FEDERAL UNIVERSITY OF PELOTAS

POST-GRADUATE PROGRAM IN EPIDEMIOLOGY

PLATINO SURVEY – BRAZILIAN SAMPLE

REPORT

This report was prepared by

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1. INTRODUCTION

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

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

The main objective of the Platino study is to measure COPD prevalence in 5 Latin American metropolitan areas. The specific objectives are:

- ✓ To measure and compare COPD prevalence using different definitions, including ATS, ERS, GOLD, FIXED RATIO AND SYMPTOMS;
- ✓ 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 (Menezes, 2002, Platino Project).

This report describes the main results of the São Paulo study, the first 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 São Paulo, through multi-stage cluster sampling.

2.2. Sampling

The sample size calculations required 800 subjects to estimate a prevalence of up to 30% with a margin of error of less than 4 percent points (Menezes, 2002, Platino Project). To allow for non-response we aimed at obtaining 68 census tracts in larger metropolitan area of Sao Paulo, and to select 15 households, on average, from each tract. We expected approximately an average of one person aged 40 years or more per household.

The metropolitan area was divided into two strata: the city of SP, and its suburbs (comprising all other municipalities around SP). Table 1 shows the population of each stratum and the proportion of the sample expected in each area, with the respective size sample.

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

Stratum	*Population*		*Sample (subjects)*	*Sampling fraction/10,000*
	N	**%**	**n**	**n/N**
SÃO PAULO CITY	3,060,554	61.9%	631	2,06
SUBURBS	1,884,585	38.1%	389	2,06
METROPOLITAN REGION (MR)	4,945,139	100%	1020	2,06

Population data were obtained from the 2000 National Demographic Census.

2.2.1. Selection of census tracts

For purposes of the annual National Household Surveys (NHS), a master sample of all census tracts in SPMA was prepared by the Census Bureau. This master sample is self-weighting, and was used to select the census tracts (CT) for the present survey. This master sample included 271 census tracts in the city of SP and 184 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 (SP and other municipalities) and within each zone, they were ranked by mean family income level as measured in the 2000 Census. A systematic sample was then obtained with probability proportionate to size, taking into account the number of households (average 200-300) in each tract.

Figure 1 - Selection of the 42 census tracts in São Paulo stratified by geographical zone and by family income.

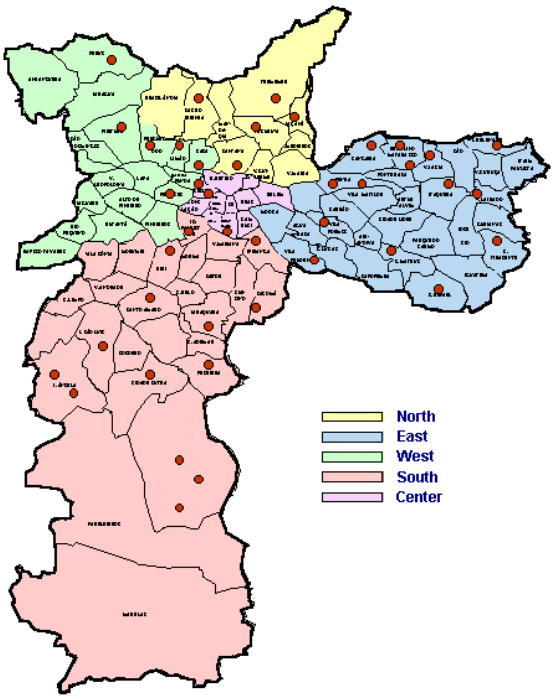

Figure 2 - Selection of the 26 census tracts in São Paulo stratified by geographical zone and by family income.

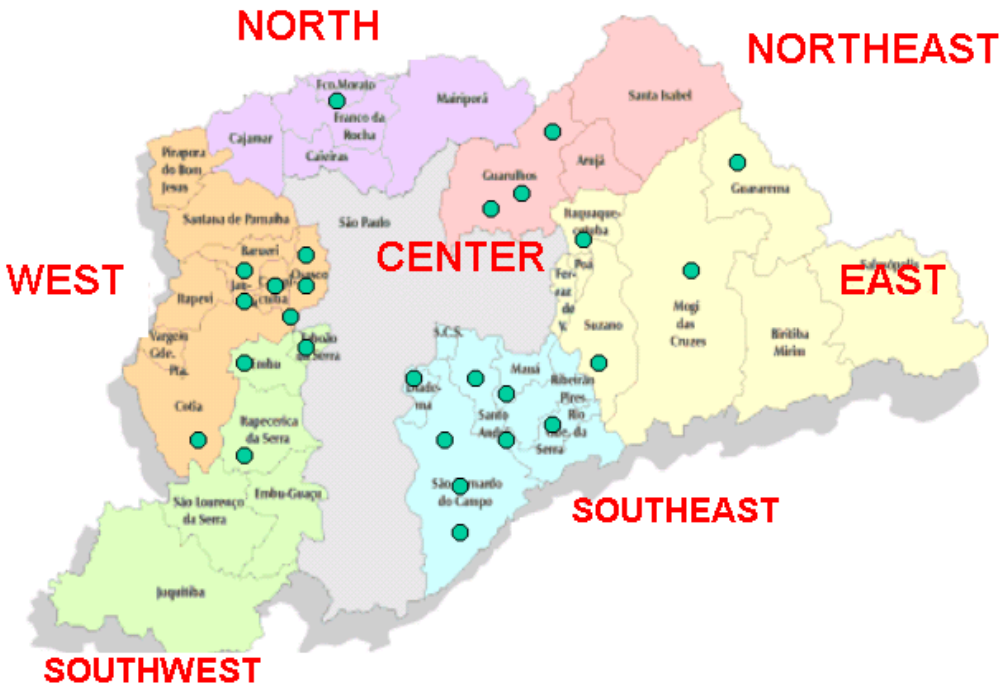

Table 2. Sampling of census tracts by stratum

Stratum	*N*	*B*	*Census tracts* *a = (n/b)*
SÃO PAULO CITY	631	15	42
SUBURBS	389	15	26
METROPOLITAN REGION (MR)	***1020***	*--*	***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 2000 during the National Census. The ratio of households counted in 2003 over those counted in 2000 represented a correction factor for population growth. This ratio was multiplied by 15 households to find out how many households should be selected in each tract (for example if the number of households

increased by 20% between 2000 and 2003 we selected 18 instead of 15 households in that tract). Households were systematically selected from the full updated listing prepared in 2003, by selecting one in every "x" household, where "x" represents the ratio between the total 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 post bronchodilator use according to the following criterion: FEV1/FVC < 70%, where FEV1 is the forced expiratory volume in the first second, and FVC is forced vital capacity (Viegi, 2000).

Prevalence of COPD was also analyzed according to other criteria:

- ✓ Global Obstructive Lung Disease (GOLD, 2001) - FEV1/FVC<70 and FEV1<80% predicted;.
- ✓ European Respiratory Society (ERS, 1993) - FEV1/FVC <88% of predicted in men and < 89% predicted in women;
- ✓ American Thoracic Society (ATS, 1994) - FEV1/FVC below 5th percentile and FEV1<100% predicted;
- ✓ For the analyses of lung function measurements, the NHANES Mexican-American reference values were used (NHANES, 1994).

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

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

2.3.2. Risk factors

The following risk factors were investigated:

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

The subject's anthropometric status (weight, height, and abdominal circumference) were 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 São Paulo study, no subjects fulfilled these criteria.

