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ABSTRACT

Introduction: Bundles of care are gaining popularity for treating acute severe illness.

Objective: To describe compliance with bundle of care elements (individually and as a 'bundle') for patients treated for chronic obstructive pulmonary disease (COPD) exacerbations in the emergency department (ED).

Methods: Retrospective observational study of patients presenting in the 2014 calendar year with an ED diagnosis of COPD. The primary outcomes of interest were compliance with key bundle of care elements (individually and as a 'bundle'). Analysis is descriptive.

Results: 381 patients were studied. Median age was 71 (IQR 64-80), 59% were male and 77% arrived by ambulance. Median duration of symptoms was 3 days (IQR 2-6 days). Compliance with the bundle elements was 90% for administration of controlled oxygen therapy (if oxygen given), 87% for administration of inhaled bronchodilators, 79% for administration of systemic corticosteroids, 75% of administration of antibiotics if evidence of infection, 77% for taking of a blood gas in non-mild disease, 98% for taking of a chest xray and 74% for administration of NIV if pH <7.3. Compliance with all appropriate elements of the defined bundle of care was 49%.

There was no difference in mean length of stay for admitted patients ($p=0.44$), in-hospital mortality ($p=1.00$) or re-admission within 30 days ($p=0.72$) by bundle compliance

Conclusion: Compliance with individual assessment and treatment recommendations was generally high, however compliance with the overall recommended bundle was only 49%. This indicates that there is an opportunity to improve care in these patients.

Key words: COPD, exacerbation, bundle of care, quality

INTRODUCTION

Exacerbations of chronic obstructive pulmonary disease (COPD) are common presentations to emergency departments (ED). Recent Australian guidelines [1] stress the importance of a number of assessments and treatments in the acute phase of care in order to optimize outcomes. These include the use of controlled oxygen therapy, inhaled bronchodilators, corticosteroids, antibiotics if there is clinical, laboratory or chest xray (CXR) evidence of infection, the taking of a chest xray, blood gas analysis for cases classified as more than mild and non-invasive ventilation (NIV) in patients with significant respiratory acidosis. There is limited data regarding compliance with each of these elements in Australasian ED.

In addition, there is growing evidence that a bundle of care approach increases compliance with guidelines and may improve outcomes. A bundle of care is a small set of evidence-based practices that when performed collectively and reliably improve patient outcomes.[2] Examples include central line bundles, ventilator bundles and sepsis bundles.[2,3]

The objectives of this study were to describe compliance with key bundle of care elements (individually and as a 'bundle') for patients treated for COPD exacerbations in the ED.

METHODS

This was a retrospective observational study performed by medical record review. It was conducted in the EDs of two metropolitan teaching hospitals in Melbourne, Australia. The EDs have a combined annual census of approximately 100,000 patients.

Patients were eligible for inclusion if they presented in the calendar year 2014 and were adult (age >40 years) with an ED discharge diagnosis coded as COPD exacerbation. Age over 40 was arbitrarily chosen in order to screen out patients more likely to have other conditions such

as asthma. Patients were excluded if the medical record was missing, they left without medical treatment, were not an ED presentation or the case was miscoded (it was clearly not COPD).

Data was collected onto a piloted data collection form. Data collected included demographics, co-morbidities, chronic medications, clinical and investigation features, treatment in ED, ED disposition and outcome. Data collectors were trained to collect the required data and provided with a data dictionary but not blinded to the objectives of the study. The data collection form is available at online appendix A. It should be noted that during the study period the EDs did not have proformas or checklists to guide management of COPD. Delivery of controlled oxygen therapy was defined as provision of oxygen therapy if required by use of nasal prongs, a venturi-type system or NIV in severe cases. Disease severity describes the severity of this exacerbation and was classified as described by the treating clinician in the medical record; it was a subjective assessment based on all available clinical and investigation data. It should be noted that the ED does not have access to acute spirometry for confirmation of diagnosis and classification of severity. Oxygen saturation was recorded as the first measurement in the ED, recognizing that a significant proportion of patients arriving by ambulance were already receiving oxygen therapy at ED arrival. pH has been reported as either arterial or venous pH which have been found to have close agreement.[4] The participating EDs routinely use venous blood gas parameters to guide initial care so we are unable to report arterial pCO₂ distribution.

