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The PLATINO Study: Contributions to COPD Knowledge

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ABSTRACT

The PLATINO study was a large survey in Latin America, originally aimed to describe the epidemiology of chronic obstructive pulmonary disease (COPD). A baseline, cross-sectional, population-based survey was conducted in five major cities: São Paulo (Brazil), Santiago (Chile), Mexico City (Mexico), Montevideo (Uruguay), and Caracas (Venezuela). A follow-up study was completed five to nine years later in three of five original centres. This review provides information from the Spanish acronym: Latin American Project for Research in Pulmonary Obstruction (PLATINO Study) on COPD epidemiology in the region (prevalence, accurate/inaccurate diagnosis, and treatment). Available data on disease risk factors, clinical patterns, follow-up prevalence, and diagnosis stability over time, as well as mortality, are also presented. **(BRN Rev. 2017;3:3-17)**

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BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a major global problem with high prevalence, morbidity, and mortality. In Latin America the situation is complex due to the fast epidemiologic and demographic transition, with increases in chronic diseases as a result of the aging population.

Few studies have assessed COPD epidemiology in Latin America[1-3]. The PLATINO study (Spanish acronym: Latin American Project for Research in Pulmonary Obstruction) was the first large survey in Latin America to assess the COPD burden in five low- and middle-income countries: São Paulo (Brazil), Santiago (Chile), Mexico City (Mexico), Montevideo (Uruguay), and Caracas (Venezuela)[2,3]. These sites represent different geographical areas of Latin America and the largest metropolitan area in each participating country. The Proyecto Latinoamericano de Investigación en Obstrucción Pulmonar (PLATINO Study) baseline study was conducted from 2002 to 2004 as an initiative of the Asociación Latinoamericana del Tórax (ALAT) (Fig. 1). Data from this study have filled an important knowledge gap in the COPD epidemiology in Latin America and have allowed analysing different characteristics of the disease in an unbiased population.

The cross-sectional nature of the PLATINO baseline study (a visit at one point in time) did not provide temporal data and thus does not allow analysing some important COPD outcomes. Therefore, after five years, a follow-up study was conducted in three of the original five PLATINO sites (Fig. 2).

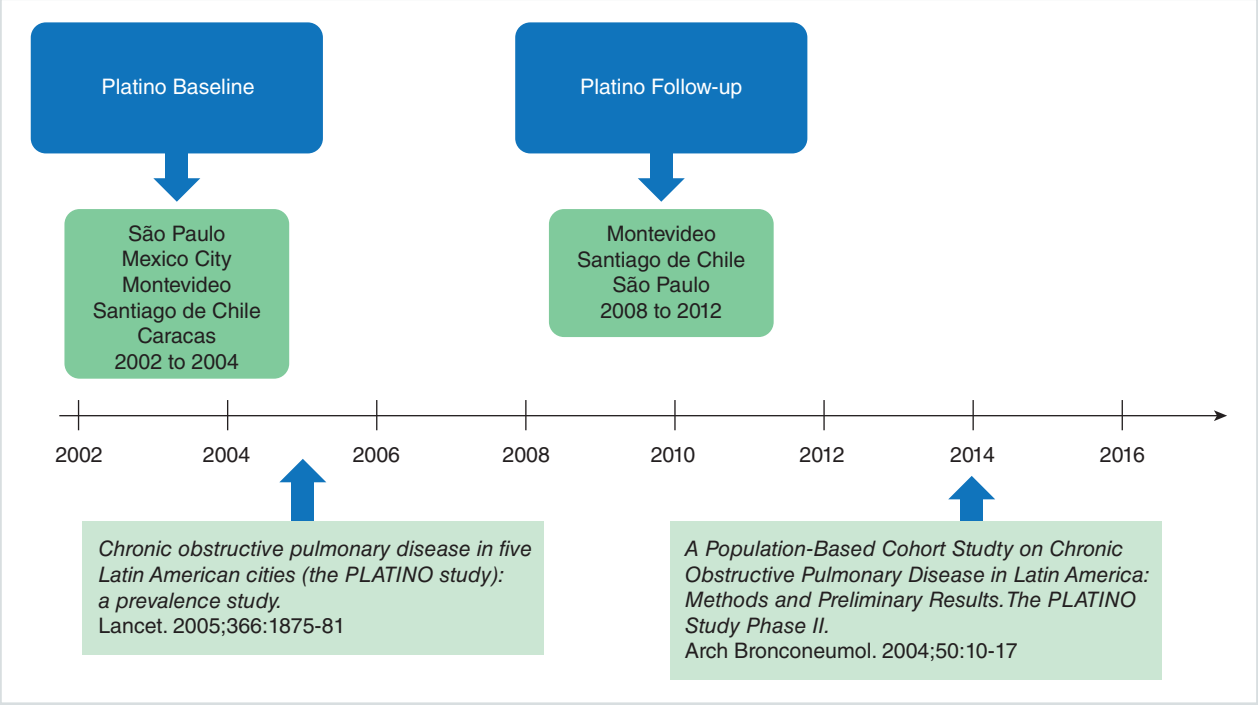

Figure 1. The PLATINO study chronology.

