Complete Summary

GUIDELINE TITLE

Chronic obstructive pulmonary disease. National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care.

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Chronic Conditions. Chronic obstructive pulmonary disease. National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. Thorax 2004 Feb;59 Suppl 1:1-232. [491 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- April 02, 2008, Relenza (zanamivir): GlaxoSmithKline informed healthcare professionals of changes to the warnings and precautions sections of prescribing information for Relenza. There have been reports (mostly from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who are receiving neuraminidase inhibitors, including Relenza.
- March 4, 2008, Tamiflu (oseltamivir phosphate): Roche and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of neuropsychiatric events associated with the use of Tamiflu, in patients with influenza. Roche has updated the PRECAUTIONS section of the package insert to include the new information and guidance under the Neuropsychiatric Events heading.
- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic obstructive pulmonary disease (COPD), including chronic bronchitis, emphysema, and chronic airflow limitation/obstruction

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Critical Care
Family Practice
Geriatrics
Internal Medicine
Nursing
Physical Medicine and Rehabilitation
Pulmonary Medicine
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Dietitians
Health Care Providers
Hospitals
Nurses
Occupational Therapists
Patients
Physical Therapists
Physicians
Public Health Departments
Respiratory Care Practitioners
Students

GUIDELINE OBJECTIVE(S)

- To develop a clinical guideline on the management of chronic obstructive pulmonary disease for use in the National Health Service (NHS) in England and Wales
- To offer best practice advice on the identification and care of patients with chronic obstructive pulmonary disease (COPD)
- To define the symptoms, signs, and investigations required to establish a diagnosis of COPD
- To define the factors that are necessary to assess the severity of COPD, provide prognostic information, and guide best management
- To provide guidance on the pharmacological and nonpharmacological treatment of patients with stable COPD and on the management of exacerbations
- To discuss the interface with surgery and intensive therapy units

TARGET POPULATION

Adults who have a clinical working diagnosis of chronic obstructive pulmonary disease (COPD), including chronic bronchitis, emphysema, and chronic airflow limitation/obstruction

Note: The guideline does not cover the management of people with asthma, bronchopulmonary dysplasia, and bronchiectasis, nor does it cover children.

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Identification of signs and symptoms and risk factors for chronic obstructive pulmonary disease (COPD)
2. Spirometry (note: reversibility testing not routinely recommended)
3. Further investigations, as needed, including chest radiograph, full blood count, body mass index, alpha-1 antitrypsin measurement, serial domiciliary peak flow measurement, transfer factor for carbon monoxide, computed tomography scan, electrocardiogram, echocardiogram, pulse oximetry, sputum culture
4. Identification of early disease to facilitate interventions to slow disease progression
5. Assessment of severity of COPD
6. Referral for specialist advice

Management of Stable COPD

1. Smoking cessation (pharmacological [bupropion/nicotine replacement therapy] and nonpharmacological approaches)
2. Short-acting and long-acting bronchodilator therapy, including $beta_2$-agonist and/or anticholinergic
3. Theophylline
4. Inhaled and oral corticosteroid therapy
5. Combination therapy

6. Drug delivery systems, including inhalers, spacers, and nebulisers
7. Nonpharmacological interventions, including pulmonary rehabilitation, lifestyle advice and education in self-management techniques
8. Management of anxiety and depression
9. Nutritional factors
10. Oxygen therapy (long-term oxygen therapy [LTOT], ambulatory oxygen therapy, and short- burst oxygen therapy)
11. Noninvasive ventilation
12. Management of pulmonary hypertension and cor pulmonale
13. Pneumococcal vaccination, influenza vaccination, and antiviral therapy
14. Surgery referral (bullectomy, lung volume reduction, lung transplant)
15. Mucolytic therapy
16. Delivery of care by multidisciplinary team
17. Follow-up
18. Palliative care

Note: The following interventions are not recommended:

1. Angiotensin-converting enzyme inhibitors, calcium channel blockers, alpha-blockers, or digoxin in the treatment of cor pulmonale
2. Alpha-1 antitrypsin replacement therapy in the management of patients with alpha-1-antitrypsin deficiency
3. Treatment with alpha-tocopherol and beta-carotene supplements
4. Antitussive therapy in the management of stable COPD
5. Prophylactic antibiotic therapy in the management of stable COPD

Management of COPD exacerbations

1. Assessment of need for hospital treatment
2. Investigations of exacerbation (e.g., chest radiograph, arterial blood gas, electrocardiogram, full blood count, theophylline level, sputum sample, blood cultures, pulse oximetry)
3. Consideration of hospital-at-home and assisted discharge schemes
4. Pharmacological management, including inhaled bronchodilators, delivery systems for inhaled therapy, systemic corticosteroids, antibiotics, theophylline, respiratory stimulants.
5. Oxygen therapy
6. Noninvasive ventilation
7. Invasive ventilation and intensive care
8. Respiratory physiotherapy
9. Monitoring recovery and discharge planning

