

8 Management of exacerbations of COPD

8.1 Introduction

Exacerbations, particularly those that result in admission to hospital, are significant events in the natural history of COPD. They are distressing and disruptive for patients, and account for a significant proportion of the total costs of caring for patients with COPD.

Much of the research into the epidemiology, pathology and management of exacerbations has been hampered by the lack of an agreed uniform definition. This is in part due to the inherent difficulties in defining exacerbations³⁸⁸. The GDG propose the definition that follows.

8.2 Definition of an exacerbation

An exacerbation is a sustained worsening of the patient's symptoms from his or her usual stable state that is beyond normal day-to-day variations, and is acute in onset. Commonly reported symptoms are worsening breathlessness, cough, increased sputum production and change in sputum colour. The change in these symptoms often necessitates a change in medication.

8.3 Consequences of having an exacerbation

In the UK, hospitalisation or management in a hospital-at-home scheme is a major event in the natural history of COPD, heralding a significant worsening of prognosis. See section 2.4.1. for the methodology underpinning this section.

▷ Evidence statements

In patients admitted to hospital in the UK with an exacerbation of COPD a retrospective audit of 1400 admissions has shown that 34% were **re-admitted** and 14% had **died** within 3 months³⁵⁰. III

In a Spanish study of patients admitted to hospital with an exacerbation of COPD 63% were **readmitted** within 1 year³⁸⁹. III

The factors associated with an increased risk of readmission were:

- ≥ 3 admissions in the previous year (Hazard Ratio 1.66, 95%CI 1.16 to 2.39)
- FEV₁ % predicted (Hazard Ratio 0.97, 95%CI 0.96 to 0.99)
- PaO₂ (Hazard Ratio 0.88, 95%CI 0.79 to 0.98)
- lower levels of physical activity (Hazard Ratio 1.85, 95%CI 1.16 to 2.94)
- need for an anticholinergic bronchodilator (Hazard Ratio 1.81, 95%CI 1.11 to 2.94)³⁸⁹.

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A study in the USA of patients admitted to an ITU with an exacerbation of COPD (median FEV₁ = 0.8 L, mean age = 70, 78% had ≥ 2 co-morbid illnesses) has shown that the 2, 6, 12 and 24 month **mortality rates** were 20%, 33%, 43% and 49% respectively³⁹⁰. **III**

Studies of a cohort of patients observed in the community have shown that **symptoms** and **peak expiratory flow rates** recover slowly after an exacerbation. **III**

The median (and inter quartile range) for recovery of symptoms was 7 days (IQR 4-14 days) and for recovery of peak expiratory flow was 6 days (IQR 1-14 days).

Recovery of PEFr to baseline was not complete in 24.8% at 35 days and 7.1% at 91 days³⁹¹.

Studies in the same cohort have shown that patients experiencing frequent exacerbations (more than 2.92 per year) have more rapid **lung function decline** (40.1 ml/yr [95% CI 38 to 42 ml/yr] vs 32.1 ml/yr [95%CI 31 to 33 ml/yr] $p < 0.05$)³⁹². **III**

Studies in the same cohort have also shown that **health related quality of life** measured using the SGRQ was significantly worse in patients experiencing frequent exacerbations (3 or more per year) (Total score -15.1 [95% CI -22.3 to -7.8, $p < 0.0005$]; Symptoms score -21.9 [95% CI -29.7 to -14.0, $p < 0.0005$]; Activities score -12.2 [95% CI -21.2 to -5.3, $p < 0.001$]; Impacts score -14.1 [95% CI -22.9 to -5.6, $p < 0.002$])³⁹³. **III**

▷ Health economics evidence statements

The costs of an exacerbation of COPD to the health care system have been estimated by Andersson et al (2002)³⁹⁴ and Price et al (1999)³⁹⁵ and have been estimated according to the severity of the exacerbation (see also section 14).

Andersson et al (2002)³⁹⁴.

Costs given in SEK, converted to GB£ by using purchasing power parities for 2002 from the OECD (www.oecd.org).

Mild	£7.94
Mild/moderate	£23.43
Moderate	£139.74
Severe	£1,446.48

Price M J et al(1999)³⁹⁵.

Mild	£14.81
Moderate	£95.20
Severe	£1,658.59

The cost of an exacerbation clearly depends on the severity of the exacerbation and there is a considerable difference in cost between a mild exacerbation and a severe exacerbation. This is mostly due to the requirement for hospitalisation for severe exacerbations.

▷ GDG consensus statements

The **long term outcomes** of exacerbations of COPD managed in the community in the UK are not known. **IV**

8.4 Causes of an exacerbation

A number of factors are known to cause exacerbations of COPD. Although bacteria can be cultured from the sputum of patients with stable COPD there is evidence that they are also responsible for exacerbations. Viruses are also important aetiological agents, particularly during winter months. Non-infectious agents are also responsible for some exacerbations. See section 2.4.1. for the methodology underpinning this section.

▷ GDG consensus statements

The following factors are known causes of exacerbations of COPD³⁹⁶. **IV**

Infections	Rhinoviruses (common cold)
	Influenza
	Parainfluenza
	Coronavirus
	Adenovirus
	Respiratory Syncytial Virus
	<i>C. pneumoniae</i>
	<i>H. influenzae</i>
	<i>S. pneumoniae</i>
	<i>M. catarrhalis</i>
	<i>Staph. aureus</i>
	<i>P. aeruginosa</i>
	Common pollutants
Particulates	
Sulphur dioxide	
Ozone	

The cause of the exacerbation may be unidentifiable in up to 30% of exacerbations. **IV**

8.5 Symptoms of an exacerbation

Exacerbations may lead to different constellations of symptoms, of varying severity, in different patients. There is no single defining symptom of an exacerbation, but changes in breathlessness, cough and sputum production are common. See section 2.4.1. for the methodology underpinning this section.

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▷ GDG consensus statements

Exacerbations of COPD can be associated with the following symptoms: **IV**

- increased dyspnoea
- increased sputum purulence
- increased sputum volume
- increased cough
- upper airway symptoms (e.g. colds and sore throats)
- increased wheeze
- chest tightness
- reduced exercise tolerance
- fluid retention
- increased fatigue
- acute confusion.

Chest pain and fever are uncommon features of COPD exacerbations and should prompt a search for other aetiologies. **IV**

8.6 Differential diagnosis of an exacerbation

Other conditions may present with similar symptoms in patients with COPD. These must be considered and excluded when making a diagnosis of an exacerbation. See section 2.4.1. for the methodology underpinning this section.

▷ GDG consensus statements

Other causes of similar symptoms in patients with COPD are: **IV**

- pneumonia
- pneumothorax
- left ventricular failure/pulmonary oedema
- pulmonary embolus
- lung cancer
- upper airway obstruction
- pleural effusion
- recurrent aspiration.

8.7 Assessment of the severity of an exacerbation

Some exacerbations are mild and self-limiting. These are frequently managed by patients at home without consulting healthcare professionals. Other exacerbations are severe, carry a risk of death and require hospitalisation. A number of factors can be used to assess the severity of an exacerbation. Not all will be present, but the occurrence of any of these should alert the clinician. See section 2.4.1. for the methodology underpinning this section.

▷ GDG consensus statements

The following signs are features of a severe exacerbation:

IV

- marked dyspnoea
- tachypnoea
- pursed lip breathing
- use of accessory muscles (sternomastoid and abdominal) at rest
- acute confusion
- new onset cyanosis
- new onset peripheral oedema
- marked reduction in activities of daily living.