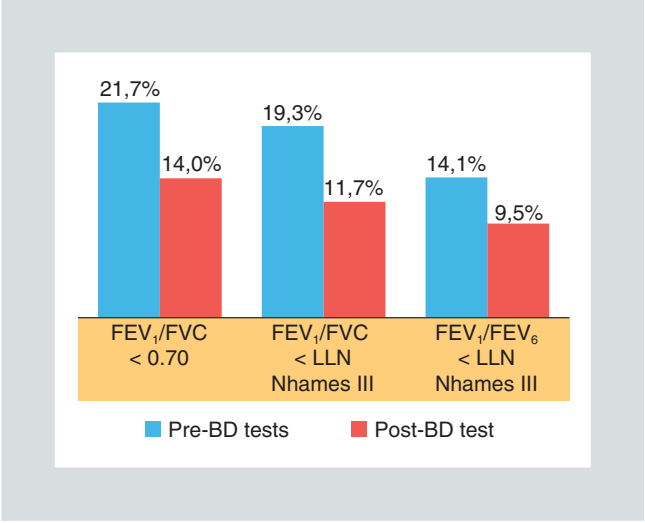

Figure 2. COPD prevalence in the PLATINO baseline population by different spirometric criteria before and after the use of bronchodilator.
BD: bronchodilator; FEV_1: forced expiratory volume in 1 second; FEV_6: forced expiratory volume in 6 seconds; FVC: forced vital capacity; LLN: lower limit of normal.

This review provides information from the PLATINO study on COPD epidemiology in the region (prevalence, accurate/inaccurate diagnosis, and treatment of disease). It also provides information on risk factors, clinical characteristics of patients with spirometric COPD diagnosis, prevalence in the follow-up study, diagnosis stability over time, and mortality.

DESIGN AND GENERAL CHARACTERISTICS OF THE PLATINO BASELINE STUDY

The PLATINO baseline study included all adults ≥ 40 years old living in the selected households[2,3]. Information was collected on several factors potentially associated with COPD (demographics, smoking habits, years of education, respiratory symptoms, exacerbation, comorbidities, respiratory medication use, and prior spirometry)[2,3]. Subjects performed spirometry pre- and post-bronchodilator (post-BD). A total of 1,000 subjects were interviewed in Sao Paulo, 1,063 in Mexico City, 943 in Montevideo, 1,208 in Santiago, and 1,357 in Caracas and spirometry was undertaken in 99%[2,3]. The overall response rate (including spirometry) was 83.7% in São Paulo, 79.5% in Santiago, 68.9% in Mexico City, 80% in Montevideo, and 71.7% in Caracas[2,3].

CONTRIBUTION TO THE EPIDEMIOLOGY AND COPD BURDEN IN LATIN AMERICA

Prevalence and risk factors

COPD is a leading cause of global morbidity and mortality, associated with a high economic and social burden[4,5]. There are many studies of COPD prevalence and their results document wide variations across countries and regions and between different groups within countries[1,3,6].

Overall COPD prevalence in the PLATINO study by the post-BD forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) < 0.70 criteria was 14.3% (ranging from 7.8% in Mexico City to 19.7% in Montevideo)[3]. Global prevalence by the lower limit of normal (LLN) criteria of post-BD FEV_1/FVC ratio was 11.7% and even lower when using the post-BD FEV_1/VEF_6 < LLN criteria (9.5%)[7]. A survey in five Colombian cities found a COPD prevalence ranging from 6.2 to 13.5%[1]. These findings suggest that the burden of COPD in Latin America is high, and that prevention of the disease is a public health priority in the region.

In all PLATINO cities, there was a consistent pattern of higher prevalence in men, older people, those with less education and lower body-mass index (BMI), and greater tobacco exposure[3]. The prevalence of COPD in all sites was significantly higher in men than in women (combined prevalence in males 18.9%, and 11.3% in females)[3]. The Burden of Obstructive Lung Diseases (BOLD), a study with similar methodology to PLATINO, subsequently reported a COPD prevalence of GOLD stage ≥ 2 of 10.1% overall, 11.8% for men, and 8.5% for women[8]. These results, in accordance with the PLATINO findings, support the higher prevalence of disease in men worldwide.