Exclusion criteria for spirometry – presence in the last three months of thoracic or abdominal surgery, heart attack, eye surgery (or retinal detachment), hospitalization for any heart problem, current treatment for tuberculosis, self reported pregnancy or pulse rate above 120 beats/minute. Sixteen 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 Tanita® 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 horizontally around the waist over the midpoint; 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 400 mg) was then administered

by inhalation, and the test was repeated 15 minutes later, with the same criteria. All spirometric examinations were carried out with the subject seated, wearing a nose clip and a disposable mouthpiece.

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

2.6. Personnel and training

The team for carrying out the training was composed by the main coordinator of the study, two experts in spirometry from Mexico, the local principal investigator, three field work supervisors, a nutritionist, and 17 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 field work lasted from 13/01 to 31/05/2003. The study team included three scouts, 17 interviewers working in pairs (all of whom were physiotherapists), three field supervisors, two local spirometry supervisors and a secretary.

All field methods were tested in a pilot study carried out in December 2002 in a middle-class area in São Paulo city.

The logistic of the field work 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 subway, 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 PI of the study was also checking the spirometries daily and working with the interviewers to correct any inaccuracies detected by him or by the Mexican team. Results of the regular quality control procedures, which confirmed that average measurement quality was 80% or higher throughout the study period, can be obtained from our homepage.

Interviews – 10% of the interviews were repeated by the supervisors. Two to three weeks after the interview, the supervisors contacted the subject interviewed and repeated six questions from the main questionnaire to assess reliability.

Anthropometry – Half way through the field work (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 Paulista School of Medicine in SP. 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 in a rehabilitation centre.

2.11. Processing of data

All questionnaires were photocopied, and the originals were sent to the Coordinating Centre (CC), while the copy remained in São Paulo. 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 São Paulo, 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 0.5% at the household level, 13.0% at the individual questionnaire level, and 2.1% for spirometry. The overall rate of non-response was 15.3%, obtained by multiplying the response rates. Exactly 1,000 subjects were interviewed, of whom 963 also completed the spirometric examination.

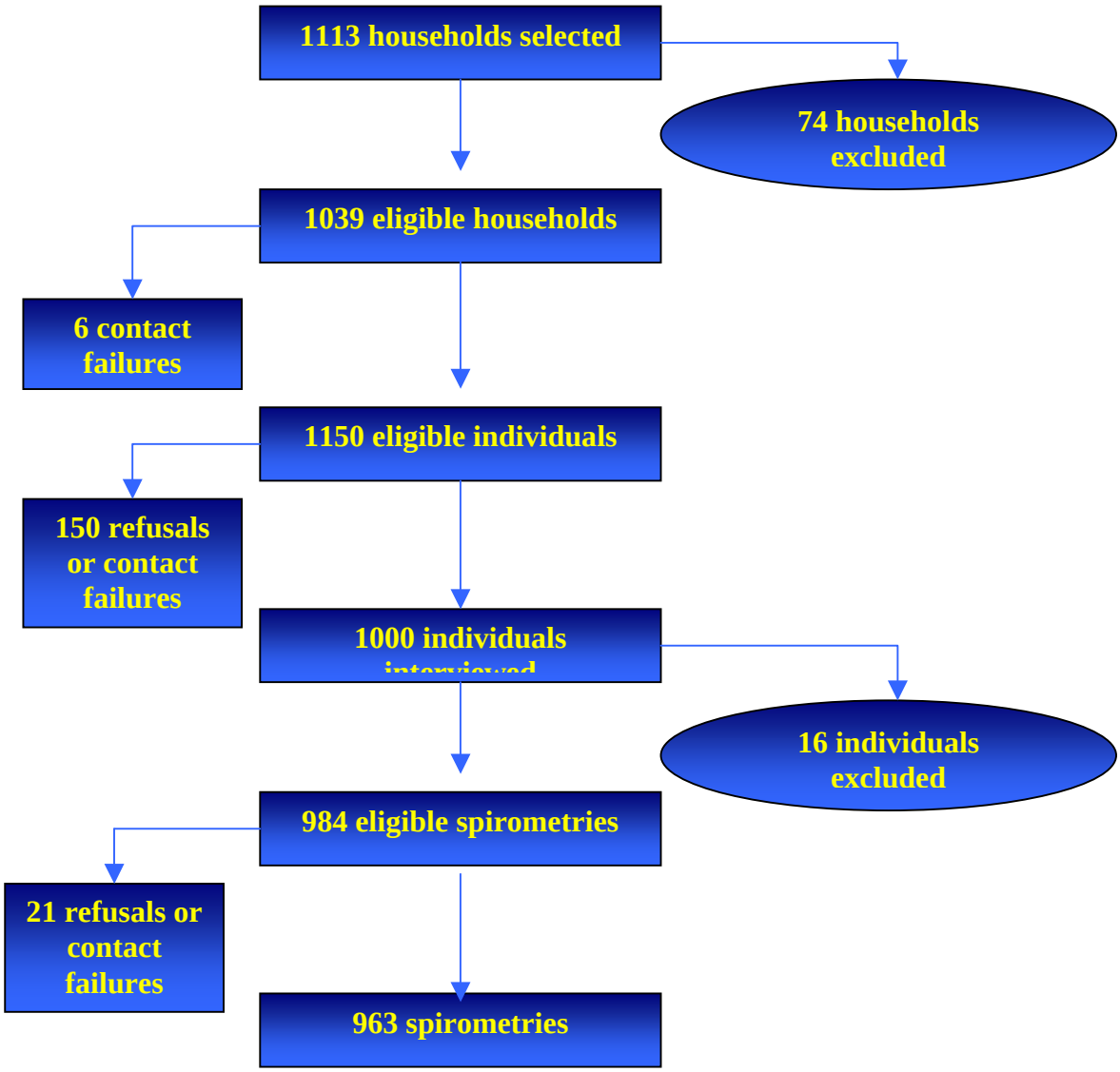

Figure 3. Number of households and individuals included in the different phases of the study.

Even for the 150 non-responders, we tried to obtain information on sex, age and smoking status; 94 (63%) answered these questions. This information was then extrapolated to the 150 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	16.6%
Females	10.0%
Age	
40-49	11.3%
50-59	13.0%
≥ 60	15.4%
Current smoking status	
No	12.5%
Yes	14.8%

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.

