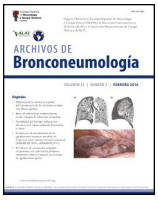
Arch Bronconeumol. 2018;54(5):260–269

Sociedad Española de Neumología y Cirugía Torácica SEPAR

ARCHIVOS DE Bronconeumología

www.archbronconeumol.org



Original Article

Prevalence of COPD in 6 Urban Clusters in Argentina: The EPOC.AR Study☆

Andrés L. Echazarreta,[a,*] Sergio J. Arias,[b] Ricardo del Olmo,[c] Eduardo R. Giugno,[d] Federico D. Colodenco,[c] Santiago C. Arce,[e] Juan C. Bossio,[b] Gustavo Armando,[b] Joan B. Soriano[f], Grupo de estudio EPOC.AR[◊]

[a] *Hospital Interzonal Especializado de Agudos y Crónicos San Juan de Dios, La Plata, Argentina*
[b] *Instituto Nacional de Enfermedades Respiratorias Emilio Coni, Ministerio de Salud de la Nación, Santa Fe, Argentina*
[c] *Hospital María Ferrer , Ciudad Autónoma de Buenos Aires, Argentina*
[d] *Hospital Dr. Antonio A. Cetrángolo, Zona Norte de Gran Buenos Aires, Argentina*
[e] *Instituto de Investigaciones Médicas A. Lanari, Universidad de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina*
[f] *Instituto de Investigación Hospital Universitario de la Princesa (IISP), Universidad Autónoma de Madrid, Madrid, Spain*

ARTICLE INFO

Article history:
Received 26 June 2017
Accepted 28 September 2017
Available online 5 April 2018

Keywords:
COPD
EPOC.AR
Argentina
Prevalence
Smoking

ABSTRACT

Introduction: The prevalence of chronic obstructive pulmonary disease (COPD) has not been studied in Argentina.
Objectives: To determine the prevalence and relevant clinical characteristics of COPD in a representative sample.
Material and methods: We performed a cross-sectional study in a population of adults aged ≥40 years randomly selected by cluster sampling in 6 urban locations. Subjects answered a structured survey and performed pre- and post-bronchodilator spirometry (PBD). COPD was defined as FEV_1/FVC ratio <0.7 predicted value. The total prevalence was estimated for each cluster with its 95% confidence interval (CI).
Results: Of 4599 surveys and 3999 spirometries, 3469 were considered of adequate quality (86.8%) for our study. The prevalence of COPD was 14.5% (CI: 13.4–15.7). The distribution of COPD cases according to FEV1 (GOLD 2017) was stage 1: 38% (CI: 34–43); stage 2: 52% (CI: 47–56); stage 3: 10% (CI: 7–13); and stage 4: 1% (CI: 0–2), and according to the refined ABCD (GOLD 2017) assessment: A: 52% (CI: 47–56); B: 43% (CI: 39–48); C: 1% (CI: 0–2); D: 4% (CI: 2–6). The rate of underdiagnosis was 77.4% (CI: 73.7%–81.1%) and diagnostic error 60.7% (CI: 55.1%–66.3%). A significant association was found between COPD and age (OR 3.77 in individuals 50–59 years of age and 19.23 in those >80 years), male gender (OR 1.62; CI: 1.31–2), smoking (OR 1.95; CI: 1.49–2.54), low socioeconomic status (OR 1.33; CI: 1.02–1.73), and previous tuberculosis (OR 3.3; CI: 1.43–7.62).
Conclusions: We estimate that more than 2.3 million Argentineans have COPD, with high rates of underdiagnosis and diagnostic error.

☆ Please cite this article as: Echazarreta AL, Arias SJ, del Olmo R, Giugno ER, Colodenco FD, Arce SC, et al. Prevalencia de enfermedad pulmonar obstructiva crónica en 6 aglomerados urbanos de Argentina: el estudio EPOC.AR. Arch Bronconeumol. 2018;54:260–269.

* Corresponding author.
E-mail address: aechaza@gmail.com (A.L. Echazarreta).

◊ Members of the EPOC.AR study group are listed in Appendix A.

Prevalencia de enfermedad pulmonar obstructiva crónica en 6 aglomerados urbanos de Argentina: el estudio EPOC.AR

Palabras clave:
Enfermedad pulmonar obstructiva crónica
EPOC.AR
Argentina
Prevalencia
Tabaquismo

R E S U M E N

Introducción: La prevalencia de la enfermedad pulmonar obstructiva crónica (EPOC) en Argentina no había sido estudiada.
Objetivos: Determinar la prevalencia de EPOC y rasgos clínicos relevantes en una muestra representativa.
Material y métodos: Estudio de corte transversal en población ≥40 años en 6 aglomerados urbanos seleccionada aleatoriamente mediante muestreo por conglomerados. Se aplicó una encuesta estructurada y espirometrías pre y postbroncodilatador (PBD). Se definió EPOC en quienes presentaban un cociente FEV_1/FVC PBD <0,7. Se estimó la prevalencia total y para cada aglomerado con intervalo de confianza del 95% (IC).
Resultados: Se realizaron 4.599 encuestas y 3.999 espirometrías, de las cuales 3.469 fueron útiles (86,8%). La prevalencia de EPOC fue de 14,5% (IC: 13,4-15,7). La distribución de los casos compatibles con EPOC según FEV_1 (GOLD-2017) fue: 1: 38% (IC: 34-43); 2: 52% (IC: 47-56); 3: 10% (IC: 7-13); y 4: 1% (IC: 0,-2) y de acuerdo al modelo combinado ABCD (GOLD 2017): A: 52% (IC: 47-56); B: 43% (IC: 39-48); C: 1% (IC: 0-2) y D: 4% (IC: 2-6). El subdiagnóstico fue del 77,4% (IC 73,7-81,1%) y el error diagnóstico de 60,7% (IC 55,1-66,3%). Encontramos asociación significativa de presencia de EPOC con edad (OR 3,77 en 50-59 años a 19,23 en >80 años), sexo masculino (OR: 1,62; IC: 1,31-2), tabaquismo (OR: 1,95; IC: 1,49-2,54), nivel socieconómico bajo (OR: 1,33; IC: 1,02-1,73) y antecedentes de tuberculosis (OR: 3,3; IC: 1,43-7,62).
Conclusiones: Se estima que más de 2,3 millones de argentinos padecen EPOC con elevada tasa de subdiagnóstico y error diagnóstico.