The primary outcomes of interest were compliance with key bundle of care elements (individually and as 'bundles') for patients treated for COPD exacerbations in the ED. For bundle elements inhaled bronchodilators and systemic corticosteroids, these were regarded as complied with if administered either in ED or the pre-hospital setting (by ambulance paramedics). Antibiotics were considered given if received in ED or taking current course at ED arrival. Secondary outcomes of interest were comparison of mortality, length of stay (LOS) and

re-admission within 30 days between groups with and without bundle of care compliance. For this study, the bundle of care was defined as controlled oxygen therapy after initial assessment (if oxygen administered), administration of inhaled bronchodilators, systemic corticosteroids and antibiotics (if there is clinical, laboratory or CXR evidence of infection), the taking of a chest xray, blood gas analysis for cases classified as more than mild and non-invasive ventilation in patients with pH <7.3. These reflect the key recommendations of the COPD-X plan.[1]

Inter-rater reliability of data collection was assessed for 40 patients for the items age, gender, past history of heart failure (HF), smoking status, use of venturi system to administer oxygen, administration of non-invasive ventilation (NIV), administration of intravenous (IV) corticosteroids, antibiotics and inhaled beta sympathomimetic agents. Agreement was 100% for gender, use of venturi system for oxygen delivery, use of NIV and administration of IV corticosteroids (kappa 1.00). It was 98% for administration of antibiotics and inhaled beta sympathomimetic agents (kappa 0.95). It was 95% for age (kappa 0.90) and 93% for past history of HF (kappa 0.90) and smoking status (kappa 0.85).

Analysis was by descriptive statistics – percent with 95% confidence intervals (CI) and mean with standard deviation (SD) for those following a normal distribution and median and inter-quartile range (IQR) as appropriate. For the comparisons of mortality and LOS, Chi Square or Fishers Exact Test, t-test and Mann-Whitney U test were used using Analyse-It™ software.

Regarding sample size, the study was powered to detect a difference in LOS between bundle compliance groups (8 days vs. 6 days, standard deviation 6 days, $p < 0.05$, two-sided test). This would require approximately 300 admitted cases. The rationale for choosing these LOS were the data that mean LOS is a multi-country comparison was approximately 8 days [5] and that a two day reduction in LOS is clinically meaningful for both patients and the health system. As the admission rate of COPD is approximately 75% (local data), we aimed to collect data from at

least 360 eligible cases. These were chosen as the first 30 cases coded as COPD in each month and an additional 25 random cases to allow for exclusions as described above. While cases were not consecutive, we believe that this approach is unlikely to have introduced any systematic bias. The project was approved as a quality assurance project by the Western Health Low Risk Ethics Panel. Patient consent for data collection was not required.

RESULTS

381 patients met inclusion criteria. Median age was 71 (SD 12), 60% were male and 77% arrived by ambulance. Home oxygen therapy was used by 19%. Median duration of symptoms was 3 days (IQR 2-6 days). Exacerbations were classified as mild in 31% of cases, moderate in 55% and severe in 14%. Characteristics of the sample are summarized in table 1.

Treatment administered and outcomes are summarized in Table 2. All patients with initial oxygen saturation below 88% received oxygen therapy; 97% as controlled oxygen therapy. In the remaining cases the mode of oxygen delivery was unclear. Compliance with the bundle elements was 90% for administration of controlled oxygen therapy (if oxygen given), 87% for administration of inhaled bronchodilators, 79% for administration of systemic corticosteroids, 75% of administration of antibiotics if evidence of infection, 77% for taking of a blood gas in non-mild disease, 98% for taking of a chest xray and 74% for administration of NIV if pH <7.3. Compliance with all appropriate elements of the defined bundle of care was 49%. Compliance with the bundle of care varied with disease severity. Eighty three percent of exacerbations classified as severe received all indicated bundle elements compared with 47% of exacerbations classified as moderate and 38% of exacerbations classified as mild. (Omnibus Chi Square; $p < 0.0001$)

There was no difference in mean LOS for admitted patients (t-test, $p=0.44$), in-hospital mortality (Fishers test, $p=1.00$) or re-admission within 30 days (Chi Square, $p=0.72$) by bundle compliance

DISCUSSION

Our data shows that while compliance with individual assessment and treatment recommendations is generally high, compliance with the overall recommended bundle is only 49%. No difference in LOS, re-admission within 30 days or inpatient mortality based on bundle compliance was shown.