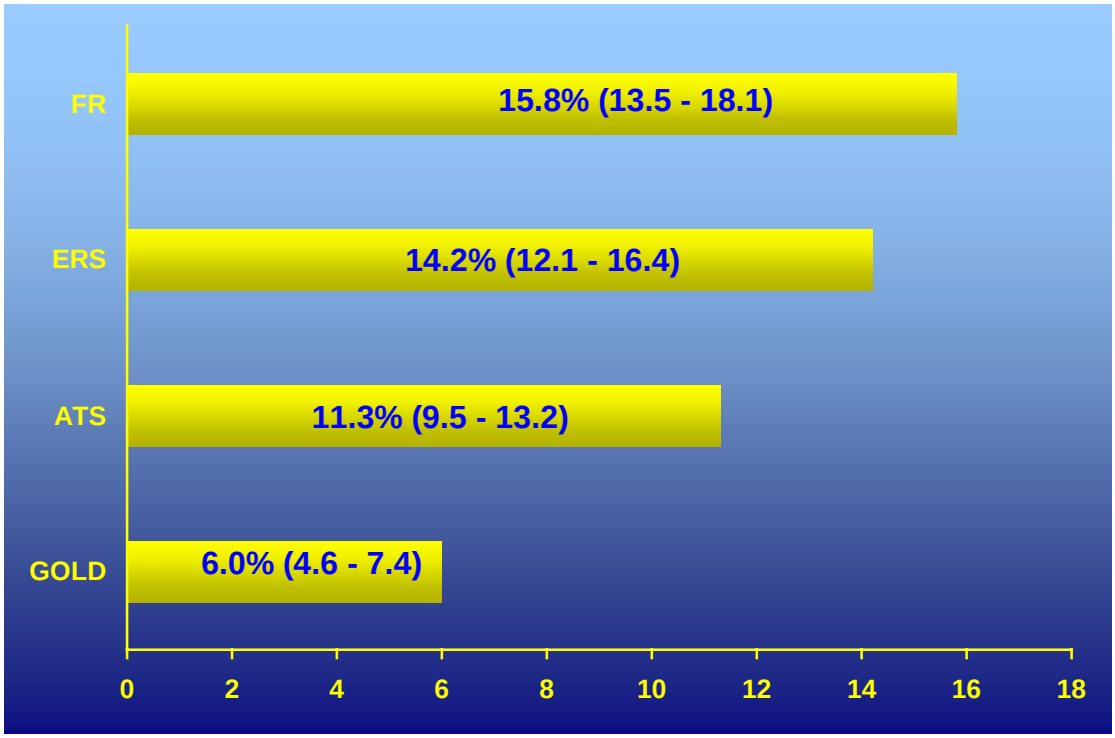

Figure 4. Prevalence of COPD based on different spirometric criteria.

The fixed ratio (FR) criterion showed the highest prevalence, of 15.8%, followed by the ERS (14.2%), ATS94 (11.3%) and GOLD (6.0%) 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. A set of Brazilian reference values are also available (Pereira, 1992) and the GOLD estimate was repeated using these references, and the estimated prevalence was 5.9% instead of 6.0%. Table 4 shows that only 9 of the 963 individuals were classified differently according to the two references. The kappa statistic for agreement was equal to 0.92.

Table 4. Comparison of COPD classification (GOLD criterion) using the NHANES and Brazilian reference curves for lung function.

Prevalence of COPD (GOLD – Brazilian reference)	*Prevalence of COPD (GOLD – NHANES reference)*		*Total*
	Present	*Absent*	
Present	53	4	57
Absent	5	901	906
Total	58	905	963

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 0.97 and 0.87, respectively. Design effects substantially greater than 1.0 are of concern, but was not the case for these outcome measures.

3.2.2 Clinical criteria

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

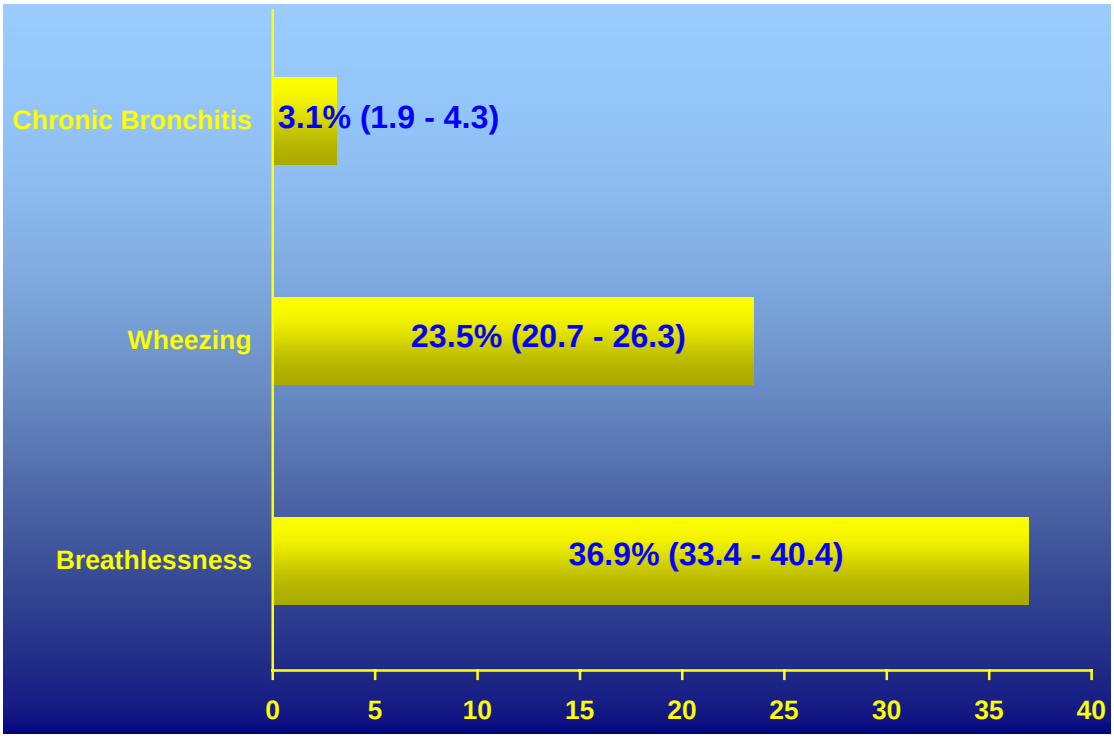

Figure 5. Prevalence of reported respiratory symptoms.

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 3.1%. Breathlessness due to exercise, and wheezing in the last 12 months were reported, respectively, by 36.9% and 23.5% 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 0.45 for cough and 0.39 for sputum, showing that agreement was intermediate to poor.

Figure 6 shows the prevalence of reported medical diagnoses of bronchitis, emphysema, asthma and COPD. Except for asthma which reached 10% of the subjects, each of the other conditions were reported by fewer than 4% of those interviewed. A medical diagnosis of either chronic bronchitis, emphysema or COPD was reported by 5.3% of all subjects.