8.8 Assessment of need for hospital treatment

Most patients with an exacerbation of COPD can be managed at home but a few need hospital treatment. This may be because of the severity of the exacerbation, the need for therapies that are not available to that patient at home (such as oxygen or nebulised bronchodilators), or the need for specialist interventions such as non-invasive ventilation. The decision about referral to hospital involves an assessment of the severity of symptoms (particularly the degree of breathlessness, the presence of cyanosis or peripheral oedema and the level of consciousness), the presence of co-morbidities, whether or not the patient is already receiving long term oxygen therapy, the level of physical functioning, and the patient's ability to cope at home. See section 2.4.1. for the methodology underpinning this section.

R135**RECOMMENDATIONS**

Factors that should be used to assess the need to treat patients in hospital are listed in table 15.

Grade D

Table 15 Factors to consider when deciding where to treat the patient

Factor	Treat at home	Treat in hospital
Able to cope at home	Yes	No
Breathlessness	Mild	Severe
General condition	Good	Poor/deteriorating
Level of activity	Good	Poor/confined to bed
Cyanosis	No	Yes
Worsening peripheral oedema	No	Yes
Level of consciousness	Normal	Impaired
Already receiving LTOT	No	Yes
Social circumstances	Good	Living alone/not coping
Acute confusion	No	Yes
Rapid rate of onset	No	Yes
Significant comorbidity (particularly cardiac disease and insulin-dependant diabetes)	No	Yes
Changes on chest radiograph	No	Present
Arterial pH level	≥ 7.35	< 7.35
Arterial Pao ₂	≥ 7 kPa	< 7 kPa

8.9 Investigation of an exacerbation

The diagnosis of an exacerbation is made clinically and does not depend on the results of investigations; however, in certain situations, investigations may assist in ensuring appropriate treatment is given. Different investigation strategies are required for patients managed in hospital (who will tend to have more severe exacerbations) and those managed in the community. See section 2.4.1. for the methodology underpinning this section.

Changes in lung function at the time of an exacerbation are usually small and are not helpful in routine practice.

Patients may present for the first time with an exacerbation of COPD. In this situation patients need assessing and their diagnosis confirmed as described in section 6.

Sending sputum samples for culture in primary care is of very limited value because empirical therapy is effective and should be prescribed promptly if the sputum is purulent.

RECOMMENDATIONS FOR PRIMARY CARE

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In patients with an exacerbation managed in primary care:

Grade D

- sending sputum samples for culture is not recommended in routine practice.
- pulse oximetry is of value if there are clinical features of a severe exacerbation.

RECOMMENDATIONS FOR PATIENTS REFERRED TO HOSPITAL

R137

In all patients with an exacerbation referred to hospital:

Grade D

- a chest radiograph should be obtained
- arterial blood gas tensions should be measured and the inspired oxygen concentration must be recorded
- an ECG should be recorded (to exclude comorbidities)
- a full blood count should be performed and urea and electrolyte concentrations should be measured
- a theophylline level should be measured in patients on theophylline therapy at admission
- if sputum is purulent, a sample should be sent for microscopy and culture
- blood cultures should be taken if the patient is pyrexial.

8.10 Hospital-at-home and assisted discharge schemes

Over the last few years there has been considerable interest in hospital-based rapid assessment units and early discharge schemes for patients with exacerbations of COPD. Rapid assessment units aim to identify those patients that can safely be managed at home with additional nursing and medical input rather than being admitted³⁹⁷. Early discharge schemes aim to facilitate the early discharge of patients admitted with an exacerbation of COPD³⁹⁸. Rapid assessment units generally involve a full assessment of the patient at the hospital by a multidisciplinary team and discharge to the community with appropriate support. This may include additional equipment (e.g. a nebuliser and compressor or an oxygen concentrator), nursing supervision from visiting respiratory nurse specialists, and increased social service input. Patients remain under the care of the hospital consultant but GPs are made aware of the fact that they are receiving home care. Early discharge schemes aim to identify patients in hospital who could be discharged before they have fully recovered by providing increased support in their homes.

When reviewing the evidence in this area account was taken of the site of assessment together with the length of stay in hospital before transferring home. It was important to distinguish between those schemes that constitute hospital-at-home and those that were referred to as assisted or early discharge. Assisted or early discharge schemes by their very nature involved hospital admission and usually at least one over-night stay.

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Four RCTs were found³⁹⁹⁻⁴⁰², one qualitative study⁴⁰³, one survey⁴⁰⁴ and one service evaluation³⁹⁷ which were applicable to hospital-at-home care. One RCT⁴⁰⁵ relates to early discharge. All but the qualitative research⁴⁰³ and the survey⁴⁰⁴ were situation specific to COPD exacerbations.

The GDG acknowledged that it was difficult to distinguish what constitutes hospital-at-home and early discharge from the papers reviewed and agreed not to make a distinction based on the minimum time spent in hospital. The GDG felt that the important distinction was whether services could be initiated at any time of day, seven days per week, with the obvious implications on resources and impact on the primary care.

▷ Evidence statements

There were no significant differences in **FEV₁**³⁹⁹⁻⁴⁰¹ or **readmission rates**³⁹⁹⁻⁴⁰² between hospital and home care for patients with COPD exacerbations. There were also no significant differences between the two groups for the **number of days in care**⁴⁰¹. **Ib**

There were no significant differences in **mortality** rates between those patients cared for as part of a hospital-at-home scheme and in-patients⁴⁰⁰⁻⁴⁰². **Ib**

Two studies showed no significant differences between the groups for **HRQL (SGRQ)** (subgroup analysis)⁴⁰⁰, **chronic respiratory disease questionnaire (CRDQ)**³⁹⁹. One Spanish study showed significant improvement in **SGRQ**⁴⁰². **Ib**

There were no significant differences between the groups for **symptom scores**⁴⁰¹. **Ib**

In relation to **additional support services** Skwarska et al³⁹⁹, found that GPs and carers did not differ significantly between hospital-at-home and in-patient care during an 8 wk follow up period. **Ib**

There were no significant differences in the **satisfaction scores** with the care package for either patient or carers between the two groups⁴⁰¹. **Ib**

Qualitative research, using a grounded theory approach (n=29) in a population of older patients (65 to 89 years) highlighted that the likelihood of surviving illness was the most important **determinant of preference** for home or hospital care in acute illness. For some, home care was seen as a low intensity service. Factors influencing perceptions included social support, self-reliance and past experience with illness⁴⁰³. This study is limited by the geographical location of the research (USA) where differences in payment of healthcare systems may affect the patient's preference for site of care. This study is also not specific to COPD patients. **III**

Cotton et al⁴⁰⁵, n=81 found on an intention to treat basis that a policy of early discharge reduced **in-patient stay** from a mean of 6.1 days (range 1 to 13 days) with conventional management to 3.2 (range 1 to 16) days with an early discharge scheme. This study is limited by its relatively small sample size. **Ib**

There were no significant differences in the number of patients that were **readmitted** in each group, the number of **additional days readmitted patients spent in hospital** or the **mortality rate**⁴⁰⁵.

