ERJ Express. Published on October 22, 2015 as doi: 10.1183/13993003.01391-2014

ORIGINAL ARTICLE
IN PRESS | CORRECTED PROOF

Risk of death and readmission of hospital-admitted COPD exacerbations: European COPD Audit

Sylvia Hartl[1,2], Jose Luis Lopez-Campos[3], Francisco Pozo-Rodriguez[4], A. Castro-Acosta[4], M. Studnicka[5], Bernhard Kaiser[5] and C. Michael Roberts[6]

Affiliations: [1]Ludwig Boltzmann Institute of COPD and Respiratory Epidemiology, Vienna, Austria. [2]Dept of Respiratory and Critical Care, Otto Wagner Hospital, Vienna, Austria. [3]Hospital Universitario Virgen del Roc, Seville, Spain. [4]Respiratory Dept and Research Institute, doce de Octubre University Hospital, CIBERES, Madrid, Spain. [5]Respiratory Dept, Paracelsus Medical University Salzburg, Salzburg, Austria. [6]Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK.

Correspondence: S. Hartl, Dept of Respiratory and Critical Care, Otto Wagner Hospital, Sanatoriumstrasse 2, 1140 Vienna, Austria. E-mail: sylvia.hartl@wienkav.at

ABSTRACT Studies report high in-hospital and post-discharge mortality of chronic obstructive pulmonary disease (COPD) exacerbations varying depending upon patient characteristics, hospital resources and treatment standards. This study aimed to investigate the patient, resource and organisational factors associated with in-hospital and 90-day post-discharge mortality and readmission of COPD exacerbations within the European COPD Audit. The audit collected data of COPD exacerbation admissions from 13 European countries.

On admission, only 49.7% of COPD patients had spirometry results available and only 81.6% had blood gases taken. Using logistic regression analysis, the risk associated with in-hospital and post-discharge mortality was higher age, presence of acidotic respiratory failure, subsequent need for ventilatory support and presence of comorbidity. In addition, the 90-day risk of COPD readmission was associated with previous admissions. Only the number of respiratory specialists per 1000 beds, a variable related to hospital resources, decreased the risk of post-discharge mortality.

The European COPD Audit identifies risk factors associated with in-hospital and post-discharge mortality and COPD readmission. Addressing the deficiencies in acute COPD care such as making spirometry available and measuring blood gases and providing noninvasive ventilation more regularly would provide opportunities to improve COPD outcomes.

@ERSpublications
Hospital-admitted COPD exacerbation needs better risk stratification: spirometry and gas analysis improve outcomes http://ow.ly/RTbdk

This article has supplementary material available from erj.ersjournals.com

Received: July 30 2014 | Accepted after revision: Aug 17 2015

Conflict of interest: Disclosures can be found alongside the online version of this article at erj.ersjournals.com

Support statement: This study was supported by the European Respiratory Society. Funding information for this article has been deposited with FundRef.

Introduction

Chronic obstructive pulmonary disease (COPD) exacerbation is common, and is associated with high in-hospital and post-discharge mortality, reported in the literature as varying from 2.5% to 30% depending upon subject characteristics and the setting of the investigation [1–6]. In a recent systematic review and meta-analysis, a number of characteristics of COPD patients as well as comorbidities were significantly associated with increased mortality [7]. National studies from the UK and Spain have in contrast focused on the influence of treatment standards and resources across hospitals on COPD mortality and readmission. Both countries used audits to collect clinical data of patients hospitalised with COPD exacerbation, and the related standards of care and organisational resources. In 2010/11, the audit methodology was used for the first time in a European COPD Audit in 13 countries to investigate the variations of care and resources across Europe [8].The variability of resources across European hospitals in this COPD audit was substantial, but greater resources in larger hospitals did not guarantee better access to care and the standards of care as described in guideline recommendations were fulfilled in only 15.3% of patients across all hospitals [8, 9].

The current study aimed to investigate the patient, resource and organisational factors associated with the outcomes in-hospital and 90-day post-discharge mortality and 90-day post-discharge readmission in patients with COPD exacerbation seen within the European COPD Audit. We believe that the identification of such factors in a "real-world setting" will provide the future opportunity to implement interventions, leading to better standards of care and better outcomes for patients.