Introduction

Chronic obstructive pulmonary disease is a major cause of disability, morbidity and mortality that affects many individuals during their economically productive years, and places a heavy burden on healthcare and monetary resources.[1] Data from the World Health Organization suggest that in 2015 more than 3 million individuals worldwide died of COPD; 90% of these deaths occurred in low and middle-income countries. The data also predict an increase in morbidity and mortality in the next 15 years, due to accumulated exposure to smoking and aging of the population.[2–4]

This situation is compounded by widespread failure to properly evaluate COPD, with either overdiagnosis in patients with symptoms caused by other entities, or underdiagnosis in patients who do have the disease.[5–8] There is a lack of awareness of COPD that prevents patients from taking steps to improve their quality of life and life expectancy by, for example, giving up smoking and incorporating physical activity and better eating habits into their daily routine.

Population-based epidemiological studies conducted in several Latin American cities showed a COPD prevalence ranging from 6% to 19.7%.[9–11]

In Argentina, a middle-income country with approximately 44 million inhabitants, 90% of whom live in urban locations, mainly in Buenos Aires and surrounding areas, the COPD mortality rate in 2015 was 24.3 per 100 000 inhabitants between 40 and 74 years of age, adjusted for age and sex, 1.2 times the rate registered in 2014. In total, 38% of these deaths occurred in people under the age of 65 years: the mortality rate among men had reduced, but it increased among women and economically productive adults.[12]

To date, no population studies with standardized questionnaires and home spirometry have been conducted to determine the prevalence of COPD in Argentina. The EPOC.AR study was designed by the Argentine Association of Respiratory Medicine and the National Institute of Respiratory Diseases of the Ministry of Health to estimate the prevalence of COPD in Argentina, to obtain data for the design of population health promotion initiatives, and to improve regional epidemiological references.

Methods

Study design

This was a multicenter population-based cross-sectional study. Participants were randomly selected from 6 urban areas in Argentina, using cluster sampling, in order to establish the prevalence of COPD and evaluate the clinical and sociodemographic characteristics of patients, treatment, and risk factors.

The study was conducted between August 2014 and May 2016. The following urban clusters were selected: La Plata, Rosario, Autonomous City of Buenos Aires, Northern Region of Gran Buenos Aires, Córdoba and Mendoza. The sample size was calculated on the basis of an 8% prevalence, as determined by the PLATINO study,[9] with a 95% confidence interval, a design effect of 1.5, and a total accuracy (6 urban areas) of ±1.15%, for which 3207 patients with completed questionnaires and postbronchodilator spirometries needed to be recruited. Taking into account an estimated response rate of 75%, the number of households to be contacted was 4276.

Study population

Men and women ≥40 years of age were included from the 6 selected urban clusters. The sample was selected by multistage probability cluster sampling based on cartographic area units, described in greater detail in the supplementary material. All selected individuals (1 single subject per household) were invited to participate in the study, and if they agreed, they were asked to sign an informed consent form. The following exclusion criteria were defined and applied: mental disorders or inability to make decisions, history of thoracic or abdominal surgery in the last 3 months, residence in institutions, current COPD exacerbation, and others described elsewhere[9] (see supplementary material). Contraindications for performing spirometry were also taken into account.[13,14]

Definition of chronic obstructive pulmonary disease

Data collected included an evaluation of bronchial obstruction by pre- and postbronchodilator spirometry as a primary study objective. COPD was defined as a postbronchodilator FEV_1/FVC ratio<0.7, and the GOLD 2017 classification was used to define the degree of obstruction and multidimensional ABCD assessment.[15] The analysis was also performed using the lower limit of normal (LLN) method.[16] All subjects were asked about any previous medical diagnosis of emphysema, chronic bronchitis or COPD.

Procedures and quality control spirometry

A study team consisting of an interviewer and a spirometry technician performed the procedures in the home of each subject. The structured interview, CAT questionnaire,[17] and mMRC[18] were first completed by all subjects (see supplementary material). Blood pressure and anthropometric measurements were obtained using a previously validated portable ultrasonic measuring board and digital weighing scale (SECA 804, Hamburg, Germany) (see supplementary material).

Spirometry was then performed before and after inhalation of 400 mcg salbutamol (Ventolin® HFA, GSK), using a measured dose device with spacer. As in similar studies,[9] spirometers equipped with an ultrasonic sensor (EasyOne NDD; Zurich, Switzerland) were used according to the standard technique.[14] Devices were calibrated every day with a 3 L syringe. Studies were analyzed according to the 3 criteria previously described in other publications.[14,19,20] The acceptability of the spirometries was determined according to Enright's A, B, and C criteria,[19] with the NHANES III reference equation.[21] During the field work period, spirometries were sent electronically to the Central Spirometry Committee once a week, where they were reviewed by 2 blinded evaluators who analyzed each spirometry and determined the number of acceptable maneuvers obtained according to ATS/ERS criteria.[14]

The performance of the technicians was evaluated every week according to the acceptability criteria of the spirometries they had conducted, and retraining was offered, if necessary (see supplementary material).

Ethical aspects

The study and written informed consent form were initially reviewed and approved by the Provincial Bioethics Committee (#344/14), Rosario City, Argentina. The ethical, regulatory, teaching and research aspects of the study were then reviewed and approved by regional and local authorities (ethics committees from each urban area).

Statistical analysis

The estimated prevalence of each variable was presented with the absolute value, percentage and respective 95% confidence interval (CI) for the overall study population and for each subgroup of interest.

A bivariate analysis was performed to establish the possible factors associated with COPD. Odds ratio (OR) with CI was used as a measure of association. A multivariate analysis was then performed using logistic regression, and variables that were considered relevant were included in the adjustment of the model. The logistic regression analysis model was performed using the stepwise method, and the adjusted ORs obtained with the complete model were analyzed. The ORs of the adjusted model were also calculated with their CI, and for these, the level of significance of

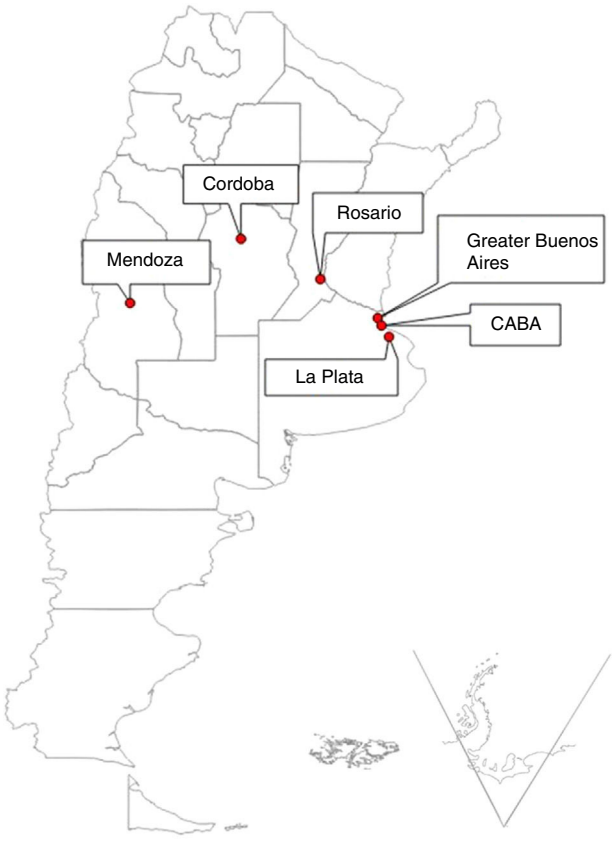


Fig. 1. Geographic location of the urban clusters selected for the study. La Plata (9.8 meters above sea level [masl]), Rosario (22.5 masl), Autonomous City of Buenos Aires-CABA (16 masl), Greater Buenos Aires (North Region, 16 masl), Cordoba (106 masl) and Mendoza (746 masl).