▷ Health economics evidence statements

Seven small studies were found. Some studies were specific to patients with severe COPD. Many of the studies had methodological limitations and were not full economic evaluations, they only gave limited details of cost. One study suggested that there was an increase in overall healthcare costs for hospital-at-home. This was mainly because of an increased use of GP services and other primary care resources, as well as the cost of the hospital-at-home care. This means that costs may be shifted to primary care when patients spend fewer days in the hospital and use the hospital-at-home scheme⁴⁰⁶.

There is limited evidence that a hospital-at-home scheme is more expensive than inpatient care, as it shifts resource use to primary care⁴⁰⁶. In a Spanish study based around tertiary referral hospitals, hospital-at-home was cheaper in the short term than conventional care⁴⁰².

There is limited evidence that a supported discharge scheme may be cheaper than usual inpatient care³⁹⁹.

RECOMMENDATIONS

R138	Hospital-at-home and assisted discharge schemes are safe and effective and should be used as an alternative way of managing patients with exacerbations of COPD who would otherwise need to be admitted or stay in hospital.	Grade A
R139	The multi professional team required to operate these schemes should include allied health professionals with experience in managing patients with COPD, and may include nurses, physiotherapists, occupational therapists and generic health workers.	Grade D
R140	There are currently insufficient data to make firm recommendations about which patients with an exacerbation are most suitable for hospital-at-home or early discharge. Patient selection should depend on the resources available and absence of factors associated with a worse prognosis, e.g. acidosis.	Grade D
R141	Patient's preferences about treatment at home or in hospital should be considered.	Grade D

8.11 Pharmacological management

8.11.1 Inhaled bronchodilators

Increased breathlessness is a common feature of an exacerbation of COPD. This is usually managed by taking increased doses of short-acting bronchodilators. The GDG has not reviewed the evidence for the effects of these drugs in this context but has considered their efficacy as bronchodilators in section 7.3.

As well as taking increased doses of bronchodilators at the time of an exacerbation, these drugs may be given using different delivery systems. This is considered in the next section.

8.11.2 Delivery systems for inhaled therapy during exacerbations

Bronchodilators are used to treat the increased breathlessness that occurs during exacerbations. Some patients who normally inhale these drugs from hand held inhalers use nebulised therapy during exacerbations. In this section the evidence underpinning this practice is reviewed. See section 2.4.1. for the methodology underpinning this section.

▷ Evidence statement

One meta analysis was found⁴⁰⁷ of bronchodilator delivery in acute airflow obstruction. **Ia**

Subgroup analysis of 48 patients from 3 studies with COPD gave a small but non-significant treatment effect size (favouring wet nebulization) of 0.23 (95% CI -0.35 to 0.81)⁴⁰⁷.

▷ GDG consensus statements

Hand-held inhalers (when used with spacer devices and a good inhaler technique) and nebulisers are equally effective in achieving bronchodilation in COPD exacerbations¹⁶⁵. **IV**

For low dose bronchodilator therapy - for example, 100-400 mg salbutamol or terbutaline - treatment with a metered dose inhaler is more convenient whilst a nebuliser can deliver higher doses more easily¹⁶⁴. **IV**

Breathless patients are less likely to be able to inspire slowly or breath hold for optimum lung deposition from a metered dose inhaler¹⁶⁴. **IV**

Nebulisers are widely used in most hospitals because they are regarded as more convenient for healthcare staff to administer and because less patient education or cooperation is required. This statement is based on ERS recommendations¹⁶⁵. **IV**

This usage does not imply that nebulised therapy is superior and this should be made clear to patients and their relatives¹⁶⁵. **IV**

A nebuliser has the advantage of being independent of effort or breathing pattern when a patient is distressed. This means that a patient can begin nebulised treatment using a mask or a mouthpiece while the medical attendant can continue with other tasks. The use of a metered dose inhaler in this situation would require the medical attendant (or respiratory therapist or nurse) to stand by the patient and supervise or administer multiple doses of treatment, possibly more than 20, at one minute intervals¹⁶⁴. **IV**

Nebulised treatment might have a further beneficial effect due to its physical properties. Inhaled droplets may alter mucus viscosity in the airways and nebulised terbutaline or saline may help patients with bronchiectasis to expectorate. Whether this is also true in acute COPD is not known¹⁶⁴. **IV**

Theoretically a mouthpiece may be better as it avoids nasal deposition of drugs, although no advantage has been found in two small clinical studies in stable asthma and COPD. **IV**

Patients may prefer a face mask, especially when acutely breathless, a situation where patients are likely to mouth breathe and thus diminish the theoretical disadvantages of the face mask. A mouthpiece may avoid the risk of ocular complication with anticholinergic agents¹⁶⁵.

RECOMMENDATIONS

R142	Both nebulisers and hand-held inhalers can be used to administer inhaled therapy during exacerbations of COPD.	Grade A
R143	The choice of delivery system should reflect the dose of drug required, the ability of the patient to use the device and the resources available to supervise the administration of the therapy.	Grade D
R144	Patients should be changed to hand-held inhalers as soon as their condition has stabilised because this may permit earlier discharge from hospital.	Grade D
R145	If a patient is hypercapnic or acidotic the nebuliser should be driven by compressed air, not oxygen (to avoid worsening hypercapnia). If oxygen therapy is needed it should be administered simultaneously by nasal cannulae.	Grade D
R146	The driving gas for nebulised therapy should always be specified in the prescription.	Grade D

8.11.3 Systemic corticosteroids

This section focuses on the area of oral or systemic steroids (excluding inhaled steroids) in relation to exacerbations of COPD. Three systematic reviews were identified⁴⁰⁸⁻⁴¹⁰ relating to the use of oral / systemic steroids in the treatment of COPD exacerbations.

The trials within each of the systematic reviews were mostly small to moderate in sample size with short to medium term follow up of a maximum of 6 months. Drug preparations, dosages and routes of administration also varied significantly.

The GDG was aware of methodological limitations in the Bullard et al paper⁴¹¹ which was included in the above systematic reviews. After transfer from emergency care blinding was broken and 12 patients (10%) crossed protocol. In addition to this there appeared to be an error in reporting the data for lung function parameters. The results reported being outside of the boundaries of the 95% confidence interval. This error was evident in the PEF_R and FEV₁ data for the non-steroid group. The FEV₁ 0-6 hour data may have been incorporated into the Wood Baker et al systematic review⁴⁰⁹ within the FEV₁ meta-analysis. Comments pertaining to this are noted on the Cochrane Internet site within the comments section (McCrary 1999). When reviewing the FEV₁ meta analysis weighted % the Bullard⁴¹¹ data only contributed 7.7%. The other two systematic reviews^{408;410} did not undertake any meta analysis. Hence the Bullard paper has been excluded from the evidence statements made below.

In addition to the three systematic reviews, one additional randomised controlled trial was found⁴¹² (n=199, 10 days follow-up), using oral prednisolone and a placebo.

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The GDG also observed that the dose of steroids used in the North American studies was considerably higher than the doses used in the UK. In addition to this, although there are data on the incidence of acute adverse events, there are no data on the long term consequences of frequent courses of oral steroids.