That compliance with the overall bundle was only 49% is somewhat disappointing. We were unable to identify any other study reporting compliance with the complete COPD-X guideline [1] (or similar) bundle of care in ED so are unable to compare this figure with other hospitals/ countries. Deficits are shared fairly evenly across administration of systemic corticosteroids, administration of antibiotics if there was evidence of infection and analysis of blood gases in the case of non-mild disease, with a smaller contribution of the non-use of NIV in patients with respiratory acidosis. While lack of knowledge may be a contributor, it is more likely that the major reasons for missing bundle elements are human error with underlying reasons such as time constraints in ED, distraction and competing patient priorities as several patients are being processed by a doctor at any given time, imperfect memory and cognitive overload. One approach suggested to address deficits in care provided includes the introduction of a COPD proforma or checklist. Using this approach, Sen et al demonstrated improvements in categorization of respiratory failure, administration of controlled oxygen therapy and appropriate referral for NIV.[6] They did not examine other pharmacological elements of care. Similarly, McCarthy et al showed that a proforma improved compliance with defined treatments.[7] This approach may be effective because it makes doctors aware of, or reminds them about,

guideline-based care. An alternative approach to improving compliance would be the use of a clinical informatics approach such as computer-assisted decision support which has been proven to improve patient safety and has been recommended by the US Agency for Healthcare Research and Quality.[8] This can range from simple reminder systems to monitor-based colour-coded bundle compliance visual alerts to computerized ventilator management[10] and is already being used in a range of conditions in ED and ICU.

There is limited previously published data on guideline compliance for ED treatment of COPD in Australia. Considine et al [9] in a study of ED care for COPD in 5 hospitals in 2006-7 reported that inhaled bronchodilators were administered in 71% of patients, systemic corticosteroids in 56% and NIV in 50% of patients with respiratory acidosis (defined as $\text{pH} < 7.35$). They did not collect data on antibiotic or oxygen administration or taking of CXR or blood gases. They also only looked at items individually rather than as a bundle. Pleasingly, our results show significant improvement (86% vs 71% for inhaled bronchodilators, 79% vs 56% for systemic corticosteroids and 74% vs 50% for use of NIV in respiratory acidosis). A North American study [10] (1999-2001) reported a CXR rate of 87%, blood gas analysis in 48% of patients, inhaled beta-agonists in 91%, systemic corticosteroids in 62% and antibiotics in 28% of patients. Again, our results compare favorably. Reasons for this improvement might include better awareness of evidence-based therapies/ guidelines and changes to ambulance treatment protocols allowing bronchodilators and corticosteroids to be administered pre-hospital.

Rates of controlled oxygen use in our study were high. This is probably due to a sustained nursing education campaign over several years that has seen incremental improvements in the appropriate use of oxygen therapy in patients with COPD. A high proportion of patients were classified as requiring antibiotics according to the criteria applied in this study. While compliant

with the spirit of the guideline, the clinical criterion of increased or purulent sputum and the investigation criteria of $WCC > 12$ and $CRP > 10$ may have over-called potential bacterial infection as viral infection can also result in these features. This is an area of ongoing controversy.

It is not surprising that compliance with an ED bundle for COPD did not impact mortality or LOS. The in-hospital mortality rate in our study was at the lower end of rates reported in the literature which range from 2% to 7.7% (median approx. 5%).[11-17] Our study was not powered for this endpoint. Length of stay was similar to other contemporary reports.[13-14] ED care is only a small part of the treatment. Length of stay in particular is more likely to be impacted by treatment on the wards and co-morbidities than by ED care.

This study has some limitations that should be considered when interpreting its results. Data collection was retrospective with potential issues of missing data.[18] Sampling was not consecutive and therefore there is potential for selection bias, however we believe this is unlikely. This is a single site study (two hospitals within one health service) and may not be generalizable to other sites or health systems. We did not confirm diagnosis or severity using spirometry. This was not available in the participating ED and is rarely used in acute ED practice. The age cut-off of 40 years or older was arbitrarily chosen. It may have screened out some patients with true COPD but the number is likely to be small. We are unable to report arterial pCO_2 distribution and its relationship to treatment as the participating ED routinely use venous blood gas analysis to guide initial care. Given that severity assessment in the ED environment integrates clinical assessment (ability to speak, pulse rate, work of breathing, etc), investigation findings such as CXR and blood gas analysis and that venous blood gas analysis has been shown to have excellent agreement for pH [4] and to be an accurate screening tool for arterial hypercarbia [19], we do not consider the lack of an arterial pCO_2 to have a major impact on our findings. We did not collect reasons why specific treatments or assessments were

not used. There may have been legitimate reasons for their omission so our data may be an under-estimate of compliance with the management bundle.