In PLATINO the risk factors with the highest etiological fractions for COPD were age, current smoking, indoor coal exposure, and dust exposure in the workplace[3]. Attributable risk for COPD was 52% for ≥ 60 years of age, and for modifiable factors the risk was 27% for current smokers, 11% for coal exposure ≥ 10 years, and 9% for dust exposure in workplace ≥ 10 years[3]. Other factors, including male sex, poor education, biomass exposure, history of tuberculosis, low BMI, and childhood admission due to respiratory problems, presented an attributable risk < 10%[3].

The BOLD study also assessed the associations between spirometric-defined COPD and main risk factors. Similar to PLATINO, they found significant associations between COPD and smoking, environmental tobacco exposure, age, education, tuberculosis, hospitalization for respiratory illness before the age of 10 years, a family history of COPD, and number of years worked in dusty jobs[9].

COPD diagnosis problems in epidemiologic studies

COPD surveys have identified important differences in the distribution of the disease prevalence and underdiagnosis. In PLATINO, COPD underdiagnosis (individuals without a prior diagnostic label consistent with COPD with airflow limitation) was 89% and misdiagnosis 64% (individuals with prior COPD medical diagnosis without airflow limitation)[10]. Only 20% of the surveyed individuals had performed a spirometry at some time in their lives. Underdiagnosis was associated with younger age, lower severity of airway obstruction, fewer respiratory symptoms (cough, phlegm, wheezing, shortness of breath), and no prior diagnosis of asthma[10].

Lamprecht et al.[11] reported an overall COPD underdiagnosis prevalence of 81.4% in national and international population surveys [BOLD, PLATINO, Epidemiologic Study of COPD in Spain (EPI-SCAN) and Prevalence of COPD in Prevalence of Chronic Obstructive Pulmonary Disease in five Colombian cities (PREPOCOL)]. Underdiagnosis was associated with male sex, younger age, never and current smoking, lower education, no previous spirometry, and milder airflow limitation[11].

These results confirm COPD underdiagnosis as a major health problem and highlight the need to improve diagnoses worldwide.

COPD undertreatment and overtreatment

Despite the availability of national and international COPD guidelines, evidence from real-life studies suggests that inadequate COPD treatment is common[12,13].

PLATINO showed that less than 25% of patients with spirometric COPD criteria had received any respiratory medication in the previous year[14]. Among those with previous correct COPD diagnosis, three-quarters (75.6%) were receiving any respiratory medication (43% inhaled medication and 36% bronchodilators)[14]. In addition, the majority of patients used the medication based on symptoms rather than on a regular basis, independently of disease severity[14].

Another PLATINO subanalysis, focused on the use of bronchodilators inhaled or corticosteroids in persons with little evidence of chronic respiratory disease, indicated that these medications are frequently used in individuals ≥ 40 years old without a previous diagnosis of asthma, COPD, or the presence of airway obstruction[15]. Over 50% of subjects using medication for airflow limitation were not obstructed. Therefore, respiratory medication also appears to be used in subjects incorrectly diagnosed as COPD[15].

In light of these evidences, investments should also be made in terms of improving COPD treatment and encouraging appropriate therapies among primary care physicians to limit the risks and costs associated with undertreatment and overtreatment and improve patient outcomes.

CONTRIBUTION TO THE CHARACTERISTICS OF THE DISEASE AND POTENTIAL COPD PHENOTYPES

The PLATINO baseline study offers an opportunity for analysing characteristics of the disease and potential patient subgroups in a large population-based sample.

Regional spirometric reference values and acute bronchodilator responsiveness in COPD

Since PLATINO participants were included by population-sampling methods, spirometric reference values before and after bronchodilators were generated from individuals without a history of respiratory disease. Proposed values represent a step forward for better spirometry in Latin America[16,17].

Acute bronchodilator responsiveness (BDR) is an area of discussion in COPD. In a selected COPD population, Calverley et al.[18] reported more than three-quarters of patients had an improvement in expiratory airflow over the generally accepted minimum clinically important difference (100 ml). Data from the Understanding the Potential Long-Term Impacts on Function with Tiotropium (UPLIFT) cohort indicated that 53.9% of patients demonstrated 12% and 200 ml FEV_1 improvement after the administration of two bronchodilators[19]. In the Lung Health Study, approximately 20% of COPD patients demonstrated initial FEV_1 response ≥ 200 ml[20].

Along this line, a sub-analysis of PLATINO assessed the acute BDR in subjects with and without airway obstruction. Over two-thirds of COPD subjects had no acute BDR[21]. Depending on the criterion used, the proportion of subjects with acute BDR ranged between 15.0-28.2% in the COPD group, 11.4-21.6% in reversible obstructed individuals, and 2.7-7.2% in healthy respiratory subjects[21]. In the

COPD group, 28% met the ATS criteria for acute BDR. An FVC acute BDR was more common than FEV_1 response; 24% had isolated FEV_1 reversibility, 38% isolated FVC reversibility, and 38% both[21]. There was a substantial overlap in FEV_1 and FVC changes after bronchodilator use in individuals with COPD and those with reversible obstruction, which makes it difficult to determine a threshold for separating these groups[21].