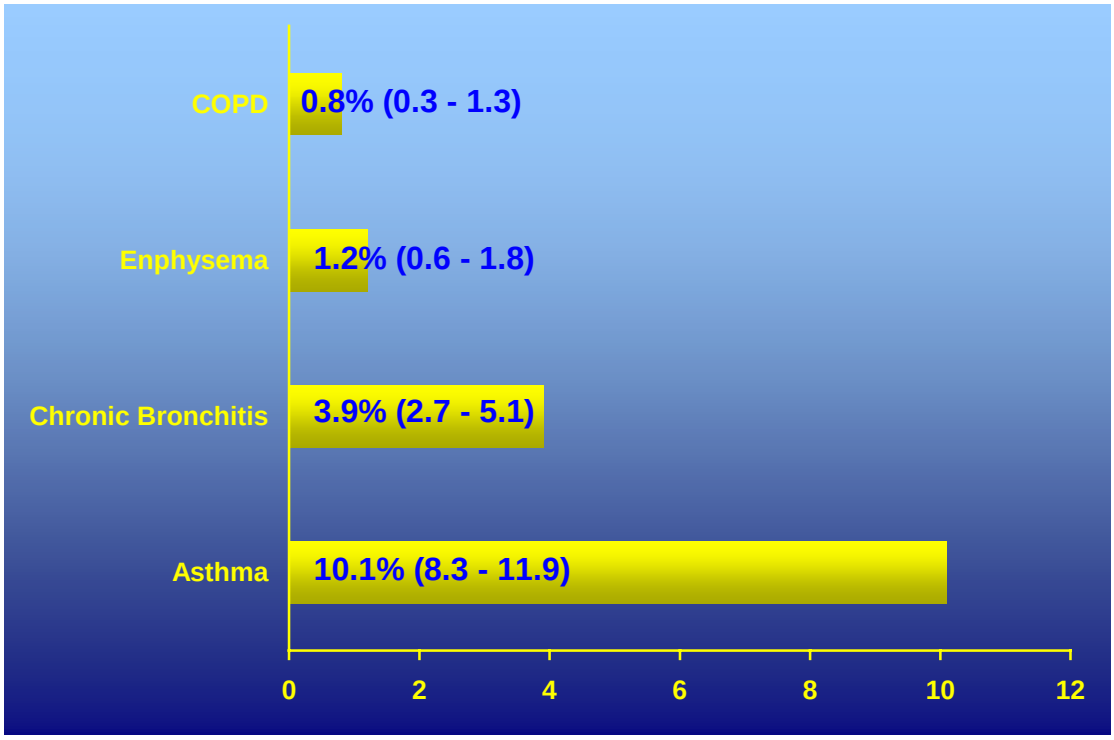

Figure 6. Prevalence of reported medical diagnoses of lung conditions.

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 the symptoms of bronchitis was 7.9% and its specificity 97.9%. Positive and negative predictive values were 41.4% and 85.0%, 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 symptoms of chronic bronchitis through questionnaire	*Prevalence of COPD (fixed ratio)*		*Total*
	Present	*Absent*	
Present	12	17	29
Absent	140	794	934
Total	152	811	963

Similar results were obtained when clinical symptoms were compared to the GOLD criterion (Table 6). Sensitivity was 10.3% and specificity 97.5%; positive and negative predictive values were 20.7% and 94.4%, 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 symptoms of chronic bronchitis through questionnaire	*Prevalence of COPD (GOLD - NHANES reference)*		*Total*
	Present	*Absent*	
Present	6	23	29
Absent	52	882	934
Total	58	905	963

These analyses were repeated for self-reported COPD, defined as either chronic bronchitis or breathlessness, or both. Sensitivity increased from 7.9% to 46.1%, but specificity decreased from 97.9% to 63.8% (Table 7). The positive predictive value was 19.3% and the negative predictive value 86.2%.

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	70	292	362
Absent	82	514	596
Total	152	806	958

For the GOLD criterion, the sensitivity of self-reported COPD was 53.4% and its specificity 63.2% (Table 8). The positive and negative predictive values were respectively 8.6% and 95.5%.

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	31	331	362
Absent	27	569	596
Total	58	900	958

Therefore, diagnoses based on clinical symptoms evidently fail 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 366 subjects who reported breathlessness, 101 (27.6%) presented a change in FEV1 post-bronchodilator use greater or equal than 12% (or 200 ml) test, thus suggesting the presence of asthma. This explains why the specificity of the combined diagnosis (Tables 7 and 8) was reduced sharply.

3.4. Risk factors for COPD

3.4.1. Distribution of the sample according to risk factors

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

Slightly more than half of all subjects were female, as was expected given the greater longevity of women. Subjects were concentrated in the 40-49 year age group. The average age was 55.2 years (SD 11.3). Most subjects classified themselves as white, followed by mulatto and blacks. Native Brazilians and Asians were rare. Approximately 15% 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 father, as a proxy for the social class of their family. The average length of schooling of the studied subjects was 5.9 years (SD 4.9). About one in four subjects were unable to inform about their fathers' schooling level, and about one half reported that their fathers had never attended school.

About one in four (24%) of the subjects contacted were smokers, and a further third (33.1%) were ex-smokers; 42.9% had never smoked. Current smokers accounted for 30.2% of the men and 19.0% of the women. When 10% of the sample were re-interviewed for quality control, the Kappa statistic for smoking was equal to 0.95, showing a very high degree of repeatability. The lifetime exposure to active smoking was also assessed; 19% 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 30.1%.

Almost half of the sample (45.1%) presented values of waist circumference above the proposed cut-off (88 cm for females and 102 cm for males). Overweight and obese subjects (BMI $\geq$ 25 kg/m^2) comprised almost two thirds of the sample (62.7%). The prevalence for males was 58.1% and for females 66.3%. Only 2.9% of all subjects reported having been admitted to a hospital due to a respiratory illness during childhood. Exposure to dust in the work-place for 10 years or more was reported by 33.7%.

Four sources of domestic smoke were studied: coal was used for cooking by 14.4% of all subjects and for heating by 1.7%; the corresponding exposures to biomass (mainly wood) were 47.5% and 6.4%. Due to the low frequency of exposure to heating fuels, these variables were collapsed into two: exposure to coal and exposure to domestic biomass fuels.

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

Variable	*Percentage*
Sex	
Men	44.2%
Women	55.8%
Age	
40-49	39.0%
50-59	32.0%
≥ 60	29.0%
Skin color / ethnicity	
White	57.5%
Mulatto	27.6%
Black	10.4%
Native Brazilians	2.3%
Asian	2.2%
Family history of CODP, bronchitis or emphysema	
No	14.7%
Yes	85.3%
Schooling level (years)	
0-2	23.4%
3-4	30.9%
5-8	22.7%
≥ 9	23.0%
Schooling of the father	
None	46.6%
Some	26.2%
Do not know	27.2%

a. There were up to 4 missing values in the variables listed in the table, among 1000 subjects.

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

Variable	*Percentage*
Smoking status	
Never smoked	42.9%
Ex-smoker	33.1%
Current smoker	24.0%
Lifetime cigarettes smoked	
Never smoked	43.4%*
≤1 pack-years	16.4%
1.1-10 pack-years	20.9%
>10 pack-years	19.3%
Passive smoking	
No	69.9%
Yes	30.1%
Hospital admission for respiratory illness during childhood	
No	97.1%
Yes	2.9%
Lifetime exposure to dust in workplace	
Never	43.0%
1-9 years	23.9%
≥ 10 years	33.1%
Exposure to coal stove for cooking or heating	
No	85.0%
Yes	15.0%
Exposure to biomass stove for cooking or heating	
No	50.9%
Yes	49.1%
Waist circumference	
Below cut-off	54.9%
Above cut-off (≥88 cm for females or ≥102 for males)	45.1%
Body mass index (kg/m^2)	
<18.5	2.2%
18.5 – 24.9	35.1%
25 – 29.9	37.3%
≥ 30	25.4%

* For current smoking status there is only 1 missing value, while for lifetime cigarettes smoked there are 11. This explains why the percentage of non-smokers is slightly different from the percentage of subjects with no lifetime exposure.

3.4.2. Crude analyses of main risk factors

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

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

Gender

Men tended to perform less well than women according to spirometric criteria, except for ERS (Table 11). One should bear in mind that the equations used for assessing spirometric results were already stratified by sex.

In terms of symptoms, men were slightly more likely to fulfill the criteria for chronic bronchitis but the difference was not significant ($P=0.19$). Women, on the other hand were more likely to report breathlessness ($P<0.001$), and wheezing prevalence was similar in both sexes ($P=0.7$). Conditions requiring a medical diagnosis tended to be more often reported by women, but the difference was only significant for asthma. COPD was seldom reported.

