Clinical Audit of COPD Patients Requiring Hospital Admissions in Spain: AUDIPOC Study

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Abstract

Backgrounds: AUDIPOC is a nationwide clinical audit that describes the characteristics, interventions and outcomes of patients admitted to Spanish hospitals because of an exacerbation of chronic obstructive pulmonary disease (ECOPD), assessing the compliance of these parameters with current international guidelines. The present study describes hospital resources, hospital factors related to case recruitment variability, patients’ characteristics, and adherence to guidelines.

Methodology/Principal Findings: An organisational database was completed by all participant hospitals recording resources and organisation. Over an 8-week period 11,564 consecutive ECOPD admissions to 129 Spanish hospitals covering 70% of the Spanish population were prospectively identified. At hospital discharge, 5,178 patients (45% of eligible) were finally included, and thus constituted the audited population. Audited patients were reassessed 90 days after admission for survival and readmission rates. A wide variability was observed in relation to most variables, hospital adherence to guidelines, and readmissions and death. Median inpatient mortality was 5% (across-hospital range 0–35%). Among discharged patients, 37% required readmission (0–62%) and 6.5% died (0–35%). The overall mortality rate was 11.6% (0–50%). Hospital size and complexity and aspects related to hospital COPD awareness were significantly associated with case recruitment. Clinical management most often complied with diagnosis and treatment recommendations but rarely (<50%) addressed guidance on healthy life-styles.

Conclusions/Significance: The AUDIPOC study highlights the large across-hospital variability in resources and organization of hospitals, patient characteristics, process of care, and outcomes. The study also identifies resources and organizational characteristics associated with the admission of COPD cases, as well as aspects of daily clinical care amenable to improvement.

Introduction

The existence of variations in clinical practice and clinical appropriateness has been recognized for decades [1]. Two methods, both developed in the late 1980s, of exploring and dealing with these variations are Evidence-Based Medicine and Clinical Audits [2,3]. These approaches are of particular relevance for the development of evidence-based clinical practice guidelines and the generation of real-life information that may eventually feed-back to the further refinement of guidelines [4].

Chronic Obstructive Pulmonary Disease (COPD) is a major health problem of increasing incidence. COPD is currently the 5th most common cause of death in the world, with the World Health Organization (WHO) predicting that it will rank 4th by 2030 [5]. In Spain, the prevalence of COPD is about 10% of the adult population [6]. Many COPD patients suffer episodes of exacerbation (ECOPD) during the course of their disease...
which impact negatively on their health status and prognosis, and constitute a major portion of the total health care costs of the disease [7].

Two British multicentre COPD clinical audits reported wide variability in interventions and outcomes. [8,9] Other smaller audits have followed [10,11], showing wide variations between different hospitals and between different countries in patient care, which is frequently not consistent with published guidelines. Interestingly, considerable variation in case recruitment and characteristics of cases across hospitals has also been described. This variation has been traditionally associated to temporal and geographical factors [12-14]. However, no studies have been carried out to assess the importance of these variations and the factors associated to them. Identifying organizational or clinical factors potentially associated with the admission to hospital and diagnosis of COPD cases ("case recruitment") may therefore be of interest in efforts to improve the quality of health care afforded to such patients.

This paper presents for the first time the results of the AUDIPOC study, a national clinical audit carried out in Spain that sought to: 1) describe hospital resources and organizational patterns of hospitals in Spain delivering care for patients with ECOPD; 2) analyse the variability among hospitals in COPD case recruitment and associated factors; 3) describe patient characteristics, clinical interventions and outcomes, both at the patient and hospital level; and 4) inform on the adequacy of care as per current clinical practice guidelines.

Methods

Study Design and Ethics

The methods of the AUDIPOC study have been described in detail elsewhere [15]. Briefly, AUDIPOC is a cross-sectional study with prospective case ascertainment of consecutive ECOPD hospital admissions from November 1st to December 31st, 2008, and retrospective data gathering from medical records. Patients were followed-up for 90 days after hospital admission with a view to include in the analysis two clinically relevant outcomes: mortality (in-hospital and out-hospital) and readmissions. The ethics committee of each participating hospital approved the study and the need of blindly evaluating the clinical performance, an ethics committee of each participating hospital approved the study and the need of blindly evaluating the clinical performance, an informed consent was waived.