Subsequently, BOLD provided reference values for BDR worldwide that confirm guideline estimates for a clinically significant level of BDR in bronchodilator testing[22]. They found that the BDR threshold for people with chronic airflow limitation was lower when asthma was excluded, with considerable overlap between the groups. They also found that the proportion with reversibility measured by changes in FEV_1 generally decreased as COPD severity increased, while that measured by changes in FVC increased with increasing COPD severity.

The PLATINO findings are consistent with other epidemiologic studies[20,22], suggesting that acute BDR in COPD is minor and less than considered as significant. Greater bronchodilator increase in FVC compared to FEV_1 support the use of lung volume-based measures (volume response) of reversibility in addition to FEV_1-based measures (flow response). Finally, all the studies consistently indicate that BDR has limited diagnostic value in differentiating asthma from COPD.

COPD screening

Limited spirometry availability is an important barrier for confirming COPD diagnosis.

Normal pre-BD peak expiratory flow (PEF) in adults may rule out clinically significant COPD. Combined data from two population-based studies (PLATINO and BOLD) was used to assess whether PEF (pre-BD) identified spirometric-confirmed post-BD airflow obstruction[23]. A PEF screening cut-off point of 70% predicted effectively ruled out COPD patients in GOLD grades 3-4 (NPV: 99.9%)[23]. Additionally, using this cut-off point as a screening tool to rule out severe airflow limitation, only 12% of subjects with COPD risk factors would require confirmatory spirometry[23]. The addition of PEF measurement to a simple screening questionnaire may rule out patients with severe-to-very severe COPD without the need of confirmatory pre- and post-BD spirometry testing[23].

Subsequently, BOLD compared the screening efficiency of differently staged algorithms that used questionnaire data and/or PEF to identify persons at risk for COPD and, hence, needing confirmatory spirometry[24]. For moderate-to-severe COPD, the use of questionnaire data alone permitted high sensitivity (97%), but required confirmatory spirometry in 80% of participants. Using PEF confirmatory spirometry was needed in only 19-22% of subjects, with 83-84% sensitivity[24]. For severe COPD, PEF achieved 91-93% sensitivity, requiring confirmatory spirometry in 9%. Cost analysis suggested that staged screening algorithm using only PEF initially, followed by confirmatory spirometry as needed, was the most cost-effective case-finding strategy.

The results support the use of PEF as a simple, cost-effective, initial screening tool for conducting COPD case-finding in adults aged ≥ 40 years.

COPD and comorbidities

Comorbidities are frequent in COPD and contribute to disease expression, disease burden, and survival[25-28]. In a large cohort of COPD patients undergoing pulmonary rehabilitation, the authors reported at least one chronic comorbidity in 51% of patients[29]. Comorbidities, defined as other chronic medical conditions, including coronary artery disease, diabetes mellitus, osteoporosis, and muscle weakness, are common in COPD, but their prevalence varies between studies[30].

In PLATINO, the number of comorbidities was significantly higher in subjects with COPD compared with non-COPD subjects, regardless of their smoking status[31]. Reported comorbidities in decreasing frequency were: any cardiovascular disease, hypertension, peptic ulcer, heart disease, diabetes, cerebrovascular disease, asthma, and lung cancer[31]. Age, female sex, and higher BMI were the main factors associated with comorbidities[31]. The number of self-reported comorbidities was associated with a deterioration in general health status independently of the COPD status[31].

These findings indicate that comorbidities are frequent in COPD. Therefore, an active search and approach for the most important comorbidities is recommended, and essential to improve disease management.

Sex and COPD expression

The perception that COPD is a disease of older male smokers is obsolete; COPD affects both men and women worldwide[32].

Although sex-specific COPD data are limited, some evidences from selected COPD populations support sex differences in the clinical expression of the disease. In general, women with COPD compared to men seem to be younger, smoke less, have lower BMI and socioeconomic status, report more anxiety and depression, have lower exercise capacity, and worse symptoms and health-related quality of life[33-38]. However, at similar severity by BODE index and FEV_1, women have significantly better survival than men[39].

In the entire PLATINO population, females reported more dyspnoea and physical limitations and worse general health status than males[40]. A higher proportion of females with COPD compared with males reported their general health status as fair-to-poor (41 versus 34%)[40]. The distribution of COPD severity was similar between genders, but actively smoking females had more severe obstruction than males, despite similar smoking exposure[40].

