

# 

**Citation:** Calle Rubio M, Soler-Cataluña JJ, López-Campos JL, Alcázar Navarrete B, Rodríguez González-Moro JM, Soriano JB, et al. (2019) Assessing the clinical practice in specialized outpatient clinics for chronic obstructive pulmonary disease: Analysis of the EPOCONSUL clinical audit. PLoS ONE 14(2): e0211732. https:// doi.org/10.1371/journal.pone.0211732

**Editor:** Konstantinos Kostikas, National and Kapodistrian University of Athens, SWITZERLAND

Received: November 30, 2018

Accepted: January 18, 2019

Published: February 6, 2019

**Copyright:** © 2019 Calle Rubio et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Data Availability Statement:** All relevant data are within the manuscript and its Supporting Information files.

**Funding:** This study has been promoted and sponsored by the SEPAR. We thank Boehringer Ingelheim for its financial support to carry out the study. The funders had no role in study design, data collection, analysis, decision to publish or preparation of this manuscript RESEARCH ARTICLE

# Assessing the clinical practice in specialized outpatient clinics for chronic obstructive pulmonary disease: Analysis of the EPOCONSUL clinical audit

Myriam Calle Rubio<sup>1,2®</sup>, Juan José Soler-Cataluña<sup>3®</sup>, José Luis López-Campos<sup>4,5®</sup>, Bernardino Alcázar Navarrete<sup>6®</sup>, José Miguel Rodríguez González-Moro<sup>7®</sup>, Joan B. Soriano<sup>8®</sup>, Manuel E. Fuentes Ferrer<sup>2,9</sup>, Juan Luis Rodriguez Hermosa<sup>1,2®</sup>\*

 Pulmonology Department, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Hospital Clínico San Carlos, Madrid, Spain, 2 Medical Department, School of Medicine, Universidad Complutense de Madrid, Madrid, Spain, 3 Pulmonology Department, H. de Arnau de Villanova, Valencia, Spain, 4 Respiratory Disease Medical-Surgical Unit. Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/Universidad de Sevilla, Spain, 5 CIBER de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain, 6 Pulmonology Department, Hospital de Alta Resolución de Loja, Granada, Spain, 7 Pulmonology Department, H. Universitario Principe de Asturias, Alcalá de Henares, Madrid, Spain, 8 Instituto de Investigación Hospital Universitario de la Princesa (IISP), Universidad Autónoma de Madrid, Madrid, Spain, 9 Preventative Medicine CMU, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain

These authors contributed equally to this work.
 \* jlrhermosa@yahoo.es

# Abstract

# Background

Chronic obstructive pulmonary disease (COPD) is one of the main reasons for healthcare appointments and use of healthcare resources. In recent years, clinics specializing in COPD have been developed to offer improved care and optimization of recourses for patients with high complexity and frequent decompensations. However, little is known about the clinical practice in this clinical model specializing in COPD. The objectives of this study were to assess the prevalence, characteristics of specialized COPD outpatient respiratory clinics and to evaluate clinical practice in this healthcare model.

# Methods

EPOCONSUL is a Spanish nationwide, observational, cross-sectional, clinical audit with prospective case recruitment including the clinical records for 4508 COPD cases from outpatient respiratory clinics over a 12-month period (May 2014–May 2015). The study evaluated clinical practice in 2378 cases from 28 hospitals with both general and specialized COPD outpatient respiratory clinics.

# Results

Only 28 (47.5%) centers had an outpatient clinic specializing in COPD, which was characterized by longer patient visits and a higher prevalence of written protocols compared to a



Competing interests: This study was partly funded by Boehringer Ingelheim. Myriam Calle Rubio has received speaker fees from Boehringer Ingelheim, AstraZeneca, GlaxoSmithKline, Menarini, and Novartis and consulting fees from GlaxoSmith¬Kline, Gebro Pharma and Novartis, Juan José Soler-Cataluña has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Esteve, Ferrer, GSK, Menarini, Mundipharma, Novartis and and consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Esteve, GSK, Mundipharma and Novartis. Jose Luis Lopez Campos has received fees for giving conferences, scientific advising, participation in clinical studies or draft of publications for (alphabetical order): Almirall, AstraZeneca, Bayer, Boehringer Ingelheim, Cantabria Pharma, Chiesi, Esteve, Faes, Ferrer, Gebro Pharma, GlaxoSmithKline, Grifols, Menarini, MSD, Novartis, Pfizer, Rovi, Teva y Takeda. Bernardino Alcázar Navarrete reports personal fees from GSK, grants, personal fees and non-financial support from Novartis AG, personal fees and non-financial support from Boehringer Ingelheim, personal fees and non-financial support from Chiesi, grants, personal fees and nonfinancial support from Laboratorios Menarini, personal fees from Gebro, personal fees from Astra- Zeneca, outside the submitted work. None of these are related to this work. José Miguel Rodríguez González- Moro has received fees for giving conferences from Astra-Zeneca, GSK, Boehringer Ingelheim, Teva, Novartis and Chiesi. J.B. Soriano declares having received grants from 2014 to date from Linde via Hospital Universitario de La Princesa, and has participated in speaking activities, advisory committees and consultancies during the period 2014-2018 sponsored by Almirall, AstraZeneca, Boehringer Ingelheim, CHEST, Chiesi, ERS, Esteve, GEBRO, Grifols, GSK, Linde, Lipopharma, Mundipharma, Novartis, Pfizer, RiRL, Rovi, Sandoz, SEPAR and Takeda, outside the submitted work. Manuel E. Fuentes Ferrer does not have conflicts of interest Juan Luis Rodriguez Hermosa has received speaker fees from Boehringer Ingelheim and Gebro Pharma. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; CPG, clinical practice guidelines; GesEPOC, Spanish National Guidelines for COPD care; IQR, interquartile range; BMI, body mass index; LAMA, long-acting antimuscarinic agents; LABA, long-acting beta-2 agonists; ICS, inhaled corticosteroids. general clinic. Patients treated in a specialized clinic had greater obstruction severity, a higher degree of dyspnea and also suffered from more comorbidities. The majority of patients at both types of clinic were classified as high risk (81.1% versus 83%, p = 0.384) according to GesEPOC criteria. Clinical control of COPD was more frequent at specialized clinics, with significant differences in non-severe patients (70.5% versus 56.1%, p < 0.001). Testing was done more frequently in specialized clinics, with better adherence to good clinical practice recommendations.

## Conclusion

A specialized COPD outpatient clinic is a healthcare model found in few pulmonology departments that treats more severe patients and those with increased comorbidities. The COPD patients treated in a specialized clinic had a better clinical control, as defined by impact and clinical stability. It is a healthcare model to offer improved care with a higher degree of adherence to guidelines.