Therefore, males tended to have higher prevalence of spirometric diagnoses, but conditions with a medical diagnosis did not show a clear gender pattern, except for asthma which was more common among women. This difference may be explained by different 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 chronic bronchitis also tended to increase with age, but the differences were not significant. No clear age patterns were found for breathlessness or wheezing. In terms of medical diagnoses, only emphysema showed an increase with age.

Smoking

Table 11 shows that, also as expected, smoking was strongly associated with all spirometric outcomes. Prevalence among smokers were increased by two to threefold among smokers relative to non-smokers, while ex-smokers tended to present intermediate levels. All associations were significant. Smokers were also more likely to report wheezing symptoms ($P<0.001$) but not breathlessness or chronic bronchitis. There was no clear association between smoking and medically diagnosed conditions, rather surprisingly, but this may be explained by careseeking patterns.

Schooling

The number of years of formal education was inversely associated with all spirometric diagnoses (Table 11), although the association with ERS was of borderline significance ($P=0.07$). Low education was also associated with a significantly higher prevalence of symptoms of breathlessness and wheezing, while the association with symptomatic chronic bronchitis was nearly significant ($P=0.08$). On the other hand, no associations were found with medically diagnosed conditions.

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=0.09*	*P=0.4*	*P=0.11*	*P=1.0*	*P=0.19*	*P<0.001*	*P=0.7*	*P=0.4*	*P=0.5*	*P=0.03*	*P=0.7*
Males	18.0%	6.8%	13.1%	14.3%	3.9%	26.7%	22.9%	2.9%	0.9%	7.7%	0.9%
Females	14.0%	5.4%	9.9%	14.2%	2.5%	45.0%	24.0%	4.7%	1.4%	12.7%	0.7%
Age#	*P<0.001*	*P<0.001*	*P=0.02*	*P<0.001*	*P=0.07*	*P=0.5*	*P=0.3*	*P=1.0*	*P=0.03*	*P=0.9*	*P=0.7*
40-49	8.4%	2.9%	8.9%	9.9%	2.1%	36.3%	24.9%	4.9%	0.5%	10.5%	0.8%
50-59	16.2%	6.8%	11.7%	15.3%	2.5%	35.7%	23.4%	1.6%	0.6%	8.5%	0.6%
60-94	25.7%	9.6%	14.3%	19.1%	5.2%	39.2%	21.8%	5.2%	2.8%	11.1%	1.0%
Smoking#	*P=0.003*	*P=0.02*	*P<0.001*	*P=0.004*	*P=0.17*	*P=0.2*	*P<0.001*	*P=0.8*	*P=0.4*	*P=0.2*	*P=0.3*
Current	21.9%	8.4%	21.5%	21.5%	5.9%	35.9%	37.2%	2.9%	1.7%	9.2%	1.3%
Past	15.5%	7.0%	9.5%	12.0%	1.5%	33.9%	21.5%	5.1%	1.2%	8.2%	0.9%
Never	12.5%	3.9%	6.9%	11.7%	2.8%	39.9%	17.5%	3.5%	0.9%	12.2%	0.5%
Schooling (years)#	*P=0.003*	*P=0.04*	*P=0.03*	*P=0.07*	*P=0.08*	*P<0.001*	*P=0.05*	*P=0.8*	*P=0.5*	*P=0.6*	*P=0.5*
0-2	22.1%	7.2%	15.8%	17.6%	5.6%	45.0%	26.2%	5.2%	0.9%	9.4%	0.4%
3-4	16.3%	7.8%	11.2%	15.0%	2.3%	40.3%	26.3%	4.2%	2.3%	12.7%	1.6%
5-8	14.4%	4.5%	9.5%	13.1%	2.7%	36.7%	22.1%	2.7%	0.4%	7.6%	0.4%
9 or more	10.4%	4.1%	9.0%	11.3%	2.2%	24.5%	18.7%	3.5%	0.9%	9.6%	0.4%
All subjects	15.8%	6.0%	11.3%	14.2%	3.1%	36.9%	23.5%	3.9%	1.2%	10.1%	0.8%
Number in sample	963	963	963	963	1000	1000	1000	999	999	999	1000

* 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 29% more likely than women to present with COPD/FR, but the difference was not quite significant (P=0.09). Individuals aged 60 or over were three times more likely to present with COPD/FR than those aged 40-49 years. There were no significant associations with skin color. There was no association between a family history of bronchitis, emphysema or COPD and the spirometric results.

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

Smoking was also strongly associated with COPD/FR. Ex-smokers had 24% higher risk, and current smokers showed an increase of 76%. A strong dose-response association was also found with lifetime consumption of cigarettes. Reported passive smoking in the past two weeks was not significantly associated with the outcome.

Hospital admissions due to respiratory disease did not show any association with COPD/FR. Reported exposure to dust in the workplace for 10 years or more was associated with a 52% increase in the risk of COPD. Exposure to coal smoke in the home also increased the prevalence of COPD/FR by 50%, while exposure to domestic biomass smoke was not associated with the outcome.

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.

A possible difference was observed for only one exposure. Subjects reporting a respiratory disease admission in childhood showed a 75% higher prevalence of COPD/GOLD, but this difference was not significant (P=0.3).

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			0.09*
Men	18.0%	1.29 (0.96; 1.73)	
Women	14.0%	1.00	
Age			<0.001#
40-49	8.4%	1.00	
50-59	16.2%	1.94 (1.40; 2.69)	
≥ 60	25.7%	3.08 (2.22; 4.27)	
Skin color / ethnicity			0.4*
White	16.2%	1.00	
Mulatto	12.8%	0.79 (0.55; 1.15)	
Black	18.6%	1.15 (0.74; 1.77)	
Native Brazilians	21.7%	1.34 (0.60; 3.01)	
Asian	22.7%	1.40 (0.61; 3.23)	
Family history of COPD, bronchitis or emphysema			0.9*
No	15.7%	1.00	
Yes	16.3%	1.04 (0.65; 1.66)	
Schooling level			0.003#
0-2	22.1%	2.13 (1.28; 3.55)	
3-4	16.3%	1.58 (0.97; 2.57)	
5-8	14.4%	1.39 (0.80; 2.43)	
≥ 9	10.4%	1.00	
Schooling of the father			0.7*
None	16.0%	1.00	
Some	13.9%	0.87 (0.61; 1.25)	
Do not know	17.1%	1.10 (0.72; 1.58)	

* 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			0.003#
Never smoked	12.5%	1.00	
Ex-smoker	15.5%	1.24 (0.87; 1.74)	
Current smoker	21.9%	1.76 (1.23; 2.52)	
Lifetime cigarettes smoked			0.001#
Never smoked	12.5%	1.00	
≤1 pack-years	11.7%	0.94 (0.58; 1.52)	
1.1-10 pack-years	19.6%	1.57 (1.08; 2.29)	
>10 pack-years	23.2%	1.86 (1.27; 2.71)	
Passive smoking			0.3*
No	15.0%	1.00	
Yes	17.7%	1.18 (0.87; 1.59)	
Hospital admission for respiratory illness during childhood			0.8*
No	15.9%	1.00	
Yes	13.8%	0.87 (0.34; 2.22)	
Lifetime exposure to dust at the workplace			0.02#
Never	13.7%	1.00	
1-9 years	13.0%	0.95 (0.60; 1.49)	
≥ 10 years	20.8%	1.52 (1.09; 2.12)	
Exposure to coal stove for cooking or heating			0.03*
No	14.7%	1.00	
Yes	22.1%	1.50 (1.05; 2.14)	
Exposure to biomass stove for cooking or heating			0.8*
No	15.5%	1.00	
Yes	16.2%	1.04 (0.78; 1.40)	