Methods

Study design

The methods of the European COPD Audit have been published elsewhere [8]. Briefly, the audit was designed as a pilot to evaluate clinical practice standards and patient- and resource-related factors for clinical processes of care and outcomes of hospital-admitted COPD exacerbations. The European COPD Audit is an observational study with an 8-week prospective consecutive case ascertainment of COPD exacerbation admissions in 13 European countries. The study period ran from October 25 to December 19, 2010 or from January 3 until February 27, 2011 according to the seasonal peak of COPD exacerbations of the participating countries. During this period, each participating hospital completed a pre-defined dataset about the resources and the organisation of acute COPD care listed in online supplementary table s1. For the risk prediction models, respiratory acidosis was stratified as severe with a pH<7.25 and mild with a pH 7.25–7.35 [10, 11]. The staff resources, *i.e.* respiratory specialists or physiotherapists, were standardised per 1000 beds. The Charlson Comorbidity Index (CCI) was assessed on admission [12]. All patients were screened on admission for interim case ascertainment of COPD exacerbation by a senior clinician. The time period between admission and discharge was the basis used to calculate in-hospital mortality, and the 90 days period following discharge was used to calculate 90-day post-discharge mortality and 90-day readmission risk.

Statistics

Statistical analyses was performed with the SPSS version 17.0 and SAS. The significance level was set to 5%. For description of the study population, means±SD, frequencies and percentages were used for continuous variables and categorical variables when appropriate. Group comparisons for means were evaluated by t-tests or ANOVA models (including pairwise *post hoc* Scheffé tests) and the differences in frequencies by crosstabs (including the Chi-squared test). The effects of risk factors were evaluated by logistic regression analysis and random effects models controlled for country effect.

Results

422 hospitals from 13 European countries participated in the clinical audit assessing outcomes of hospital-admitted COPD exacerbations in a real-world setting. The case management reflects the standards of care of the individual hospital. Case ascertainment is shown in figure 1.

Characteristics of the patients hospitalised with exacerbated COPD are presented in table 1. The leading symptom on admission was dyspnoea (96.2%). Only 81.6% of COPD patients (13 069/16 016) had blood gases taken on admission and 45.4% of them (5933/13 069) had carbon dioxide retention (>6 kPa), including 16.6% (2164/13 069) with pronounced retention (>8 kPa). 18.8% (2452/13 041) demonstrated respiratory acidosis; of those, 78.3% (1921/2452) were classified as mild, whereas 21.7% (531/2452) were classified as severe.

Only 45.0% of patients with mild acidosis received ventilatory support (865/1921), whereas 77.2% (410/531) of severely acidotic patients were ventilated. Comparing the basic demographics of ventilated and nonventilated patients, there were no differences with regard to the distribution in age or smoking history,

DOI: 10.1183/13993003.01391-2014

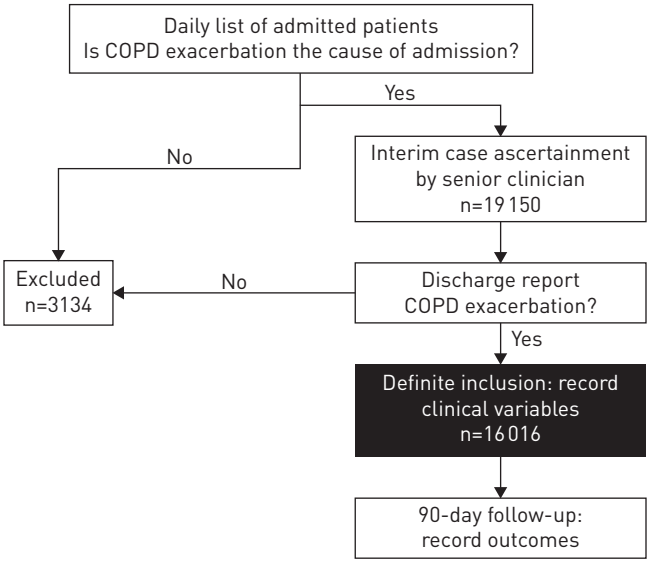

FIGURE 1 Algorithm of case ascertainment of chronic obstructive pulmonary disease (COPD) exacerbation.

but there were more COPD GOLD (Global Initiative for Chronic Obstructive Lung Disease) stage IV patients in the ventilated group (39.5% (478/1210) *versus* 23.0% (1551/6753)).

On admission, 49.7% (7958/16 016) patients had spirometry results available which could be categorised into GOLD severity stages: 25.6% were classified as GOLD IV (2098/7958), 45.5% as GOLD III (3737/7958), 26.5% (2175/7958) as GOLD II and 2.4% (195/7958) as GOLD I. Mean CCI was higher in GOLD I and II than in GOLD III and IV (2.5±1.7 *versus* 2.2±1.5, p=0.001).

37.6% (6026/16 016) of the patients reported COPD without any other comorbidity, whereas the most frequent comorbidities were cardiovascular diseases (40.5%, 6491/16 016), diabetes (19.9%, 3181/16 016) and chronic pulmonary diseases (20.8%, 3328/16 016) (details in online supplementary table s2).