# Introduction

Often, one of the most important problems in the structure and organization of healthcare is the management of chronicity and patient complexity. According to data from the World Health Organization (WHO), chronic disease is the cause of 60% of deaths worldwide and results in 75% of public health costs. Furthermore, it is estimated that chronic disease will account for 60% of all disease worldwide by 2020 and will be responsible for 73% of deaths around the world [1–3].

In recent years, important changes have taken place in both the design and organization of healthcare services, such as the distribution of resources according to epidemiological criteria, with the aim of offering healthcare based on greater scientific and technological quality with efficiency criteria [4, 5]. New healthcare strategies need to be applied which focus on more continuous and personalized patient care which is also multidisciplinary, proactive and planned out. Identifying the most appropriate level of care to treat patients is essential to reach a degree of efficiency that allows system sustainability. As a result, in recent years, specific programs have been proposed focusing on healthcare for patients with complex chronic disease such as COPD [6, 7].

COPD is considered the paradigm of chronicity as it is an illness with a high prevalence [8] and morbidity and mortality [9], which is associated with an elevated consumption of health-care resources [10], thus justifying the implementation of specialized clinics in terms of epidemiology and impact.

A specialized clinic is characterized by a team of expert professionals treating highly complex patients (homogeneous case mix) with the aim of offering comprehensive multidisciplinary care focused on the patient and based on beneficial scientific evidence. This formula has been proven to be ideal in terms of efficiency and quality of patient care, both from the scientific and technical and of course organizational and economic perspectives [11–12]. In recent years, outpatient clinics specializing in COPD have been set up in a number of healthcare centers. However, little is known about the clinical practice in this clinical model specializing in COPD. The EPOCONSUL study is the first national audit to analyze medical care for COPD in pulmonology departments in Spain. This paper uses the EPOCONSUL database in order to determine the prevalence and characteristics of specialized COPD clinics in pulmonology departments in Spain, as well as to analyze the characteristics of the patients and medical care in specialized COPD clinics.

# Materials and methods

The methodology of the EPOCONSUL audit has been extensively described elsewhere [13]. Briefly, the COPD audit promoted by the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) was designed to evaluate clinical practice as well as clinical and organizational factors related to managing patients with COPD across Spain. It was designed as an observational, cross-sectional study. Recruitment was intermittent over a single year (May 2014–May 2015). Every 2 months, each investigator recorded the clinical records of the first 10 patients identified as being diagnosed with COPD and seen in the outpatient respiratory clinic (general or specializing in COPD). Subsequently, the patients identified were reevaluated to determine if they met the inclusion/exclusion criteria described in S1 Table. The information collected was historical in nature for the clinical data from the last and previous visits, and information about hospital resources was concurrent. 46 variables associated with the hospitals and 153 associated with the patients were collected. Data from this study is included in S1 File and S2 File.

A total of 59 centers participated (33.7% of those potentially eligible) from 16 of the 17 Spanish autonomous communities (excluding La Rioja). The distribution of hospitals in the different regions and participating investigators are included in <u>S1 Appendix</u>. In order to evaluate the clinical practice for COPD patients in Spain in specialized COPD outpatient respiratory clinics versus general outpatient respiratory clinics, cases audited from 28 hospitals with both general and specialized outpatient respiratory clinics available were analyzed.

The centers were classified according to their size (small or large) as measured by: the number of beds per center  $\geq$ 500, the number of inpatient respiratory beds  $\geq$ 20, the number of pulmonology staff members  $\geq$ 5, and the number of annual outpatient respiratory visits  $\geq$ 10,000. All the criteria needed to be met to be considered large.

The level of risk was defined according to the Spanish National Guidelines for COPD Care (GesEPOC) criteria (post-bronchodilator FEV1%, degree of dyspnea and history of exacerbations) described in S2 Table [14].

COPD control was evaluated based on two components: impact and stability [15, 16]. Impact can be classified as low or high according to patients' clinical features (degree of dyspnea or COPD Assessment Test score) adjusted for the degree of disease severity defined by FEV1 or even by the BODEx. Stability was defined as the absence of exacerbations in the previous six months. These criteria are described in <u>S3 Table</u>.

In order to evaluate the degree of current CPG implementation of the main recommendations in the 2017 Spanish National Guidelines for COPD Care (GesEPOC) [14] and the 2016 Global Initiative for Chronic Obstructive Lung Disease (GOLD) [17] in both general and specialized outpatient respiratory clinics, we established the cut-off point as fulfilling  $\geq$ 50% of criteria for good clinical practice evaluated in each category (clinical evaluation of the patient, COPD evaluation and therapeutic intervention).

The protocol was approved by the Ethics Committee at the Hospital Clínico San Carlos (Madrid, Spain; internal code 14/030-E). Additionally, in accordance with current research laws in Spain, the ethics committee at each participating hospital evaluated and agreed to the study protocol. The need for informed consent was waived due to the non-interventional

nature of the study, the anonymization of data and the need to blindly evaluate the clinical performance. This circumstance was clearly explained in the protocol and the ethical committees approved this procedure. To avoid modifications to the usual clinical practice and preserve the blinding of the clinical performance evaluation, the medical staff responsible for the outpatient respiratory clinic was not informed about the audit. Data was entered remotely at each participating location to a centrally-controlled server.

#### Statistical analysis

The statistical analysis was carried out using the IBM SPSS statistical package (IBM Corporation, Armonk, New York, USA), version 23.0. Quantitative variables were expressed as mean and standard deviation (SD), and median and interquartile range were presented for asymmetric continuous variables. Qualitative variables were expressed by absolute and relative frequency (percentage). The chi-square test was used to compare qualitative variables in the specialized COPD and general outpatient respiratory clinic groups. Quantitative variables in the two risk groups were compared using the Student's t-test for symmetric variables or the nonparametric Mann–Whitney U test for asymmetric variables. All variables that were statistically significant in the univariate model were included in this model. In all tests of the hypothesis, the null hypothesis was rejected with a type I error or an error of less than 0.05.

## Results

#### Population

A total of 4508 clinical records of patients treated in outpatient respiratory clinics from 59 hospitals were audited. Of this cohort, only 2378 patients audited from 28 hospitals with available outpatient clinic settings (general versus specialized) were included in the analysis. The sampling process was detailed in an epidemiology flow chart and described in Fig 1.

## **Center characteristics**

Hospital center characteristics according to availability of a specialized COPD outpatient clinic are summarized in <u>S4 Table</u>. There were no significant differences found regarding size nor center characteristics such as being a public university center. There were few centers with a specialized COPD outpatient clinic (28 centers, 47.5%).