* 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			0.4*
Men	6.8%	1.26 (0.75; 2.10)	
Women	5.4%	1.00	
Age			<0.001#
40-49	2.9%	1.00	
50-59	6.8%	2.37 (1.21; 4.66)	
≥ 60	9.6%	3.33 (1.73; 6.39)	
Skin color / ethnicity			0.6*
White	5.8%	1.00	
Mulatto	5.3%	0.92 (0.49; 1.70)	
Black	9.3%	1.61 (0.83; 3.15)	
Native Brazilians	4.4%	0.76 (0.10; 5.88)	
Asian	9.1%	1.58 (0.41; 6.05)	
Family history of COPD, bronchitis or emphysema			0.16*
No	5.6%	1.00	
Yes	8.5%	1.52 (0.84; 1.75)	
Schooling level			0.04#
0-2	7.2%	1.78 (0.82; 3.85)	
3-4	7.8%	1.93 (0.93; 3.99)	
5-8	4.5%	1.11 (0.45; 2.77)	
≥ 9	4.1%	1.00	
Schooling of the father			0.8*
None	6.7%	1.00	
Some	5.6%	0.83 (0.46; 1.52)	
Do not know	5.3%	0.80 (0.39; 1.62)	

* 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			0.02#
Never smoked	3.9%	1.00	
Ex-smoker	7.0%	1.78 (0.90; 3.53)	
Current smoker	8.4%	2.16 (1.07; 4.35)	
Lifetime cigarettes smoked			0.003#
Never smoked	3.9%	1.00	
≤1 pack-years	2.6%	0.66 (0.22; 2.04)	
1.1-10 pack-years	10.1%	2.57 (1.24; 5.34)	
>10 pack-years	9.5%	2.42 (1.21; 4.84)	
Passive smoking			0.6*
No	5.8%	1.00	
Yes	6.6%	1.13 (0.71; 1.82)	
Hospital admission for respiratory illness during childhood			0.3*
No	5.9%	1.00	
Yes	10.3%	1.75 (0.56; 5.54)	
Lifetime exposure to dust at the workplace			0.05#
Never	4.6%	1.00	
1-9 years	6.1%	1.33 (0.67; 1.61)	
≥ 10 years	8.0%	1.75 (1.00; 3.07)	
Exposure to coal stove for heating			0.007*
No	5.1%	1.00	
Yes	11.0%	2.15 (1.24; 3.71)	
Exposure to biomass stove for heating			0.7*
No	6.3%	1.00	
Yes	5.7%	0.91 (0.56; 1.98)	

* Wald test for heterogeneity # Wald test for trend

3.4.4. Multivariable analyses

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

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

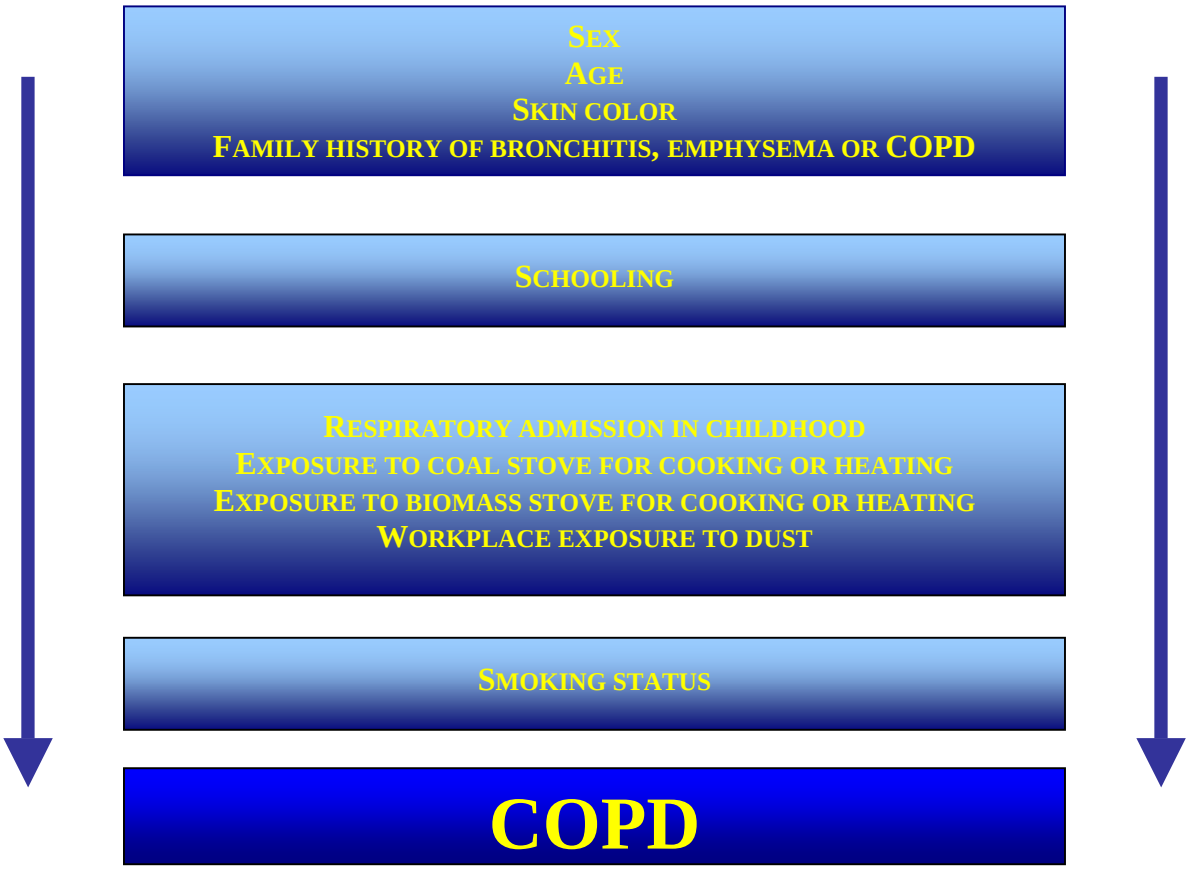

Figure 7. Conceptual framework for guiding the multivariable analyses.

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

FR criteria

Table 16 shows the results of the GOLD/FR outcome. The effects of sex, age, skin color and family history were very similar to those obtained in the unadjusted analyses. Because skin color and family history had P levels greater than 0.20, they were excluded from the model because they cannot confound the effect of other exposures due to their lack of association with the outcome.

In the second level of analyses, schooling for up to two years was associated with a 51% increase in COPD/FR, a marked reduction from the crude analyses in which there was a 113% increase; this variable was not quite significant (P=0.14). The crude

association of schooling with COPD was being confounded by age, because older subjects had both lower schooling and poor lung function.

History of respiratory admission and exposure to biomass smoke were not significant. Workplace dust exposure, which had been associated in the crude analyses, showed a borderline level of association (P=0.08) after adjustment. The same P level as observed for domestic exposure to coal smoke, which was associated with a 40% increase in the prevalence of COPD/FR.

Smoking and continued to be significantly associated with the outcome. Smokers had a 104% increase relative to non-smokers, compared to a 76% increase in the crude analyses.

Therefore, the adjusted analyses showed significant effects of age and smoking. Sex, schooling, workplace exposure to dust and domestic exposure to coal smoke showed associations with P levels between 0.06 and 0.14.