▷ Evidence statements

Three systematic reviews⁴⁰⁸⁻⁴¹⁰ all reviewed virtually the same RCTs. The reviews demonstrated a significant effect in favour of steroids over placebo for **FEV₁ for at least 72 hours**. In the meta analysis by Wood Baker et al⁴⁰⁹ of 6 RCTs, the WMD was 120 ml (95% CI; 5ml to 190ml). **Ia**

One additional RCT was found⁴¹². This trial also demonstrated significant improvements in **FEV₁ up to 36 hours** with a mean difference of 160ml (95% CI; 9ml to 240ml) in favour of the intervention compared to placebo. **Ib**

Davies et al⁴¹³, Niewoehner et al⁴¹⁴ and Thompson et al⁴¹⁵ (all trials included in the systematic reviews) measured **FEV₁** at multiple time points over differing time frames. These trials found statistically significant improvements occurred in the first 3 to 5 days of corticosteroid treatment compared to the control⁴⁰⁸. **Ia**

Maltais et al⁴¹² and Thompson⁴¹⁵ demonstrated a statistically significant improvement in arterial **PaO₂** in the first 72 hours in favour of the steroid group compared to placebo <0.05. **Ib**

Significantly shorter **duration of hospitalisation** was demonstrated by Niewoehner et al⁴¹⁴ (p=0.03) and Davies et al⁴¹³ (p=0.027) in favour of the steroids compared to placebo. **Ib**

In one further study with no objective assessment of fitness for discharge, Maltais⁴¹² found no significant differences in the mean duration of hospitalisation between steroid and placebo groups. **Ib**

A meta analysis of 5 RCTs found no statistically significant differences between the steroid and control groups for **mortality**⁴⁰⁹. **Ia**

The systematic review by McCrory et al⁴⁰⁸ highlighted the current debate around **duration** of steroid treatment and **dose** during COPD exacerbations^{413;414;416}. **Ia**

Niewoehner et al⁴¹⁴ included a randomised comparison between a 2 and 8-week course of systemic corticosteroids. Findings demonstrated that there were no important clinical differences in clinical outcomes between the two courses.

There is still debate about the optimal dose and duration of treatment of steroids. "Small studies suggest that even lower doses⁴¹³ and even shorter courses of treatment⁴¹⁶ may be effective".

Meta analysis by Wood Baker et al⁴⁰⁹ of 5 RCTs showed a significantly beneficial effect of steroids compared to placebo at reducing **treatment failure**, OR 0.50 (95% CI; 0.32 to 0.79). It should be noted however that there was significant heterogeneity between the trials p=0.0071. This was potentially due to differences in operational definitions between the trials. **Ia**

Three RCTs^{413;414;416} were combined in a meta analysis by Wood Baker et al⁴⁰⁹ for **adverse events**. “Overall, patients receiving corticosteroid treatment were 2.7 times more likely to have an adverse drug reaction than those receiving placebo”.

Ia

Niewoehner et al⁴¹⁴ (n=271) found that a greater proportion of patients in the steroid compared to placebo group required treatment for hyperglycaemia (15% vs. 4%, p=0.002). 67% of the steroid treated patients with hyperglycaemia had diabetes. Maltais et al⁴¹² also found an increased incidence of hyperglycaemia. The hyperglycaemia was asymptomatic in patients in both studies and there was no increase in the onset of diabetes.

Ib

RECOMMENDATIONS

R147	In the absence of significant contraindications oral corticosteroids should be used, in conjunction with other therapies, in all patients admitted to hospital with an exacerbation of COPD.	Grade A
R148	In the absence of significant contraindications, oral corticosteroids should be considered in patients managed in the community who have an exacerbation with a significant increase in breathlessness which interferes with daily activities.	Grade B
R149	Patients requiring corticosteroid therapy should be encouraged to present early to get maximum benefits (see recommendations 122-126).	Grade D
R150	Prednisolone 30mg orally should be prescribed for 7 to 14 days.	Grade D
R151	It is recommended that a course of corticosteroid treatment should not be longer than 14 days as there is no advantage in prolonged therapy.	Grade A
R152	For guidance on stopping oral corticosteroid therapy it is recommended that clinicians refer to the BNF.	Grade D
R153	Osteoporosis prophylaxis should be considered in patients requiring frequent courses of oral corticosteroids.	Grade D
R154	Patients should be made aware of the optimum duration of treatment and the adverse effects of prolonged therapy.	Grade D
R155	Patients, particularly those discharged from hospital, should be given clear instructions about why, when and how to stop their corticosteroid treatment.	Grade D

8.11.4 Antibiotics

Bacteria can be isolated from sputum samples during periods of stability in COPD but are also associated with exacerbations. Antibiotics are commonly prescribed for episodes of purulent sputum. The bacteria that have been isolated during exacerbations are generally sensitive to most broad-spectrum antibiotics. There has been controversy about whether antibiotics have a benefit in exacerbations and more specifically about whether their use should be restricted to patients with purulent sputum. Early studies included patients with clinically defined “chronic bronchitis” rather than COPD as defined by airflow obstruction. This makes extrapolation difficult⁴¹⁷.

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There have been two recent publications^{408;418} that have assimilated the evidence base (including the meta analysis by Saint et al⁴¹⁹) relating to the use of antibiotics during COPD exacerbation. These publications were of rigorous methodological quality and hence the evidence statements cited below are mainly based upon their content.

In addition, three other studies were found⁴²⁰⁻⁴²² that following critical appraisal were also worthy of inclusion.

Because of the uncertainty over the role of antibiotics in the management of exacerbations of COPD and the methodological limitations of studies that aim to determine the relative efficacy of different antibiotic drugs without including a placebo comparison, the GDG have only considered studies that include a placebo comparison. The antibiotic drugs that were studied included tetracycline, doxycycline, chloramphenicol, penicillin, streptomycin, ampicillin, amoxicillin and cotrimoxazole compared to placebo. The fact that there was no agreed definition of an exacerbation limits the interpretation of these studies.

▷ Evidence statements

A meta analysis of nine trials⁴¹⁹ cited in⁴⁰⁸ found a small but statistically significant effect favouring antibiotics over placebo in patients with **exacerbations of COPD**. Effect size 0.22 (95% CI, 0.1 to 0.34). **Ia**

Four studies⁴²³⁻⁴²⁵ all cited by AHRQ⁴⁰⁸ and Allegra et al⁴²² assessed whether there was a relationship between **severity of exacerbation** and the effectiveness of antibiotic use. **Ia**

Three of these studies suggest that the worse the COPD severity of exacerbation (lung function impairment (FEV₁, PEFr), purulence of sputum) then the greater the degree of benefit from antibiotics. **Ib**

Anthonisen et al⁴²³ showed a relationship of better outcomes with antibiotic versus placebo treatment based upon the severity of exacerbations. **Type 1 exacerbations (increased amount and purulence of sputum and dyspnoea)** benefited the most with resolution of symptoms in 63% of the antibiotic treated exacerbations and 43% of the placebo group. Patients with type-3 exacerbation (who met none of the three criteria) did not show any benefit. **Ib**

Berry et al⁴²⁵ assessed the severity of exacerbation at presentation on a 4-point scale (baseline, mild, moderate or severe). Mild exacerbations demonstrated no significant difference. For patients presenting with **moderate or severe exacerbations**, the antibiotic group had significantly less severe symptoms on days 2 and 7 (but were not significant at two weeks). **Ib**

Allegra 2001 (n=46) in a retrospective data analysis of a previously reported RCT, re-clustered patients on the basis of severity of baseline lung function. The original RCT compared amoxicillin-clavulanic acid to placebo in patients with exacerbations of chronic bronchitis. The improvement or success rate vs. the failure rate was significantly different in **severe exacerbation** patients compared to those with exacerbations of a less severity. **Ib**

In relation to the use of quinolones, the SIGN publication on Community Management of Lower Respiratory Tract Infection⁴¹⁸ cites Davies et al⁴²⁶. Although quinolones have **Ib**

performed equally well in clinical trials, no clinical superiority over other antibiotics has yet been shown⁴²⁶.

