

Citation: López-Campos JL, Abad Arranz M, Calero-Acuña C, Romero-Valero F, Ayerbe-García R, Hidalgo-Molina A, et al. (2016) Guideline Adherence in Outpatient Clinics for Chronic Obstructive Pulmonary Disease: Results from a Clinical Audit. PLoS ONE 11(3): e0151896. doi:10.1371/journal. pone.0151896

Editor: Konstantinos Kostikas, University of Athens Medical School, SWITZERLAND

Received: January 4, 2016

Accepted: March 4, 2016

Published: March 17, 2016

Copyright: © 2016 López-Campos et al. This is an open access article distributed under the terms of the <u>Creative Commons Attribution License</u>, 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 paper. Individual data are available at Fundación Neumosur (<u>http://www.neumosur.net/</u>), upon request.

Funding: This study was financially supported by an unrestricted grant from Laboratorios Menarini, SA (Barcelona, Spain).

Competing Interests: This study was financially supported by an unrestricted grant from Laboratorios Menarini, SA (Barcelona, Spain). This does not alter **RESEARCH ARTICLE**

Guideline Adherence in Outpatient Clinics for Chronic Obstructive Pulmonary Disease: Results from a Clinical Audit

Jose L. López-Campos^{1,2}*, Maria Abad Arranz¹, Carmen Calero-Acuña^{1,2}, Fernando Romero-Valero³, Ruth Ayerbe-García⁴, Antonio Hidalgo-Molina³, Ricardo I. Aguilar-Pérez-Grovas⁴, Francisco García-Gil⁵, Francisco Casas-Maldonado⁶, Laura Caballero-Ballesteros⁵, María Sánchez-Palop⁶, Dolores Pérez-Tejero⁷, Alejandro Segado⁷, Jose Calvo-Bonachera⁸, Bárbara Hernández-Sierra⁸, Adolfo Doménech⁹, Macarena Arroyo-Varela⁹, Francisco González-Vargas¹⁰, Juan J. Cruz-Rueda¹⁰

 Unidad Médico-Quirúrgica de Enfermedades Respiratorias, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/Universidad de Sevilla, Seville, Spain, 2 CIBER de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain, 3 Hospital Puerta del Mar, Cádiz, Spain, 4 Hospital Juan Ramón Jiménez, Huelva, Spain, 5 Hospital Universitario Reina Sofía, Córdoba, Spain, 6 Hospital Universitario San Cecilio, Granada, Spain, 7 Hospital Infanta Margarita, Cabra, Córdoba, Spain, 8 Hospital Torrecárdenas, Almería, Spain, 9 Hospital Regional Universitario de Málaga, Málaga, Spain, 10 Hospital Universitario Virgen de las Nieves, Granada, Spain

* lcampos@separ.es

Abstract

Objectives

Previous clinical audits of COPD have provided relevant information about medical intervention in exacerbation admissions. The present study aims to evaluate adherence to current guidelines in COPD through a clinical audit.

Methods

This is a pilot clinical audit performed in hospital outpatient respiratory clinics in Andalusia, Spain (eight provinces with more than 8 million inhabitants), including 9 centers (20% of the public centers in the area) between 2013 and 2014. Cases with an established diagnosis of COPD based on risk factors, clinical symptoms, and a post-bronchodilator FEV₁/FVC ratio of less than 0.70 were deemed eligible. The performance of the outpatient clinics was benchmarked against three guidance documents available at the time of the audit. The appropriateness of the performance was categorized as excellent (>80%), good (60–80%), adequate (40–59%), inadequate (20–39%), and highly inadequate (<20%).

Results

During the audit, 621 clinical records were audited. Adherence to the different guidelines presented a considerable variability among the different participating hospitals, with an excellent or good adherence for symptom recording, MRC or CAT use, smoking status



the authors' adherence to PLOS ONE policies on sharing data and materials. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. evaluation, spirometry, or bronchodilation therapy. The most outstanding areas for improvement were the use of the BODE index, the monitoring of treatments, the determination of alpha1-antitrypsin, the performance of exercise testing, and vaccination recommendations.

Conclusions

The present study reflects the situation of clinical care for COPD patients in specialized secondary care outpatient clinics. Adherence to clinical guidelines shows considerable variability in outpatient clinics managing COPD patients, and some aspects of the clinical care can clearly be improved.

Introduction

Clinical audits have emerged as an overarching tool to measure the adequacy of clinical practice in a given health care setting and temporal context. Far from being simply a collection of information, clinical audits have shown their role in highlighting the gaps between the health care that patients receive and the recommended practices [1]. Accordingly, audits and feedback are being used to improve health care across all areas and to evaluate clinical care for different diseases and in different health care settings [2].

COPD is a disease of the first magnitude in terms of morbidity and mortality $[\underline{3}]$, with a wide prevalence in the population $[\underline{4}]$ and a considerable impact on the health system $[\underline{5}, \underline{6}]$. It follows that health care of the patient with COPD should employ the highest quality standards for its potential impact on the lives of patients. Accordingly, COPD is one of the key diseases in which clinical audits have a special relevance.

Until the last few years, clinical audits for COPD were not very common. The United Kingdom [7], recently followed by Spain [8, 9], has been leading the audit process in COPD over the last several decades. Additionally, several countries have recently started their own audit projects [10–12], and very recently, a European Clinical COPD Audit was carried out in 13 European countries [13, 14]. These audits have provided relevant information about medical intervention in a hospital ward for patients admitted with COPD exacerbation [14], the resources available [15], and the interrelationship between resources and clinical practice [16]. However, there is virtually no experience in auditing COPD patients' care in an outpatient facility, with only one preliminary attempt recently carried out in Italy [17].

The information regarding how COPD patients are treated in outpatient settings would provide very relevant information on the process of care and might show important areas of improvement that could complete the picture obtained in the hospital setting. Based on our previous audit experiences, we have developed a clinical audit for COPD patients in the outpatient setting [18]. In the present manuscript, we describe the main results of a clinical audit in terms of guideline adherence in outpatient clinics of specialized secondary care centers. The results of this audit will serve to set the scenario for an improvement in health care for COPD patients.