Major outcomes: mortality

1727 patients, *i.e.* 10.8% of those admitted with exacerbated COPD, died during the observational period of the audit. 790 (45.7%) of hospitalised COPD patients died while still in hospital, whereas 937 (54.3%) died during the 90-day post-discharge follow-up. 35 patients were not discharged until the end of the 90-day follow-up, and two were lost to follow-up and were therefore excluded from the analysis of post-discharge mortality and readmission. In a stepwise logistic regression analysis, resource-, patient- and treatment-related factors (for the detailed list, see online supplementary table s1) were tested for increased/reduced risk of in-hospital and post-discharge mortality.

The risk of in-hospital mortality was independently associated with patient-related factors such as age, presence of respiratory acidosis and CCI. Of the treatment-related factors, only ventilatory support was significantly associated with in-hospital mortality (table 2).

For the 90-day post-discharge analyses, in-hospital deaths (790/16 016) and patients who were still hospitalised at the end of the 90-day post-discharge follow-up were excluded from the analysis, leaving a total of 15 191 patients. The significant variables associated with the 90-day post-discharge mortality are presented in table 3.

Similar to the results of in-hospital mortality, the patient-related factors age, CCI, presence of respiratory acidosis and additionally previous admissions increased the risk for post-discharge mortality, while the presence of diabetes decreased it. The number of respiratory specialists per 1000 beds also decreased post-discharge mortality.

Survival curves for the 90-day post-discharge observation period according to the severity of acidosis and the type of ventilatory support are shown in figures 2 and 3. Nonacidotic patients had a survival of 90.9% (9625/10 589) compared with 83.9% (1612/1921) for mild acidotic patients and 71.9% (382/531) for severe acidotic patients. The survival probability of invasively ventilated patients was 64.4% (141/219) compared with 80.4% for noninvasively ventilated patients (1663/2068) and 91.0% for those who had no need for ventilatory support (11 959/13 142), reflecting the severity of underlying respiratory failure.

TABLE 1 Characteristics of patients admitted with exacerbated COPD (N=16 016)

Sex	
Male	10 865 (67.8)
Smoking status n=15 181	
Current smoker	5012 (31.3)
Ex-smoker	9317 (58.2)
Never-smoker	852 (5.3)
Age years	
Total	70.8±10.8
Male	71.4±10.4
Female	69.5±11.3
BMI kg·m^{-2} n=9011	
Total	26.6±6.5
Male	26.6±5.9
Female	26.7±7.5
Symptoms on admission	
Dyspnoea increase	15 409 (96.2)
Sputum increase	10 373 (64.8)
Sputum colour change	8134 (50.8)
Previous admissions during last 12 months n=14 641	
0	6907 (47.2)
1	3498 (23.9)
>1	4236 (28.9)
FEV_1 % predicted n=7958	44.0±17.5
GOLD stage in spirometry-proven COPD n=7958	
I	195 (2.4)
II	2175 (26.5)
III	3737 (45.5)
IV	2098 (25.6)
Blood gas analysis	
pH n=13 041	
>7.35	10 589 (81.2)
7.25–7.35	1921 (14.7)
<7.25	531 (4.1)
P_{aCO_2} kPa n=13 069	
>6	5933 (45.4)
>8	2164 (16.6)
Ventilatory support n=15 496	
No ventilatory support	13 142 (84.8)
Only NIV	2068 (13.3)
Only IV	219 (1.4)
NIV and IV	67 (0.4)
X-ray n=15 765	
Normal	3555 (22.2)
Any pathology	12 212 (76.2)
Medication on admission n=16 016	
Systemic corticosteroids	13 187 (82.3)
Antibiotics	13 773 (86.0)

Data are presented as mean±SD or n (%). BMI: body mass Index; FEV_1: forced expiratory capacity in 1 s; GOLD: Global Initiative for Chronic Obstructive Lung Disease; COPD: chronic obstructive pulmonary disease; P_{aCO_2}; arterial carbon dioxide tension; IV: invasive ventilation; NIV: noninvasive ventilation.

In the group of COPD patients with spirometric classification available, severity of lung function impairment was significantly associated with 90-day post-discharge mortality (figure 4).

Major outcomes: readmission

Exacerbated and discharged COPD patients (n=15 191) were followed for 90 days and the readmission rate determined. 35.1% (5337/15 191) were readmitted within 90 days. In bivariate analysis, a higher proportion of readmitted patients was in COPD IV compared with non-readmitted (29.5%, 851/2880 *versus* 22.5%, 1131/5016). Readmitted patients had a higher mortality (13.4%, 714/5337) than non-readmitted patients (2.3%, 223/9854) (Chi-squared test, p=0.0001). In the logistic regression analysis patient-related factors age, CCI and previous admissions increased the risk of readmission, while diabetes decreased it. Similar to mortality, the need for ventilatory support increased the likelihood of readmission (table 4).