#### **Respiratory unit resources**

The respiratory unit resources according to availability of a specialized COPD outpatient clinic are summarized in <u>S5 Table</u>. No differences were found in the services portfolio or number of resources available in pulmonology departments according to whether they included a specialized COPD outpatient clinic except for the annual number of visits, which was higher in departments that had a specialized COPD clinic model.

#### Outpatient clinic respiratory resources

Available resources according to type of clinic are described in Table 1. In the specialized clinic model, more time was available for the first visit ( $\geq 20$  minutes, 67.9% versus 50%, p = 0.010) and for follow-up visits ( $\geq 15$  minutes, 71.4% versus 46.4%, p = 0.039). Protocols were more frequently available in the specialized clinic model (25% versus 3.2%, p = 0.022). No differences were found with regard to nurses available or inhalation therapy educational programs.



Fig 1. The sampling process described in a STROBE flow chart. A total of 4508 clinical records of patients treated in outpatient respiratory clinics from 59 hospitals were audited. Of this cohort, only 2378 patients audited from 28 hospitals with available outpatient clinic settings (general versus specialized COPD) were included in the analysis.

https://doi.org/10.1371/journal.pone.0211732.g001

## Audited patient characteristics and clinical conditions

The demographic and clinical characteristics according to type of clinic are shown in Table 2. Statistically significant differences were found for all variables except sex, age and BMI. Patients treated at a specialized clinic were characterized as having a higher degree of comorbidity according to the Charlson index, and also had a greater degree of dyspnea and more severe degree of obstruction. In addition, other clinical characteristics were more frequent such as the presence of criteria for chronic bronchitis, a symptom suggesting asthma and the emphysema phenotype according to GesEPOC. Triple therapy was the option most commonly used in both types of clinic, although it was more frequent in specialized clinics along with oxygen therapy, home respiratory support and rehabilitation programs. The majority of patients at both the specialized and general clinics were classified as high risk (81.1% versus 83%, p = 0.384). Table 3 shows the distribution of criteria that define high-risk patients

Characteristics of the outpatient respiratory clinic	General outpatient respiratory clinic	Specialized COPD outpatient clinic	P-Value
Length of initial outpatient respiratory visit in minutes, median (P25-75)	19 (15–30)	20 (15–30)	0.063
<20 min, (%)	50	32.1	0.010
≥20 min, (%)	50	67.9	
Length of follow-up outpatient respiratory visit in minutes, median (P25- 75)	12 (10–15)	15 (12–15)	0.084
<15 min, (%)	53.6	28.6	0.039
≥15 min, (%)	46.4	71.4	
Nurse available, (%)	46.4	53.6	0.452
Inhalation technique educational program available	25.8	35.7	0.572
Written COPD protocol available	3.2	25	0.022

#### Table 1. Resources in general and specialized COPD outpatient respiratory clinics.

https://doi.org/10.1371/journal.pone.0211732.t001

according to GesEPOC. Patients meeting the three criteria were more common at specialized clinics (31.9% versus 24.1%, p = 0.014). The most frequent criteria for high risk was a degree of dyspnea  $\geq$ 2 mMRC at a general clinic and severe obstruction (FEV1 <50%) at specialized clinics. Fig 2 shows the level of COPD control at both types of clinic. Clinical control of COPD was more common in specialized clinics among non-severe patients (70.5% versus 56.1%, p <0.001). There were no significant differences in severe patients (38.6% versus 43.5%, p = 0.159).

#### Diagnostic procedures during follow-up

The main diagnostic procedures performed during follow-up are described in Table 4. In patients treated at a specialized clinic, it was more common to perform functional evaluation tests such as lung volume measurement (47.6% versus 38.2%; p <0.001), the diffusing capacity test (50.8% versus 45.9%; p <0.02) and the 6-minute walk test (44.2% versus 20.5%; p <0.001). Thoracic computerized axial tomography (CAT) was also more common at specialized clinics (60.7% versus 53.9%; p <0.001).

# Actions taken at the time of the last follow-up visit

Table 5 includes the main clinical actions taken during the last audited visit. At specialized clinics, it was more common to evaluate degree of dyspnea (92.5% versus 78.1%; p <0.001), take a patient history of exacerbations (78.4% versus 67%; p <0.001), comorbidities (82.4% versus 75.1%; p <0.001) and level of physical activity (63.1% versus 37%; p <0.001). Patient characterization by phenotype according to GesEPOC (53.7% versus 44%; p = 0.001), revision of inhalation technique (41.7% versus 27.8%; p = 0.001) and the use of the CAT questionnaire (31% versus 16.5%; p = 0.001) were also more frequent.

## Adherence to good clinical practice criteria

<u>Table 6</u> describes the adherence to the main recommendations in clinical practice guidelines (CPG) at both types of clinic, showing that specialized clinics better adhere to the main CPG recommendations.

# Discussion

This paper provides data on clinical practice and the characteristics of patients treated in specialized COPD outpatient clinics compared to general clinics in pulmonology departments in Spain for the first time.