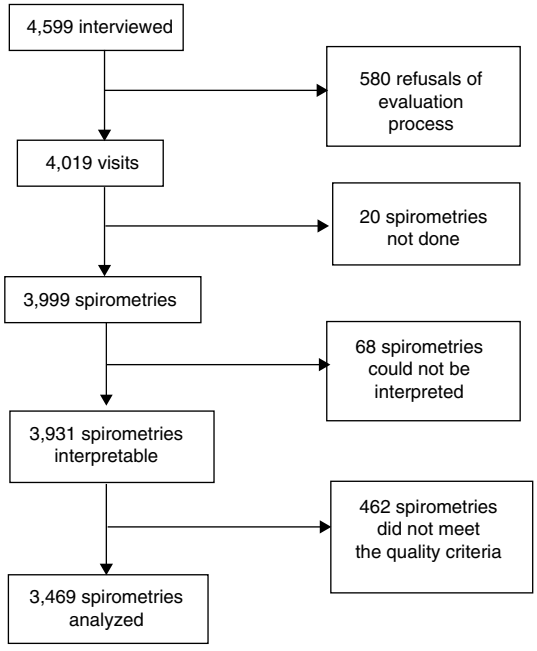


Fig. 2. EPOC.AR study flow chart.

Table 1
Participant characteristics.

Variables	No.	%
Urban cluster		
Cordoba	499	14.4
Greater Buenos Aires	691	19.9
Autonomous City of Buenos Aires	697	20.1
Rosario	466	13.4
La Plata	694	20.0
Mendoza	422	12.2
Sex		
Male	1461	42.1
Female	2008	57.9
Age group		
40–49	873	25.2
50–59	1020	29.4
60–69	888	25.6
70–79	527	15.2
≥80	161	4.6
Nutritional status		
Underweight	16	0.5
Normal weight	730	21.0
Overweight	1239	35.7
Obese	1470	42.4
ND	14	0.4
Socio-economic status		
C1 (middle-high)	405	11.7
C2 (middle)	643	18.5
C3 (middle-low)	1111	32.0
D1 D2 (low)	1301	37.5
ND	9	0.3
Education		
None	8	0.2
Primary	1201	34.6
Secondary	1409	40.6
Higher studies	391	11.3
University	448	12.9
ND	12	0.3
Living conditions (number of people per room)		
Up to 1	2514	72.5
1–2	770	22.2
2–3	122	3.5
3–4	12	0.3
More than 4	14	0.4
ND	37	1.1
Type of housing		
House	2833	81.7
Shanty/improvised housing constructed with waste material	25	0.7
Apartment	578	16.7
Tenement/hotel/other	7	0.2
ND	26	0.7
Smoking		
Active smoker	1213	35.0
Former smoker	1226	35.3
Never smoker	1030	29.7
Occupational exposure		
Yes	1946	56.1
No	1508	43.5
ND	15	0.4
Environmental or indoor pollution		
Yes	1462	42.1
No	2007	57.9
Heart disease		
Yes	1550	44.7
No	1919	55.3
Diabetes		
Yes	409	11.8
No	3036	87.5
ND	24	0.7
Cerebrovascular accident, hemorrhage, or ischemia		
Yes	43	1.2
No	3409	98.3
ND	17	0.5
Tuberculosis		
Yes	29	0.8
No	3435	99.0
ND	5	0.1
Total	3469	100

ND: no data.

the differences between odds was analyzed using the Chi-square method, with a level of significance set at 5%.

Results

In total, 4599 homes were visited in the 6 selected urban clusters, and preliminary clinical and spirometric data were collected from 3999 subjects (86.9%) (Figs. 1 and 2). The Central Spirometry Committee monitored the quality of the spirometries and rejected 530 tests (13.2%), so the final study population with eligible clinical and spirometric data comprised 3469 subjects (75.4% of the total visits), of which 2008 were women (57.9%) (Fig. 2).

Sociodemographic and clinical characteristics of the participants are shown in Tables 1 and 2 and Appendix B, Tables A1 and A2 of the supplementary material.

Prevalence of chronic obstructive pulmonary disease

COPD prevalence was 14.5% (CI: 13.4–15.7), 18.4% (CI: 16.4–20.4) in men and 11.7% in women (CI: 10.3–13.1), and increased in each decade of life analyzed, from 3.2% (CI: 2.0–4.4) in subjects younger than 50 years of age to 30.4% (CI: 23.3–37.5) in patients 80 years of age or older (Table 3 and Fig. 3). Prevalence was higher in subjects with lower educational levels: 16.7% in subjects with primary education only (CI: 14.5%–18.8%); and lower socio-economic status: 17.8% in the lowest category (CI: 15.8%–19.9%). Overall COPD prevalence and differences among the urban clusters did not vary significantly after direct adjustment for sex, age, and education (Appendix B, Fig. A2 of the supplementary material).

When the LLN criterion was applied, prevalence was 9.4%, *n*: 325 (CI: 8.4%–10.3%) (Table 4 and Appendix B, Tables A3 and A4 of the supplementary material), and a good correlation for spirometric diagnosis of obstruction was observed between both methods (k=0.735; CI: 0.700–0.770; P<.05). However, 187 cases (37.1%) classified as obstructive according to the GOLD criteria were considered normal according to the LLN method (Appendix B, Table A4 of the supplementary material), and when both spirometric criteria were compared, the prevalence of COPD in the older subgroups was lower with the LLN method (Table 4).

Severity of COPD according to spirometric obstruction (GOLD 2017) was: (1) mild 38% (CI: 34–43); (2) moderate 52% (CI: 47–56), (3) severe 10% (CI: 7–13); and (4) very severe 1% (CI: 0–2). The GOLD 2017 ABCD multidimensional assessment[15,22] distribution was as follows: (A) 52% (CI: 47–56), (B) 43% (CI: 39–48), (C) 1% (CI: 0–2), and (D) 4% (CI: 2–6) (Fig. 4).