Methodology

This is a pilot clinical audit performed in hospital outpatient respiratory clinics in the region of Andalusia, Spain (eight provinces with more than 8 million inhabitants). The methodology has been extensively reported previously [18]. Briefly, 20% of centers in the area were invited to

participate in this audit. The selection of centers was based on participation in previous audits and was voluntary. Participating centers were categorized as regional hospitals (Highly ranked hospitals offering all medical specialties and providing care to the entire regional population), specialty hospitals (Hospitals offering a higher number of medical specialties than district hospitals and providing care to the entire province in which they are located), and district hospitals (Hospitals offering basic medical specialties and providing care to the population of the town in which they are located, including close villages located at a maximum of 1 hour away). As a pilot study, randomization was not performed, and, therefore, we did not aim to achieve a representative sampling.

Cases with an established diagnosis of COPD based on risk factors, clinical symptoms, and a post-bronchodilator FEV_1/FVC ratio of less than 0.70 were deemed eligible [19]. Because our goal was to assess the usefulness of formally scheduled regular follow-up visits, only cases with at least 1 year of follow-up were included in the audit. Patients who underwent a first diagnostic visit or presented with an exacerbation were not eligible. Similarly, subjects with significant respiratory comorbidities that could have an impact on the COPD treatment approach were excluded at the local investigator's discretion.

Based on our previous experience, we estimated that 80 cases per center would be required for this pilot study. The 1-year audit took place between October 2013 and September 2014. Recruitment was performed in 4 three-month periods (October–December 2013, January– March 2014, April–June 2014, and July–September 2014). At the beginning of each period, investigators were instructed to identify consecutive COPD cases at the beginning of each trimester until the desired sample size of 20 per trimester was reached.

The performance of the outpatient clinics was benchmarked against clinical guidelines available at the time of the audit. Throughout the study period, two guidelines—GOLD 2013 [19] and the Spanish National Guideline for COPD (GesEPOC) [20]–were widely and uniformly used in Spain. We therefore carefully reviewed the two guidelines to extract the main statements for the purpose of benchmarking the audited performances. We also considered the 2009 Spain Health-Care Quality Standards in COPD, which were active at the time of the audit [21]. The appropriateness of the outpatient performances in relation to such statements was categorized as excellent (>80%), good (60–80%), adequate (40–59%), inadequate (20–39%), and highly inadequate (<20%).

The audit was approved by the Ethics Committee of the Hospital Universitario Virgen del Rocío (code: 2013PI/201). Clinical records were anonymized in the database by assigning a numerical code through an algorithm. No personal information was registered that could be used directly or indirectly to identify an individual. The relationship between the audit code and the clinical history number was kept locally and was the local investigator's responsibility. Because of the retrospective nature of the study, the anonymization of data, and the lack of active research interventions, the need for informed consent was waived. The Ethics Committee was aware of this circumstance, clearly explained in the protocol, and approved this procedure.

Statistical Analysis

All computations were performed using the Statistical Package for Social Sciences, version 20.0 (SPSS; IBM Corporation, Somers, NY, USA). Clinical variables are presented as the mean and standard deviations or absolute and relative frequencies, as appropriate. The variability was expressed by using the inter-hospital range (IHR), which represents the highest and lowest mean value from the participant centers. The significance of this variability was explored by the chi-squared test or ANOVA between the different participant centers. The alpha error was set at 0.05.

Results

During the audit, 621 clinical records from 9 hospitals were audited. The characteristics of the participant centers are summarized in <u>table 1</u>. The majority were big university hospitals with beds ranging from 220 to 1367.

The characteristics of the audited cases are summarized in <u>table 2</u>. Cases were typically male, in the seventh decade of life, with a considerable proportion of current smokers, a homogeneous distribution of comorbidities, and moderate to severe lung function impairment.

Adherence to recommendations regarding clinical assessment, phenotypes and treatment monitoring is summarized in tables <u>3–5</u>. Some items were not recorded because they were not included in the audit as per the scientific committee decision. Fulfillment of the different criteria was variable. Even in items with an excellent adherence to the guidelines, the variability of the results, as measured by the IHR range, was considerable. Although most of the items in Q1 and Q2 from <u>table 2</u> were independently evaluated in most patients, the fulfillment of all the items occurred in a lower proportion of cases. Using CAT and MRC scores and recording tobacco use were relatively high, the former with good adherence and the latter with excellent adherence, also showing an important variability. Unfortunately, the GesEPOC recommendations on disease phenotypes and the GOLD patient stratification were followed with an inadequate adherence. Additionally, the GesEPOC recommendation to use the BODE or BODEx indexes to evaluate severity had a highly inadequate adherence. Regarding treatment monitoring (Q9 from <u>table 2</u>), guideline adherence varied depending on the item. However, the adherence was highly inadequate when considering all four items together for one patient.

Adherence to recommendations on the diagnostic tests is summarized in table 6. The performance of a spirometry in the audited visit showed good adherence but with considerable variability. Similarly, the performance of this spirometry after a bronchodilator presented an adequate adherence with very high variability. The indication for a CT scan followed the recommendations in all cases except for 9, in which the indication was not specified in the clinical record. The indications for a CT scan to exclude other associated diseases included suspected neoplasm in 32 (56.1%) cases, lung infiltrates in 8 (14.0%) cases, lung transplant evaluation in 5 (8.8%) cases, hemoptysis in 4 (7.0%) cases, pleural diseases in 4 (7.0%) cases, and other in 4 (7.0%) cases. Determination of serum α 1-antitrypsin concentrations was clearly inadequate. Monitoring of physical activity had good adherence. However, the performance of a cardiopulmonary test was clearly highly inadequate. In addition, the six-minute walking test was conducted in 110 cases (17.7%) with IHR of 0–82.5%.

Adherence to recommendations regarding treatment is summarized in tables 7 and 8. Antitobacco recommendations for active smokers presented good adherence, but with considerable variability. However, adherence to the recommendation for other non-pharmacological treatment was inadequate for the influenza vaccination and exercise recommendations and lower for the pneumococcal vaccination. The type of pneumococcal vaccination was not recorded as per the scientific committee decision. Other treatments, such as long-term oxygen therapy, were not evaluated because the audit did not record blood gas values to assess the correct indication.