Participating Hospitals

All 225 acute care hospitals of the public Spanish National Health System listed in the 2008 Registry of the Ministry of Health [16] were invited to participate. Each hospital’s catchment population was estimated from the proportion of the corresponding regional population census (January 1st, 2009) that was assigned for admission to that particular hospital [17].

Ascertainment of Cases

The inclusion of patients in the AUDIPOC study followed a two-step process. First, clinical notes of all cases hospitalized by the Emergency Department (ED) were reviewed daily to identify one or more of 13 clinical conditions compatible with the diagnosis of ECOPD (table 1); these patients were labelled as interim ECOPD cases. Second, these cases were reassessed at hospital discharge against a list of definite inclusion and exclusion criteria (table 1) to identify cases with a clinical diagnosis of ECOPD, that were labelled as definite ECOPD cases [15].

Data Acquisition and Processing

Hospitalization and follow-up data were obtained from clinical records and entered into a web-based application that was monitored daily to identify errors, inconsistencies and missing values during the audit. Once the audit had ended, two quality controls were established. Firstly, independent auditors re-entered data for 28 relevant variables for a random sample of 1897 patients (15% of all interim cases). Secondly, after a preliminary data description that was made to identify extreme values and inconsistencies, the database entered a data cleaning process [18]. Those values considered extreme or found to have inconsistencies with other related variables were sent to local investigators to check and send back the correct value.

Guidelines Adherence Evaluation

The main recommendations regarding hospital care of ECOPD patients were identified from three different guidelines (GOLD 2010 [19], NICE 2010 [20] and SEPAR/ALAT 2009 [21]), and the degree of compliance with these recommendations was investigated in the AUDIPOC database.

Statistical Analysis

Results at a patient level are presented as percentages or medians, interquartile ranges (IQR) and ranges, as appropriate. Results at a hospital level are presented as medians IQR and ranges of data grouped for all patients within each hospital (i.e. clustered). Inter-rater agreement between the initial set of data and the re-entered by independent auditors was calculated as Cohen’s kappa coefficient. Between-hospital variability in case recruitment was modelled using Bayesian multivariate analysis [22,23]. Bayesian analysis is a method of statistical inference that allows the investigator to explicitly incorporate the distribution of prior beliefs and expert knowledge (prior probability distribution) concerning parameters such as means, variances and regression coefficients underlying random variables, with the currently observed data and the assumed probability model to obtain posterior probability distributions. To determine which hospital resource and organizational related attributes were associated with the variable “ratio of observed to expected number of interim cases,” we used a Poisson probability regression model. For the “proportion of interim cases ultimately considered definite cases,” a binomial probability regression model was fitted.

The above models were built allowing for the quantification of the extra-variability in the response variables via a random effects term. Uninformative prior distributions were used to assign prior probabilities to all values for each parameter, including the regression coefficients and the variance associated with the hospital-level random effects term. The Markov Chain Monte Carlo (MCMC) method was used [24], to simulate posterior distributions of all parameters in the final model. In order to maximize the quality of the sampling of the posterior distributions, one million iterations were run for each of the two models; one half to verify convergence, and the other half for statistical inference. Results were expressed with the mean posterior probability and its 25–75% limits of credibility, and with an estimated average Odds Ratio. These credible intervals indicate that the true population parameter lies in this interval with a probability of 50%.

Results

A total of 11,564 interim ECOPD cases were hospitalized during the study period. At discharge, 5,178 patients fulfilled all the inclusion and none of the exclusion criteria and were therefore
Characteristics of Participating Hospitals

Included in the audit as definite ECOPD cases. Not-included cases were slightly older (78 vs. 75 yrs.), more often females (47 vs. 12%) and were less frequently diagnosed on admission with conditions related to COPD (20 vs. 80%) or at discharge with a primary diagnosis of COPD (18 vs. 82%). Regarding the internal consistency of the data recorded, it is of note that the inter-rater agreement was high, with 68% of Cohen’s kappa coefficients >0.61 and only one <0.40 (Table S1 in the online Appendix).

