cooking**		0.93*
	No	1.00	
	Yes	0.99 (0.70; 1.39)	
3	**Exposure to coal stove for heating or cooking**		0.89*
	No	1.00	
	Yes	1.02 (0.73; 1.44)	
4	**Smoking status**		0.001#
	Never smoked	1.00	
	Ex-smoker	1.15 (0.76; 1.75)	
	Current smoker	2.16 (1.41; 3.30)	

* 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**		<0.001*
	Men	1.77 (1.31; 2.40)	
	Women	1.00	
1	**Age**		<0.001#
	40-49	1.00	
	50-59	1.72 (1.20; 2.46)	
	≥ 60	2.50 (1.67; 3.75)	
1	**Skin color / ethnicity**		0.46*
	White	1.00	
	Mulatto	0.89 (0.63; 1.26)	
	Black	0.46 (0.08; 2.74)	
	Indians	1.08 (0.55; 6.15)	
	Asian	0.94 (0.15; 5.65)	
1	**Family history of COPD, bronchitis or emphysema**		0.34*
	No	1.00	
	Yes	1.23 (0.80; 1.89)	
2	**Schooling level**		0.48#
	0-2	1.29 (0.79; 2.12)	
	3-4	0.95 (0.57; 1.61)	
	5-8	1.04 (0.72; 1.50)	
	≥ 9	1.00	
3	**Hospital admission for respiratory illness during childhood**		0.55*
	No	1.00	
	Yes	1.24 (0.61; 2.51)	
3	**Lifetime exposure to dust at the workplace**		0.36#
	Never	1.00	
	1-9 years	0.78 (0.50; 1.19)	
	≥ 10 years	1.21 (0.85; 1.71)	
3	**Exposure to biomass stove for heating or cooking**		0.73*
	No	1.00	
	Yes	1.06 (0.75; 1.50)	
3	**Exposure to coal stove for heating or cooking**		0.60*
	No	1.00	
	Yes	0.92 (0.67; 1.26)	
4	**Smoking status**		0.001#
	Never smoked	1.00	
	Ex-smoker	1.04 (0.69; 1.56)	
	Current smoker	2.52 (1.21; 3.55)	

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