As expected, long-acting bronchodilators (LABD) are widely used in COPD. However, patients using one LABD who had persistent dyspnea received two LABDs in only 32.4% of cases, suggesting a need for improvement in treatment selection. The number of patients with indications for ICS use (severe and very severe disease with frequent exacerbations) was 42 (6.7%), of which all but two were already receiving ICS. Altogether, 62.5% of all cases used ICS. Phosphodiesterase-4 inhibitors were not frequently used even for those patients with indications.

Centre	Туре	University hospital	Catchment population	Total number of beds
Centre 1	Specialty hospital	Yes	325,723	699
Centre 2	Specialty hospital	Yes	221,436	770
Centre 3	District hospital	No	200,000	220
Centre 4	Regional hospital	Yes	461,555	1197
Centre 5	Regional hospital	Yes	442,523	1200
Centre 6	Regional hospital	Yes	296,868	600
Centre 7	Regional hospital	Yes	270,000	448
Centre 8	Regional hospital	Yes	370,000	1100
Centre 9	Regional hospital	Yes	554,981	1367

Table 1. Characteristics of the participant centers.

doi:10.1371/journal.pone.0151896.t001

Discussion

The present study is the first clinical audit on COPD outpatient clinic performance and provides a comprehensive picture of clinical care for COPD patients in this setting. Although it is a non-randomized pilot study, the information presented here reflects the real-life situation of clinical care in the outpatient setting. Adherence to clinical guidelines varies considerably in outpatient clinics managing COPD patients, with strengths and weaknesses in clinical care.

Clinical audits are conceived as tool to summarize the clinical performance of health care over a specified period of time and are aimed at providing information to health professionals to allow them to assess and adjust their performance [2]. In practical terms, health professionals can receive feedback on their performance based on data derived from their routine practice. While it seems intuitive that health care professionals would be prompted to modify their clinical practice if they received feedback that was inconsistent with that of their peers or accepted guidelines, the importance of this change may not be extremely relevant and is influenced by several factors [9]. Accordingly, audits should be followed not only by feedback but also by an implementation program [23].

Table 2. Clinical characteristics	s of the audited cases (n = 621).
-----------------------------------	-----------------------------------

	Average*	Inter-hospital range	P-Value [†]
Age (years)	68.3 (9.8)	64.7–69.7	NS
Male gender (n)	527 (84.9)	51.7–94.8	< 0.001
Current smokers (n)	142 (22.9)	13.8–37.5	< 0.001
Tobacco history (pack-year)	54.7 (30.5)	42.5–66.6	< 0.001
Comorbidities (Charlson)	2.15 (1.5)	1.8–2.4	NS
Psychiatric comorbidities (n)	126 (20.3)	12.3–24.1	NS
Cardiovascular comorbidities (n)	163 (26.2)	18.2–37.5	NS
Previous neoplasms (n)	92 (14.8)	8.6–21.0	NS
Time from diagnosis (years)	5.5 (5.9)	1.06–6.9	0.033
Previous hospitalizations (n)	0.9 (1.6)	0.1–1.3	< 0.001
Body mass index (kg/m ²)	28.2 (5.3)	26.0–29.6	0.009
FVC (%)	74.6 (20.7)	63.7–98.4	< 0.001
FEV1 (%)	51.9 (19.7)	42.7–59.1	0.001

* Average value expressed as the mean (standard deviation) or absolute (relative) frequency depending on the nature of the variable.

[†] Calculated for the variability between centers using ANOVA or Chi-square, depending on the nature of the variable.

Table 3. Recommendations regarding the clinical assessments.

PLOS ONE

Recommendation	Average value*	Inter-hospital range	P value [†]
Q1. GOLD 2013. COPD assessment must consider the following aspects of the disease:			
Current level of patient's symptoms: dyspnea recorded	560 (90.2)	69.1–100	< 0.001
Severity of the spirometric abnormality	510 (82.1)	52.5-100	< 0.001
Exacerbation risk	556 (89.5)	57.5–98.7	< 0.001
Presence of comorbidities	Not recorded		
All three recorded items	437 (70.4)	30.0–95.0	< 0.001
Q2. GOLD 2013. At each visit, inquire about changes in symptoms since the last visit, including:			
Cough and sputum	551 (88.7)	62.5–100	< 0.001
Breathlessness	560 (90.2)	69.1–100	< 0.001
• Fatigue	Not recorded		
Activity limitation	403 (64.9)	24.7–100	< 0.001
Sleep disturbances	Not recorded		
All three recorded items	362 (58.3)	22.2-100	< 0.001
Q3. GOLD 2013. GOLD recommends the use of:			
• The Modified British Medical Research Council (mMRC) questionnaire, or	489 (78.7)	33.3–100	< 0.001
The COPD Assessment Test (CAT).	108 (17.4)	0–93.8	< 0.001
Any of the two	489 (78.7)	33.3–100	< 0.001

* Average value expressed as the mean (standard deviation) or absolute (relative) frequency depending on the nature of the variable.

[†] Calculated for the variability between centers using ANOVA or Chi-square, depending on the nature of the variable. Percentages refer to the whole population (n = 621) unless otherwise indicated. GOLD 2013: Global Initiative for Obstructive Lung Disease 2013 [19]; SEPAR 2009: SEPAR Health-Care Quality Standards 2009 [21]; GesEPOC 2012: Spanish National Guideline for COPD [22].

doi:10.1371/journal.pone.0151896.t003

Although clinical performance has been exhaustively studied during COPD admissions, the situation in outpatient clinics has only been evaluated in one preliminary report in Italy [17]. That study analyzed clinical histories with a limited number of variables and did not analyzed the variability of clinical care. Other studies have evaluated the rates of adherence to GOLD

Table 4. Recommendations regarding the clinical phenotypes and multidimensional evaluation.