#### Table 2. Characteristics of the audited cases at both general and specialized outpatient respiratory clinics.

	Global n = 2378	Global % or median (P25-75)	General outpatient respiratory clinic n = 1369 (57.6%)	Specialized COPD outpatient clinic n = 1009 (42.4%)	P-Value
Gender (male), (%)	2378	84.6	84.7	84.5	0.954
Age (years), m (SD)	2378	69.37 (9.76)	69.61 (9.88)	69.05 (9.58)	0.164
<u>≤55, (%)</u>		8.5	8.7	8.1	0.199
≥70, (%)		50.5	51.9	48.8	0.342
Active smokers, (%)	2378	31.7	38.5	22.4	< 0.001
Smoking pack-years, median (P25-75)	2378	45(35-68.4)	45 (30-60)	50 (38–79.7)	< 0.001
BMI kg/m2, m (SD)	2378	27.91 (5.50)	27.86 (5.48)	27.98 (5.53)	0.598
BMI ≤21 kg/m2, (%)	2378	8	8.4	7.4	0.401
Charlson index, m (SD)	2378	2.82 (2.17)	2.77 (2.18)	2.88 (2.15)	
$\overline{\text{Charlson index } \geq 3, (\%)}$	2378	43.1	41.3	45.6	0.040
Dyspnea (MRC-m)	2378				< 0.001
0–1, (%)		27.9	22.9	34.8	
≥2, (%)		45	39.6	52.2	
Missing, (%)		11.3	15.6	5.5	
Level of dyspnea not referred to, (%)		15.8	21.9	7.5	
CAT questionnaire >10, (%)	539	64.4	63.7	64.9	0.785
Chronic bronchitis, (%)	2378	43	40.1	46.9	< 0.001
Chronic colonization, (%)	2378	5.3	4.8	6	0.197
Emphysema phenotype (GesEPOC 2017), (%)	1145	17.9	15.6	20.5	0.037
History of asthma or symptoms suggestive of asthma, (%)	2378	31.5	29	35	0.002
Post-BD FEV <sub>1</sub> %, m (SD)	2378	49.59(17.26)	50.91 (16.96)	47.79 (17.51)	< 0.001
Post-BD FEV <sub>1</sub> <50%		52.5	48.6	57.7	< 0.001
Number of moderate/severe exacerbations in the last year, median (P25-75)	1708	(0-2)	1.28 (1.48)	1.28 (1.39)	0.874
Number of hospitalizations in the last year, median (P25-75)	1472	0.5 (0-1)	0.56(1.00)	0.65 (1.01)	0.052
High risk level (GesEPOC 2017), (%)	1388	82	83	81.1	0.384
BODEx, m(SD)	197	3.45 (1.95)	3.01 (1.60)	3.84 (2.15)	0.003
GOLD group, (%)	590				< 0.001
<u>A</u>		22.5	19.3	24.1	
B		18	29.4	12.7	
<u>C</u>		17.8	19.3	17.1	
<u>D</u>		41.7	32.1	46.2	
COPD Phenotype (GesEPOC 2017)	2378				< 0.001
Non-exacerbator, (%)		28.3	26.5	30.7	
Exacerbator, (%)		19.8	17.5	23	
Missing, (%)		51.9	56	46.3	
Drug treatment for COPD, (%)	2391				0.003
LAMA monotherapy		11.9	12.9	10.4	
LAMA-LABA combination		25.4	25.7	24.8	
LABA+ ICS combination		8.1	8.9	7	
Triple therapy		48.3	46.8	50.5	
Quadruple therapy		6.3	5.6	7.4	
Long-term oxygen therapy, (%)	2378	26.6	20.5	31.5	< 0.001
Home ventilation, (%)	2378	8.9	6.6	12.1	< 0.001

(Continued)

#### Table 2. (Continued)

	Global n = 2378	Global % or median (P25-75)	General outpatient respiratory clinic n = 1369 (57.6%)	Specialized COPD outpatient clinic n = 1009 (42.4%)	P-Value
Respiratory rehabilitation, (%)	2378	10.8	7.5	15.4	< 0.001

BMI: body mass index; BODE: body mass index, airflow obstruction, dyspnea, and exercise capacity; BODEx: body mass index, airflow obstruction, dyspnea and severe exacerbations; post-BD FEV1%: post-bronchodilator FEV1 percent predicted; Triple therapy: LABA: long-acting beta-2 agonists + LAMA: long-acting antimuscarinic agents + ICS: inhaled corticosteroids; Quadruple: long-acting muscarinic antagonist/long-acting -2 adrenergic agonist/inhaled corticosteroids/other drug (roflumilast or theophylline or long-term antibiotic); GOLD: Global Initiative for Chronic Obstructive Lung Disease; GesEPOC: Spanish National Guidelines for COPD; CAT: COPD Assessment Test.

https://doi.org/10.1371/journal.pone.0211732.t002

COPD is a widely prevalent disease, 10% in those aged 40–80 [18]. The disease is progressive and is often associated with a high degree of comorbidity and mortality, ranked as the fifth leading cause of death in Spain at present [19, 20]. It is currently a priority in healthcare system plans [21] as it is associated with a substantial demand for care. COPD is one of the main reasons for healthcare appointments and use of healthcare resources, both for primary and specialized care. In Spain, the disease accounts for 10-12% of primary care visits, 35-40% of pulmonology visits and is responsible for 7% of hospitalizations [22]. The average healthcare cost generated by each Spanish patient is estimated to be 3538 euros/year, of which more than 85% corresponds to costs for hospitalizations due to exacerbations [23]. As a result, patients with highly complex cases and frequent decompensation will have a higher social health impact due to frequent hospitalizations [24].

Systematized healthcare has been shown to improve quality of life and prognosis in complex chronic patients, in addition to lowering the cost of care (reducing hospitalizations and length of hospital stays, lowering the number of ER visits, appropriate use of medication, etc.) [25, 26]. This data warrants the need to adapt current mechanisms in COPD care and to reshape the care model, guaranteeing specialized units for patients with high complexity and frequent decompensations such as specialized clinics. As a result, clinics specializing in COPD have been developed in recent years to offer improved care and optimization of recourses [27, 28, 12].

The results of our study show that a clinic specializing in COPD is a healthcare model found in few pulmonology departments (in 47.5%), despite the fact that the majority of the

Table 3. Distribution of high-risk patients accordin	ng to criteria that define their high-risk level at both	1 clinic models.		
No. of high-risk criteria met	Patients with a high level of risk in general outpatient respiratory clinics (n = 551)	Patients with a high level of risk in specialized COPD outpatient clinics (n = 587)	P-Value	
A single criterion, n (%)	192 (34.8%)	189 (32.2%)	0.014	
Only degree of dyspnea $\geq 2$ (mMRC)	105 (54.7%)	67 (35.4%)	]	
Only FEV1 <50% predicted	44 (22.9%)	81 (42.9%)		
Only $\geq$ 2 exacerbations and/or $\geq$ 1 hospitalization	43 (22.4%)	41 (21.7%)		
Two criteria, n (%)	226 (41%)	211 (35.9%)		
Degree of dyspnea $\geq$ 2 (mMRC) and FEV1<50%	103 (45.6%)	117 (55.5%)		
Degree of dyspnea $\geq 2$ (mMRC) and [ $\geq 2$ exacerbations and/or $\geq 1$ hospitalization]	78 (34.5%)	57 (27%)		
FEV1 <50% and [ $\geq$ 2 exacerbations and/or $\geq$ 1 hospitalization]	45 (19.9%)	37 (17.5%)		
Three criteria, n (%)	133 (24.1%)	187 (31.9%)		

#### Т

FEV1: post-bronchodilator FEV1 percent predicted; mMRC: modified Medical Research Council.

https://doi.org/10.1371/journal.pone.0211732.t003





Fig 2. Control of COPD adjusted for severity in both outpatient clinic models. In patients with mild to moderate severity (BODEx  $\leq 2$  points or FEV1  $\geq 50\%$ ), to establish a situation of optimal control of COPD, the following criteria must be met: low impact [dyspnea (mMRC) 0-1 and/or CAT <10 points] and stability defined as the absence of exacerbations in the last 6 months. In severe/very severe patients (BODEx >2 points or FEV1 <50%), to establish a situation of optimal control of COPD, the following criteria must be met: low impact [dyspnea (mMRC) 0-2 and/or CAT ≤16 points] and stability defined as the absence of exacerbations in the last 6 months.

https://doi.org/10.1371/journal.pone.0211732.g002

hospitals participating in the audit were public university hospitals with training for medical specialists. We found no differences with regard to specialized clinic availability, center characteristics or the resources available in the pulmonology department such as medical staff or diagnostic procedures, except for a higher number of visits to pulmonology departments that included a clinic specializing in COPD. The low prevalence of clinics specializing in COPD in Spain is not in line with current guidelines established in COPD action plans for patients with a high degree of intervention and greater complexity [29, 21] in which follow-up falls on the referred hospital specialist in a separate clinic characterized by a higher degree of specialization and training in COPD.