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

Level¨	*Variable*	*PR (CI95%)*	*P-value*
1	**Sex**		0.06*
	Men	1.32 (0.99; 1.76)	
	Women	1.00	
1	**Age**		<0.001#
	40-49	1.00	
	50-59	1.94 (1.40; 2.67)	
	≥ 60	3.11 (2.24; 4.31)	
1	**Skin color / ethnicity**		0.6*
	White	1.00	
	Mulatto	0.87 (0.61; 1.25)	
	Black	1.21 (0.79; 1.87)	
	Native Brazilians	1.32 (0.60; 2.86)	
	Asian	1.35 (0.65; 2.80)	
1	**Family history of COPD, bronchitis or emphysema**		0.9*
	No	1.00	
	Yes	1.05 (0.66; 1.66)	
2	**Schooling level**		0.14#
	0-2	1.51 (0.91; 2.50)	
	3-4	1.20 (0.73; 1.97)	
	5-8	1.27 (0.73; 2.20)	
	≥ 9	1.00	
3	**Hospital admission for respiratory illness during childhood**		0.7*
	No	1.00	
	Yes	1.18 (0.49; 2.89)	
3	**Lifetime exposure to dust at the work-place**		0.08#
	Never	1.00	
	1-9 years	1.04 (0.66; 1.64)	
	≥ 10 years	1.36 (0.96; 1.93)	
3	**Exposure to biomass stove for heating or cooking**		0.4*
	No	1.00	
	Yes	0.88 (0.66; 1.17)	
3	**Exposure to coal stove for heating or cooking**		0.08*
	No	1.00	
	Yes	1.40 (0.96; 2.03)	
4	**Smoking status**		<0.001#
	Never smoked	1.00	
	Ex-smoker	1.23 (0.88; 1.72)	
	Current smoker	2.04 (1.41; 2.95)	

* 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. Although men had a 28% higher prevalence, the difference was not significant (P=0.3). Age was positively associated with the outcome, with a 233% increase for those aged 60 years or more. Skin color was not associated with COPD/GOLD. Subjects with a family history of CODP shows a 54% increase in prevalence, but this was not significant (P=0.16).

In the second level of analyses, schooling for up to two years was associated with a 25% increase in COPD/GOLD, a non-significant difference (P=0.4). The crude effect of schooling was being confounded by age again.

Subjects exposed for 10 years or more to dust at the workplace had a 75% increase in prevalence (P=0.05). Domestic exposure to coal smoke led to a 106% increase in prevalence (P=0.02), while hospital admission due to respiratory disease in childhood was associated with a 116% increase (P=0.19). Exposure to biomass smoke was not associated with COPD.

Smoking continued to be significantly associated with the outcome. Smokers had a 157% increase relative to non-smokers, compared to an 81% increase for ex-smokers.

In short, the adjusted analyses showed significant effects of age, exposure to dust and coal, and smoking. Family history (P=0.16), schooling (P=0.4) and hospital admission due to respiratory disease in childhood (P=0.19) showed associations in the expected direction but that were not significant. These results were quite comparable with those observed in the multivariable analyses of COPD/FR, as shown by the prevalence ratios in Tables 9 and 10. 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**		0.3*
	Men	1.28 (0.77; 2.12)	
	Women	1.00	
1	**Age**		<0.001#
	40-49	1.00	
	50-59	2.37 (1.21; 4.66)	
	≥ 60	3.33 (1.73; 6.39)	
1	**Skin color / ethnicity**		0.5*
	White	1.00	
	Mulatto	1.00 (0.54; 1.85)	
	Black	1.70 (0.87; 3.30)	
	Native Brazilians	0.74 (0.10; 5.52)	
	Asian	1.51 (0.43; 5.27)	
1	**Family history of COPD, bronchitis or emphysema**		0.16*
	No	1.00	
	Yes	1.54 (0.84; 2.81)	
2	**Schooling level**		0.4#
	0-2	1.25 (0.57; 2.74)	
	3-4	1.46 (0.67; 3.19)	
	5-8	1.01 (0.42; 2.47)	
	≥ 9	1.00	
3	**Lifetime exposure to dust at the work-place**		0.05#
	Never	1.00	
	1-9 years	1.65 (0.81; 3.35)	
	≥ 10 years	1.75 (0.99; 3.09)	
3	**Hospital admission for respiratory illness during childhood**		0.19*
	No	1.00	
	Yes	2.16 (0.67; 6.90)	
3	**Exposure to biomass stove for heating or cooking**		0.4*
	No	1.00	
	Yes	0.88 (0.66; 1.17)	
3	**Exposure to coal stove for heating or cooking**		0.02*
	No	1.00	
	Yes	2.06 (1.16; 3.65)	
4	**Smoking status**		0.01#
	Never smoked	1.00	
	Ex-smoker	1.81 (0.89; 3.65)	
	Current smoker	2.57 (1.19; 5.53)	

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

3.4.5. COPD and anthropometry

Subjects with waist circumference above the proposed 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 circumference. While the average of FEV1 was 2.73 (SD 0.77) for subjects below the cut-off point, it was 2.37 (SD 0.77) for those above. The same trend was observed for forced vital capacity (FVC), with averages of 3.65 (SD 0.90) and 3.18 (SD 0.94) for subjects below or above the cut-off points, respectively (P<0.001). Significant higher results (P=0.04) of the FEV1/FVC ratio were found among subjects above the cut-off point compared with those below. However, when waist circumference was treated as a continuous variable, no significant associations were found with FEV1, FVC or FEV1/FVC ratio, indicating possible non-linearity.

The association between BMI and COPD is summarized in Figure 8. Overall, prevalence of COPD was higher in the low-BMI group (<18.5kg/m^2) and no differences were found among the remaining categories.

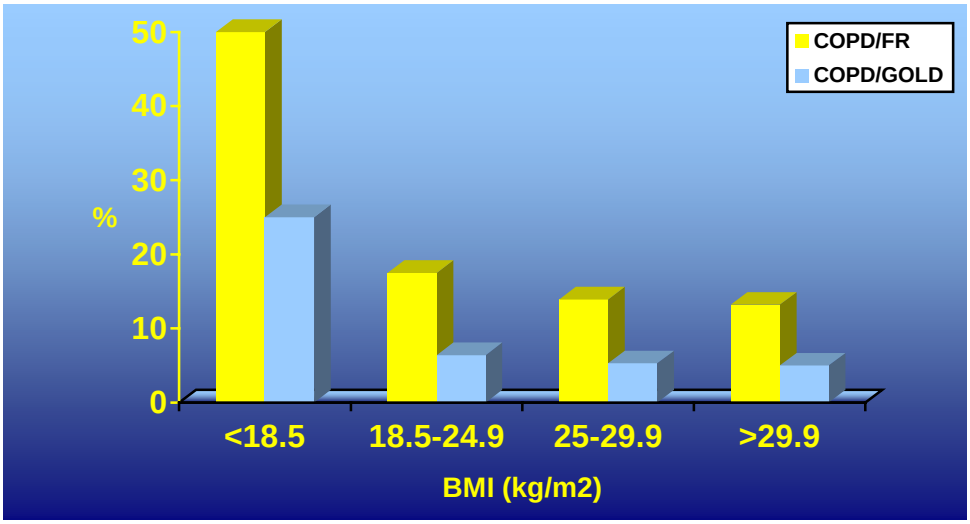

Figure 8. Relationship between COPD (FR and GOLD criteria) and body mass index (BMI).