Recommendation	Average value*	Inter-hospital range	P value [†]
Q4. GesEPOC. The clinical phenotype of COPD should be established in all patients:			
Cases with GesEPOC phenotype established after the visit	294 (47.3)	8.6–95.0	< 0.001
Q5. The impact of COPD on an individual patient combines the symptomatic assessment with the patient's spirometric classification and/or risk of exacerbations			
Cases with GOLD classification established	224 (36.1)	3.4–100	< 0.001
Cases with either GOLD or GesEPOC classifications established	328 (52.8)	10.3–90.0	< 0.001
Cases with both GOLD and GesEPOC classifications established	95 (15.3)	1.2-49.4	< 0.001
Q6. GesEPOC. The severity of a patient with COPD is determined by the BODE index.	60 (9.7)	0–32.5	< 0.001
Q7. GesEPOC. Alternatively, the BODEx index can be used for patients with mild-to-moderate COPD.			
Use of the BODEx index in the cohort	145 (23.3)	0–96.3	< 0.001
 Use of the BODEx index in those with post-bronchodilator FEV1 > 50% 	24 (15.9)	0–100	< 0.001

* Average value expressed as the mean (standard deviation) or absolute (relative) frequency depending on the nature of the variable.

[†] Calculated for the variability between centers using ANOVA or Chi-square, depending on the nature of the variable. Percentages refer to the whole population (n = 621) unless otherwise indicated. GOLD 2013: Global Initiative for Obstructive Lung Disease 2013 [19]; SEPAR 2009: SEPAR Health-Care Quality Standards 2009 [21]; GesEPOC 2012: Spanish National Guideline for COPD [22].

Table 5. Recommendations regarding treatment monitoring.

Recommendation	Average value*	Inter-hospital range	P value [†]
Q8. GOLD 2013. At each visit, determine current smoking status and smoke exposure:			
Smoking status verified	591 (95.2)	72.4–100	< 0.001
Pack-years calculated	558 (89.9)	68.8–100	< 0.001
Both items evaluated	533 (85.8)	62.1–100	< 0.001
Q9. GOLD 2013 recommends monitoring of:			
 Dosages of various medications: ICS dose recorded (n = 397) 	372 (93.7)	50–100	< 0.001
Adherence to the regimen	327 (52.7)	3.4–92.6	< 0.001
Inhaler technique	Not recorded		
Effectiveness of the current regime at controlling symptoms: dyspnea recorded	560 (90.2)	69.1–100	< 0.001
Side effects of treatment	145 (23.3)	4.9–66.7	< 0.001
All four items recorded	93 (15.0)	0–44.4	< 0.001

* Average value expressed as the mean (standard deviation) or absolute (relative) frequency depending on the nature of the variable.

[†] Calculated for the variability between centers using ANOVA or Chi-square, depending on the nature of the variable. Percentages refer to the whole population (n = 621) unless otherwise indicated. GOLD 2013: Global Initiative for Obstructive Lung Disease 2013 [19]; SEPAR 2009: SEPAR Health-Care Quality Standards 2009 [21]; GesEPOC 2012: Spanish National Guideline for COPD [22].

doi:10.1371/journal.pone.0151896.t005

Table 6. Recommendations regarding the diagnostic tests.

Recommendation	Average value*	Inter-hospital range	P value [†]
Q10. GOLD 2013. Decline in lung function is best tracked by spirometry performed at least once a year	497 (80.0)	30–100	< 0.001
Q11. GOLD 2013. Spirometry should be performed after the administration of an adequate dose of a short-acting inhaled bronchodilator to minimize variability	352 (56.7)	0–94.9	< 0.001
Q12. GOLD 2013. A chest X-ray is valuable in excluding alternative diagnoses and establishing the presence of significant comorbidities	426 (68.6)	19.2–100	< 0.001
Q13. GOLD 2013. Computed tomography (CT) of the chest is not routinely recommended			
Cases with CT scan performed	96 (15.5)	2.5-37.5	< 0.001
Q14. GesEPOC. Indications for a chest CT scan are $(n = 96)$:			
Diagnosis of bronchiectasis	14 (14.6)	0–33.3	0.021
Exclusion of other associated lung diseases	57 (59.4)	0–100	0.001
Diagnosis and evaluation of emphysema	16 (16.7)	0–100	0.002
Indication not available	9 (9.4)	0–46.7	< 0.001
Q15. SEPAR 2009. Serum α 1-antitrypsin concentrations should be determined for all COPD patients at least once			
 Serum α1-antitrypsin concentrations evaluated at some time point 	190 (30.6)	2.5-62.3	< 0.001
Q16. GOLD 2013. Monitoring of physical activity may be more prognostically relevant prognosis than evaluating exercise capacity	403 (64.9)	24.7–100	< 0.001
Q17. SEPAR 2009. Patients with severe or very severe COPD should undergo the following test at least one time: maximal exercise test ($n = 174$)	1 (0.6)	0–50	< 0.001

* Average value expressed as the mean (standard deviation) or absolute (relative) frequency depending on the nature of the variable.

[†] Calculated for the variability between centers using ANOVA or Chi-square, depending on the nature of the variable. Percentages refer to the whole population (n = 621) unless otherwise indicated. GOLD 2013: Global Initiative for Obstructive Lung Disease 2013 [19]; SEPAR 2009: SEPAR Health-Care Quality Standards 2009 [21]; GesEPOC 2012: Spanish National Guideline for COPD [22].



Table 7. Recommendations regarding non-pharmacological treatment.

Recommendation	Average value*	Inter-hospital range	P value [†]
Q18. GesEPOC. It is recommended to offer all smokers with COPD advice to quit supported by medical/ psychological counseling			
 Current smokers receiving anti-tobacco recommendations (n = 142) 	107 (75.4)	20–95.8	< 0.001
Q19. SEPAR 2009. Influenza vaccination should be recommended for all COPD patients	269 (43.3)	2.5–93.8	< 0.001
Q20. SEPAR 2009. Pneumococcal vaccination should be offered to patients with severe COPD and to all COPD patients aged 65 years and older			
 Use of pneumococcal vaccine among those with indication (n = 463) 	96 (20.7)	0–43.8	< 0.001
Q21. SEPAR 2009. Regular exercise should be recommended for all COPD patients	276 (44.4)	2.5-88.9	< 0.001

* Average value expressed as the mean (standard deviation) or absolute (relative) frequency depending on the nature of the variable.