DOI: 10.1183/13993003.01391-2014

TABLE 2 Logistic regression model for the risk associated with in-hospital mortality (n=16 016)

	OR (95% CI)	p
Age years	1.064 (1.054–1.074)	0.0001
Charlson Comorbidity Index points	1.137 (1.087–1.189)	0.0001
Ventilatory support: yes	3.667 (2.997–4.486)	0.0001
Respiratory acidosis		
Mild *versus* normal	1.582 (1.286–1.945)	0.0001
Severe *versus* normal	2.313 (1.721–3.109)	

Respiratory acidosis is categorised as: severe, pH<7.25; mild, pH 7.25–7.35; normal, pH>7.35. Results are from a random effects model adjusting for country.

Discussion

This study presents the largest European dataset of prospectively collected real-world data of quality of care and outcomes for hospital-admitted COPD exacerbation. The study confirms the findings from smaller national audits and highlights gaps in quality of care in many European countries when compared with evidence-based recommendations, and importantly provides insights into where interventions could be made which might improve outcomes for patients.

Acidotic respiratory failure on admission and the subsequent need for ventilatory support were found to be important and consistent predictors of in-hospital mortality and post-discharge mortality. The only factor associated with a reduced risk of death during the 90-day post-discharge follow-up was the number of respiratory specialists per 1000 beds.

Respiratory acidosis, reflecting the severity of the exacerbation, was a finding in 18.8% of admitted patients with blood gases available. National COPD audits from the UK and Spain [13, 14] have reported similar proportions of respiratory acidosis, and this European audit confirms the previous findings. Respiratory acidosis, when split into severe (pH<7.25) and mild (pH 7.25–7.35) as a surrogate of the severity of the exacerbation, was a strong predictor of in-hospital and post-discharge mortality. It is therefore of concern that 18.5% of patients were assessed and managed without this information. Blood gas analysis is recommended in COPD guidelines [15, 16] and although incomplete adherence to these recommendations was first reported in the 1997 UK COPD Audit [17], it is concerning to report similar figures across Europe 13 years later.

Respiratory acidosis is considered a modifiable condition in the acute setting and noninvasive ventilation (NIV) is one of the very few interventions with strong evidence from the published literature to effectively reduce mortality [18–20]. The high mortality of COPD patients with severely impaired respiratory function has been noted since the early 1990s [1, 21, 22], but was improved by early ventilation for mild respiratory acidosis in randomised controlled trials (RCTs) [21]. These survival benefits are incompletely transferred into everyday practice, as exemplified by a 45.0% ventilation rate of mild acidotic patients in the present study. Moreover, the number of intubated patients after NIV failure was very small, indicating

TABLE 3 Logistic regression model for the risk associated with 90 day post-discharge mortality (n=15 191)

	OR (95% CI)	p
Age year	1.037 (1.029–1.046)	0.0001
Charlson Comorbidity Index points	1.128 (1.074– 1.185)	0.0001
Diabetes	0.661 (0.531–0.822)	0.0002
Respiratory acidosis		
Mild *versus* normal	1.187 (0.957–1.472)	0.0160
Severe *versus* normal	1.858 (1.312–2.632)	
Ventilatory support: yes	2.147 (1.811–2.542)	0.0001
Respiratory specialists per 1000 beds	0.995 (0.989–0.999)	0.0269
Previous admission (one or more)	1.622 (1.297–2.030)	0.0001

Respiratory acidosis is categorised as: severe, pH<7.25; mild, pH 7.25–7.35; normal, pH>7.35. Results are from a random effects model adjusting for country.