3.5. Additional analyses

3.5.1. Co-morbidity

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

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

Table 18. Lifetime prevalence of selected medical diagnoses.

Condition	*Prevalence*
Hypertension	40.6%
Gastritis	31.2%
Heart problem	15.3%
Diabetes	11.7%
Stroke	3.3%
Tuberculosis	2.8%
Lung cancer	0.8%

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

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

Condition	*COPD (FR criteria)*		*COPD (GOLD criteria)*	
	Prevalence	*P*	*Prevalence*	*P*
Heart problem		0.5		0.9
Yes	14.0%		5.9%	
No	16.1%		6.1%	
Hypertension		0.3		1.0
Yes	17.3%		6.0%	
No	14.8%		6.0%	
Diabetes		0.3		0.3
Yes	19.4%		8.3%	
No	15.3%		5.7%	
Lung cancer		0.008		0.4
Yes	50.0%		12.5%	
No	15.5%		6.0%	
Stroke		0.8		0.6
Yes	14.3%		3.6%	
No	15.9%		6.1%	
Tuberculosis		0.12		0.2
Yes	26.9%		11.5%	
No	15.5%		5.9%	
Gastritis		0.3		0.4
Yes	17.6%		7.0%	
No	15.0%		5.6%	

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 17.9%, while it is 26.2% according to COPD/GOLD. Therefore, about one in 4-5 COPD cases would be prevented by smoking control.

We have also calculated attributable risks of low schooling level (0-2 years), exposure to coal, hospital admissions due to respiratory disease in childhood and workplace exposure to dust. The attributable risks of low schooling were 10.3% and

7.4% for the COPD/FR and COPD/GOLD criteria, respectively. For exposure to coal, the same values were 5.7% and 13.7%. Hospital admissions due to respiratory disease in childhood presented attributable risks of 0.5% and 3.3% for COPD/FR and COPD/GGOLD, respectively. Finally, the corresponding figures for workplace exposure to dust for 10 years or more were 10.6% and 19.8%.

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 three of the four spirometric criteria used. However, these associations were greatly reduced after controlling for smoking status. The male/female prevalence ratio was 1.32 for COPD/FR, but when we control for smoking, the value is 1.13. For the COPD/GOLD indicator, the value decreased from 1.28 to 1.11. For the ATS criteria, these values were 1.33 and 1.07. This shows that most of the excess in COPD among males is due to the fact that they smoke more often.

3.6. Medical management

Overall, 7.9% of the individuals reported having used medicines for lung or respiratory problems in the previous 12 months (Table 20). The prevalence rates for COPD/FR positive and negative were, respectively, 18.4% and 5.9% (P<0.001). The most frequently used drugs were salbutamol, fenoterol, aminophylline and ipratropium (Table 20). Among salbutamol users, 62.5% used it via syrup, which is not recommended, while only 37.5% used sprays or inhalation. Most subjects (84.6%) reported using this drug only for symptomatic relief, which is also inadequate.

Although influenza immunization is recommended for all COPD patients, only 30.9% of those who were COPD/FR positive reported being vaccinated in the previous year, compared to 20.9% of the remainder (P<0.001).

Subjects were asked if they had ever been submitted to spirometry. The lifetime frequency was 10.1%, almost the same for COPD/FR positive (10.5%) and negative (9.5%). On the other hand, this prevalence was strongly associated with schooling level; 4.3% among subjects with 0-2 years of formal education; 9.1% in the 3-4 years group; 9.3% of the 5-8 years group; and 17.8% of the 9 years or more.

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

Drug	*N*	*Percentage*
Acebrophylline	2	1.7%
Aceclofenac	1	0.8%
Acetylcysteine	4	3.4%
Ambroxol	2	1.7%
Aminophylline	16	13.4%
Beclomethasone	4	3.4%
Betamethasone	1	0.8%
Bromhexin	1	0.8%
Budesonide	1	0.8%
Carbosisteine	1	0.8%
Ephedrine	3	2.5%
Epinastine	1	0.8%
Fenoterol	19	16.0%
Formoterol	3	2.5%
Ipratropium	13	10.9%
Predinisone	3	2.5%
Salbutamol	21	17.6%
Triamcinolone	2	1.7%
Clobutinol	1	0.8%
Guaifenesin	1	0.8%
Flunisolide	1	0.8%
Others	18	15.1%
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.

Quality of life indicator	*Prevalence according to COPD/FR status*		*P*
	Positive	*Negative*	
Difficulty in carrying out moderate physical activities	9.9%	5.7%	0.06
Difficulty in carrying out intense physical activities	13.2%	5.9%	<0.001
Any limitation due to physical health in the past year	21.7%	14.3%	0.02
Any limitation in the workplace due to physical health	17.1%	16.1%	0.7
Any limitation due to mental health in the past year	23.0%	16.3%	0.05
Any limitation in the workplace due to mental health	18.4%	14.2%	0.16

An additional question inquired whether lung disease affected daily activities in the past year. Of COPD/FR positive subjects, 17.1% answered affirmatively, while 8.5% of the remainder did so (P=0.002).

3.8. Economic impact of COPD

Formal employment in the previous 12 months was reported by 57.1% individuals (47.4% among COPD/FR positive and 60.0% among the negative; P=0.004). This difference disappeared, however, after adjustment for age, because both COPD and unemployment were more common among older subjects.

Among the 429 individuals who did not work in the previous years, 2.1% reported that this was due to lung disease.

Approximately one in ten individuals (10.2%) reported having limited leisure activities due to health problems. The percentages were 13.8% and 8.5% among COPD/FR positive and negative subjects, respectively (P=0.04).

4. DISCUSSION

This is the final report from the first site of the PLATINO study. As such, the present results have to be interpreted with caution because, for most comparisons being made, the required sample size will only be reached after data from 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 and recommendations for other study sites. A full discussion of the implications of the study will be prepared after data collection in all sites is completed.

4.1 Discussion of methodological issues

The positive aspects of the study include the relatively high response rate of 84.7%. Given the size of the study area and the high levels of violence, with the consequent reluctance of the population to welcome strangers, the response rate is remarkable. Men, however, were more likely to refuse participation than women. 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 2% of those eligible accepted 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 15.8% 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 (6.0%) 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 5.3% of all subjects.

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 age, smoking and exposure to coal smoke were significantly associated with COPD. Possible associations were also detected with sex, schooling, and exposure to dust in the workplace. A comparison of our results with the medical literature will be carried out after the final analyses.

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

Regarding case-management, important problems were identified. Most subjects with COPD do not take medication that could substantially improve their condition, and those who take such medication often do it inappropriately, both in terms of the route of administration and of its frequency. Preventive interventions are also inadequate; only one in three of the diseased, for example, receive flu vaccination in the previous year. Finally, diagnostic procedures were poor; the percentages of subjects who ever underwent spirometry were similar among the COPD positive and negative.

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

4.3. Conclusions

The São Paulo survey showed that the study protocol was adequate, having resulted in 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 study was carried out in a timely fashion. Field work lasted four months, as planned, and the present final report has been concluded ten months after interviewer training was started.

The experience gained in São Paulo was already employed in the implementation of the study in Mexico City and Montevideo, and will be used in the next sites to be added to the study.

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

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

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

* Wald test for heterogeneity # Wald test for trend

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

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

* Wald test for heterogeneity # Wald test for trend

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

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

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

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

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

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