With regard to available resources, our study found that more time was available for both the first visit and follow-up visits at specialized clinics and protocols were also more commonly available. These two tools are considered crucial, since having ample time during the visit improves communication with the patient, reduces the need for tests and reduces possible

	Global (n = 2378)		General outpatient respiratory clinic (n = 1369)	Specialized COPD outpatient clinic (n = 1009)	P-Value
	N	% or median (P25- 75)	% or median (P25-75)	% or median (P25-75)	
Referred from, n (%)	1857				< 0.001
Primary care		41.7	49.3	31.1	
Emergency room		8.5	9.9	6.5	
Other inpatient department		18.8	19.1	18.3	
Other specialties		31	21.6	44	
Follow-up frequency, n (%)	2326				< 0.001
Less than 6 months		54.6	53.7	55.9	
6–12 months		30.1	33.6	25.4	
More than 12 months		15.3	12.7	18.7	
Follow-up time (years), median (P25-75)	2378	4 (2–7)	4 (2-6)	4 (2-6)	0.002
Bronchodilator reversibility testing, n (%)	2378	60.7	61.4	59.7	0.396
Arterial blood gases measured on any occasion, n (%)	2378	60.8	58.1	64.3	0.003
Alfa-1- AT serum level testing available, n (%)	2378	25.7	22.6	29.9	< 0.001
Lung volumes measured on any occasion, n (%)	2378	42.2	38.2	47.6	< 0.001
Diffusion capacity measured on any occasion, n (%)	2378	48	45.9	50.8	0.02
6-min walk test performed on any occasion, n (%)	2378	30.6	20.5	44.2	< 0.001
Cardiopulmonary exercise testing performed on any occasion, n (%)	2378	4.4	2.7	6.6	<0.001
BODE index calculated on any occasion, n (%)	2378	19.8	11	31.6	< 0.001
Chest CT scan performed on any occasion, n (%)	2378	56.8	53.9	60.7	< 0.001

#### Table 4. Medical care and diagnostic procedures during follow-up in both outpatient clinic models.

Abbreviations: Alpha-1 AT: alpha-1 antitrypsin; BODE: body mass index, airflow obstruction, dyspnea and exercise capacity; BODEx: body mass index, airflow obstruction, dyspnea and severe exacerbations; BD test: bronchodilator test; CT: computed tomography; CAT: COPD assessment test.

https://doi.org/10.1371/journal.pone.0211732.t004

mistakes in treatment [30]. The application of protocols and clinical guidelines is also a fundamental tool to improve efficiency and reduce variability in care provided [31].

In our study, patients treated at clinics specializing in COPD had a higher rate of comorbidity. Chronic expectoration and the emphysema phenotype were also more common. These findings are in line with numerous studies that have shown that the presence of comorbidities, cough with chronic expectoration and emphysema are associated with a higher risk of exacerbations, a worse prognosis and higher mortality [32, 33]. In both general outpatient respiratory clinics and those specialized in COPD, the majority of COPD patients were classified as high risk according to the GesEPOC criteria (post-bronchodilator FEV1%, degree of dyspnea and history of exacerbations) described in S2 Table [13, 34], although it must be noted that patients who met the three criteria defining high risk with a higher degree of dyspnea and obstruction severity were more common at specialized clinics. These differential aspects in the clinical characteristics of patients and the origin of the visit could suggest that, at centers with both types of clinics, patients who are more complex or "fragile" or the patients who need complex treatment (home ventilation or respiratory rehabilitation) are strategically selected for referral to the specialized COPD outpatient respiratory clinics from other specialties rather than the general outpatient respiratory clinic to which patients are generally referred from primary care. Nevertheless, one limitation to bear in mind is that referral criteria could not be evaluated as it was not available.

#### Table 5. Actions taken at the time of the last follow-up visit in both outpatient clinic models.

	Global (n = 2378)		General outpatient respiratory clinic (n = 1369)	Specialized COPD outpatient clinic (n = 1009)	P-Value
	N	% or median (IR)	% or median (IR)	% or median (IR)	Р
Evaluation of dyspnea severity, n (%)	2378	84.2	78.1	92.5	< 0.001
Number of moderate or severe exacerbations in the last 12 months recorded, n (%)	2378	71.8	67	78.4	< 0.001
Data on regular exercise recorded, n (%)	2378	48.1	37	63.1	< 0.001
Comorbidities identified in the medical record, n (%)	2378	78.2	75.1	82.4	< 0.001
COPD severity defined in the report by which criteria, n (%)	2378	74.4	66.6	85	< 0.001
FEV1		80.2	85.1	74.9	
BODE		14.5	7.9	21.6	
BODEx		5.3	7	3.5	
COPD GOLD type defined in the report, n (%)	2378	24.8	13.7	39.9	< 0.001
COPD phenotype according to GesEPOC defined in the report, n (%)	2378	48.1	44	53.7	< 0.001
CAT questionnaire completed on any occasion, n (%)	2378	22.7	16.5	31	< 0.001
Treatment adherence evaluated, n (%)	2378	46.4	34.6	62.3	< 0.001
Inhalation technique evaluated, n (%)	2378	33.7	27.8	41.7	< 0.001
Degree of satisfaction with inhalation device evaluated, n (%)	2378	21	18.4	24.5	< 0.001
Adverse effects of medication recorded, n (%)	2378	28.9	22.1	38.2	< 0.001
Specific intervention for smoking cessation in active smokers offered, n (%)	1625	27.7	22.4	33.4	< 0.001
Regular exercise recommended during the visit, n (%)	2378	49.8	37	67.2	< 0.001
Influenza annual vaccination recorded, n (%)	2378	50.2	41	62.6	< 0.001
Pneumococcal vaccination recorded, n (%)	2378	29.2	27.8	31.1	0.083
Any change in current medication advised, n (%)	2378	22.5	20.7	24.8	0.022

https://doi.org/10.1371/journal.pone.0211732.t005

A relevant result is the fact that patients treated in a specialized clinic, despite being more severe in terms of disease burden, had a better clinical control of their COPD, as defined by impact and clinical stability [15], with significant differences in patients with a mild or moder-ate degree of severity (70.5% versus 56.1%, p <0.001). This data suggests that clinical control may be an achievable therapeutic objective for a significant number of patients with COPD in a healthcare model with a higher degree of adherence to guidelines like the specialized clinic, according to information from our study. Nevertheless, this is a cross-sectional analysis that does not evaluate long-term clinical data.