CONCLUSION

Compliance with individual assessment and treatment recommendations was generally high, however compliance with the overall recommended bundle was only 50%. This indicates that there is an opportunity to improve care in these patients. No difference in LOS, re-admission within 30 days or inpatient mortality based on bundle compliance was shown.

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COMPETING INTERESTS

None to declare

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Table 1. Characteristics of the sample

Characteristic	Result	Missing data
Age (years, mean, SD)	71 (12)	0
Gender (male, N, %, 95% CI)	227, 60% (55-64%)	0
Co-morbidities		
Heart failure (N, %, 95% CI)	103, 27% (23-32%)	0
Diabetes (N, %, 95% CI)	101, 27% (22-31%)	0
Ischaemic heart disease (N, %, 95% CI)	108, 28% (24-33%)	0
Smoker (N, %, 95% CI)	142, 37% (33-42%)	0
Chronic medications		
Inhaled beta-sympathomimetics (N, %, 95% CI)	329, 86% (83-89%)	0
Inhaled anti-cholinergics (N, %, 95% CI)	272, 71% (67-78%)	0
Inhaled corticosteroids (N, %, 95% CI)	250, 66% (61-70%)	0
Oral corticosteroids (N, %, 95% CI)	97, 25% (21-30%)	0
Antibiotics (N, %, 95% CI)	58, 15% (12-19%)	0
Home oxygen (N, %, 95% CI)	71, 19% (15-23%)	0
Diuretic (N, %, 95% CI)	151, 40% (35-45%)	0
Xanthine (N, %, 95% CI)	3, 0.8% (0.3-2.3%)	0
Mode of arrival (ambulance, N, %, 95% CI)	294, 78% (74-82%)	5
Duration of symptoms (median, IQR)	3, 2-6	23
Severity of exacerbation		49
Mild (N, %, 95% CI)	103, 31% (26-36%)	
Moderate (N, %, 95% CI)	181, 55% (49-60%)	
Severe (N, %, 95% CI)	48, 14% (11-19%)	
Clinical features		
Respiratory rate ≥ 30 (N, %, 95% CI)	89, 23% (19-28%)	2

Blood pressure <100 (N, %, 95% CI)	26, 7% (5-10%)	1
Temperature ≥ 38.5 C (N, %, 95% CI)	33, 9% (6-12%)	9
Pulse rate ≥ 120 (N, %, 95% CI)	65, 17% (14-21%)	1
Oxygen saturation on air <88% (N, %, 95% CI) *Note: all other patients were on supplemental oxygen at initial assessment	104, 37% (31-42%)	97*
Clinical evidence of infection (N, %, 95% CI)	160, 42% (37-47%)	0
Investigations		
White cell count >12 (N, %, 95% CI)	131, 35% (31-40%)	10
pH < 7.3 (arterial or venous, N, %, 95% CI)	40, 16% (12-21%)	128 – blood gas not performed
CXR performed (N, %; 95% CI)	373, 98% (96-99%)	0
Infiltrate on CXR (N, %; 95% CI)	133, 36% (31-41%)	0