These findings indicate that manifestations of COPD may differ in females; therefore, a multi-disciplinary approach for COPD in women is required, including increased awareness, risk minimization, and a greater clarity of specific factors affecting the risk, disease progression, and treatment.

Body mass index and COPD

The BMI is identified as an independent prognostic factor for COPD, with a clear association between decreased BMI and increased mortality[41,42].

A progressive increment in the proportion of COPD subjects was observed as BMI decreased in the PLATINO population[43]. Compared with non-COPD subjects, the proportion of COPD subjects with BMI < 25 kg/m^2 (underweight and normal-weight categories) was higher, and lower in the obese category[43]. In men with COPD, aging, current smoking, and severe airway obstruction were the main factors associated with lower BMI, whereas in women these were current smoking, lower education, and severe airway obstruction[43].

These results are in line with a recent BOLD analysis, which showed, after adjustment for confounders, that in subjects with chronic airflow limitation, low BMI was more frequent (OR: 2.23; 95% CI: 1.75-2.85), and conversely, obesity was less frequent (OR: 0.78; 95% CI: 0.65-0.94). All these results clearly indicate an association between lower BMI and COPD[44].

Exacerbation frequency

COPD exacerbations are important events associated with an accelerated decline in lung function, poor quality of life, and increased mortality[45-49]. They are the most common conditions requiring hospital admission, contributing substantially to the economic burden of disease[50-53].

In the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study, approximately 20% of patients with GOLD stage 2 and 47% of those with stage 4 were classified as "frequent exacerbators" (defined as two or more exacerbations annually)[54].

Less than one-third of the PLATINO baseline population reported ever having had an exacerbation, 7.9% reported having an exacerbation in the past-year, with 6.2% requiring a doctor visit and 2% requiring hospitalization[55]. The proportion of individuals with an exacerbation increased as airway obstruction worsened (4.2% in GOLD stage 1 versus 28.9% in grades 3-4)[55]. The other factors associated with having an exacerbation were dyspnoea and prior diagnosis of asthma[55]. The highest proportion (> 55%) of COPD patients categorized as mild-to-moderate explains the lower frequency of individuals with an exacerbation compared to selected COPD populations. However, they consistently indicate that exacerbations become more frequent as the severity of COPD increases.

Chronic bronchitis phenotype

The presence of chronic bronchitis (CB) in COPD patients has been associated with worse quality of life and symptoms, and increased disease severity and risk of exacerbation[56-58]. The reported prevalence of CB ranges from 14 to 74% of all COPD patients, probably due to varying definitions, different study populations, and study designs[56,58,59].

In PLATINO, the proportion of COPD subjects with CB defined as the presence of phlegm most days, ≥ 3 months/years for ≥ 2 years, was 14.4%[60] and was associated with increased disease severity (lower pulmonary function, more respiratory symptoms and exacerbations), worse health status, and more physical activity limitation[60]. These findings are in line with

those reported in selected COPD patients and support the fact that CB is associated with worse COPD outcomes.

Asthma-COPD overlap syndrome

Both COPD and asthma are common chronic airway diseases in adults, and therefore, the coexistence in some individuals is likely and has been recognized as asthma-COPD overlap syndrome (ACOS).

Proposed definitions for ACOS vary widely and include patients with: (i) COPD and previous asthma diagnosis; (ii) spirometric COPD definition and significant reversibility; and (iii) asthma and persistent airflow limitation.

The prevalence of ACOS in the general population ranges from 1.6 to 4.5% in different studies[61]. If only COPD subjects are included, the prevalence of ACOS ranges from 12.1 to 55.2%[61]. The wide variation in prevalence is related to the diagnostic criteria applied, together with the population being studied.

Figure 3 shows the prevalence of ACOS in PLATINO using different definitions and different denominators for calculating the prevalence. In general, subjects with ACOS had more respiratory symptoms, worse lung function, used more respiratory medication, and had more hospitalizations and exacerbations and worse general health status[62]. After adjusting for confounders, ACOS was associated with higher risk for exacerbations and hospitalizations and worse general health status compared with COPD-only subjects[62].