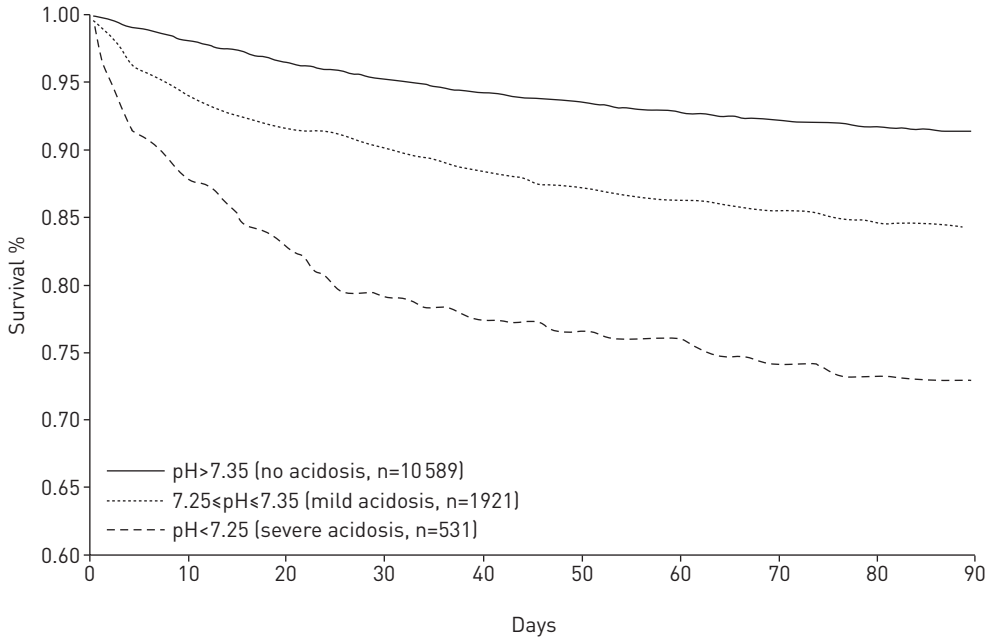

FIGURE 2 Survival curves of the 90-day post-discharge follow-up according to severity of respiratory acidosis; n=13 041.

that NIV was a ceiling therapy for most of the cases who died after NIV. Reasons for delaying or withholding NIV are dependent on physicians' decisions, but may also be influenced by the availability of NIV and access to the intensive care unit (ICU) for COPD patients, as first reported by Roberts *et al.* [14] and confirmed by this European COPD Audit [9]. This is alarming when guidelines recommend that NIV should be delivered in a dedicated setting and ICU admission should be considered in respiratory failure for COPD [16]. It is likely to be key that the medical team with the appropriate knowledge and skills is on hand to make these critical decisions. It is noteworthy that the audit demonstrated an association between reduced post-discharge mortality and the ratio of respiratory specialists to beds, which supports the view that early access to specialists may be the optimum service model.

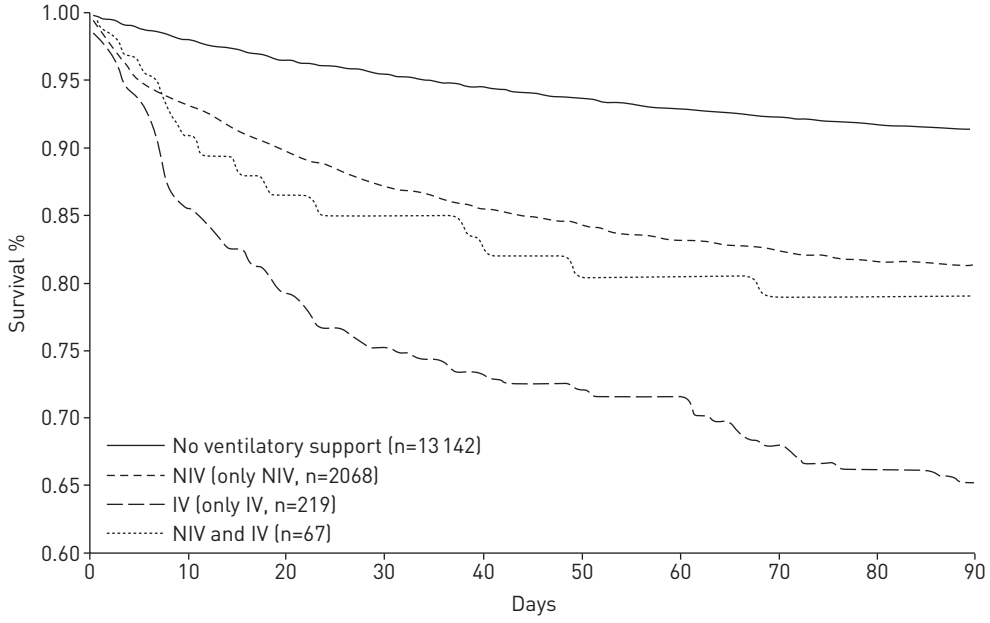

FIGURE 3 Survival curves of the 90-day post-discharge follow-up according to the type of ventilatory support during hospital stay; n=15 429. NIV: noninvasive ventilation; IV: invasive ventilation.