Table 2. Treatment and outcome in ED

Treatment	Result
Controlled oxygen therapy after initial nurse assessment, if oxygen administered (N/denominator, %, 95% CI)	265/294, 90% (86-93%)
Inhaled bronchodilator (beta sympathomimetic, anti-cholinergic or both; N, %; 95% CI)	332, 87% (83-90%)
Systemic corticosteroid (oral or IV; N, %; 95% CI)	301, 79% (75-83%)
Antibiotics if evidence of infection (purulent sputum, fever >38, raised WCC ≥ 12 or CRP ≥ 10 , CXR shows infection) (N/denominator, %, 95% CI)	217/289, 75% (70-80%)
Blood gas if moderate or severe illness or oxygen saturation <90% (N/denominator, %, 95% CI)	219/271, 81% (76-85%)
CXR taken (N, %; 95% CI)	373, 98% (96-99%)
NIV if pH <7.3 (N/denominator, %, 95% CI)	29/40, 73% (57-84%)
Compliance with all applicable bundle elements (N, %; 95% CI)	186, 49% (44-54%)
Outcome	
Admitted to hospital ward (N, %; 95% CI)	288, 76% (71-80%)
Length of stay –median, days, IQR (admitted patients; N=287) Note: 1 inter-hospital transfer with incomplete data	5, 4-8
In-hospital mortality – admitted patients (N/denominator, %, 95% CI)	11/287, 3.8% (2.2-6.7%)
Re-admission to hospital ward within 30 days (N, %; denominator; 95% CI)	
Patients admitted to ward at index visit *There were 11 in-hospital deaths	73/278*, 26% (21-32%)
Patients discharged from ED at index visit	24/92, 26% (18-36%)

COPD BUNDLE CASE REPORT FORM

1. CASE NUMBER & DEMOGRAPHICS

Case number

Date of arrival in ED / / (day/month/year)

Gender Male ☐ Female ☐

Year of birth Age

2. CO-MORBIDITIES

NOTE: If not documented, assume absent

Condition	Present	Absent	Condition	Present	Absent
Chronic cardiac failure	☐ (2)	☐ (1)	Active or recent (<1 year) smoker	☐ (2)	☐ (1)
Diabetes mellitus	☐ (2)	☐ (1)	Ischaemic heart disease/ Prior MI	☐ (2)	☐ (1)
Asthma	☐ (2)	☐ (1)			

3. USUAL MEDICATION (CHRONIC USE)

NOTE: If not documented, assume absent

Name/Class	No	Yes	Name/ Class	No	Yes
Inhaled beta-sympathomimetics e.g. salbutamol, salmeterol (alone or in combination)	☐ (1)	☐ (2)	Home oxygen	☐ (1)	☐ (2)
Inhaled anti-cholinergic agent	☐ (1)	☐ (2)	Diuretic	☐ (1)	☐ (2)
Inhaled corticosteroid (alone or in combination)	☐ (1)	☐ (2)	Leukotriene receptor antagonist	☐ (1)	☐ (2)
Oral corticosteroid	☐ (1)	☐ (2)	Xanthine e.g. Theophylline	☐ (1)	☐ (2)
Antibiotic	☐ (1)	☐ (2)			

4. MODE OF ARRIVAL

Self, private car – go to question 6 ☐ (1)
Ambulance - go to question 5 ☐ (2)
Not recorded ☐ (3)

COPD BUNDLE CASE REPORT FORM

5. PRE-HOSPITAL TREATMENT BY AMBULANCE (leave blank if did not come by ambulance)

Treatment	No	Yes	Treatment	No	Yes
Oxygen	☐ (1)	☐ (2)	Corticosteroid (any route)	☐ (1)	☐ (2)
Non-invasive ventilation	☐ (1)	☐ (2)	Inhaled beta-agonist	☐ (1)	☐ (2)
Endotracheal intubation and mechanical ventilation	☐ (1)	☐ (2)	IV beta-agonist	☐ (1)	☐ (2)
Adrenaline	☐ (1)	☐ (2)			

6. INITIAL ASSESSMENT

Duration of symptoms (days, number) ☐ Not recorded (999)

Ability to speak ☐ None (1) ☐ Phrases (2) ☐ Sentences (3)
☐ Normal (4) ☐ Not recorded (5)

Auscultation (chose one that best applies) ☐ Normal (1) ☐ Wheeze (2) ☐ Basal creps (3)
☐ Widespread creps (4) ☐ Local rhonchi/bronchial breathing (5) ☐ Widespread rhonchi (6)
☐ Signs of pneumothorax (7) ☐ Signs of pleural effusion (8) ☐ Not recorded (9)

For the items below, use worst value in the first hour of ED care

Respiratory rate (number) ☐ Not recorded (999)

Systolic BP (number) ☐ Not recorded (999)

Temperature (number) ☐ Not recorded (999)

Pulse rate (number) ☐ Not recorded (999)

Oxygen saturation on air, if known (number) ☐ Not recorded (999)

Oxygen saturation on oxygen (number) ☐ Not recorded (999)