Nouira et al⁴²⁰ undertook a small RCT (n=90) assessing the efficacy of oral ofloxacin in patients with severe exacerbation of COPD requiring ventilation. In relation to **deaths**, 4% (n=2) of patients receiving ofloxacin and 22% (n=10) in the placebo group died in hospital (ARR 17.5%, 95% CI 4.3 to 30.7, p=0.01). Treatment with ofloxacin significantly reduced the need for **additional courses of antibiotics** (ARR 28.4%, 95% CI 12.9 to 43.9, p=0.0006). **Duration of mechanical ventilation** and **hospital stay** was significantly shorter in the antibiotic group than placebo group (absolute difference 4.2 days, 95% CI, 2.5 to 5.9) and (absolute difference 9.6 days, 95% CI, 3.4 to 12.8) respectively.

Ib

Sin et al⁴²¹ undertook a large population based retrospective cohort study (n=26301) to determine the association between outpatient use of oral antibiotics and 30-day all-cause mortality following hospitalisation in a group of elderly COPD patients. Patients who used antibiotics within 30-days of the index hospitalisation date experienced lower odds for all-cause 30-day **mortality** after hospitalisation than those who did not receive antibiotics. (OR 0.83, 95% CI, 0.75 to 0.92). In relation to antibiotic use, macrolides had the lowest relative odds for mortality (OR 0.58, 95% CI 0.47 to 0.73) and fluoroquinolones had the highest relative odds (OR 0.98, 95% CI 0.84 to 1.15).

III

▷ Health economics evidence statements

A pharmacoeconomic review was found, looking at the cost effectiveness of antibiotic therapy⁴²⁷. This concluded that due to the small number of economic evaluations and the nature of the designs, it was not possible to make a definitive statement recommending which specific antibacterial should be preferred on cost effectiveness grounds for the management of acute bacterial exacerbations of chronic bronchitis and future research is suggested.

Key points from the review by Morris et al⁴²⁷ are:

- accurate diagnosis is a key factor affecting the cost effectiveness of antibacterials, in order to avoid unnecessary prescribing
- initial empirical treatment antibiotics which are more effective but usually more costly in terms of drug acquisition price are likely to be more cost effective. This is mainly due to reducing the high costs associated with treatment failure.

A decision analytic model which was included in the review, constructed by Backhouse et al⁴²⁸, supported the use of amoxicillin-clavulnic acid as first and second line therapy over amoxicillin. Even though this drug has a higher acquisition cost, its higher efficacy rate was found to reduce the cost of treatment failure. The model was based on a general practice setting in the UK from the perspective of the NHS. The model was constructed in 1995, did not include side effects and there are concerns over the quality of the clinical data used in the model. Many of the studies were uncontrolled, had small sample sizes, differed in operational definitions of treatment success and study endpoints and are now considered old. We cannot be confident that this model applies to current conditions and there is too much uncertainty over the effectiveness data used to recommend the results. Further research is suggested on this issue⁴²⁸.

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One study⁴²⁹ undertook an economic evaluation alongside a trial to estimate the incremental cost per quality adjusted life year (QALY) of ciprofloxacin vs. usual antibacterial care. In a subgroup analysis of patients with severe chronic bronchitis, ciprofloxacin was more cost effective, dominating usual antibacterial care.

RECOMMENDATIONS

R156	Antibiotics should be used to treat exacerbations of COPD associated with a history of more purulent sputum.	Grade A
R157	Patients with exacerbations without more purulent sputum do not need antibiotic therapy unless there is consolidation on a chest radiograph or clinical signs of pneumonia.	Grade B
R158	Initial empirical treatment should be an aminopenicillin, a macrolide, or a tetracycline. When initiating empirical antibiotic treatment prescribers should always take account of any guidance issued by their local microbiologists.	Grade D
R159	When sputum has been sent for culture, the appropriateness of antibiotic treatment should be checked against laboratory culture and sensitivities when they become available.	Grade D

8.11.5 Theophylline and other methylxanthines

As well as their apparent actions as bronchodilators, theophylline also appears to increase respiratory drive^{430;431} and this appears capable of overcoming some of the respiratory depression present during exacerbations⁴³². For these reasons they have been used to treat patients admitted to hospital with an exacerbation.

The GDG were aware of one systematic review⁴³³ relating to the use of methylxanthines for exacerbations of COPD. All other abstracts identified by the literature search were either already included in the systematic review⁴³³ or were excluded due to use in stable COPD patients^{68;94;146;434;435} or small sample size⁴³⁶.

▷ Evidence statements

The systematic review⁴³³ identified three RCTs and one abstract with a total sample size of n=169. Methylxanthines were compared to placebo in patients with exacerbations of COPD. However, the following limitations were noted: the mean age of subjects was low (mean age 65 years), limited outcome measures e.g. changes in FEV₁ were used, and only three trials⁴³⁷⁻⁴³⁹ plus one abstract⁴⁴⁰ were available for review. These studies had relatively small sample sizes (n=50, 52, 39 respectively). There were no significant differences in **pulmonary function** or **symptom scores**. **Ia**

▷ GDG Consensus statement

The GDG concluded that there was inadequate evidence to recommend a change from the current clinical practice of using intravenous theophylline to treat exacerbations of COPD. **IV**

RECOMMENDATIONS

R160	Intravenous theophylline should only be used as an adjunct to the management of exacerbations of COPD if there is an inadequate response to nebulized bronchodilators.	Grade D
R161	Care should be taken when using intravenous theophylline because of interactions with other drugs and potential toxicity if the patient has been on oral theophylline.	Grade D
R162	Theophylline levels should be monitored within 24 hours of starting treatment and subsequently as frequently as indicated by the clinical circumstances.	Grade D

8.11.6 Respiratory stimulants

During exacerbations some patients develop hypercapnic ventilatory failure. This is now usually managed using non-invasive ventilation (see section 8.13), but centrally acting drugs have also been used to stimulate respiratory drive. These drugs have a short duration of action and must be given by intravenous infusion.

One systematic review⁴⁴¹ was found and one RCT⁴⁴² which looked at the role of respiratory stimulants in patients with exacerbations of COPD. Both papers had methodological limitations, which included lack of detail of power calculations, small sample size, and lack of operational definitions.

The Greenstone et al systematic review⁴⁴¹ identified 4 RCTs (n=176 in total). One study compared doxapram with placebo⁴⁴³ but approximately 40% of patients had a pH > 7.35 at entry and patients had an age range of 21 to 78 years. Another unblinded RCT by Angus et al⁴⁴⁴ compared doxapram with NIV (n=17). The third study⁴⁴⁵ contained in the review⁴⁴¹ compared doxapram with other stimulants not currently used. The fourth study contains data from an unpublished study⁴⁴⁶ comparing doxapram with non-invasive ventilation. No numerical data is available for inclusion into the analyses.

An additional RCT⁴⁴² was found which compared oral almitrine to placebo (n=23) but there was no power analysis. There was a general lack of methodological detail (e.g. randomisation, concealment and blinding processes). Only 74% of patients completed the study. The data was analysed on an intention to treat basis.