DOI: 10.1183/13993003.01391-2014

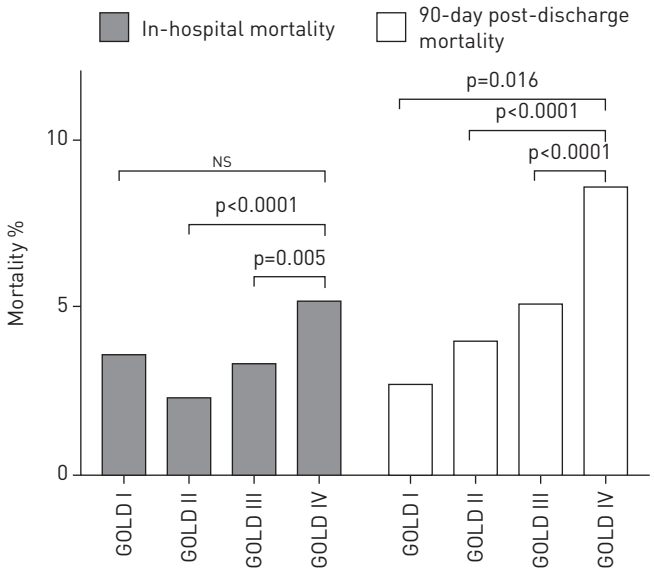

FIGURE 4 In-hospital mortality and 90 day post-discharge mortality according to COPD GOLD stages ($FEV_1/FVC<70\%$; GOLD I, FEV_1 % predicted >80%; GOLD II, FEV_1 % predicted 80–50%; GOLD III, FEV_1 % predicted 50–30%; GOLD IV, FEV_1 % predicted <30%) by Scheffé's paired post hoc test; n=7958 (49.7% total). NS: nonsignificant; GOLD: Global Initiative for Chronic Obstructive Lung Disease; COPD: chronic obstructive pulmonary disease; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

On the basis of these findings, we recommend that European hospitals develop a COPD care pathway which includes the analysis of arterial blood gases on admission and a subsequent decision model for acidotic patients to receive NIV as indicated by a respiratory specialist comparable with the acute intervention model for myocardial infarction [23].

We observed a 35.1% readmission rate for all patients discharged within 90 days, which was also strongly related to post-discharge mortality. Readmission is still considered to be avoidable and led to the establishment of a penalty system for readmission within 30 days in the USA [24–26]. However, the prediction of readmission is still poor and most of the published data fail to show any improvement of readmission rates in COPD as a result of financial penalties [26, 27]. In our study, readmission was related to the risk factor of previous admissions, thereby possibly reflecting the frequent exacerbator phenotype.

Pulmonary rehabilitation programmes following acute exacerbation of COPD have effectively reduced readmission and mortality [28, 29]. Moreover the inclusion of a number of interventions into a discharge care bundle [30, 31] has also been shown to reduce readmission rates. Identification of the risk factors highly associated with readmission rate would allow more vigorous post-discharge care bundles to be tailored for these patients.

The CCI, but no specific disease group, although a fair number of specific comorbidities was investigated, was associated with increased in-hospital and post-discharge mortality.

The lower risk of readmission and post-discharge mortality associated with diabetes confirmed the findings of previous smaller studies [32, 33], but does not elucidate the possible underlying mechanisms. The thesis of the protective potential of a higher body mass index in diabetic patients has been discussed by McGhan *et al.* [32], but is still speculative. Another explanation model is that comorbidities may include unidentified treatment options which in diabetes therapy might lead to less blood sugar escalation

TABLE 4 Logistic regression model for the 90-day readmission risk in subjects discharged with COPD (n=15 191)

	OR (95% CI)	p
Age years	1.013 (1.010–1.017)	0.0001
Charlson Comorbidity Index points	1.093 (1.066–1.121)	0.0001
Comorbid chronic pulmonary diseases	1.133 (1.036–1.239)	0.0063
Ventilatory support	1.133 (1.036–1.239)	0.0015
Diabetes	0.899 (0.815–0.992)	0.034
Previous admission (one or more)	2.479 (2.301–2.671)	0.0001

Data are from a random effects model adjusting for country.

caused by systemic corticosteroid therapy considered harmful in the studies of Baker *et al.* [34] and Chakrabarti *et al.* [35].

Lung function test results to confirm the diagnosis of COPD and categorise the severity of disease were not available in >50% of patients at the time of admission. When available, COPD stage IV patients had a higher need of ventilatory support. Spirometry data available to admitting clinicians would help to confirm the diagnosis and to risk-stratify patients. The availability of spirometry would probably both influence the decision model of acute care and the discharge care bundle.

We acknowledge that the European COPD Audit has limitations as it was established as a pilot to evaluate the potential for widespread European data collection. Thus, selection bias relating to the voluntarily participating centres clearly could be an issue. Participating hospitals at the national level were not randomly recruited, which resulted in wide variations of the catchment of population between countries. Thus, results of a single country are not considered to be representative of the national COPD population. However, for countries such as the UK and Spain with the highest experience in national audits [36, 37] there were not significant differences in results when a smaller number of centres participated in the European Audit. The lack of data from European countries such as Germany and France does, however, limit the generalisation of the results across all Europe. Moreover, audit data do not compare with the standards of RCTs and the absence of spirometry in half of the included cases raises issues about the confirmation of diagnosis. Nevertheless, the audit is an accurate reflection of real-world clinical practice, and highlights the gaps between the RCT-based evidence of ideal clinical practice and the standards delivered in routine care.