Table 1. Provisional and definitive inclusion and exclusion criteria.

| Provisional inclusion of the patient upon admission |
|--------------------------------------------------|
| 1. CPOD or chronic pulmonary obstructive disease |
| 2. COB or chronic obstructive bronchitis |
| 3. CB or chronic bronchitis |
| 4. CAO or chronic airflow obstruction |
| 5. CAL or chronic airflow limitation |
| 6. Obstructive lung disease |
| 7. Asthmatic bronchitis with or without reference to acuteness, exacerbations, dyspnoea, bronchospasms, or respiratory insufficiency |
| 8. Respiratory infection, excluding pneumonia |
| 9. Bronchial infection |
| 10. Chronic, acute, or exacerbated respiratory failure, not associated with a causal effect other than CPOD |
| 11. Filial, non-filial, or undetermined dyspnoea |
| 12. Non-specific or non-filial respiratory pathology under study |
| 13. Heart Failure IF acute pulmonary oedema is not explicitly mentioned and IF accompanied by any of the terms previously described |

Inclusion and exclusion criteria

a. Definitive inclusion criteria (at least one)

1. Admitted principally for eCPOD diagnosis
2. Admitted for “respiratory pathology” (respiratory infection without radiological infiltration or pleural effusion (OR) respiratory failure (OR) right heart failure (OR) bronchitis (OR) bronchospasms (AND) historical diagnosis of CPOD (OR) a documented FEV1/FVC <0.70 in the absence of other obstructive diseases such as asthma or bronchiolitis)

b. Definitive Exclusion Criteria (any of the following):

1. Specific diagnosis: pulmonary oedema, pneumonia, pulmonary embolism, pneumothorax, rib fractures, aspiration, pleural effusion, etc. upon admission
2. Other associated respiratory pathology that determines treatment: pulmonary fibrosis, kyphsoliosis, obesity-hypoventilation, neuromuscular pathology, upper airway obstruction, bronchiectasis, extensive tuberculosis sequelae, asthma, bronchiolitis or uncontrolled bronchogenic carcinoma
3. Pathology outside the lungs that determines treatment: major cardiopathy with chronic heart failure, evolved dementia, extended neoplasia, liver or kidney failure, or other situations at the discretion of the researcher

These criteria are evaluated on the discharge report and clinical history. The cases included are those that have at least one inclusion criteria and no exclusion criteria.

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Analysis of Hospital Variability in Case Recruitment

Table 4 displays the mean and 50% credible intervals of the posterior distribution of regression coefficients in the final models, as well as the corresponding average odds ratio (OR). The positive/negative signs in front of their values indicate the same/opposite direction of effects. The number of interim ECOPD cases recruited was positively associated with variables somehow related to COPD awareness such as number of cases admitted in the year prior to the study, existence of a COPD clinical management protocol, or the availability of respiratory physicians in the ED. By contrast they were negatively associated with variables related to hospital size and complexity, including case-mix index, number of beds, existence of an early discharge scheme or domiciliary hospitalisation, number of respiratory physicians, or being a university-affiliated hospital (Table 4, upper panel). On the other hand, the proportion of interim cases that became definite was positively associated with hospital size and complexity and negatively associated with hospital COPD awareness (exceptions were university affiliated and medical training hospitals, for which the probability of an interim case becoming definite decreased) (Table 4, lower panel). Interestingly, both the number of interim ECOPD cases and the proportion of definite cases rose with the availability of hospital documents in electronic format. In any case, a large component of the hospital-related variance in the number of interim ECOPD cases recruited initially (calculated as a 43-fold change) and the proportion of interim cases that become definite...
(calculated as a 17-fold change) remained unexplained by the models fitted (Table 4).

**Characteristics of Audited Patients**

Table 5 presents the main clinical characteristics, interventions and outcomes of the 5,178 patients included in the audit, at different time points and at both the patient and hospital levels. Additional information can be found in the online supplement (Table S2 in the online Appendix). There was large variability in patient characteristics, interventions and outcomes across hospitals. Gender, age, smoking status, comorbidity, general health status (e.g. performance status), anaemia, peripheral oedema, serum albumin and creatinine levels and the frequency and severity of respiratory failure (Table S2 in the online Appendix) varied widely between patients treated in different hospitals. Further differences between hospitals were observed in relation to the availability of spirometric data, arterial blood gas analysis at the ED, and prescription of oxygen therapy, ventilation support, antibiotics, systemic/inhaled steroids, long-acting β2 agonists (LABA) and long-acting muscarinic antagonists (LAMA), as well as for other treatments (Table 5). In-hospital mortality ranged from 0 to 35% (median = 4.5%, IQR = 1.3–7.7%). Length of stay (LOS) ranged from 4 to 65 days (median = 8 days, IQR = 7–10 days) and all-cause hospital readmissions from 0 to 62% (median 34%, IQR 28–42%). Mortality during follow-up ranged from 0 to 38% (median 6%, IQR 2–9%) and the overall mortality across hospitals ranged from 0 to 50% (median 12%, IQR 8–15%).