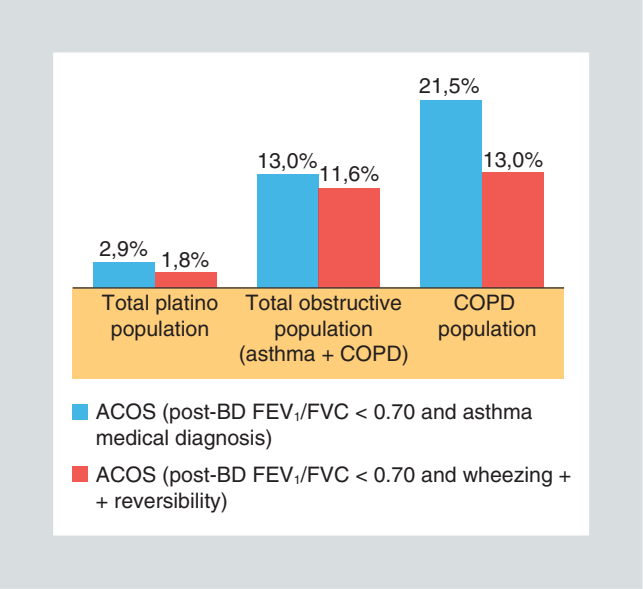

Figure 3. Asthma-COPD overlap syndrome prevalence using different definitions in the total PLATINO population, total obstructive population (asthma + COPD), and COPD population (PLATINO baseline).
BD: bronchodilator; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity ; ACOS: asthma-COPD overlap syndrome.

The results of two recent systematic reviews showed that ACOS patients have higher healthcare utilization, higher exacerbation rates, more symptoms, and lower quality of life[63,64].

In summary, the available information indicates that criteria used to define ACOS and the population used to calculate prevalence has a significant influence on prevalence. Additionally, ACOS represents a clinical phenotype associated with more frequent adverse outcomes than either asthma or COPD, which probably indicates a different management approach.

COPD in non-smokers

Although smoking is widely recognized as the most important risk factor for COPD, it is now acknowledged that the disease also occurs in non-smokers.

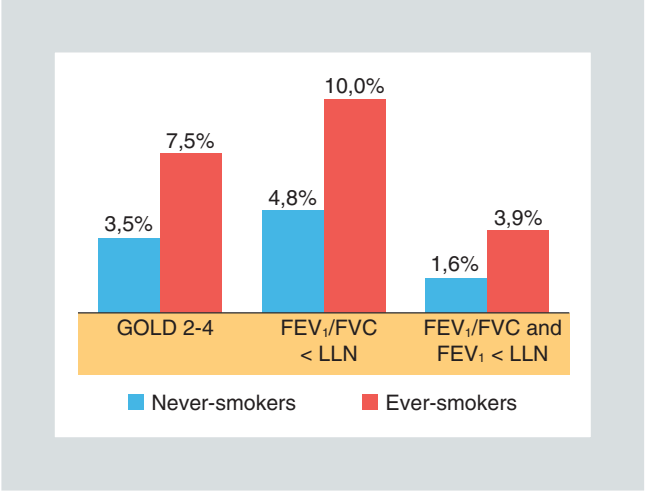

Figure 4. Population prevalence of COPD by different spirometric criteria and smoking status (PLATINO baseline).
FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; LLN: lower limit of normal.

The BOLD study described the characteristics of COPD in never-smokers and their risk factors[65]. Among never-smokers, 6.6% met the criteria for mild COPD (GOLD instead 1), and 5.6% met the criteria for GOLD grades ≥ 2. Never-smokers made up 27.7% of all COPD cases: 33.0% of all GOLD grades 1 cases and 23.3% of all GOLD grades ≥ 2 cases. Predictors of COPD in never-smokers include age, education, occupational exposure, childhood respiratory diseases, and BMI alterations[65].

Among PLATINO populations, 43% were never-smokers and 57% ever-smokers. COPD was observed in 3.5% of never-smokers and in 7.5% of ever-smokers. Figure 4 shows the COPD prevalence by different spirometric criteria and smoking status. The prevalence of COPD (GOLD grades ≥ 2) in never-smokers was 3.5%. Never-smoker patients with COPD (GOLD grades 2-4) were more likely to be older, female, with previous diagnosis of asthma and tuberculosis and higher FEV_1, response to bronchodilators, reporting more commonly exacerbations requiring medical consultation or hospitalization, and less passive smoking exposure than ever-smokers with COPD[66].

Recently, an analysis of the data from 5,176 adults (≥ 40 years) who participated in the Canadian Cohort of Obstructive Lung Disease (CanCOLD) study showed that the COPD prevalence (FEV_1/FVC < LLN) in never-smokers was 6.4%, constituting 27% of all COPD subjects[67]. Independent predictors of COPD in never-smokers and ever-smokers were older age, self-reported asthma, and lower education. In never-smokers, a history of hospitalization in childhood for respiratory illness was discriminative, while exposure to passive smoke and biomass fuel for heating was discriminative for women[67].

The results from these epidemiologic studies confirm the evidence that never-smokers comprise a substantial proportion of individuals with COPD. The main factors associated with an increased risk for COPD for both genders were: increased age, prior diagnosis of asthma, lower education levels, exposure to organic dusts in the workplace, and childhood respiratory diseases. In addition, studies suggest gender-specific risk factors for COPD in never-smoker women (exposure to passive smoke and biomass fuel for heating).