Table 2
Spirometric characteristics of participants (*n*: 3469).

Variable	Total		Males		Females	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	58.8	11.6	58.5	11.6	58.9	11.6
Weight (kg)	79.5	18.8	87.4	18.2	73.7	17.0
Height (m)	163.2	10.1	171.5	7.3	157.2	7.2
Body mass index (kg/m^2)	29.8	6.3	29.7	5.7	29.8	6.8
FVC (L) pre	3.29	0.94	3.96	0.88	2.81	0.63
%FVC predicted pre	91.9	16.1	90.8	16.1	92.7	16.0
FEV_1 (L) pre	2.51	0.78	2.99	0.78	2.16	0.56
%FEV_1 predicted pre	90.9	19.0	89.9	18.9	91.7	19.1
FEV_1/FVC pre	75.9	8.5	75.0	9.0	76.6	8.0
FVC (L) post	3.32	0.91	3.99	0.83	2.84	0.60
%FVC predicted post	92.9	15.3	91.5	15.3	93.9	15.3
FEV_1 (L) post	2.59	0.77	3.08	0.77	2.24	0.54
%FEV_1 predicted post	94	18.42	92.8	18.37	94.8	18.42
FEV_1/FVC post	77.8	8.6	76.7	9.2	78.7	9.2
Delta response FVC (ml)	28.4	262.8	35.2	325.1	23.4	205.8
% response FVC	1.43	7.70	1.44	7.14	1.42	8.08
Delta response FEV_1 (mL)	80.6	177.6	92.2	206.4	72.1	152.7
% response FEV_1	3.99	8.19	3.81	7.61	4.11	8.59

Total FVC and FEV_1 reversibility, defined as a significant postbronchodilator change of at least 12% and 200 ml in FVC and/or FEV_1, was 11.4% in the total population, with no differences between men and women (see Table A2 of the supplementary material).

Table 3
COPD prevalence. Distribution by cluster, sex, age, education, and socioeconomic status.

Variable	Total	COPD				*P*
		No.	%	95% CI		
Urban cluster						
Cordoba	499	86	17.2	13.9	20.5	<.001
Greater Buenos Aires	691	115	16.6	13.9	19.4	
Autonomous City of Buenos Aires	697	102	14.6	12.0	17.3	
Rosario	466	68	14.6	11.4	17.8	
La Plata	694	89	12.8	10.3	15.3	
Mendoza	422	44	10.4	7.5	13.3	
Sex						
Male	1461	269	18.4	16.4	20.4	<.001
Female	2008	235	11.7	10.3	13.1	
Age						
40–49	873	28	3.2	2.0	4.4	<.001
50–59	1020	115	11.3	9.3	13.2	
60–69	888	169	19.0	16.4	21.6	
70–79	527	143	27.1	23.3	30.9	
≥80	161	49	30.4	23.3	37.5	
Educational level						
None	8	2	25.0	3.2	65.1	.006
Primary	1201	200	16.7	14.5	18.8	
Secondary	1409	202	14.3	12.5	16.2	
Higher studies	391	37	9.5	6.6	12.4	
University	448	61	13.6	10.4	16.8	
No information	12	2	16.7	–	–	
Socio-economic status						
C1 (middle-high)	405	56	13.8	10.5	17.2	<.001
C2 (middle)	643	75	11.7	9.2	14.1	
C3 (middle-low)	1111	141	12.7	10.7	14.6	
D1 D2 (low)	1301	232	17.8	15.8	19.9	
No data	9	0	0.0	–	–	
Total	3469	504	14.5	13.4	15.7	

Degree of knowledge and diagnosis of chronic obstructive pulmonary disease

Only 22.6% (114/504) of the subjects with obstructive spirometry results had a previous diagnosis of COPD, chronic bronchitis or emphysema made by a doctor. This is equivalent to an underdiagnosis rate of 77.4% (CI: 73.7–81.1), with no differences between men (77%) and women (78%). Of the 504 patients with a spirometric diagnosis of COPD, only 190 (38.1%) had performed at least 1 previous spirometry.

In contrast, 176 of the 290 subjects who reported that a doctor had given them a diagnosis of pulmonary emphysema, chronic bronchitis, or COPD, did not show an obstructive spirometric pattern. This is equivalent to a diagnostic error rate of 60.7% (CI: 55.1–66.3), lower in men (49%) than in women (69%), *P*<.001.

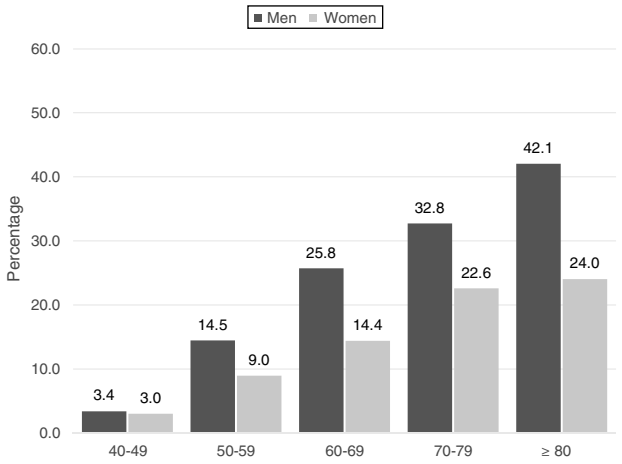


Fig. 3. COPD prevalence. Distribution by age and sex.

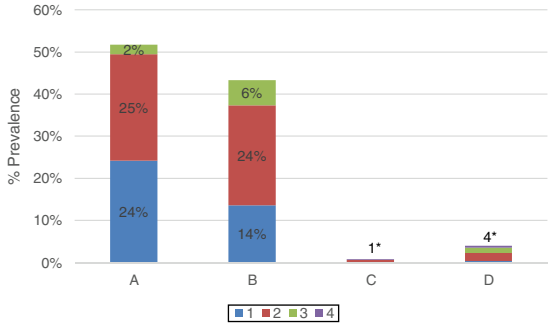


Fig. 4. Distribution of COPD cases according to GOLD 2017 multi-dimensional assessment. Prevalence of each ABCD subgroup with grades 1, 2, 3, and 4 for all COPD patients (*n*: 471). Patients in subgroup A (grade 1: 24%; grade 2: 25%; grade 3: 2%; grade 4: 0%); B (grade 1: 14%; grade 2: 24%; grade 3: 6%; grade 4: 0%); C (Total 1%*: grade 1: 0%; grade 2: 1%; grade 3: 0%; grade 4: 0%) and D (total 4%*: grade 1: 0%; grade 2: 2%; grade 3: 1%; grade 4: 0%).