**Compliance with Clinical Practice Guidelines**

Compliance with clinical practice guidelines is summarised in Table 6 (with further information available in Table S3 in the online Appendix). Although considerable variability at the hospital level was also observed, compliance with recommendations regarding diagnosis or in-hospital treatment revealed high standards of care. In contrast, the level of information included in the final discharge report was not of a high standard, since recommendations related to general health practices and lifestyle improvements were given in written form to less than 50% of discharged patients (Table 6).

**Discussion**

This is the first national clinical audit of patients hospitalized in Spain because of ECOPD. Given the high percentage of population coverage the results should provide an accurate description of the clinical characteristics of ECOPD cases, current clinical practice models, and outcomes of ECOPD treatment in Spain. Further, our results identify the hospital characteristics associated with the admission of ECOPD patients and confirm, for the Spanish National Health System, previous findings on different health-care systems concerning the variability of available resources, clinical presentation and outcomes of patients admitted to these hospitals. Finally, our study provides novel information relating to the degree of actual compliance with international guidelines. Taken together, a proactive approach to the management of this information should contribute to improvements in organizational aspects of care given to COPD patients.

**Previous Studies**

Most previous ECOPD audits included small samples of patients or hospitals, or focused on particular aspects of clinical care. Further to this, those studies involving large numbers of patients were mainly based on administrative databases [25–27]. To our knowledge, only two other nationwide clinical audits of patients hospitalized with ECOPD, and which involved the prospective recruitment of cases and collection of patient clinical record-based data, have been published to date. Both of these studies were carried out in the United Kingdom. The first was...
performed in 2003 and included 234 participating hospitals and 7514 patients. Median inpatient mortality was 7% (between-hospital IQR 3%–11%), total mortality was 15% (IQR 9%–21%), median LOS was 6 days (IQR 3–11 days) and the re-hospitalization rate was 31% (IQR 22%–40%) [8]. The second study, undertaken in 2008 and which included 232 participating hospitals and 9716 patients, reported similar updated results [9]. Overall, the results of these two studies are in keeping with those of AUDIPOC. Minor differences may be related to the distinctiveness of the British and Spanish health systems as well as to differences in the inclusion criteria used in the respective studies.

Interpretation of Findings

The general clinical profile of the patients included in the AUDIPOC study corresponded mostly to that of elderly persons (a third of whom were still smokers) with a history of previous ECOPD hospitalizations and frequent comorbidities (mostly cardiovascular). At the ED they complained of increased dyspnoea with purulent sputum. By and large, treatment during hospitalization and at discharge followed international recommendations (Tables 6 and S3). There were, however, relatively few documented interventions aimed at promoting smoking cessation, an active life-style (including rehabilitation prescription) and/or influenza or pneumococcal vaccination. Importantly, re-hospitalizations were frequent and there was remarkably high all-cause mortality (11.6%).

A more detailed analysis of our results, however, showed that there were marked variations across hospitals in terms of patient characteristics, process of care, adherence to guidelines (Tables 6 and S3), and outcomes. Although part of this variability can be explained by the relatively small number of cases provided by some hospitals, it is more likely due to one or more of the following: (1) heterogeneity of the participating hospitals in terms of size, resources and organization, case recruitment, complexity of health care delivery, (2) heterogeneity of the disease itself [28] as well as diversity of interventions undertaken; (3) thoroughness and accuracy of clinical record data collection; or (4) other, still unidentified, factors not included in the analysis, such as those related to geographical location [14]. In order to gain further insight into the relative contribution of each of these, we first investigated what hospital resources and organizational variables could be identified to explain the recruitment of ECOPD cases into the audit. To this end, we used a Bayesian approach because of its flexibility to study complex models and databases, and the fact that it generates posterior probability distributions that facilitate the interpretation of regression coefficients [29]. This identified a number of explanatory variables that seem to act in opposing directions with respect to the number of interim COPD