As far as medical care according to type of clinic, it must be noted that there are differences in diagnostic and therapeutic procedures, as it is more common to complete specific tests in a specialized clinic such as measuring lung volume, the diffusing capacity test, computerized axial tomography (CAT), or the 6-minute walk test. Actions to evaluate treatment are also more common, with better adherence to good clinical practice recommendations. These differences in actions performed would not be explained by level of patient risk, and may be related to the use of protocols or clinical pathways, having more time in the clinic and greater knowledge and interest among the professionals treating patients in the specialized clinic model, although this aspect was not evaluated. In this sense, numerous studies have shown a notable variability in COPD care in different environments which is not exclusively influenced by clinical presentation or resources available, but instead is explained by a grouping or clustering effect [35–37] based on the center or care model. This is why management using



Criteria of good clinical practice evaluated in EPOCONSUL	No. of criteria met	Global (n = 2378), (%)	Patients in general outpatient respiratory clinics (n = 1369), (%)	Patients in Specialized COPD outpatient clinic (n = 1009), (%)	P-Value
During clinical evaluation	6 criteria	22.3	17.8	27.6	< 0.001
1. Is dyspnea severity evaluated on current visit?	>3 criteria	66.9	57.6	79.5	< 0.001
2. Is the number of hospitalizations in the last 12 months recorded during current visit?	≤3 criteria	33.1	42.4	20.5	< 0.001
3. Is the number of moderate or severe exacerbations in					
the last 12 months recorded during current visit?					
4. Is current smoking habit recorded?					
6. Are comorbidities identified in the clinical record?					
During COPD evaluation	8 criteria	2.1	0.6	4.3	< 0.001
1. Is alfa-1-antitrypsin serum level determination	>4 criteria	32.6	23.9	44.4	< 0.001
available?	<1 criteria	67.4	76.1	55.6	<0.001
2. Is COPD severity defined in the report?		07.4	70.1	55.0	<0.001
3. Is COPD GOLD type defined in the report?					
4. Is COPD phenotype according to GesEPOC defined in					
the report?					
5. Is the 6M w 1 performed on any occasion?					
<ul> <li>a. Is diffusion capacity measured on any occasion?</li> <li>7. Are lung volumes measured on any occasion?</li> </ul>					
8. Is a chest CT scan performed on any occasion in the					
exacerbator phenotype?					
During therapeutic intervention	5 criteria	11.6	9.1	14.9	< 0.001
1. Is treatment adherence evaluated in any way?	>3 criteria	28.1	21.5	37.1	< 0.001
2. Is innatation technique evaluated in any way:					
4. Is exercise advised during the visit?	≤3 criteria	71.9	78.5	62.9	< 0.001
5. Have arterial blood gases been measured on any					
occasion for patients on long-term oxygen therapy?					

Table 6. Adherence to recommendations (GOLD and GesEPOC) in both outpatient clinic models.

In order to evaluate the degree of current CPG implementation of the main recommendations, we evaluated the number of criteria for good clinical practice met in each category (clinical evaluation of the patient, COPD evaluation and therapeutic intervention).

https://doi.org/10.1371/journal.pone.0211732.t006

integrated care processes and care protocols according to principles of evidence-based medicine are fundamental tools to improve efficiency, reduce variability in clinical practice and contribute to improving the quality of care. However, it is important to remember that while CPG recommendations are based on scientific evidence in order to systematize actions, COPD is a heterogeneous and complex disease with a variable clinical presentation [38].

With regard to the type of treatment according to clinic type, we must note that a high percentage of patients received inhaled corticosteroids at both types of clinic, in accordance with other national studies done at different levels of care [39], although the results of our analysis showed that triple therapy, oxygen therapy and home respiratory support were more common in specialized clinics. A change in drug treatment was also more common in specialized clinics, which may reflect more proactive care in these specialized units. However, there was no change in prescription for the majority of patients (75.2%). This infrequent changing of drug treatment in pulmonology departments is consistent with other studies in which it was associated with the presence of clinical characteristics such as a lower frequency of exacerbations and symptoms, which identify better management in a patient [40].

Finally, a few methodological limitations should be kept in mind such as the fact that center selection was not randomized and was based on having previously participated in COPD clinical audits. We must also consider the limitation intrinsic to any clinical audit, the fact that some values were not recorded as they were not available. Additionally, we must mention the

possible limitation that this was a cross-sectional study, so differences in risk of exacerbations or complications compared to patients treated in general respiratory clinics cannot be evaluated. Further clinical audits are necessary to evaluate the impact on clinically significant results. However, despite these limitations, we believe that due to its population coverage, the sample included is representative of medical attention for patients with COPD in Spain according to the type of outpatient respiratory clinic.

## Conclusions

A specialized COPD outpatient respiratory clinic is a healthcare model present in very few pulmonology departments in Spain. It is characterized by a greater amount of time reserved for patient care and creating protocols for care, although it does not have additional human resources or equipment available. This formula has been proven to offer a better clinical control of COPD with greater adherence to clinical practice guidelines. However, future studies are needed in order to evaluate whether it has an impact on clinically relevant results.

## Supporting information

**S1** Appendix. Investigators participating in the EPOCONSUL study. (DOCX)

**S1 Table.** The inclusion criteria and exclusion criteria. (DOCX)

**S2 Table. Risk stratification according to GesEPOC.** (DOCX)

S3 Table. COPD management criteria with adjustment for severity according to the BODEx index or FEV<sub>1</sub>%. (DOCX)

S4 Table. Hospital center characteristics according to availability of a specialized COPD outpatient clinic.

(DOCX)

S5 Table. Respiratory unit resources according to availability of a specialized COPD outpatient clinic.

(DOCX)

**S1 File. Data from this study.** (XLSX)

**S2 File. Data from this study.** (XLSX)

# Acknowledgments

The authors thank the investigators and the centers that participated in EPOCONSUL study. A list of the EPOCONSUL researchers is available in <u>S1 Appendix</u>.