PLATINO FOLLOW-UP STUDY CONTRIBUTION

Design and general characteristics of the study

The PLATINO longitudinal study was performed in three of the original five PLATINO

Table 1. Overall response rates of interviews and spirometry of localized subjects in the PLATINO follow-up study

	Montevideo (Uruguay)	Santiago de Chile (Chile)	Sao Paulo (Brazil)
Response only interviews, (%)	0.5	3.6	1.8
Response of interviews plus spirometry, (%)	78.6	76.7	63.2
Deaths, refusals and losses, (%)	21.0	20.0	35.0

sites, with a high follow-up rate and spirometry quality. It was performed on the same individuals, using the same spirometers and techniques[68]. Selection of the follow-up centres was determined by the level of COPD prevalence in the baseline study. The first site was Montevideo due to the highest COPD prevalence (19.7%), Santiago had the second highest prevalence (16.9%) and the highest smoking prevalence (38.6%), and Sao Paulo was third in prevalence (15.8%). The time interval between two visits in each of the centres range from 5, 6, to 9 years in Montevideo, Santiago, and Sao Paulo, respectively[68]. In Montevideo 85.6% of patients were located and interviewed, 84.7% in Santiago, and 77.7% in Sao Paulo[68]. The overall response rates of interviews and spirometry of localized subjects in the PLATINO follow-up is shown in table 1. The general quality of spirometry was ≥ 80% according to ATS criteria[68]. A total of 71 deaths were documented in Montevideo, 95 in Santiago, and 135 in Sao Paulo, and death certificates were obtained from the national mortality registries for 76.1, 88.3, and 91.8% of cases, respectively[68].

COPD prevalence over time and diagnosis stability

COPD is characterized by persistent airflow limitation; therefore, by definition, variations over time from the presence to the absence of airflow limitation are not compatible with disease diagnosis and in theory would represent COPD misdiagnosis.

Variations in the overall COPD prevalence according to different spirometric criteria were assessed using PLATINO baseline and follow-up data (Fig. 5). Using the diagnostic criteria post-BD $FEV_1/FVC < 0.70$, COPD prevalence among centres varied in the baseline study from 15.7% in Sao Paulo to 19.5% in Montevideo, and markedly in the follow-up (from 8.5% in Sao Paulo to 27.5% in Montevideo)[69]. Similar changes were observed by using the post-BD $FEV_1/FVC < LLN$ criteria (baseline from 8.5% in Santiago to 9.8% in Montevideo, and in the follow-up from 6.0% in Sao Paulo to 13.2% in Montevideo)[69]. Variations were lower using the GOLD stages 2-4 definition (baseline from 5.8% in Santiago to 7.8% in Montevideo, and in the follow-up from 5.3% in Sao Paulo to 8.4% in Montevideo) and the $FEV_1/FEV_6 < LLN$ criteria (baseline from 7.5% in Santiago to 9.7% in Montevideo and in the follow-up from 7.9% in Santiago to 10.6% in Montevideo)[69]. These changes were associated with differences in the forced expiratory time (FET) between the two surveys (shortest mean FET in Sao Paulo and longest in Montevideo)[69]. The results suggest that the FEV_1/FEV_6 ratio is associated with lower variations than FEV_1/FCV, in part