### Table 3. Characteristics of participating hospitals (N = 129).

| Variable                                      | Reported | %     | Median | Q1–Q3          | Min.– Max. |
|-----------------------------------------------|----------|-------|--------|----------------|------------|
| Catchment population (hab)                    | 129      | 224076 | 136036–340458 | 44000–787000 |
| Total beds per hospital                       | 129      | 373   | 192–599 | 61–1352        |
| Patients admitted by hospital in 2007         | 129      | 14573 | 7246–21165 | 600–90000    |
| COPD patients admitted per hospital in 2007   | 129      | 293   | 151–519 | 25–1417        |
| Total staff physicians within the hospital    | 129      | 12    | 8.00–18 | 5–50           |
| Internal Medicine Staff members               | 109      | 8     | 5.00–12 | 1–30           |
| Pulmonary Medicine Staff members              | 129      | 1.3   | 1.0–1.6 | 0.7–2.2        |
| Hospital case-mix index 2007                  | 129      | 79    |         |               |
| Universities with residents in training       | 129      | 50    |         |               |
| Pulmonary Unit                                | 129      | 84    |         |               |
| Yes, with hospital ward                       | 129      | 61    |         |               |
| Yes, without hospital ward                    | 129      | 23    |         |               |
| No                                            | 129      | 16    |         |               |
| Lung function laboratory available            | 129      | 83    |         |               |
| Availability of non-invasive ventilation      | 129      | 95    |         |               |
| Intensive care/High Dependency Unit           | 129      | 90    |         |               |
| Admissions ward                               | 129      | 87    |         |               |
| Pulmonary physicians on duty on site          | 79       | 61    |         |               |
| Written protocol for COPD                     | 129      | 44    |         |               |
| Formal pulmonary rehabilitation programme     | 129      | 28    |         |               |
| Availability for transferring COPD cases to another hospitals | 129 | 43    |         |               |
| Early discharge scheme/hospital at home       | 129      | 20    |         |               |
| Triage by physicians                          | 129      | 40    |         |               |
| Access to electronic/digital information      | 129      | 78    |         |               |
| Number of interim ECOPD cases recruited       | 129      | 80    | 41–136  | 8–365          |
| Number of definite ECOPD cases recruited      | 129      | 37    | 25–60   | 8–134          |

Q1–Q3: interquartile range.
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cases and the proportion of definite cases (Table 4). Hospital size and complexity attributes were associated with admitting fewer interim cases and selecting more definite cases from these (i.e. a more refined selection strategy), whilst the COPD awareness dimension facilitates the admission of more interim cases and selection of fewer definite cases (i.e. a less refined selection strategy). The association of access to electronic/digital information with the number of interim and definite cases suggests that the use of information technologies may increase the identification of cases and, possibly, improve the audit process. In any case, a large use of information technologies may increase the identification of hospital performance.

**Table 4.** Multivariate Bayesian analysis showing posterior distributions for the regression coefficients associated with recruitment hospital performance.

| Response variable: ratio of interim recruited to expected COPD cases | Mean posterior probability | 25% Limit of credibility | 75% Limit of credibility | OR |
|---|---|---|---|---|
| Intercept | −2.50 | −3.18 | −1.79 |
| Total patients admitted in 2007 (log N) | 0.29 | 0.19 | 0.38 | 1.33 |
| Access to electronic/digital information (Yes) | 0.23 | 0.13 | 0.34 | 1.26 |
| COPD patients admitted in 2007 (log N) | 0.20 | 0.12 | 0.28 | 1.23 |
| Access to pulmonologist in the ED (Yes) | 0.13 | 0.03 | 0.25 | 1.15 |
| Written protocol for COPD (Yes) | 0.09 | −0.01 | 0.19 | 1.09 |
| Early discharge scheme/day hospital/hospital at home (Yes) | −0.31 | −0.42 | −0.21 | 0.73 |
| Total hospital beds (log N) | −0.17 | −0.28 | −0.03 | 0.85 |
| Hospital case-mix index (units) | −0.14 | −0.26 | 0.00 | 0.87 |
| University hospital (Yes) | −0.13 | −0.25 | −0.01 | 0.86 |
| Pulmonary medicine staff (N) | −0.04 | −0.06 | −0.02 | 0.96 |
| Hospital random effects (standard deviation) | 0.70 | 0.67 | 0.73 |