The results of all of these trials should be treated with caution due to the inherent methodological limitations and in light of these it was felt to be inappropriate to present evidence statements based on these data.

▷ GDG consensus statements

Whilst the GDG acknowledges that doxapram is effective the group believe that non-invasive ventilation is more effective and is the treatment of choice for patients with respiratory failure during exacerbations of COPD.

IV

There is insufficient evidence to recommend a change from current clinical practice of using doxapram to treat respiratory failure during exacerbations of COPD. **IV**

RECOMMENDATIONS

R163

It is recommended that doxapram is used only when non-invasive ventilation is either unavailable or considered inappropriate.

Grade D

8.12 Oxygen therapy during exacerbations of COPD

During exacerbations of COPD patients develop worsening breathlessness. This may be associated with hypoxia and oxygen is commonly used to relieve the symptoms and raise arterial oxygen saturations. Patients are often given oxygen during their transfer to hospital in an ambulance, whilst being assessed at hospital and during the treatment of their exacerbation. The main aim is to prevent life-threatening hypoxia; however, in patients with COPD, this must be done with caution as some patient's respiratory drive depends on their degree of hypoxia rather than the usual dependence on hypercapnia. Thus uncontrolled oxygen therapy can result in suppression of respiratory drive, carbon dioxide narcosis and ultimately respiratory arrest.

Much of the literature concerning the use of oxygen therapy for exacerbations of COPD is old and many studies did not have control groups. Recently a group of respiratory emergency medicine and intensive care physicians in the North West of England have reviewed the literature in this area⁴⁴⁷ and developed guidelines on the use of emergency oxygen therapy for breathless patients⁴⁴⁸. These guidelines are not exclusively for patients with COPD but do make specific recommendations regarding the administration of oxygen to patients with exacerbations of COPD. The GDG has considered these recommendations when formulating its consensus statements and recommendations. See section 2.4.1. for the methodology underpinning this section.

▷ Evidence statements

During exacerbations patients with COPD may become significantly hypoxic. Three studies⁴⁴⁹⁻⁴⁵¹ have shown that the PaO₂ falls from 55-60 mmHg to 25-50 mmHg during an exacerbation. **III**

There are marked variations in the response of individual patients to oxygen. King et al⁴⁵² gave 24% oxygen to patients with exacerbations of chronic respiratory failure. They recorded a mean PO₂ of 40.4 mmHg in these patients on room air and a mean PO₂ of 57.3 mmHg after 30 to 60 minutes of 24% oxygen but 15 out of 40 patients did not increase their PO₂ beyond 50 mmHg. **IIb**

In a prospective randomised crossover study Agusti et al⁴⁵¹ gave oxygen to 18 patients with COPD, within 48 hours of an admission with acute respiratory failure. Oxygen was given via nasal prongs at 2-4 l/min and Venturi masks at 24-28%. These concentrations raised the oxygen saturation to greater than 90% immediately in all cases. Oxygen was administered for 24 hours via each device and the oxygen saturation monitored continuously. Patients subsequently had an oxygen saturation **Ib**

less than 90% for a mean of 3.7 hours using the Venturi mask and 5.4 hours using nasal prongs. In extreme cases patients were poorly oxygenated for as long as 15 hours. It was found that the oxygen saturation was between 70 and 80% for a mean of 80 minutes, between 60 and 70% for a mean of 38 minutes and between 50 and 60% for a mean of 4 minutes during these periods of poor oxygenation. Inter-subject variability was considerable.

Oxygen therapy may lead to hypercapnia and acidosis.

- Plant et al⁴⁵³, in 2000, found a significant negative correlation between pH and PaO₂ in 972 patients after oxygen therapy. The more oxygenated patients became the greater the magnitude of the subsequent respiratory acidosis. 47% of patients were hypercapnic, 20% of patients were acidotic and 4.6% of patients had a pH less than 7.25. More than 50% of hypercapnic patients were acidotic if the PaO₂ was greater than 75 mmHg⁴⁵³. **III**
- Degaute et al⁴⁵⁴ gave 35 patients with exacerbations of COPD 28% oxygen for one hour. The average PaCO₂ rose from 59 mmHg to 63 mmHg during that period. **IIb**
- Smith et al⁴⁵⁵ gave 27 patients with an exacerbation of COPD and respiratory failure 24% to 28% oxygen for four hours. Sixteen patients had increases in PaCO₂ and, in two of these, dangerous respiratory acidosis developed with the pH decreasing to below 7.25. **IIb**
- Eldridge et al⁴⁵⁶ gave oxygen at flow rates ranging from 2 to 12 litres per minute in random order for at least 20 minutes at each level to 19 patients with exacerbations of COPD. In 17 patients there were progressive rises in PaCO₂ with increasing PaO₂ and the PaCO₂ fell when the arterial PaO₂ changed from a higher to a lower value. Again, there was great variability in the increases in PaCO₂ for a given increase in PaO₂ between patients. **IIb**
- Prime and Wenstlake⁴⁵⁷ gave 100% oxygen to 35 patients with stable COPD for 30 to 40 minutes. Thirty-three had increases in PaCO₂ ranging from 1.2 to 25.4 mmHg. **IIb**
- Aubier et al⁴⁵⁸ gave 100% oxygen for 15 minutes to 22 patients with an exacerbation of COPD and respiratory failure. There was an average increase in PaCO₂ of 23 ± 5 mmHg and there was an average drop in pH from 7.34 ± 0.01 to 7.25 ± 0.02. **IIb**

Radial stabs to obtain blood for arterial blood gas analysis are not more painful than arterialised ear lobe gases⁴⁵⁹. **III**

Arterialised ear lobe gases may not accurately reflect PaO₂ but are acceptable for PaCO₂⁴⁵⁹⁻⁴⁶². **III**

▷ GDG Consensus statements

Arterialised ear lobe samples are an alternative way of obtaining arterial blood gases if there is local expertise and may be less painful for patients. **IV**

RECOMMENDATIONS

R164	The oxygen saturation should be measured in patients with an exacerbation of COPD, if there are no facilities to measure arterial blood gases.	Grade D
R165	If necessary, oxygen should be given to keep the SaO ₂ greater than 90%.	Grade C
R166	Pulse oximeters should be available to all health care professionals managing patients with exacerbations of COPD and they should be trained in their use. Clinicians should be aware that pulse oximetry gives no information about the PCO ₂ or pH.	Grade D
R167	In the interim period while the recommendation on the availability of oximeters is implemented, oxygen should be given to all patients with an exacerbation of COPD who are breathless, if the oxygen saturations are not known.	Grade D
R168	During the transfer to hospital the following points should be considered: <ul style="list-style-type: none"> • It is not desirable to exceed an oxygen saturation of 93%. Oxygen therapy should be commenced at approximately 40% and titrated upwards if saturation falls below 90% and downwards if the patient becomes drowsy or if the saturation exceeds 93-94%. • Patients with known type II respiratory failure need special care, especially if they require a long ambulance journey or if they are given oxygen at home for a prolonged period before the ambulance arrives. 	Grade D
R169	When the patient arrives at hospital, arterial blood gases should be measured and the inspired oxygen concentration noted in all patients with an exacerbation of COPD. Arterial blood gas measurements should be repeated regularly, according to the response to treatment.	Grade D
R170	The aim of supplemental oxygen therapy in exacerbations of COPD is to maintain adequate levels of oxygenation (SaO ₂ >90%), without precipitating respiratory acidosis or worsening hypercapnia. Patients with pH<7.35 should be considered for ventilatory support.	Grade D

8.13 Non invasive ventilation (NIV) and COPD exacerbations

Non invasive ventilation (NIV) is a method of providing ventilatory support that does not require the placement of an endotracheal tube. It is usually delivered via a mask that covers the nose, but occasionally a full face mask covering the nose and the mouth is required. The ventilators themselves are compact and portable.