[†] Calculated for the variability between centers using ANOVA or Chi-square, depending on the nature of the variable. Percentages refer to the whole population (n = 621) unless otherwise indicated. GOLD 2013: Global Initiative for Obstructive Lung Disease 2013 [19]; SEPAR 2009: SEPAR Health-Care Quality Standards 2009 [21]; GesEPOC 2012: Spanish National Guideline for COPD [22].

doi:10.1371/journal.pone.0151896.t007

Table 8. Recommendations regarding pharmacological treatment.

Recommendation	Average value*	Inter-hospital range	P value [†]
Q22. GesEPOC. Long-acting bronchodilators should be used as first-line treatment in all patients with chronic symptoms	590 (95.0)	86.4–100	0.001
Q23. GesEPOC. Combinations of long-acting bronchodilators should be considered for COPD patients with persistent symptoms despite monotherapy			
Use of long-acting bronchodilator combinations	453 (72.9)	56.8-84.0	0.006
 Use of long-acting bronchodilator combinations among those with indication (n = 102) 	33 (32.4)	0–47.6	NS
Q24. GOLD 2013. Long-term treatment with inhaled corticosteroids is recommended for patients with severe and very severe COPD and frequent exacerbations not adequately controlled by long-acting bronchodilators			
Use of treatment with inhaled corticosteroids	388 (62.5)	52.1-82.7	< 0.001
Q25. GOLD 2013. Long-term monotherapy with inhaled corticosteroids is not recommended in COPD			
Use of monotherapy with inhaled corticosteroids	1 (0.2)	0–1.3	NS
Q26. GOLD 2013. The use of antibiotics (other than for treating infectious exacerbations of COPD and other bacterial infections) is not currently indicated			
Cases not using antibiotics	602 (96.9)	93.8–100	< 0.001
Q27. GOLD 2013. There is some evidence that treatment with mucolytics (such as carbocysteine and N- acetyl-cysteine) may reduce exacerbations in COPD patients not receiving inhaled corticosteroids			
Use of mucolytics	53 (8.5)	0–19.8	< 0.001
 Use of mucolytics among those not receiving inhaled steroids (n = 174) 	11 (6.3)	0-22.2	0.023
Q28. GOLD 2013. The phosphodiesterase-4 inhibitor, roflumilast, may also be used in patients with chronic bronchitis and severe and very severe COPD, and frequent exacerbations not adequately controlled by long-acting bronchodilators			
Use of phosphodiesterase-4 inhibitors	76 (12.2)	6.2-21.0	NS
 Use of phosphodiesterase-4 inhibitors among those with indication (n = 31) 	12 (38.7)	0–100	NS

* Average value expressed as the mean (standard deviation) or absolute (relative) frequency depending on the nature of the variable.

[†] Calculated for the variability between centers using ANOVA or Chi-square, depending on the nature of the variable. Percentages refer to the whole population (n = 621) unless otherwise indicated. GOLD 2013: Global Initiative for Obstructive Lung Disease 2013 [19]; SEPAR 2009: SEPAR Health-Care Quality Standards 2009 [21]; GesEPOC 2012: Spanish National Guideline for COPD [22].

guidelines for COPD treatment among pulmonologists, but exclusively focusing on pharmacological treatment [24]. In the present study, we have done a comprehensive evaluation of the performance of one typical follow-up clinical visit, and, thus, the degree to which the doctor in charge follows and records the recommended information, highlighting the variability of the performance.

There are two important notes to consider regarding clinical audits. The first is related to the importance of adhering to clinical guidelines. Guidelines are general recommendations on how to provide clinical care for a particular condition. However, it is important to remember that these recommendations are not always evidence-based and that the clinical presentation of diseases is normally variable. It is not surprising to find some type of deviation from the actual recommendations for a given condition. However, the adequate degree of this deviation has not been quantified. The second is that, as a retrospective study, an audit can only evaluate the information that the staff has actually provided in writing in the clinical history. Therefore, evaluations conducted that have not been noted in the history appear as not completed in the audit. For instance, a physician may have checked the inhalation technique but did not write it down in the history. In this regard, it is important to highlight the necessity of noting all of the clinical actions and the consequences they may have for clinical care.

In addition to the information provided, this pilot study has also served as a clinical experience to improve the audit methodology for future audits for COPD in this clinical setting. Accordingly, several limitations should be considered. First, randomization would improve the representativeness of the sample. Second, this audit focused on a cross-sectional evaluation of one particular clinical visit. However, there are some items that should be evaluated with wider temporal limits. For instance, spirometry was not performed in all cases, but it is possible that the spirometry was performed in other recent visits. Third, because this was a pilot study, some of the recorded items recommended by the guidelines were not evaluated in the interest of simplifying the protocol, e.g., sleep disturbances, fatigue or blood gas results. Therefore, future audits should carefully select all of the recommendations in the guidelines. Fourth, the present study was not powered to evaluate the impact of the centers or the physicians' expertise on the results. Future clinical audits should evaluate the importance of resources and doctors' expertise on clinical outcomes. Finally, it is important to evaluate the impact of guideline adherence on clinically relevant outcomes. Accordingly, a follow-up of patients is needed to evaluate exacerbation rates and survival.

In 2012, the Spanish COPD guideline (GesEPOC) was released with a novel approach to COPD management [22]. After three years, this seems to be the right time to test the adherence to this guideline. Despite the admittedly important contribution of GesEPOC to patient evaluation [6], it seems that the implementation of this guideline is far from optimal. The two main aspects of the guideline, the categorization of patients according to clinical phenotypes and the severity evaluation according to multidimensional BODE or BODEx indexes, are not extremely common in our area. The BODE index is a good quality-of-life marker within the entire spectrum of COPD severity [25, 26]. However, one obvious limitation is the performance of the six-minute walking test needed for the BODE index, and in our area this is rarely performed; the Italian audit noted previously had a similar finding [17]. However, the BODEx index does not require any extra tests [27] and it is equally infrequently used.