| Response variable: proportion of interim COPD cases that become definite | Mean posterior probability | 25% Limit of credibility | 75% Limit of credibility | OR |
|---|---|---|---|---|
| Intercept | 1.71 | 0.97 | 2.45 |
| Hospital Case-mix (units) | 0.24 | −0.00 | 0.49 | 1.27 |
| Lung function laboratory (Yes) | 0.40 | 0.15 | 0.65 | 1.49 |
| Access to electronic/digital information (Yes) | 0.34 | 0.15 | 0.54 | 1.40 |
| Pulmonary physicians on duty on site (Yes) | 0.18 | −0.06 | 0.41 | 1.20 |
| Pulmonary medicine staff (N) | 0.03 | 0.00 | 0.05 | 1.03 |
| University Hospital (Yes) | −0.72 | −0.92 | −0.52 | 0.49 |
| Residents in training (Yes) | −0.34 | −0.54 | −0.14 | 0.71 |
| Written protocol for COPD (Yes) | −0.31 | −0.48 | −0.12 | 0.74 |
| COPD patients admitted for COPD in 2007 (log N) | −0.26 | −0.38 | −0.12 | 0.77 |
| Non-invasive ventilation (Yes) | −0.26 | −0.53 | −0.00 | 0.77 |
| Hospital random effects (standard deviation) | 1.29 | 1.23 | 1.36 |

OR: Odds Ratio.
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Strengths and Limitations

The application of strict inclusion/exclusion criteria has likely resulted in the inclusion in the AUDIPOC study of a relatively “pure” ECOPD cohort, with few patients incorrectly included. As such, the study’s results can be generalized to all patients admitted with ECOPD. An additional strength of this study is that the auditors were reasonably consistent in their re-entering of data, thus supporting the quality of the data retrieving and entry process (Table S1). On the other hand, however, a potential limitation of this study, which is intrinsic to any clinical audit, is that medical charts were used as the data source, so some missing and inconsistent values were unavoidable. To address this limitation, a thorough process of database screening and editing was undertaken and the number of extreme or inconsistent values was notably reduced. However, missing data values still remained that tended to cluster in related variables, thus contributing to cross-correlation among them and rendering the multivariate analysis particularly challenging.
Conclusions
The AUDIPOC study is the first national audit on patients hospitalized in Spain because of ECOPD. Our results confirm previous studies from other countries and show significant variability in terms of the resources and organization of hospitals, process of care and outcomes. The study also identifies for the first time a number of resources and organizational characteristics of patients with ECOPD. The results are shown in Table 5.

Table 5. Selected patient characteristics, clinical interventions and outcomes. Estimation at patient level and at hospital level.