Non invasive ventilation is now widely used for the treatment of respiratory failure occurring during exacerbations of COPD. It has many advantages over intubation and ventilation and can be used outside ITUs.

Three systematic reviews were identified⁴⁶³⁻⁴⁶⁵ and two additional RCTs^{466,467} that compared NIV (nasal or mask) to usual medical care. Conti et al⁴⁶⁷ compared NIV to conventional ventilation (endotracheal ventilation).

Factors for consideration within this topic include; 1) Operational definitions regarding what constitutes an Intensive Care Unit (ICU) differ between countries; 2) Due to the type of intervention applied (NIV) double blinding is not possible; 3) The comparator of 'standard treatment' is not always defined but include oxygen, antibiotics, bronchodilators, steroids, respiratory stimulants and methylxanthines; 4) Trials are generally of small sample size and 5) Lastly, as highlighted by Ram et al⁴⁶⁵, there is potential systematic bias in the trials as patients who failed treatment before 1 hour are missing in the one hour measurements.

The RCT by Thys et al⁴⁶⁶ had methodological limitations (sample size n=20) was stopped at the interim analysis stage as the ten patients in the placebo NIV and convention medical care group all required active ventilation (3 full endotracheal intubation). Conti et al⁴⁶⁷, for the majority of the outcomes, only provides descriptive statistics in the form of percentages rather than inferential statistics.

▷ Evidence statements

NIV compared to usual medical care decreases **mortality**. Relative risk 0.41 (95% CI; 0.26 to 0.64)⁴⁶⁵. Odds ratio (OR) 0.22; (95% CI; 0.09 to 0.54 for COPD only trials)⁴⁶⁴. Risk difference -0.13 (95%CI; -0.21 to -0.06 for COPD sub group)⁴⁶³. **Ia**

NIV compared to usual medical care decreased the need for **intubation**. Relative risk 0.42 (95%CI 0.31 to 0.59)⁴⁶⁵. OR 0.12 (95%CI; 0.05 to 0.29 for COPD only trials)⁴⁶⁴. Risk difference -0.18 (95% CI; -0.33 to -0.03 for COPD sub group)⁴⁶³. **Ia**

NIV compared to usual medical care resulted in improvement in **pH** in the first hour of treatment WMD 0.03 (95% CI; 0.02 to 0.04), **Paco₂** WMD -0.40 kPa, (95% CI; -0.78 to -0.03), and respiratory rate WMD -3.08 rpm, (95% CI; -4.26 to -1.89)⁴⁶⁵. **Ia**

NIV compared to usual medical care resulted in fewer **complications** (principally ventilator associated pneumonia) in the NIV group, relative risk (RR) 0.32, (95%CI 0.18 to 0.56)⁴⁶⁵. **Ia**

NIV compared to usual medical care resulted in a shorter **duration of hospital stay** WMD -3.24 days, (95%CI -4.42 to -2.06)⁴⁶⁵. Risk difference -5.66 (95% CI; -10.10 to -1.23 for COPD sub group)⁴⁶³. **Ia**

Although the Plant et al⁴⁹¹ paper is included in two of the systematic reviews quoted above^{463;465} this is the only study to be carried out in a general medical and respiratory ward **setting** in the UK. As such the GDG felt it worthy of presenting the outcomes of this study separately. The study compared NIV to standard treatment. Overall, NIV significantly reduced the need for intubation p=0.02 and mortality was reduced p=0.05. NIV compared to standard care also led to a rapid improvement in pH in the first hour p=0.02, a greater fall in respiratory rate at 4 hours p=0.035 and the duration of breathlessness was also reduced p=0.025. N.B. This study was *not* designed to identify the best setting to deliver NIV though. **Ib**

The GDG noted that the hospital stay mortality in the group receiving standard care was high at 20%. This compares to a hospital stay mortality quoted by Connors et al (1996)³⁹⁰ of 11%.

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▷ GDG consensus statements

Although the mean age of patients in these studies was 60 years there is no reason **IV** to suppose that the benefits are not the same in older patients.

▷ Health economics

Five papers were found. There were some methodological limitations in the papers. Keenan et al⁴⁶⁸ showed that NIV is cost effective in patients with a severe exacerbation of COPD as it is more effective and less expensive, compared to standard therapy alone.

Plant et al⁴⁶⁹ found that the addition of ward based NIV to standard treatment is cost effective when compared to standard treatment alone, with an incremental cost effectiveness ratio of -£645 per death avoided. Whilst costs are increased on the respiratory wards, these are offset by savings in the cost of ICU.

Modelling of results showed that providing a NIV service will avoid 6 deaths and 3-9 admissions to ICU per annum.

There is evidence that NIV is cost effective in patients with a severe exacerbation of COPD, being more effective and less expensive, compared to standard therapy alone. Keenan et al⁴⁶⁸, Plant et al (2003)⁴⁶⁹.

RECOMMENDATIONS

R171	NIV should be used as the treatment of choice for persistent hypercapnic ventilatory failure during exacerbations despite optimal medical therapy.	Grade A
R172	It is recommended that NIV should be delivered in a dedicated setting with staff who have been trained in its application, who are experienced in its use and who are aware of its limitations.	Grade D
R173	When patients are started on NIV there should be a clear plan covering what to do in the event of deterioration and ceilings of therapy should be agreed.	Grade D

8.14 Invasive ventilation and intensive care

Although non-invasive ventilation is the initial treatment of choice for respiratory failure during exacerbations of COPD, some patients do not respond adequately to NIV and require intubation and ventilation. Other patients have multiple organ system impairment or reduced levels of consciousness and in these settings ITU care may be the appropriate first line management option. In the past there has often been a reluctance to intubate patients with COPD or admit them to ITUs because of concerns about weaning and long term outcomes. The GDG has reviewed the evidence about the outcomes of ventilation and ITU care.

The GDG identified four descriptive case series of relevance⁴⁷⁰⁻⁴⁷³. Esteban et al⁴⁷¹ looked at the characteristics and outcomes in adult patients receiving endotracheal ventilation in a 28 day international study n=15757 involving 361 ICUs and 20 countries. The study is limited due to a heterogeneous population of ventilated patients and only limited details regarding COPD patients.

Nevins et al⁴⁷³ looked at predictors of outcome for patients with COPD requiring invasive ventilation. This was a retrospective analysis of patients with a history of COPD to identify the patient characteristics at the time of hospital admission that predicted a poor outcome.

Seneff et al⁴⁷⁰ in patients with exacerbations of COPD looked at hospital and one year survival of patients admitted to ICU.

Rieves et al⁴⁷² looked at a population of patients with severe COPD and acute respiratory failure and examined correlates for survival at the time of intubation.