The pilot study was not designed to detect barriers to the implementation of guideline recommendations, but only shows the gaps of quality of care. The intention of an audit is to identify the deficiencies of care measured against standards and then to challenge clinicians to form action plans to improve care before again measuring the quality of the care given to patients in their practice [38].

In summary, the European COPD Audit identifies areas of clinical practice which if improved should result in better outcomes for patients. It is unacceptable that half of all patients admitted with COPD do not have documented spirometry to confirm the diagnosis nor to stratify the risk to the individual. It is also unacceptable that a fifth of patients do not undergo blood gas analysis for critical decision making regarding ventilatory support. In addition, the study identifies the number of respiratory physicians as a modifiable risk factor to influence post-discharge mortality.

In conclusion, the study asks for optimising the risk stratification on admission for COPD exacerbation, identifying respiratory acidosis effectively in the first hours of an admission, deploying specialist respiratory care teams in time and following these risk factors at discharge to implement evidence-based interventions.

Acknowledgements

The authors would like to thank all the contributing clinicians across Europe and the statistical team of V. Abraira-Santos, A. Lopez-Quilez, J. Dorado and A. Schrott.

The European COPD Audit team members are as follows. Data analysis team: V. Abraira-Santos, A. Lopez-Quilez, J. Dorado and A. Schrott. National experts (by alphabetical order of country): O. Burghuber and R. Kohansal (Austria), W. Janssens and V. Heinen (Belgium), N. Miculinic and H. Puretic (Croatia), N. Tzanakis and E. Nontas Kosmas (Greece), S. McCormack and T. McDonell (Ireland), C. Farrugia Jones (Malta), J. Chorostowska-Wynimko (Poland), G. Sowula, F. Mihaltan, M. Alexandru Bogdan and I. Munteanu (Romania), I. Solovic and R. Tkacova (Slovakia), F. Pozo-Rodriguez and J. Ancochea (Spain), D. Stolz (Switzerland), M. Polatli and E. Sen (Turkey), C. Bucknall, S. Welham and C. Routh (UK). Project managers: M. Haan, M. Zarelli, E. Lechat and R.J. Buckingham. European Respiratory Society COPD Audit liaison officer: G. Joos.

References

1 Connors AF Jr, Dawson NV, Thomas C, *et al.* Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). *Am J Respir Cell Mol Biol* 1996; 154: 959–967.

2 Soler-Cataluna JJ, Martinez-Garcia MA, Roman Sanchez P, *et al.* Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax* 2005; 60: 925–931.

3 Roche N, Zureik M, Soussan D, *et al.* Predictors of outcomes in COPD exacerbation cases presenting to the emergency department. *Eur Respir J* 2008; 32: 953–961.

4 Bustamante-Fermosel A, De Miguel-Yanes JM, Duffort-Falco M, *et al.* Mortality-related factors after hospitalization for acute exacerbation of chronic obstructive pulmonary disease: the burden of clinical features. *Am J Emerg Med* 2007; 25: 515–522.

5 Chavaillon JM, Lerousseau L, David P, *et al.* Mortalité intrahospitalière au cours des exacerbations aiguës de BPCO. Étude EABPCO-CPHG du Collège des pneumologues des hôpitaux généraux (CPHG) [Intrahospital mortality during acute exacerbations of COPD. Study EABPCO-CPHG of the College of the Lung specialists of General hospitals (CPHG)]. *Rev Mal Respir* 2010; 27: 709–716.