| Variables | At patient level (N = 5,178) | At hospital level (N = 129) |
|-----------|-------------------------------|----------------------------|
| N         | % or median (IQ limits)       | Group data median | IQ limits | Range limits |
| Gender (men) | 5178 87 | 90 82–94 | 46–100 |
| Age (years) | 5178 75(68–80) | 75 73–77 | 63–85 |
| Current smoker (yes) | 4500 30 | 29 22–38 | 0–64 |
| Comorbidity >1 (yes) | 5178 38 | 38 26–46 | 9–88 |
| Performance status (moderate to severe limitations) | 3485 51 | 37 18–53 | 0–89 |
| Documented spirometry (yes) | 4191 73 | 63 42–76 | 0–100 |
| Oxygen therapy (yes) | 3403 39 | 25 17–34 | 0–75 |
| Non-invasive ventilatory support (yes) | 3403 5.2 | 6 3–9 | 0.8–22 |
| Previous admissions with ECOPD (yes) | 5178 74 | 74 65–81 | 41–100 |
| Arterial blood gases (yes) | 5178 90 | 95 88–100 | 33–100 |
| pH (units) | 4630 7.41(7.37–7.44) | 7.4 7.39–7.42 | 7.25–7.45 |
| PaCO₂ (mmHg) | 4628 45(38–55) | 46 43–49 | 38–76 |
| PaO₂ (mmHg) | 4627 57(49–66) | 56 53–60 | 30–69 |
| Chest x ray (yes) | 5178 98 | 100 97–100 | 27–100 |
| EKG (yes) | 5178 85 | 90 79–97 | 16–100 |
| Admitted under Respiratory physician (yes) | 5178 53 | 56 26–74 | 0–100 |
| Acidosis (pH<7.35) at any time (yes) | 5178 19 | 17 12–27 | 0–67 |
| Admitted to ICU/HDU (yes) | 5178 2.4 | 0 0–4 | 0–25 |
| Short Acting Beta Adrenergics (yes) | 5178 88 | 93 85–97 | 11–100 |
| Short Acting Anti Cholinergics (yes) | 5178 89 | 94 88–100 | 15–100 |
| Inhaled steroids (yes) | 5178 40 | 42 17–62 | 0–100 |
| Systemic steroids (yes) | 5178 92 | 94 89–98 | 50–100 |
| Antibiotics (yes) | 5178 90 | 92 86–95 | 55–100 |
| Oxygen therapy (yes) | 5178 96 | 98 95–100 | 53–100 |
| Ventilatory support (yes) | 5178 11 | 11 4–18 | 0–67 |
| Death in hospital (yes) | 5178 5 | 4.5 1.3–7.7 | 0.0–35.3 |
| Length of Stay (days) | 5178 8(6–12) | 8 7–10 | 4–65 |
| Long Acting Beta Adrenergics | 4919 82 | 80 70–87 | 43–100 |
| Long Acting Anti Cholinergics | 4919 67 | 67 58–77 | 25–100 |
| Inhaled steroids | 4919 84 | 81 74–89 | 56–100 |
| Systemic corticosteroids | 4919 74 | 73 62–81 | 13–100 |
| Antibiotics | 4919 53 | 49 34–67 | 8–100 |
| Oxygen therapy | 4919 45 | 43 33–53 | 7–92 |
| Non-invasive ventilatory support | 4919 6 | 5 0–9 | 0–25 |
| 90 days follow up since admission | 4919 | 37 34 28–42 | 0–62 |
| Readmissions from all causes | 4919 28 | 26 18–33 | 0–54 |
| Readmissions from COPD | 4919 | 6.9 | 6 2–9 | 0–38 |

N: Number of cases that reported data. COPD: Chronic Obstructive Pulmonary Disease. IQ limits: interquartile limits. Range limits: total range limits. doi:10.1371/journal.pone.0042156.t005

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### Table 6. Guideline statements related to clinical findings GOLD (2010)/NICE (2009)/SEPAR-ALAT (2009).

| Clinical findings                                                                 | Variable                   | Median | IRQ    | Min-Max |
|-----------------------------------------------------------------------------------|----------------------------|--------|--------|---------|
| An exacerbation of COPD is characterised by a change in the patient's baseline   | Increased dyspnoea         | 96     | 93–100 | 84–100  |
| dyspnoea, cough, and/or sputum production or colour                               |                             |        |        |         |
| An exacerbation of COPD is characterised by a change in the patient's baseline   | Increased sputum           | 64     | 54–72  | 9–100   |
| dyspnoea, cough, and/or sputum production or colour                               |                             |        |        |         |
| An exacerbation of COPD is characterised by a change in the patient's baseline   | Increased purulence        | 88     | 80–100 | 17–100  |
| dyspnoea, cough, and/or sputum production or colour                               |                             |        |        |         |
| An exacerbation of COPD is characterised by a change in the patient's baseline   | None of the symptoms       | 0      | 0–4    | 0–13    |
| dyspnoea, cough, and/or sputum production or colour                               |                             |        |        |         |
| An exacerbation of COPD is characterised by a change in the patient's baseline   | Anthonisen Type I          | 40     | 30–49  | 7–100   |
| dyspnoea, cough, and/or sputum production or colour                               |                             |        |        |         |
| An exacerbation of COPD is characterised by a change in the patient's baseline   | Anthonisen Type II         | 26     | 19–32  | 0–50    |
| dyspnoea, cough, and/or sputum production or colour                               |                             |        |        |         |
| An exacerbation of COPD is characterised by a change in the patient's baseline   | Anthonisen Type III        | 31     | 23–40  | 0–91    |
| dyspnoea, cough, and/or sputum production or colour                               |                             |        |        |         |