Only 27.6% (505/1828) of the subjects who reported symptoms of COPD (dyspnea, cough, expectoration, and wheezing) had performed at least 1 previous spirometry.

Analysis of prevalence of chronic obstructive pulmonary disease according to obstruction, exposure and symptoms

COPD prevalence varied when only the definition based on spirometric obstruction was taken into consideration (14.5%; CI: 13.4–15.7). Prevalence reduced progressively (7.2%; CI: 6.3–8.1), as exposure (smoking, occupational exposure, and indoor pollution) and symptoms (mMRC≥2 or CAT≥10) were added to the model (Table 4).

Smoking

Smoking was found to be highly prevalent; 35% of all respondents were active smokers (33.5% women; 37% men), while 35.3% were former smokers (30% women; 42.6% men) and 29.7% were never-smokers (36.5% women; 20.4% men).

COPD prevalence in the study population was 16.9% among the 2439 active or former smokers, and 8.9% among the 1030 never smokers.

Among the 504 subjects who met spirometry criteria for COPD, 412 (82%) were active or former smokers and 92 (18%) had no history of an active or former smoking habit (Table 5).

The association between smoking and COPD was significant (OR: 1.95; CI: 1.49–2.54), both in the crude analysis and after adjustment using logistic regression (Table 5). This association was maintained when smokers and former smokers were compared by sex, with a closer association observed for men. In total, 248 men (21.3%) and 164 women (12.9%) with COPD and a history of smoking were identified (Fig. 5). The corresponding OR for the association between smoking and COPD was 3.95 for men, and 1.42 for women.

Exposure to tobacco was similar in the 6 urban clusters (Appendix B, Table A5 of the supplementary material).

Adjusted analysis of risk factors and other variables related with chronic obstructive pulmonary disease

Table 5 shows the association between numbers of COPD cases with selected characteristics and spirometry-confirmed COPD, along with the OR for the crude association and the association adjusted by binary logistic regression. Sex, age, smoking (current or previous), socioeconomic status, history of tuberculosis, and a family history of asthma showed a statistically significant association with the presence of COPD. The associations with COPD persisted after adjustment by logistic regression, taking into account the

Table 4
COPD prevalence by age group, obstruction, exposure, symptoms, and spirometric criteria.

	COPD prevalence by age group			
	FEV_1/FVC PBD<0.7		FEV_1/FVC PBD<LLN	
	No.	% (95% CI)	No.	% (95% CI)
40–49 years	28	3.2 (2.0–4.4)	35	4.0 (2.7–5.3)
50–59 years	115	11.3 (9.3–13.2)	94	9.2 (7.4–11)
60–69 years	169	19.1 (16.5–21.7)	94	10.6 (8.6–12.6)
70–79 years	143	27.1 (23.3–30.9)	76	14.4 (11.4–17.4)
≥80 years	49	30.4 (23.3–37.5)	26	16.1 (10.5–21.8)
Total	504	14.5 (13.4–15.7)	325	9.4 (8.4–10.3)
	COPD prevalence by obstruction, exposure, and symptoms			
	FEV_1/FVC PBD<0.7		FEV_1/FVC PBD<LLN	
	No.	% (95% CI)	No.	% (95% CI)
Obstruction only	504	14.5 (13.4–15.7)	325	9.4 (8.4–10.3)
Obstruction and exposure	483	13.9 (12.8–15.1)	310	9.0 (8.0–9.9)
Obstruction, exposure and symptoms[a]	218	7.2 (6.3–8.1)	159	5.2 (4.5–6.0)

[a] Exposure defined as smoking+occupational exposure+indoor pollution and symptoms such as mMRC≥2 or CAT≥10.

Table 5
COPD prevalence according to selected criteria: Number and percentages by category, crude OR, and OR adjusted by logistic regression for each category.

Characteristics	COPD		No COPD		*P*	Crude OR	Adjusted OR
	*N**	%	*N**	%			
Sex							
Male	269	53.4	1192	40.2	<.001	1.70 (1.41–2.06)	1.62 (1.31–2.00)
Female	235	46.6	1773	59.8		Reference	
Age group							
40–49	28	5.6	845	28.5		Reference	
50–59	115	22.8	905	30.5	.030	3.83 (2.51–5.85)	3.77 (2.43–5.84)
60–69	169	33.5	719	24.2	<.001	7.09 (4.69–10.75)	7.19 (4.67–11.11)
70–79	143	28.4	384	13.0	<.001	11.24 (7.35–17.24)	12.04 (7.65–19.23)
≥80	49	9.7	112	3.8	<.002	13.16 (8.00–21.74)	19.23 (10.98–33.33)
Education							
Primary or none	202	40.2	1007	34.1	.707	1.20 (0.97–1.48)	1.08 (0.73–1.59)
Secondary	202	40.2	1207	40.8	.469	1.52 (1.17–1.97)	0.88 (0.62–1.24)
Higher level/university	98	19.5	741	25.1		Reference	
No information	2	0.4	10	0.3	–	–	–
Smoking							
Active or former smoker	412	82%	2027	68%	<.001	2.07 (1.63–2.63)	1.95 (1.49–2.54)
Never smoker	92	18%	938	32%		Reference	
Biomass smoke							
Yes	251	49.8	1211	40.8	.748	1.44 (1.19–1.74)	1.04 (0.84–1.28)
No	253	50.2	1754	59.2		Reference	
Occupational exposure[a]							
Yes	309	61.3	1192	40.2	.177	1.29 (1.06–1.57)	1.16 (0.94–1.44)
No	192	38.1	1773	59.8		Reference	
Heart disease							
Yes	283	56.2	1267	42.7	.608	1.72 (1.42–2.08)	1.06 (0.85–1.31)
No	221	43.8	1698	57.3		Reference	
Diabetes[a]							
Yes	51	10.1	358	12.1	.005	0.82 (0.60–1.12)	0.62 (0.45–0.87)
No	449	89.1	2587	87.3		Reference	
Lung cancer[a]							
Yes	4	0.8	5	0.2	.087	4.75 (1.27–17.73)	3.34 (0.84–13.30)
No	499	99.0	2960	99.8		Reference	
Cerebrovascular accident[a]							
Yes	7	1.4	36	1.2	.316	1.14 (0.51–2.58)	0.62 (0.25–1.58)
No	496	98.4	2913	98.2		Reference	
Tuberculosis[a]							
Yes	10	2.0	19	0.6	.005	3.14 (1.45–6.80)	3.30 (1.43–7.62)
No	493	97.8	2943	99.3		Reference	
Family history of asthma[a]							
Yes	127	25.2	728	24.6	.053	1.04 (0.83–1.29)	1.28 (1.00–1.64)
No	375	74.4	2227	75.1		Reference	
Family history of COPD[a]							
Yes	50	9.9	289	9.7	.317	1.02 (0.74–1.40)	1.20 (0.84–1.72)
No	453	89.9	2666	89.9		Reference	
Socio-economic status[a]							
C1 (middle-high)	56	11.1	349	11.8		Reference	
C2 (middle)	75	14.9	568	19.2	.582	1.35 (0.99–1.86)	1.14 (0.72–1.79)
C3 (middle-low)	141	28.0	970	32.8	.175	1.64 (1.24–2.17)	1.28 (0.89–1.83)
D1 D2 (low)	232	46.0	1069	36.2	.037	1.49 (1.19–1.87)	1.33 (1.02–1.73)
No information	0	0.0	9	0.3	–	–	–
Total	504		2965				