 DOI: 10.1183/13993003.01391-2014

6 Groenewegen KH, Schols AM, Wouters EF. Mortality and mortality-related factors after hospitalization for acute exacerbation of COPD. *Chest* 2003; 124: 459–467.
7 Singanayagam A, Schembri S, Chalmers JD. Predictors of mortality in hospitalized adults with acute exacerbation of chronic obstructive pulmonary disease. *Ann Am Thorac Soc* 2013; 10: 81–89.
8 Lopez-Campos JL, Hartl S, Pozo-Rodriguez F, *et al.* European COPD Audit: design, organisation of work and methodology. *Eur Respir J* 2013; 41: 270–276.
9 Lopez-Campos JL, Hartl S, Pozo-Rodriguez F, *et al.* Variability of hospital resources for acute care of COPD patients: the European COPD Audit. *Eur Respir J* 2014; 43: 754–762.
10 Brochard L. Non-invasive ventilation for acute exacerbations of COPD: a new standard of care. *Thorax* 2000; 55: 817–818.
11 Confalonieri M, Garuti G, Cattaruzza MS, *et al.* A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. *Eur Respir J* 2005; 25: 348–355.
12 Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–383.
13 Pozo-Rodriguez F, Lopez-Campos JL, Alvarez-Martinez CJ, *et al.* Clinical audit of COPD patients requiring hospital admissions in Spain: AUDIPOC study. *PloS One* 2012; 7: e42156.
14 Roberts CM, Stone RA, Buckingham RJ, *et al.* Acidosis, non-invasive ventilation and mortality in hospitalised COPD exacerbations. *Thorax* 2011; 66: 43–48.
15 GOLD. Global Strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2010. http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html. Date last accessed: February 4, 2012.
16 National Institute for Clinical Excellence. CG101 Chronic obstructive pulmonary disease (update): NICE guideline. https://www.nice.org.uk/guidance/cg101. Date last accessed: January 16, 2014.
17 Roberts CM, Barnes S, Lowe D, *et al.* Evidence for a link between mortality in acute COPD and hospital type and resources. *Thorax* 2003; 58: 947–949.
18 Peter JV, Moran JL. Noninvasive ventilation in exacerbations of chronic obstructive pulmonary disease: implications of different meta-analytic strategies. *Ann Intern Med* 2004; 141: W78–W79.
19 Lightowler JV, Wedzicha JA, Elliott MW, *et al.* Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. *BMJ* 2003; 326: 185.
20 Wysocki M, Richard JC, Meshaka P. Noninvasive proportional assist ventilation compared with noninvasive pressure support ventilation in hypercapnic acute respiratory failure. *Crit Care Med* 2002; 30: 323–329.
21 Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *Lancet* 2000; 355: 1931–1935.
22 Seneff MG, Wagner DP, Wagner RP, *et al.* Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of chronic obstructive pulmonary disease. *JAMA* 1995; 274: 1852–1857.
23 Silber S, Richartz B, Brilmayer M. Die ESC-Leitlinien zur perkutanen Koronarintervention (PCI) [The ESC guidelines for percutaneous coronary intervention (PCI)]. *Herz* 2006; 31: 836–848.
24 Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. *N Engl J Med* 2009; 360: 1418–1428.
25 Kangovi S, Grande D. Hospital readmissions – not just a measure of quality. *JAMA* 2011; 306: 1796–1797.
26 Gorodeski EZ, Starling RC, Blackstone EH. Are all readmissions bad readmissions? *N Engl J Med* 2010; 363: 297–298.
27 Feemster LC, Au DH. Penalizing hospitals for chronic obstructive pulmonary disease readmissions. *Am J Respir Crit Care Med* 2014; 189: 634–639.
28 Spruit MA, Pitta F, Garvey C, *et al.* Differences in content and organisational aspects of pulmonary rehabilitation programmes. *Eur Respir J* 2014; 43: 1326–1337.
29 Puhan MA, Gimeno-Santos E, Scharplatz M, *et al.* Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2011; 10: CD005305.
30 Hopkinson NS, Englebretsen C, Cooley N, *et al.* Designing and implementing a COPD discharge care bundle. *Thorax* 2012; 67: 90–92.
31 McCarthy C, Brennan JR, Brown L, *et al.* Use of a care bundle in the emergency department for acute exacerbations of chronic obstructive pulmonary disease: a feasibility study. *Int J Chron Obstruct Pulmon Dis* 2013; 8: 605–611.
32 McGhan R, Radcliff T, Fish R, *et al.* Predictors of rehospitalization and death after a severe exacerbation of COPD. *Chest* 2007; 132: 1748–1755.
33 Ng TP, Niti M, Tan WC, *et al.* Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. *Arch Intern Med* 2007; 167: 60–67.
34 Baker EH, Janaway CH, Philips BJ, *et al.* Hyperglycaemia is associated with poor outcomes in patients admitted to hospital with acute exacerbations of chronic obstructive pulmonary disease. *Thorax* 2006; 61: 284–289.
35 Chakrabarti B, Angus RM, Agarwal S, *et al.* Hyperglycaemia as a predictor of outcome during non-invasive ventilation in decompensated COPD. *Thorax* 2009; 64: 857–862.
36 Roberts CM, Ryland I, Lowe D, *et al.* Audit of acute admissions of COPD: standards of care and management in the hospital setting. *Eur Respir J* 2001; 17: 343–349.
37 Roberts CM, Stone RA, Lowe D, *et al.* Co-morbidities and 90-day outcomes in hospitalized COPD exacerbations. *COPD* 2011; 8: 354–361.
38 Boulet LP, FitzGerald JM, Levy ML, *et al.* A guide to the translation of the Global Initiative for Asthma (GINA) strategy into improved care. *Eur Respir J* 2012; 39: 1220–1229.