## **Author Contributions**

**Conceptualization:** Myriam Calle Rubio, José Luis López-Campos, Bernardino Alcázar Navarrete, José Miguel Rodríguez González-Moro, Joan B. Soriano, Juan Luis Rodriguez Hermosa. **Data curation:** José Luis López-Campos, Manuel E. Fuentes Ferrer, Juan Luis Rodriguez Hermosa.

Formal analysis: Manuel E. Fuentes Ferrer.

Funding acquisition: Myriam Calle Rubio.

- **Investigation:** Myriam Calle Rubio, Juan José Soler-Cataluña, Bernardino Alcázar Navarrete, José Miguel Rodríguez González-Moro, Juan Luis Rodriguez Hermosa.
- Methodology: Myriam Calle Rubio, Juan José Soler-Cataluña, José Luis López-Campos, Bernardino Alcázar Navarrete, Joan B. Soriano, Manuel E. Fuentes Ferrer, Juan Luis Rodriguez Hermosa.
- Resources: Myriam Calle Rubio.
- Supervision: Myriam Calle Rubio, Juan José Soler-Cataluña, José Luis López-Campos, Bernardino Alcázar Navarrete, José Miguel Rodríguez González-Moro, Joan B. Soriano, Juan Luis Rodriguez Hermosa.
- Validation: Juan José Soler-Cataluña, Bernardino Alcázar Navarrete, Juan Luis Rodriguez Hermosa.
- Visualization: Juan Luis Rodriguez Hermosa.
- Writing original draft: Myriam Calle Rubio, Juan Luis Rodriguez Hermosa.
- Writing review & editing: Myriam Calle Rubio, Juan José Soler-Cataluña, José Luis López-Campos, Bernardino Alcázar Navarrete, José Miguel Rodríguez González-Moro, Joan B. Soriano, Manuel E. Fuentes Ferrer, Juan Luis Rodriguez Hermosa.

#### References

- OMS. Estadísticas sanitarias mundiales. 2014. <u>http://www.who.int/countries/esp/es/</u> [Accessed: 11-9-2018].
- Murray CJ, Lopez AD. Measuring the global burden of disease. N Engl J Med. 2013; 369:448–57. https://doi.org/10.1056/NEJMra1201534 PMID: 23902484
- European Lung Foundation. The burden of lung disease. European lung white book. Available at: <a href="http://www.erswhitebook.org/chapters/the-burden-of-lung-disease/">http://www.erswhitebook.org/chapters/the-burden-of-lung-disease/</a> [Accessed: 11-9-2018].
- 4. Timbie JW, Fox DS, Van Busum K, Schneider EC. Five reasons that many comparative effectiveness studies fail to change patient care and clinical practice. Health Aff (Millwood). 2012; 31:2168–75.
- Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA. 2005; 294:716–24. https://doi.org/10.1001/jama.294.6.716 PMID: 16091574
- Adams SG, Smith PK, Allan PF, Anzueto A, Pugh JA, Cornell JE. Systematic review of the chronic care model in chronic obstructive pulmonary disease prevention and management. Arch Intern Med. 2007; 167:551–61. https://doi.org/10.1001/archinte.167.6.551 PMID: 17389286
- Lemmens KM, Lemmens LC, Boom JH, Drewes HW, Meeuwissen JA, Steuten LM, et al. Chronic care management for patients with COPD: a critical review of available evidence. J Eval Clin Pract. 2013; 9:734–52.
- Soriano JB, Ancochea J, Miravitlles M, Garcia-Rio F, Duran E, Munoz L, et al. Recent trends in COPD prevalence in Spain: a repeated cross-sectional survey 1997–2007. Eur Respir J. 2010; 36:758–65. https://doi.org/10.1183/09031936.00138409 PMID: 19996189
- Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. Eur Respir J. 2006; 28:523–32. https://doi.org/10.1183/09031936. 06.00124605 PMID: 16611654
- Miravitles M, Murio C, Guerrero T, Gisbert R, on behalf of the DAFNE study group. Costs of chronic bronchitis and COPD. A one year follow-up study. Chest. 2003; 123:784–91. PMID: <u>12628879</u>