[a] *n*: minor differences with totals due to missing data in that category.

concomitant presence of all the other variables. Diabetes and obesity showed an inverse association: fewer COPD patients presented concomitant diabetes and obesity (Appendix B, Tables 5 and A6 of the supplementary material).

Discussion

The EPOC.AR study is the first to contribute data on COPD prevalence in the general population in Argentina aged 40 years and over, and to our knowledge, the fourth population study conducted in Latin America.[9–11]

Unlike other COPD prevalence studies,[23–25] subjects were studied in their own homes, whereas the study design, methodology,[9–11,26] and spirometers used have been validated by other authors.[9,25,27–29] These factors, along with strict quality supervision by the Central Spirometry Committee (90% of spirometries met Enright criteria A, B or C, and no significant differences were observed in quality among the 6 centers) guarantee the validity of our results.

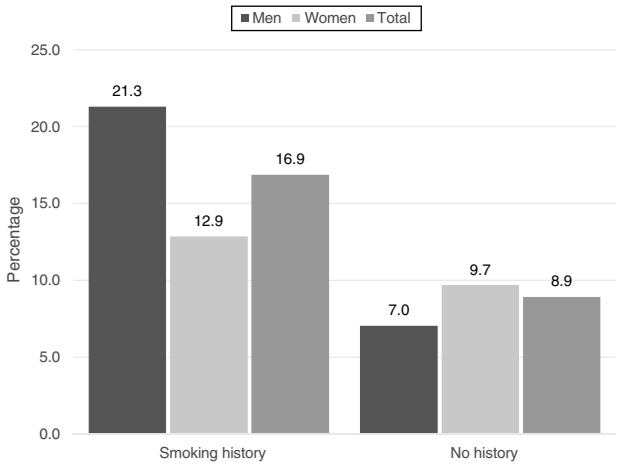


Fig. 5. COPD prevalence by smoking history (active or former smoker) or no history of smoking (never-smoker). Distribution by sex.

The NHANES III equations were selected for comparison, since they are the most widely used references equations in Argentina.[30,31] GLI 2012 theoretical equations were not used as they were not available at the time of the study.[32]

The overall prevalence of COPD in the 6 urban areas of the study was 14.5%, ranging from 10.4% in Mendoza to 17.2% in Cordoba. These results are average compared to other data from the region, in which prevalence ranges from the low levels observed in 4 cities in Peru (6%) and Mexico City (7.8%) to the higher levels found in Santiago de Chile (Chile) and Montevideo (Uruguay), 16.9% and 19.7%, respectively. This suggests that prevalence varies widely between different countries, and among the various cities of each country, as has been previously described.[9–11,33,34]

Figures emerging from Argentina and South America support the notion of a greater prevalence of the disease in the areas referred to by the World Health Organization as "the Americas",[34] and point to an increase in the worldwide caseload from an estimated 149.1 million cases (CI: 137.4–160.7) in 2005 to 174.5 million (CI: 160.2–190) in 2015; in other words, a 17% (CI: 15.1%–19%) increase in overall prevalence.[3] These same reports indicate that the disease burden is greater in urban populations than in rural areas, an important consideration in Argentina and in the region in general.

The recent publication of the GOLD 2017 strategy has enabled us to assess COPD patients on the basis of 16 different domains.[15,22] It is interesting to note that in our study, patients classified as A and B had less obstruction (9% grade 3 or 4) compared to those in categories C and D (39% grade 3 or 4), suggesting a closer than expected association between obstruction, symptoms, and exacerbations.

The significant percentage of patients with mild-to-moderate obstruction and few symptoms might explain the significant rate of underdiagnosis found in our study (77.4%). This phenomenon has already been described in the region (88.7% and 87.4% in the PLATINO and PREPOCOL studies[9,10]), as well as in other parts of the world, such as Spain, where underdiagnosis rates of 73% have been reported (EPI-SCAN[26]).

Similarly, we observed significant underuse of spirometry and high rates of diagnostic error or overdiagnosis (60.7%) in subjects with symptoms consistent with COPD.

When exposure and symptoms were added to the definition of COPD, disease prevalence fell, as might be expected, to 7.2% (GOLD 2017). The magnitude of this reduction was much greater after symptoms were taken into consideration, possibly because a high percentage of individuals presented few symptoms. In our study, the factor most strongly associated with COPD prevalence was age, also reported by other authors.[9,26] Although the prevalence of COPD measured by LLN was foreseeably lower than that obtained from the fixed ratio, the progressive increase of both spirometric criteria by age suggests the effect of a longer period of exposure. Differences in the distribution of age groups may have contributed to the differences in COPD prevalence observed among the different cities of Latin America.

The second most significant factor, in line with other studies, was smoking.[9–11,26] The reported proportion of active smokers was high (35%), and significantly more so in men. These values are higher than those described in previous surveys conducted in Argentina, in which 25.1% of respondents over 18 years of age were active smokers,[35] but similar to prevalences reported in Santiago de Chile[9] and Spain.[36] This discrepancy may be due to the different methodology employed and to differences in the study populations of the previous survey and ours. The COPD prevalence in never-smokers (8.9%) falls midway between numbers reported in Latin America (5.2%–15.9%)[9,10] and is similar to that of other regions.[26,37] Various factors, such as age, passive smoking, exposure to biomass smoke, and respiratory disease in infancy have been associated with COPD in never-smokers.[26,37]

Male sex (with a greater prevalence of smoking), low socioeconomic status, and a history of tuberculosis were associated independently with COPD, in line with previous publications.[4,9–11,26] Interestingly, we found an inverse correlation between diabetes and COPD. A positive correlation between these 2 diseases has been described,[38] but in our series, this finding may be due to the greater proportion of obese individuals among the non-COPD population.