### Diagnosis

| Variable                                                                 | Median | IRQ    | Min-Max |
|-------------------------------------------------------------------------|--------|--------|---------|
| For patients that require hospitalisation, measurement of arterial blood | 95     | 88–100 | 33–100  |
| gases is important to assess the severity of an exacerbation.            |        |        |         |
| Inspired oxygen concentration recorded in the ED                         | 93     | 73–100 | 0–100   |

### Oxygen therapy

| Variable                                                                 | Median | IRQ    | Min-Max |
|-------------------------------------------------------------------------|--------|--------|---------|
| Oxygen therapy is the cornerstone of hospital treatment of COPD         | 98     | 95–100 | 53–100  |
| exacerbations and Supplemental oxygen should be titrated to improve the |        |        |         |
| patient's hypoxemia                                                    |        |        |         |
| Pulse-oxymetry while receiving oxygen-therapy                          | 98     | 86–100 | 0–100   |

### Bronchodilators

| Variable                                                                 | Median | IRQ    | Min-Max |
|-------------------------------------------------------------------------|--------|--------|---------|
| Management of COPD exacerbations involves increasing the dose and/or    | 98     | 94–100 | 61–100  |
| frequency of existing short-acting bronchodilator therapy, preferably   |        |        |         |
| with a β₂ agonist.                                                      |        |        |         |
| Cases on short-acting bronchodilators                                   | 98     | 94–100 | 61–100  |
| Cases on short-acting β₂ agonists                                      | 93     | 85–97  | 11–100  |
| Cases on ipratropium                                                    | 94     | 88–100 | 15–100  |

### Antibiotics

| Variable                                                                 | Median | IRQ    | Min-Max |
|-------------------------------------------------------------------------|--------|--------|---------|
| Antibiotics should be given to patients with three cardinal symptoms,   | 98     | 90–100 | 50–100  |
| with two cardinal symptoms if purulence of sputum is one of the two     |        |        |         |
| symptoms, and patients that require mechanical ventilation              |        |        |         |
| Cases on antibiotics with three cardinal symptoms                       | 98     | 90–100 | 50–100  |
| Cases on antibiotics with an increase in sputum purulence              | 97     | 91–100 | 0–100   |
| Cases on ventilator support receiving antibiotics                       | 100    | 83–100 | 0–100   |

### Steroids

| Variable                                                                 | Median | IRQ    | Min-Max |
|-------------------------------------------------------------------------|--------|--------|---------|
| In the absence of significant contraindications oral corticosteroids     | 94     | 89–98  | 50–100  |
| should be used, in conjunction with other therapies, in all patients    |        |        |         |
| admitted to hospital with an exacerbation of COPD.                       |        |        |         |

### Discharge report

| Variable                                                                 | Median | IRQ    | Min-Max |
|-------------------------------------------------------------------------|--------|--------|---------|
| Opportunities for prevention of future exacerbations should be reviewed  | 43     | 23–63  | 0–100   |
| before discharge, with particular attention to smoking cessation, current|        |        |         |
| vaccination (influenza, pneumococcal vaccines), knowledge of current     |        |        |         |
| therapy including inhaler technique and how to recognize symptoms of     |        |        |         |
| exacerbations.                                                          |        |        |         |
| Anti-tobacco instructions in active smokers                               | 37     | 21–53  | 0–100   |
| Influenza vaccination instructions                                       | 0      | 0–7    | 0–100   |
| Pneumococcal vaccination instructions                                    | 0      | 0–3    | 0–100   |
| Nutritional instructions                                                 | 7      | 0–19   | 02100   |
| Inhaler technique instructions                                           | 95     | 89–100 | 30–100  |

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hospitals that may influence the routine admission of COPD cases for hospitalization, pinpointing therefore to several improbable organizational aspects. The issue of compliance with clinical practice guidelines in real life was also addressed, with some aspects that are amenable to improvement of daily clinical care also identified.

Supporting Information

Table S1 Consistency analysis of variables included in the study.

Table S2 Additional patient characteristics, clinical interventions and outcomes. Estimations at patient level and at hospital level.

Table S3 Additional guidelines assessment.

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