COPD BUNDLE CASE REPORT FORM

Clinical evidence of infection (purulent sputum, fever) ☐ No (1) ☐ Yes (2)

Severity assessment – recorded or implied ☐ Mild (1) ☐ Moderate (2) ☐ Severe (3) ☐ Not recorded (4)

7. INVESTIGATIONS (leave blank if not taken)

Troponin	☐ Not elevated (1)	☐ Elevated (2)
Haemoglobin	<input type="text"/>	g/dL
Neutrophil count	<input type="text"/>	X 10 ⁹ /L
Lactate	<input type="text"/>	mmol/L
pH (venous or arterial)	<input type="text"/>	
Arterial pCO ₂	<input type="text"/>	mmHg
d-dimer	☐ Not elevated (1)	☐ Elevated (2)

Imaging in ED (mark if done)

CXR	☐ No (1)	☐ Yes (2)
VQ scan	☐ No (1)	☐ Yes (2)
Evidence of infiltrate on CXR	☐ No (1)	☐ Yes (2)
Evidence of pneumothorax on CXR	☐ No (1)	☐ Yes (2)

8. TREATMENT IN THE EMERGENCY DEPARTMENT

INITIAL Oxygen delivery system in ED	☐ None (1)	☐ Standard Face mask e.g. Hudson mask (2)	☐ Venturi system (3)	☐ Non-rebreather mask (4)
	☐ Low flow nasal prongs (5)	☐ Humidified high flow nasal O ₂ (6)	☐ CPAP (7)	☐ BiPAP (8)
	☐ Bag valve mask (9)	☐ Mechanical ventilation (10)	☐ Oxygen given but mode unknown (11)	
Oxygen delivery systems in ED (tick all that apply)	☐ None (1)	☐ Standard Face mask e.g. Hudson mask (2)	☐ Venturi system (3)	☐ Non-rebreather mask (4)
	☐ Low flow nasal prongs (5)	☐ Humidified high flow nasal O ₂ (6)	☐ CPAP (7)	☐ BiPAP (8)
	☐ Bag valve mask (9)	☐ Mechanical ventilation (10)	☐ Oxygen given but mode unknown (11)	

COPD BUNDLE CASE REPORT FORM

Mechanical ventilation ☐ No (1) ☐ Yes (2)

Oral Antibiotics ☐ No (1) ☐ Yes (2)

IV antibiotics ☐ No (1) ☐ Yes (2)

Oral corticosteroids ☐ No (1) ☐ Yes (2)

IV corticosteroids ☐ No (1) ☐ Yes (2)

Inhaled beta-agonists ☐ No (1) ☐ Yes (2)

Inhaled anticholinergics ☐ No (1) ☐ Yes (2)

IV bronchodilators (salbutamol, adrenaline) ☐ No (1) ☐ Yes (2)

Aspiration of pneumothorax ☐ No (1) ☐ Yes (2)

Catheter drainage & UWSD/ Heimlich valve for pneumothorax ☐ No (1) ☐ Yes (2)

9. DISPOSITION FROM ED

Discharge destination

☐ Home (1)

☐ Home via ED
Short stay unit (2)

☐ Inpatient
ward (3)

☐ ICU/HDU (4)

☐ Transfer to
another hospital (5)

☐ Death in ED (6)

10. IF ADMITTED, FINAL HOSPITAL DISCHARGE

Date of hospital discharge
(day/ month/ year)

/ /

Total LOS (include day
of arrival at ED and day
of discharge; days)

Discharged alive ☐ Yes (2) ☐ No (1)

Re-admit within 30 days ☐ No (1) ☐ Yes (2)

COPD BUNDLE CASE REPORT FORM

ADMIN USE ONLY (AMK to complete):

11. COMPLIANCE WITH BUNDLE OF CARE ELEMENTS

COMPONENT	COMPLETED	NOT APPLICABLE
Controlled oxygen therapy after initial nurse contact (prongs, venturi, CPAP)		
Inhaled bronchodilators (salbutamol, ipratropium, both)		
Corticosteroids		
Antibiotics if evidence of infection (purulent sputum, fever > 38, raised WCC or CRP, CXR shows infection)		
CXR taken		
Blood gas if severity moderate, severe or SpO2 <90		
NIV if pH <7.3

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Author/s:

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