Alpha-1 antitrypsin deficiency in COPD patients is another pending issue [28]. Despite its low prevalence [29], the clinical implications of this genetic form of COPD, the possibility of a specific treatment and the accessible noninvasive diagnostic procedure make it one aspect that should be generalized. Accordingly, indications for active case searches have recently been updated in Spain [30]. However, there is disagreement about the determination of this protein in our area. Previous experiences indicate that is possible to screen for this disease [31].

Notably, some initiatives are being discussed including new screening tools, and there is a debate on the appropriateness of including it in newborn screening $[\underline{32}]$.

The use of chest radiological techniques in COPD is a current source of debate. It is now accepted that chest radiography is of no value in the diagnosis or follow-up of COPD, except for excluding alternative diagnoses and establishing the presence of significant comorbidities. In our cohort, the most common comorbidity detected in a CT scan was lung neoplasms. Of note, recent studies have investigated the role of CT scans in the early detection of lung cancer [33, 34]. In Spain, as in the rest of Europe, the experience confirms the feasibility and efficacy of lung cancer screening using low-dose CT scans [35]. However, current guidelines are not yet clear enough to recommend annual CT scan screening for COPD patients.

The most followed recommendation on non-pharmacological treatment was anti-tobacco recommendations for active smokers. Despite not being optimal, the adherence to the recommendation to quit smoking was higher than previously reported [17]. However, the vaccination recommendation showed worse adherence, especially with the pneumococcal vaccine. In this regard, it is important to highlight the potential of the vaccination to reduce invasive pneumococcal disease [36].

The pharmaceutical treatment recommendations should be followed with caution. These are results from a clinical audit and not a randomized trial, and they reflect real life prescriptions. Currently, there is an important debate on the use of ICS [37]. In Spain, a recent consensus has provided information on the correct use of inhaled corticosteroids in COPD [38]. However, ICSs are still considered to be overused and the situation in our area is not very different from that in other countries [39]. This opens the debate on ICS withdrawal [40, 41]. Interestingly, by the time this audit was performed, there was no clear recommendation on ICS withdrawal in the guideless that we could benchmark.

In conclusion, the present study reflects the situation of clinical care for COPD patients in specialized secondary care outpatient clinics. Adherence to clinical guidelines varies considerably in outpatient clinics managing COPD patients. Despite this variability, some aspects of clinical care can clearly be improved. With this pilot experiment, a nationwide clinical audit is needed to overcome some of the limitations of the pilot audit, which would include the knowledge gained. It is important that this be followed by feedback and an implementation strategy that allows us to finally improve the clinical care being provided.

Acknowledgments

The authors are grateful to all of the project researchers for their time and dedication to this project.

Author Contributions

Conceived and designed the experiments: JLLC MAA CCA. Performed the experiments: CCA FRV RAG AHM RIAPG FGG FCM LCB MSP DPT AS JCB BHS AD MAV FGV JJCR. Analyzed the data: JLLC. Wrote the paper: JLLC MAA CCA.

References

- Ivers NM, Grimshaw JM, Jamtvedt G, Flottorp S, O'Brien MA, French SD, et al. Growing literature, stagnant science? Systematic review, meta-regression and cumulative analysis of audit and feedback interventions in health care. Journal of general internal medicine. 2014; 29(11):1534–41. doi: <u>10.1007/</u> s11606-014-2913-y PMID: 24965281; PubMed Central PMCID: PMC4238192.
- Flottorp SA. Using audit and feedback to health professionals to improve the quality and safety of health care. Copenhagen European Observatory on Health Systems and Policies,: WHO. regional office for Europe; 2010. IX, 42 p. p.

- Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015; 385(9963):117–71. Epub 2014/12/23. doi: 10.1016/s0140-6736(14)61682-2 PMID: 25530442; PubMed Central PMCID: PMCPMC4340604.
- 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 (9589):741–50. doi: <u>10.1016/S0140-6736(07)61377-4</u> PMID: <u>17765523</u>.
- Montes de Oca M, Lopez Varela MV, Acuna A, Schiavi E, Rey MA, Jardim J, et al. ALAT-2014 Chronic Obstructive Pulmonary Disease (COPD) Clinical Practice Guidelines: Questions and Answers. Archivos de bronconeumologia. 2015; 51(8):403–16. Epub 2015/01/19. doi: <u>10.1016/j.arbres.2014.11.017</u> PMID: <u>25596991</u>.
- Miravitlles M. What was the impact of the Spanish COPD guidelines (GesEPOC) and how can they be improved? Archivos de bronconeumologia. 2016; 52(1):1–2. Epub 2015/06/01. doi: <u>10.1016/j.arbres.</u> <u>2015.04.001</u> PMID: <u>26026686</u>.
- Roberts CM, Ryland I, Lowe D, Kelly Y, Bucknall CE, Pearson MG, et al. Audit of acute admissions of COPD: standards of care and management in the hospital setting. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology. 2001; 17(3):343–9. PMID: <u>11405509</u>.
- Pozo-Rodriguez F, Alvarez CJ, Castro-Acosta A, Melero Moreno C, Capelastegui A, Esteban C, et al. [Clinical audit of patients admitted to hospital in Spain due to exacerbation of COPD (AUDIPOC study): method and organisation]. Archivos de bronconeumologia. 2010; 46(7):349–57. doi: <u>10.1016/j.arbres.</u> <u>2010.04.004</u> PMID: <u>20554103</u>.
- Lopez-Campos JL, Asensio-Cruz MI, Castro-Acosta A, Calero C, Pozo-Rodriguez F, Audipoc, et al. Results from an audit feedback strategy for chronic obstructive pulmonary disease in-hospital care: a joint analysis from the AUDIPOC and European COPD audit studies. PloS one. 2014; 9(10):e110394. doi: 10.1371/journal.pone.0110394 PMID: 25333953; PubMed Central PMCID: PMC4198296.
- Liaaen ED, Henriksen AH, Stenfors N. A Scandinavian audit of hospitalizations for chronic obstructive pulmonary disease. Respiratory medicine. 2010; 104(9):1304–9. doi: <u>10.1016/j.rmed.2010.03.007</u> PMID: <u>20363605</u>.
- Agabiti N, Belleudi V, Davoli M, Forastiere F, Faustini A, Pistelli R, et al. Profiling hospital performance to monitor the quality of care: the case of COPD. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology. 2010; 35(5):1031–8. doi: <u>10.1183/09031936</u>. 00056209 PMID: <u>19840969</u>.
- 12. Pretto JJ, McDonald VM, Wark PA, Hensley MJ. Multicentre audit of inpatient management of acute exacerbations of chronic obstructive pulmonary disease: comparison with clinical guidelines. Internal medicine journal. 2012; 42(4):380–7. doi: 10.1111/j.1445-5994.2011.02475.x PMID: 21395962.
- Lopez-Campos JL, Hartl S, Pozo-Rodriguez F, Roberts CM, European CAt. European COPD Audit: design, organisation of work and methodology. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology. 2013; 41(2):270–6. Epub 2012/05/19. doi: <u>10.</u> <u>1183/09031936.00021812</u> PMID: <u>22599361</u>.
- Roberts CM, Lopez-Campos JL, Pozo-Rodriguez F, Hartl S, European CAt. European hospital adherence to GOLD recommendations for chronic obstructive pulmonary disease (COPD) exacerbation admissions. Thorax. 2013; 68(12):1169–71. Epub 2013/06/05. doi: <u>10.1136/thoraxjnl-2013-203465</u> PMID: 23729193.
- Lopez-Campos JL, Hartl S, Pozo-Rodriguez F, Roberts CM, European CAt. Variability of hospital resources for acute care of COPD patients: the European COPD Audit. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology. 2014; 43(3):754–62. doi: 10.1183/09031936.00074413 PMID: 23988775.
- Pozo-Rodriguez F, Castro-Acosta A, Alvarez CJ, Lopez-Campos JL, Forte A, Lopez-Quilez A, et al. Determinants of between-hospital variations in outcomes for patients admitted with COPD exacerbations: findings from a nationwide clinical audit (AUDIPOC) in Spain. International journal of clinical practice. 2015; 69(9):938–47. Epub 2015/02/05. doi: 10.1111/ijcp.12601 PMID: 25651319.
- Nardini S, Cicchitto G, De Benedetto F, Donner CF, Polverino M, Sanguinetti CM, et al. Audit on the appropriateness of integrated COPD management: the "ALT-BPCO" project. Multidisciplinary respiratory medicine. 2014; 9(1):40. Epub 2014/08/07. doi: <u>10.1186/2049-6958-9-40</u> PMID: <u>25097757</u>; PubMed Central PMCID: PMCPMC4122534.
- Lopez-Campos JL, Abad Arranz M, Calero Acuna C, Romero Valero F, Ayerbe Garcia R, Hidalgo Molina A, et al. Clinical Audits in Outpatient Clinics for Chronic Obstructive Pulmonary Disease: Methodological Considerations and Workflow. PloS one. 2015; 10(11):e0141856. Epub 2015/11/07. doi: <u>10.</u> <u>1371/journal.pone.0141856</u> PMID: <u>26544556</u>; PubMed Central PMCID: PMCPmc4636163.

- Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. American journal of respiratory and critical care medicine. 2013; 187(4):347–65. doi: <u>10.1164/</u> rccm.201204-0596PP PMID: <u>22878278</u>.
- Miravitlles M, Soler-Cataluna JJ, Calle M, Molina J, Almagro P, Quintano JA, et al. Spanish guideline for COPD (GesEPOC). Update 2014. Archivos de bronconeumologia. 2014; 50 Suppl 1:1–16. Epub 2014/02/11. doi: 10.1016/S0300-2896(14)70070-5 PMID: 24507959.
- Soler-Cataluna JJ, Calle M, Cosio BG, Marin JM, Monso E, Alfageme I. [Health-care quality standards in chronic obstructive pulmonary disease]. Archivos de bronconeumologia. 2009; 45(4):196–203. Epub 2009/03/24. doi: <u>10.1016/j.arbres.2008.05.008</u> PMID: <u>19304362</u>.
- Miravitles M, Soler-Cataluna JJ, Calle M, Molina J, Almagro P, Quintano JA, et al. Spanish COPD Guidelines (GesEPOC): pharmacological treatment of stable COPD. Spanish Society of Pulmonology and Thoracic Surgery. Archivos de bronconeumologia. 2012; 48(7):247–57. doi: <u>10.1016/j.arbres.</u> 2012.04.001 PMID: 22561012.
- 23. Stephenson M, McArthur A, Giles K, Lockwood C, Aromataris E, Pearson A. Prevention of falls in acute hospital settings: a multi-site audit and best practice implementation project. International journal for quality in health care: journal of the International Society for Quality in Health Care / ISQua. 2015. Epub 2015/12/19. doi: 10.1093/intqhc/mzv113 PMID: 26678803.
- Asche CV, Leader S, Plauschinat C, Raparla S, Yan M, Ye X, et al. Adherence to current guidelines for chronic obstructive pulmonary disease (COPD) among patients treated with combination of long-acting bronchodilators or inhaled corticosteroids. International journal of chronic obstructive pulmonary disease. 2012; 7:201–9. doi: <u>10.2147/COPD.S25805</u> PMID: <u>22500120</u>; PubMed Central PMCID: PMCPMC3324995.
- Sanchez-Salcedo P, de Torres JP. BODE Index: A Good Quality of Life Marker in Chronic Obstructive Pulmonary Disease Patients. Archivos de bronconeumologia. 2015; 51(7):311–2. Epub 2015/04/26. doi: 10.1016/j.arbres.2015.03.003 PMID: 25910549.
- Nonato NL, Diaz O, Nascimento OA, Dreyse J, Jardim JR, Lisboa C. Behavior of Quality of Life (SGRQ) in COPD Patients According to BODE Scores. Archivos de bronconeumologia. 2015; 51 (7):315–21. Epub 2015/01/28. doi: <u>10.1016/j.arbres.2014.02.017</u> PMID: <u>25622995</u>.
- Soler-Cataluna JJ, Martinez-Garcia MA, Sanchez LS, Tordera MP, Sanchez PR. Severe exacerbations and BODE index: two independent risk factors for death in male COPD patients. Respiratory medicine. 2009; 103(5):692–9. Epub 2009/01/10. doi: 10.1016/j.rmed.2008.12.005 PMID: 19131231.
- Sorroche PB, Fernandez Acquier M, Lopez Jove O, Giugno E, Pace S, Livellara B, et al. Alpha-1 Antitrypsin Deficiency in COPD Patients: A Cross-Sectional Study. Archivos de bronconeumologia. 2015; 51(11):539–43. Epub 2015/03/25. doi: 10.1016/j.arbres.2015.01.008 PMID: 25800328.
- Perez-Rubio G, Jimenez-Valverde LO, Ramirez-Venegas A, Camarena A, Sansores RH, Flores-Trujillo F, et al. Prevalence of alpha-1 antitrypsin high-risk variants in Mexican mestizo population and their association with lung function values. Archivos de bronconeumologia. 2015; 51(2):80–5. Epub 2014/ 12/03. doi: 10.1016/j.arbres.2014.09.010 PMID: 25454901.
- Casas F, Blanco I, Martinez MT, Bustamante A, Miravitlles M, Cadenas S, et al. Indications for active case searches and intravenous alpha-1 antitrypsin treatment for patients with alpha-1 antitrypsin deficiency chronic pulmonary obstructive disease: an update. Archivos de bronconeumologia. 2015; 51 (4):185–92. Epub 2014/07/17. doi: 10.1016/j.arbres.2014.05.008 PMID: 25027067.
- Chorostowska-Wynimko J. Targeted screening programmes in COPD: how to identify individuals with alpha1-antitrypsin deficiency. European respiratory review: an official journal of the European Respiratory Society. 2015; 24(135):40–5. doi: <u>10.1183/09059180.00010614</u> PMID: <u>25726553</u>.
- Teckman J, Pardee E, Howell RR, Mannino D, Sharp RR, Brantly M, et al. Appropriateness of newborn screening for alpha1-antitrypsin deficiency. J Pediatr Gastroenterol Nutr. 2014; 58(2):199–203. Epub 2013/10/15. doi: <u>10.1097/mpg.0000000000196</u> PMID: <u>24121147</u>; PubMed Central PMCID: PMCPMC3901803.
- de Koning HJ, Meza R, Plevritis SK, ten Haaf K, Munshi VN, Jeon J, et al. Benefits and harms of computed tomography lung cancer screening strategies: a comparative modeling study for the U.S. Preventive Services Task Force. Annals of internal medicine. 2014; 160(5):311–20. doi: <u>10.7326/M13-2316</u> PMID: <u>24379002</u>; PubMed Central PMCID: PMC4116741.
- National Lung Screening Trial Research T, Church TR, Black WC, Aberle DR, Berg CD, Clingan KL, et al. Results of initial low-dose computed tomographic screening for lung cancer. The New England journal of medicine. 2013; 368(21):1980–91. doi: <u>10.1056/NEJMoa1209120</u> PMID: <u>23697514</u>; PubMed Central PMCID: PMC3762603.
- Sanchez-Salcedo P, Berto J, de-Torres JP, Campo A, Alcaide AB, Bastarrika G, et al. Lung cancer screening: fourteen year experience of the Pamplona early detection program (P-IELCAP). Archivos de

bronconeumologia. 2015; 51(4):169–76. Epub 2015/02/03. doi: <u>10.1016/j.arbres.2014.09.019</u> PMID: <u>25641356</u>.

- von Gottberg A, de Gouveia L, Tempia S, Quan V, Meiring S, von Mollendorf C, et al. Effects of vaccination on invasive pneumococcal disease in South Africa. The New England journal of medicine. 2014; 371(20):1889–99. doi: 10.1056/NEJMoa1401914 PMID: 25386897.
- Marcos PJ, Huerta A, Marquez-Martin E. 2014 GesEPOC and Systemic Steroids in chronic obstructive pulmonary disease (COPD) Exacerbation: An Update. Archivos de bronconeumologia. 2015; 51 (7):360. Epub 2014/07/16. doi: <u>10.1016/j.arbres.2014.05.007</u> PMID: <u>25022785</u>.
- Alcazar Navarrete B, Casanova C, Miravitlles M, de Lucas P, Riesco JA, Rodriguez Gonzalez-Moro JM, et al. "Correct use of inhaled corticosteroids in chronic obstructive pulmonary disease": a consensus document. Archivos de bronconeumologia. 2015; 51(4):193–8. Epub 2014/12/30. doi: <u>10.1016/j.</u> <u>arbres.2014.11.001</u> PMID: <u>25540900</u>.
- Price D, West D, Brusselle G, Gruffydd-Jones K, Jones R, Miravitlles M, et al. Management of COPD in the UK primary-care setting: an analysis of real-life prescribing patterns. International journal of chronic obstructive pulmonary disease. 2014; 9:889–904. doi: <u>10.2147/COPD.S62750</u> PMID: <u>25210450</u>; PubMed Central PMCID: PMC4154894.
- Rodriguez Roisin R, Arismendi E. Inhaled corticosteroids withdrawal in severe patients with chronic obstructive pulmonary disease: a wisdom decision? Archivos de bronconeumologia. 2015; 51(2):57–8. Epub 2015/01/08. doi: <u>10.1016/j.arbres.2014.11.003</u> PMID: <u>25563900</u>.
- Rossi A, Guerriero M, Corrado A, Group OAS. Withdrawal of inhaled corticosteroids can be safe in COPD patients at low risk of exacerbation: a real-life study on the appropriateness of treatment in moderate COPD patients (OPTIMO). Respiratory research. 2014; 15:77. doi: <u>10.1186/1465-9921-15-77</u> PMID: 25005873; PubMed Central PMCID: PMC4122053.