Our study has limitations that should be pointed out. The study population, like other population studies,[9–11,26] was predominantly female. This could be due to the greater likelihood of women being at home at the time of the interview, particularly during the morning, and a greater willingness among women to perform the study procedures. The total amount of data lost due to refusal to participate and poor quality spirometries was similar to that previously reported.[9,10] The main causes for failure to conduct the evaluations were refusal to participate because of lack of time or absence of the subject from home at the time of the appointment. Although we cannot rule out the influence of a potential selection bias, the analysis of another publication that evaluated non-responders seems to conclude that this factor is not significant.[9]

Conclusions

On the basis of our results, we estimate that over 2.3 million people in Argentina may have COPD. The high prevalence of smoking underlines the need to place emphasis on anti-smoking campaigns. The high rate of underdiagnosis, the underuse of spirometry and the high rate of diagnostic error or overdiagnosis show that health strategies are needed to raise awareness of the disease among the population and among healthcare professionals. The data collected from the study will be useful for identifying other characteristics of the disease in Argentina (comorbidities, therapeutic modalities, and access to treatment) and for incorporating and assessing the new domains established by the recently published GOLD strategy.

Funding

This study was funded by an educational grant from GSK (7SCO117383). The sponsor did not participate in the study design, data collection, data analysis and interpretation, or in the drafting of this article.

Conflict of interests

The authors state that they have no conflict of interests.

Acknowledgements

We thank in particular Raúl Bozzo from IC Projects and his secretary Alicia Parera for their constant assistance during the conduct of this study.

AAMR Scientific Committee: María Cristina Borrajo (Pcia. de Buenos Aires, Sección Tabaquismo AAMR 2013), Juan Arturo Precerutti (CABA, Sección Neumonología Clínica AAMR 2013), Eduardo Armando Schiavi (CABA), Guillermo Menga (CABA), Santiago Enrique Rossi (CABA, Sección Imágenes AAMR 2013), Ana María López (Córdoba), Miguel Alberto Penizzotto (Corrientes), Pablo Saez Scherbovsky (Mendoza, Sección de Inmunología y Enfermedades Obstructivas AAMR 2013), Gustavo Enrique Zabert (Neuquén), Carlos Sebastián Wustten (Paraná), Hector Daniel Schönfeld (Puerto Madryn, Presidente AAMR 2013–2014), Juan Carlos Figueroa Casas (Rosario), Marcelino de Vega (Salta), Ramón Ángel Rojas (Tucumán).

Spirometry technicians, nurses, and doctors

La Plata: Valeria González; Mónica Zarate; Patricia Madeo Gómez; Rocío Berardi; María del Carmen Sánchez. *Rosario*: Malvina Piana; Nadia Soledad Neumayer; María Celeste Pellicciotti; Valeria Soledad Milano; Rodolfo Navarrete; Maria Florencia Nannini. *Greater Buenos Aires:* María Agustina D'Agostino; María de los Ángeles Basavilbaso; María Virginia Sandlien; María Sol Badano; Carolina Erhardt; Aldana Andrea Colombo Rey; Angélica Marcela Schaffer; Bárbara Elizabeth Schaffer; Carla Ronco; Maria Golè. *Autonomous City of Buenos Aires:* Susana Quevedo; Elizabeth M. Sangiovanni; María Cristina Burgos; Cecilia Fernández; Lucas Sheridan; Andrea Dardowski; Tania Rodríguez; Alberto Levi. *Cordoba:* Marcos Elías; Noelia Arrillaga; Claudia Fernández; Manuel Ferreyra; Ana Carolina Markiewicz; María Victoria Batistella; Gabriel Eduardo Luna; Julio Andrés Moyano Casco; Vanesa Perrone; Andrea Guzman; Juan Ponce; Erica Ivana Cuestas. *Mendoza:* Diana Salvioli; Gustavo A. Torres; Alfredo R. Moran; Andrea S. Mancinelli; Nicolás Cangiani; Héctor Varas; Gerardo Malberti; Daniel A. Sánchez; Pablo Guarnieri; Adrian Armoa; Leandro E. Diaz; Gianina Coletto; Natalia Valletto; Maria Laura Ríos; Pablo Moyano; Nuri Nahir Plata. *Central Spirometry Committee:* Santiago C. Arce; Ricardo del Olmo; Adrian Ceccatto; Mariano H. Fielli; Juan M. Lucchelli; Evelin N. Sureda.

Appendix A. Members of the EPOC.AR Study Group.

Principal investigators and co-investigators: La Plata: Mario Macuso (Hospital San Juan de Dios de la Plata) and Eduardo Maniago (Hospital San Roque de Gonnet). Rosario: Walter Gardeñez (Hospital Provincial del Centenario) and Marcelo Figueroa Casas (Instituto Cardiovascular de Rosario). Vicente López and Gran Buenos Aires: Patricia Malamud (Hospital del Tórax Dr. Antonio Cetrángolo) and Álvaro Alonso (Sanatorio Las Lomas). CABA: Santiago Auteri and Martín Fernández (Hospital María Ferrer). Mendoza: Ramón Alchapar and Diana Salvioli (Hospital J.N. Lencinas) and Carlos Elías (INSARES). Córdoba: Susana Lühning (Hospital Nacional de Clínicas) and Juan Pablo Casas (Sanatorio Allende Cerro).

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.arbr.2017.09.017.