▷ Evidence statements

The mean **duration of mechanical ventilation** for COPD patients compared to acute respiratory distress syndrome (ARDS) patients was 5.1 vs. 8.8 respectively $p < 0.001$ ⁴⁷¹. However Nevins et al 2001⁴⁷³ identified a mean duration of ventilation of 9 days (median 4 days). III

Duration of weaning was non significant between the two groups⁴⁷¹. III

Length of hospital stay in ICU was 1.2 days in the COPD patients compared to 24.5 days in the ARDS patients, $p = 0.07$, whilst **length of stay in hospital** was 21.2 days in the COPD group versus 24.5 days in the ARDS group $p = 0.07$ ⁴⁷¹. Nevins et al⁴⁷³ identified a mean duration of hospital stay of 22 days in COPD patients requiring ventilation. III

The **mortality** rate in ICU for patients who received ventilation for an exacerbation of COPD was estimated at 22%. Patient receiving mechanical ventilation due to acute decompensation of COPD had a significantly lower mortality than patients receiving mechanical ventilation because of acute respiratory failure (ARF) of other aetiologies. COPD OR 0.70; (95% CI 0.59 to 0.83); $p < 0.001$ compared to coma OR 1.31; (95%CI; 1.19 to 1.45); $p < 0.001$ ⁴⁷¹. III

There was a high mortality rate for those patients who required >72 hrs mechanical ventilation compared to those with <72 (37% vs. 16%; $p < 0.01$), those without previous episodes of mechanical ventilation (33% vs. 11%; $p < 0.01$) and those with a failed extubation attempt (36% vs. 7%; $p = 0.0001$)⁴⁷³. III

NIV can be successfully used to shorten duration of mechanical ventilation ($p = 0.002$)⁴⁷⁴. Ib

▷ GDG consensus statements

The decision on which patients with exacerbations of COPD will benefit from intubation is difficult and involves balancing health status with an estimate of expectation of survival. Factors that are likely to influence this decision are prior functional status, BMI, requirement for oxygen when stable, co-morbidities and previous ITU admissions. IV

RECOMMENDATIONS

R174	Patients with exacerbations of COPD should receive treatment on intensive care units, including invasive ventilation when this is thought to be necessary.	Grade C
R175	During exacerbations of COPD, functional status, BMI, requirement for oxygen when stable, co-morbidities and previous admissions to intensive care units should be considered, in addition to age and FEV ₁ , when assessing suitability for intubation and ventilation. Neither age nor FEV ₁ should be used in isolation when assessing suitability.	Grade D
R176	NIV should be considered for patients who are slow to wean from invasive ventilation.	Grade A

8.15 Respiratory physiotherapy and exacerbations

Physiotherapy has traditionally been used to assist sputum clearance during exacerbations of COPD. The GDG have looked at the evidence regarding the role of respiratory physiotherapy. Physiotherapists are also involved in the reablement of patients prior to discharge but the GDG have not looked at the evidence base for this aspect of management.

An extensive literature search of the role of respiratory physiotherapy was undertaken, which identified 62 potential papers. Of these 46 were excluded from the abstract. Sixteen papers were retrieved and a further 10 were excluded upon full paper review. Six papers were critically appraised. Two systematic reviews were identified^{408;475}, two RCTs^{476;477} and two quasi-experimental studies^{478;479}.

Interventions included postural drainage, chest percussion, vibration, chest shaking, directed coughing, forced exhalation, and expiration under positive pressure (PEP mask).

There was little research in this area and there were methodological limitations inherent in the studies identified. Limitations included heterogeneous populations, Jones et al 2002⁴⁷⁵ (COPD stable and exacerbations, asthmatics, cystic fibrosis) and McCrory 2001⁴⁰⁸ (stable, exacerbations and post exacerbation population), small sample sizes (Bellone et al 2000⁴⁷⁶ n=10, Wollmer et al 1985⁴⁷⁹ n=10) and hence potentially significant under powering, short-term interventions, short term outcome assessments or did not report suitable outcome data⁴⁰⁸. Many of the trials precluded meta analysis due to the diversity of patient groups and outcomes⁴⁷⁵. One RCT by Bellone 2000⁴⁷⁸ on the effects of using a PEP mask included selected patients with mucus hyper secretion making it difficult to be sure that the results of this small study (n=27) can be generalised.

The results of most of these trials^{408;475-477;479} should be treated with caution due to the inherent methodological limitations and in light of this the GDG felt it inappropriate to present evidence statements based on these studies.

▷ Evidence statements

Bellone et al⁴⁷⁸ (n=27) looked at the short term effects of using a PEP mask in patients with exacerbation of COPD and mild acidosis requiring NIV who were hyper-secreting mucus. **Ib**

Sputum production was significantly higher in the PEP mask plus assisted coughing group (10g) compared to the control group (5g) of assisted coughing alone (p<0.01)⁴⁷⁸.

Weaning time from NIV was found to be significantly lower in the intervention group (5 days vs 7 days) p<0.01⁴⁷⁸.

Brown et al (n=24) looked at the effect of short term mechanical vibration on sputum production and found a significant increase at 60 minutes but not over 24 hours⁴⁸⁰. **Ib**

RECOMMENDATIONS

R177

Physiotherapy using positive expiratory pressure masks should be considered for selected patients with exacerbations of COPD, to help with clearing sputum.

Grade B

8.16 Monitoring recovery from an exacerbation

In patients admitted to hospital or managed in a hospital-at-home or assisted discharge scheme it is important to monitor the response to treatment. This allows appropriate reduction in additional support that patients are receiving and require, and determination of the timing of discharge.

RECOMMENDATIONS

R178

Patients' recovery should be monitored by regular clinical assessment of their symptoms and observation of their functional capacity.

Grade D**R179**

Pulse oximetry should be used to monitor the recovery of patients with non-hypercapnic, non-acidotic respiratory failure.

Grade D**R180**

Intermittent arterial blood gas measurements should be used to monitor the recovery of patients with respiratory failure who are hypercapnic or acidotic, until they are stable.

Grade D**R181**

Daily monitoring of PEF or FEV₁ should not be performed routinely to monitor recovery from an exacerbation because the magnitude of changes is small compared with the variability of the measurement.

Grade D

8.17 Discharge planning

Advanced discharge planning can help to reduce the risk of readmission and reduce unnecessary hospital bed occupancy. Discharge planning involves an assessment of the patients fitness for discharge and assessment of their needs once back in the community.

A hospital admission gives an opportunity for spirometry to be performed on patients who may not otherwise have had this measured. Measurements taken at the time of admission or soon after may give an unrepresentative assessment of the severity of airflow obstruction and thus it is of more value to perform spirometry close to the time of discharge when the patient will be closer to their normal functional state. See section 2.4.1. for the methodology underpinning this area.

RECOMMENDATIONS

R182	Spirometry should be measured in all patients before discharge.	Grade D
R183	Patients should be re-established on their optimal maintenance bronchodilator therapy before discharge.	Grade D
R184	Patients who have had an episode of respiratory failure should have satisfactory oximetry or arterial blood gas results before discharge.	Grade D
R185	All aspects of the routine care that patients receive (including appropriateness and risk of side effects) should be assessed before discharge.	Grade D
R186	Patients (or home carers) should be given appropriate information to enable them to fully understand the correct use of medications, including oxygen, before discharge.	Grade D
R187	Arrangements for follow-up and home care (e.g. visiting nurse, oxygen delivery, referral for other support) should be made before discharge.	Grade D
R188	Before the patient is discharged, the patient, family, and physician should be confident that he or she can manage successfully. When there is remaining doubt a formal activities of daily living assessment may be helpful.	Grade D



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