- Domingo Ribas C. Efectividad y eficiencia de una consulta externa monográfica de asma. Arch Bronconeumol. 2001; 37: 274–80. PMID: <u>11412525</u>
- 12. Domingo Ribas C. Efectividad y eficiencia de una consulta monográfica hospitalaria para pacientes con EPOC e insuficiencia respiratoria. Arch Bronconeumol. 2006; 42:104–12. PMID: 16545247
- Calle M, Alcázar B, Soriano JB, Soler-Cataluña JJ, Rodríguez JM, Fuentes M, et al. Clinical audit of COPD in outpatient respiratory clinics in Spain: the EPOCONSUL study. Int J Chron Obstruct Pulm Dis. 2017; 12:417–26.
- Miravitiles M, Soler-Cataluña JJ, Calle M, Molina J, Almagro P, Quintano JA, et al. Guía española de la enfermedad pulmonar obstructiva crónica (GesEPOC) 2017. Tratamiento farmacológico en fase estable. Arch Bronconeumol. 2017; 53:324–35. https://doi.org/10.1016/j.arbres.2017.03.018 PMID: 28477954
- Soler-Cataluña JJ, Alcázar-Navarrete B, Miravitlles M. The concept of control of COPD in clinical practice. Int J Chron Obstruct Pulm Dis. 2014; 9:1397–405.
- Duarte Araújoa A, Hespanhol V, Correia de Sousa J. ¿Es útil el concepto de control de la EPOC?: evaluación del éxito terapéutico a partir de la valoración del estado de salud en relación con la EPOC. Arch Bronconeumol. 2017; 53:530–1.
- Vogelmeier CF, Criner GJ, Martinez 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. *Am J Respir Crit Care Med.* 2017; 195:557–82. https://doi.org/10.1164/rccm. 201701-0218PP PMID: 28128970
- Ancochea J, Badiola C, Durán-Taulería E, García Río 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-yearolds: protocol summary. Arch Bronconeumol. 2009; 45:41–7. https://doi.org/10.1016/j.arbres.2008.06. 001 PMID: 19186298
- Soriano JB, Lamprecht B, Ramirez AS, Martinez-Camblor P, Kaiser B, Alfageme I, et al. Mortality prediction in chronic obstructive pulmonary disease comparing the GOLD 2007 and 2011 staging systems: a pooled analysis of individual patient data. *Lancet Respir Med.* 2015; 3:443–50. <u>https://doi.org/10.</u> 1016/S2213-2600(15)00157-5 PMID: 25995071
- Ministerio de Sanidad, Servicios Sociales e Igualdad. Informe anual del Sistema Nacional de Salud, 2015. Available at:http://www.mscbs.gob.es/estadEstudios/estadisticas/sisInfSanSNS/ tablasEstadisticas/Inf\_Anual\_SNS\_2015.1.pdf21. [Accessed: 11-9-2018].
- Estrategia en EPOC del Sistema Nacional de Salud. Plan de Calidad para el Sistema Nacional de Salud. Madrid: Ministerio de Sanidad y Politica Social; 2009. Available at: http://www.mscbs.gob.es/ organizacion/sns/planCalidadSNS/pdf/EPOC\_version\_junio\_2014.pdf [Accessed: 11-9-2018].
- Álvarez-Sala Walther JL, Cimas Hernando E, Molina París J, Naberan Toña K, Simonet Aineto P, Masa Jiménez J F, et al. Recomendaciones para la atención al paciente con enfermedad pulmonar obstructiva crónica. Aten Primaria. 2001; 28: 491–500. PMID: 11718646
- Soriano J.B, Miravitlles M. Datos epidemiológicos de EPOC en España. Arch Bronconeumol. 2007; 43 Supl 1:2–9.
- Chapman KR, Mannino DM, Soriano JB, Vermeire PA, Buist AS, Thun MJ, et al. Epidemiology and costs of chronic obstructive pulmonary disease. Eur Respir J. 2006; 27:188–207. <u>https://doi.org/10. 1183/09031936.06.00024505 PMID: 16387952</u>
- Morales-Asensio JM. Gestion de casos y cronicidad compleja: conceptos, modelos, evidencias e incertidumbres. Enferm Clin. 2014; 24:23–34. https://doi.org/10.1016/j.enfcli.2013.10.002 PMID: 24314797
- Contel J.C, Muntané B, Camp L. La atención al paciente crónico en situación de complejidad: el reto de construir un escenario de atención integrada. Aten Primaria. 2012; 44:107–13. https://doi.org/10.1016/ j.aprim.2011.01.013 PMID: 21636176
- Casas A, Troosters T, Garcia-Aymerich J, Roca J, Hernandez C, Alonso A et al. Integrated care prevents hospitalisations for exacerbations in COPD patients. Eur Respir J. 2006; 28: 123–30. <u>https://doi.org/10.1183/09031936.06.00063205</u> PMID: 16611656
- Jonkman NH, Westland H, Trappenburg JC, Groenwold RH, Bischoff EW, Bourbeau J, et al. Characteristics of effective self-management interventions in patients with COPD: individual patient data metaanalysis. Eur Respir J. 2016; 48:55–68. https://doi.org/10.1183/13993003.01860-2015 PMID: 27126694
- 29. Ministerio de Sanidad y Politica Social. Plan de Calidad para el Sistema Nacional de Salud. Estrategia para el abordaje de la Cronicidad en el Sistema Nacional de Salud. 2012. Available at: http://www.mscbs.gob.es/organizacion/sns/planCalidadSNS/pdf/ESTRATEGIA\_ABORDAJE\_CRONICIDAD.pdf [Accessed: 11-9-2018].

- Outomuro D, Actis AM. "Tiempo de consulta ambulatoria". Rev Med Chile 2013; 141: 361–6. <u>https://doi.org/10.4067/S0034-98872013000300012</u> PMID: 23900328
- Burgers J, Smolders M, van der Weidjen T, Davis D, Grol R. Clinical practice guidelines as a tool for improving patient care. En: Improving patient care. The implementation of change in health care. 2nd Edition. Grol R, Wensing M, Eccles M, Davis D. eds. Oxford: Wiley Blackwell; 2013. pp. 91–110.
- Divo M, Cote C, De Torres JP, Casanova C, Marin JM, Pinto-Plata V, et al; BODE Collaborative Group. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2012; 186:155–6. https://doi.org/10.1164/rccm.201201-0034OC PMID: 22561964
- Prescott E, Lange P, Vestbo J. Chronic mucus hypersecretion in COPD and death from pulmonary infection. Eur Respir J. 1995; 8:1333–8 PMID: 7489800
- Calle Rubio M, Rodríguez Hermosa JL, Soler-Cataluña JJ, López-Campos JL, Alcázar Navarrete B, Soriano JB, et al. Medical Care According to Risk Level and Adaptation to Spanish COPD Guidelines (Gesepoc): The Epoconsul Study. Arch Bronconeumol.2018; 54: 270–9, https://doi.org/10.1016/j. arbres.2017.11.015 PMID: 29361320
- Pozo-Rodríguez F, López-Campos JL, Álvarez-Martínez CJ, Castro-Acosta A, Agüero R, Hueto J, AUDIPOC Study Group, et al. Clinical audit of COPD patients requiring hospital admissions in Spain: AUDIPOC study. PLoS One. 2012; 7:e42156. <u>https://doi.org/10.1371/journal.pone.0042156</u> PMID: 22911875
- 36. Calle Rubio M, López-Campos JL, Soler-Cataluña JJ, Alcázar Navarrete B, Soriano JB, Rodríguez González-Moro JM, et al. EPOCONSUL Study. Variability in adherence to clinical practice guide lines and recommendations in COPD outpatients: a multi-level, cross-sectional analysis of the EPOCONSUL study. Respir Res. 2017; 18:200. https://doi.org/10.1186/s12931-017-0685-8 PMID: 29197415
- Jones R, Roberts M. National cohort data from Sweden to the national COPD audit in England and Wales: grand designs for quality improvement. Prim Care Respir J. 2014; 23:7–8. https://doi.org/10. 4104/pcrj.2014.00013 PMID: 24553824
- Lugtenberg M, Burgers JS, Clancy C, Westert GP, Schneider EC. Current guidelines have limited applicability to patients with comorbid conditions: a systematic analysis of evidence-based guidelines. PLoS One. 2011; 6:e25987. https://doi.org/10.1371/journal.pone.0025987 PMID: 22028802
- Calle M, Casamor R, Miravitlles M. Identification and distribution of COPD Phenotypes in clinical practice according to Spanish COPD Guidelines: the FENEPOC study. Int J Chron Obstruct Pulmon Dis. 2017; 12: 2373–83. https://doi.org/10.2147/COPD.S137872 PMID: 28848338
- Lopez-Campos JL, Navarrete BA, Soriano JB, Soler-Cataluña JJ, González-Moro JM, Ferrer ME, et al. Determinants of medical prescriptions for COPD care: an analysis of the EPOCONSUL clinical audit. Int J Chron Obstruct Pulmon Dis. 2018; 13:2279–88. <u>https://doi.org/10.2147/COPD.S160842</u> PMID: 30100718