References

1. Burney P, Jarvis D, Perez-Padilla R. The global burden of chronic respiratory disease in adults. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 2015;19:10–20.
2. Organización Mundial de la salud (OMS). Enfermedad pulmonar obstructiva crónica (EPOC). Nota descriptiva; 2016, November. Available from: http://www.who.int/mediacentre/factsheets/fs315/es/
3. GBD 2015 Disease and injury incidence and prevalence collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Lond Engl. 2016;388:1545–602.
4. Grigsby M, Siddharthan T, Chowdhury MA, Siddiquee A, Rubinstein A, Sobrino E, et al. Socioeconomic status and COPD among low- and middle-income countries. Int J Chron Obstruct Pulmon Dis. 2016;11:2497–507.
5. Soriano JB, Zielinski J, Price D. Screening for and early detection of chronic obstructive pulmonary disease. Lancet. 2009;374:721–32.
6. Martinez CH, Mannino DM, Jaimes FA, Curtis JL, Han MK, Hansel NN, et al. Undiagnosed obstructive lung disease in the United States. Associated factors and long-term mortality. Ann Am Thorac Soc. 2015;12:1788–95.
7. Parron Collar D, Pazos Guerra M, Rodriguez P, Gotera C, Mahíllo-Fernández I, Peces-Barba G, et al. COPD is commonly underdiagnosed in patients with lung cancer: results from the RECOIL study (Retrospective study of COPD Infradiagnosis in Lung Cancer). Int J Chron Obstruct Pulmon Dis. 2017;12:1033–8.
8. Kaplan A, Thomas M. Screening for COPD: the gap between logic and evidence. Eur Respir Rev. 2017;26.
9. Menezes AM, Perez-Padilla R, Jardim JR, Muiño A, Lopez MV, Valdivia G, et al. Chronic obstructive pulmonary disease in five Latin American cities (The PLATINO Study): a prevalence study. Lancet. 2005;366:1875–81.
10. Caballero A, Torres-Duque CA, Jaramillo C, Bolívar F, Sanabria F, Osorio P, et al. Prevalence of COPD in five Colombian cities situated at low, medium, and high altitude (PREPOCOL study). Chest. 2008;133:343–9.
11. Jaganath D, Miranda JJ, Gilman RH, Wise RA, Diette GB, Miele CH, et al. Prevalence of chronic obstructive pulmonary disease and variation in risk factors across four geographically diverse resource-limited settings in Peru. Respir. Res. 2015;16:40.
12. Instituto Nacional de Enfermedades Respiratorias (INER) Emilio Coni. Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) Carlos G. Malbrán. Ministerio de Salud-Argentina: mortalidad por enfermedad pulmonar obstructiva crónica (EPOC) de 40 a 74 años en Argentina. 1980–2015. PRO.E.P.C.DOC.TEC 05/17-INER-ANLIS-MSAL. Available from: http://www.anlis.gov.ar/iner/wp-content/uploads/2016/04/Mortalidad-por-Enfermedad-Pulmonar-Obstructiva-Cronica-EPOC-DE-40-a-74-A%C3%B1os-en-Argentina-1980-2015.pdf [accessed 20.06.17].
13. Miller MR, Crapo R, Hankinson J, Brusasco V, Burgos F, Casaburi R, et al. General considerations for lung function testing. Eur. Respir. J. 2005;26:153–61.
14. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur. Respir. J. 2005;26:319–38.
15. Vogelmeier CF, Criner GJ, Martínez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: GOLD executive summary. Arch. Bronconeumol. 2017;53:128–49.
16. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur. Respir. J. 2005;26:948–68.
17. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD assessment test. Eur. Respir. J. 2009;34:648–54.
18. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax. 1999;54:581–6.
19. Enright PL, Johnson LR, Connett JE, Voelker H, Buist AS. Spirometry in the lung health study. 1. Methods and quality control. Am. Rev. Respir. Dis. 1991;143:1215–23.
20. Vollmer WM, Gislason T, Burney P, Enright PL, Gulsvik A, Kocabas A, et al. Comparison of spirometry criteria for the diagnosis of COPD: Results from the BOLD study. Eur. Respir. J. 2009;34:588–97.
21. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am. J. Respir. Crit. Care Med. 1999;159:179–87.
22. From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2017. Available from: http://goldcopd.org [accessed 20.06.17].
23. Schiavi E, Stirbulov R, Hernandez Vecino R, Mercurio S, Di Boscio V, Puma Team. COPD screening in primary care in four Latin American countries: methodology of the PUMA study. Arch. Bronconeumol. 2014;50:469–74.
24. Guerriero M, Caminati M, Viegi G, Senna G, Cesana G, Pomari C. COPD prevalence in a North-Eastern Italian general population. Respir. Med. 2015;109:1040–7.
25. Buist AS, McBurnie MA, Vollmer WM, Gillespie S, Burney P, Mannino DM, et al. International variation in the prevalence of COPD (The BOLD Study): a population-based prevalence study. Lancet. 2007;370:741–50.
26. Miravitlles M, Soriano JB, García-Río F, Muñoz L, Duran-Tauleria E, Sanchez G, et al. Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities. Thorax. 2009;64:863–8.
27. Walters JA, Wood-Baker R, Walls J, Johns DP. Stability of the EasyOne ultrasonic spirometer for use in general practice. Respirology. 2006;11:306–10.
28. Perez-Padilla R, Vazquez-Garcia JC, Marquez MN, Jardim JR, Pertuzé J, Lisboa C, et al. The long-term stability of portable spirometers used in a multinational

study of the prevalence of chronic obstructive pulmonary disease. Respir. Care. 2006;51:1167–71.
29. Barr RG, Stemple KJ, Mesia-Vela S, Basner RC, Derk SJ, Henneberger PK, et al. Reproducibility and validity of a handheld spirometer. Respir. Care. 2008;53:433–41.
30. Arce SC, De Vito EL. Ecuaciones espirométricas utilizadas en la Argentina y su implicancia diagnóstica. Respirar. 2012;3:S142.
31. Perez-Padilla R, Valdivia G, Muino A, López MV, Márquez MN, Montes de Oca M, et al. Spirometric reference values in 5 large Latin American cities for subjects aged 40 years or over. Arch. Bronconeumol. 2006;42:317–25.
32. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. ERS Global Lung Function Initiative. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the Global Lung Function 2012 equations. Eur. Respir. J. 2012;40:1324–43.
33. Ancochea J, Badiola C, Duran-Tauleria E, Garcia Rio F, Miravitlles M, Muñoz L, et al. The EPI-SCAN survey to assess the prevalence of chronic obstructive pulmonary disease in Spanish 40-to-80-year-olds: protocol summary. Arch. Bronconeumol. 2009;45:41–7.
34. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, et al. Global and regional estimates of COPD prevalence: systematic review and meta-analysis. J Global Health. 2015;5:020415.
35. Ministerio de Salud de la Nación, Argentina. Tercera Encuesta Nacional de Factores de Riesgo para Enfermedades No Transmisibles. Available from: http://www.Msal.Gob.Ar/images/stories/bes/graficos/0000000544cnt-2015_09_04_encuesta_nacional_factores_riesgo.Pdf [accessed 20.06.17].
36. Ministerio de Sanidad Servicios Sociales e Igualdad, España. Informe a las Cortes Generales de evaluación del impacto sobre la salud pública de la Ley 42/2010. Available from: Https://www.msssi.gob.es//ciudadanos/proteccionSalud/tabaco/InformesTabaco.htm [accessed 20.06.17].
37. Tan WC, Sin DD, Bourbeau J, Hernandez P, Chapman KR, Cowie R, et al. Characteristics of COPD in never-smokers and ever-smokers in the general population: results from the CanCOLD study. Thorax. 2015;70:822–9.
38. Leone N, Courbon D, Thomas F, Bean K, Jégo B, Leynaert B, et al. Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. Am. J. Respir. Crit. Care Med. 2009;179:509–16.