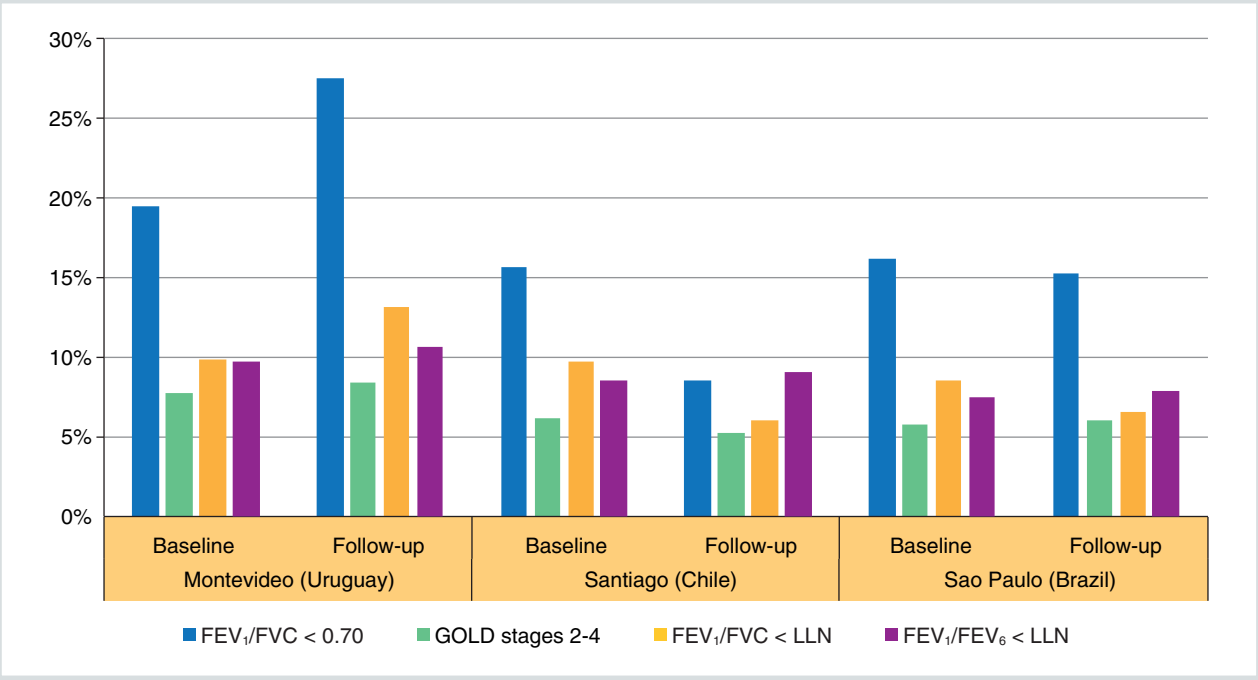

Figure 5. Changes in the COPD prevalence (%) after the use of bronchodilator by different spirometric criteria in the PLATINO follow-up study.
FEV_1: forced expiratory volume in 1 second; FEV_6: forced expiratory volume in 6 seconds; FVC: forced vital capacity; LLN: lower limit of normal.

due to FVC varying with the duration of the forced exhalation[69].

Inconsistency in the COPD diagnosis over time in the PLATINO follow-up study was also assessed and defined as the percentage of participants with a change in diagnosis of airflow limitation (either a new diagnosis in the second evaluation or the presence of airflow obstruction in the first evaluation but not in the second). Inconsistent diagnoses occurred with all COPD spirometric criteria, but were more common when using the post-BD $FEV_1/FVC < 0.70$ criterion (11.7%)[70]. Post-BD FEV_1/FVC < LLN criterion showed an intermediate inconsistency (6.5%), FEV_1/FEV_6 < LLN criterion 5.9%, and the lowest value was for GOLD grades 2-4 (4.1%)[70]. Using FEV_1/FEV_6 < LLN or GOLD stage 2-4 as the criterion for airflow obstruction reduces inconsistencies in the COPD diagnosis over time[70].

These analyses provide important information on the variations and changes of the COPD diagnosis over time and the factors associated with these changes.

General mortality in the PLATINO study population

COPD and poor lung function are important predictors for all-cause cardiovascular and respiratory mortality[71-73].

Mortality rates according to COPD status and lung function measured at baseline were analysed in PLATINO. Deaths were more common among men, and survival curves were similar in all sites[74]. Cardiovascular and respiratory disease and cancer were the main causes of death. Cardiovascular disease was the leading cause of death for both sexes in Santiago and Sao Paulo, and for men in Montevideo, followed by cancer and respiratory deaths[74].

Spirometric criteria for COPD at baseline was associated with all-cause mortality (HR: 1.43 for $FEV_1/FVC < LLN$; 2.01 for GOLD 2-4; 1.46 for GOLD 1-4; 1.50 for $FEV_1/FEV_6 < LLN$)[74]. For cardiovascular mortality, significant associations were found: GOLD grades 2-4 (HR: 2.68) and GOLD 1-4 (HR: 1.78)[74]. Including lung cancer among respiratory causes of mortality, the results were quite similar.

The FEV_1 was a better predictor of mortality than FVC[74]. Low FEV_1 was a predictor for all causes and respiratory mortality in both genders and for cardiovascular mortality in men, whereas FVC was not associated with overall mortality[74]. COPD and low FEV_1 are important predictors for overall and cardiovascular mortality in Latin America[74].

These findings are consistent with the literature, although it is controversial as to which parameter shows the greatest predictive ability from evidence coming from cohort studies[71-73].

CONCLUSION

The PLATINO baseline and follow-up studies, beyond providing data on COPD epidemiology, offer an opportunity to characterize disease clinical features, management, stability of diagnosis, and mortality associated factors in Latin America.

CONFLICT OF INTEREST

Dr. Montes de Oca has nothing to disclose, Dr. Lopez Varela reports personal fees from Boehringer Ingelheim, personal fees from Novartis, personal fees from AstraZeneca, outside the submitted work.

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