MAJOR OUTCOMES CONSIDERED

- Signs and symptoms
- Activities of daily living
- Lung function, as measured by forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), and peak expiratory flow
- Arterial oxygen saturation
- Exercise capacity/tolerance
- Quality of life
- Hospitalisation

- Number or duration of exacerbations
- Morbidity
- Mortality
- Cost measures, including cost effectiveness
- Quality adjusted life year

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searching for the Evidence

There were four stages to evidence identification and retrieval:

1. The technical team set out a series of specific clinical questions (see Appendix A of the original guideline document [full version]) that covered the issues identified in the project scope. The Consensus Reference Group met to discuss, refine, and approve these questions as suitable for identifying appropriate evidence within the published literature.
2. A total of 120 questions were identified. The technical team and project executive agreed that a full literature search and critical appraisal process could not be undertaken for all of these areas due to the time limitations within the guideline development process. The technical team identified questions where it was felt that a full literature search and critical appraisal was essential.
3. The Information Scientist developed a search strategy for each evidence-based question to identify the available evidence. Identified titles and abstracts were reviewed for relevance to the agreed clinical questions and full papers obtained as appropriate.
4. The full papers were critically appraised and the pertinent data entered into evidence tables that were then reviewed and analysed by the Guideline Development Group as the basis upon which to formulate recommendations. The evidence tables are available at http://thorax.bmjjournals.com/content/vol59/supp_1.

Literature Search

Limited details of the searches with regard to databases and constraints applied can be found in Appendix A of the original guideline document (full version). In general no formal contact was made with authors of identified studies, but occasionally it was necessary to contact authors for clarification of specific points. Additional contemporary articles were identified by the Guideline Development Group on an ad hoc basis. Stakeholder evidence identified via a process established by the National Institute for Clinical Excellence was incorporated

where appropriate. Both were assessed for inclusion by the same criteria as evidence provided by the electronic searches.

Searches were re-run at the end of the guideline development process, thus including evidence published up to the end of May 2003. Studies recommended by stakeholders or Guideline Development Group members that were published after this date were not considered for inclusion. This time-point should be the starting point for searching for new evidence for future updates to this guideline.

Literature Search for Economic Evidence

While evidence on cost effectiveness was extracted from the main searches wherever it existed, this was rare. It was necessary to undertake a separate search for information on the potential costs and benefits of the interventions and management strategies considered in this guideline. These searches were carried out by the health economist. The Guideline Development Group realised that few formal cost effectiveness analyses would be identified; therefore, the search for economic evidence was very broad and designed to identify information about the resources used in providing a service or intervention and/or the benefits that can be attributed to it. No study design criteria were imposed a priori (i.e., the searches were not limited to randomised control trials or formal economic evaluations). Further details of the searches for economic evidence are given in section 15, Appendix E of the original guideline document (full version).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Hierarchy of Evidence

Levels of Evidence

Ia: Evidence from systematic reviews or meta-analysis of randomised controlled trials

Ib: Evidence from at least one randomised controlled trial

IIa: Evidence from at least one controlled study without randomisation

IIb: Evidence from at least one other type of quasi-experimental study

III: Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies

IV: Evidence from expert committee reports or opinions and/or clinical experience of respected authorities

The guideline development group also identifies evidence from the National Institute for Clinical Excellence (NICE) guidelines or Health Technology Appraisal programme and evidence from Health Service Circulars (HSC) as follows:

NICE: Evidence from NICE guidelines or Health Technology Appraisal programme

HSC: Evidence from Health Service Circulars

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Synthesising the Evidence

Abstracts of articles identified from the searches were screened for relevance. Hard copies were ordered of papers that appeared to provide useful evidence relevant to each clinical question. Each paper was assessed for its methodological quality against pre-defined criteria using a validated quality appraisal tool. Papers that met the inclusion criteria were then assigned a level according to the evidence hierarchy (see Rating Scheme for the Strength of the Evidence in this summary). Owing to practical limitations, the selection, critical appraisal, and data extraction were undertaken by one reviewer only. Evidence was considered carefully by the Guideline Development Group (GDG) for accuracy and completeness.

Each clinical question dictated the appropriate study design that was prioritised in the search strategy. In addition certain topics within any one clinical question at times required different evidence types to be considered. Randomised control trials (RCTs) were the most appropriate study design for a number of clinical questions, as they lend themselves particularly well to research into medicines. They were not, however, the most appropriate study design for all clinical questions. For example, the evaluation of diagnostic tests is more suited to alternative research designs. Furthermore, RCTs are more difficult to perform in areas such as rehabilitation and lifestyle, where interventions may be tailored to the needs of the individual. As such, pharmaceutical interventions tend to be placed higher in the evidence hierarchy than other equally important interventions. This should not be interpreted as a preference for a particular type of intervention or as a reflection of the quality of the evidence, particularly for those clinical areas where non-RCT evidence is valid and most appropriate.

Where available, evidence from well-conducted systematic reviews was appraised and presented. Trials included within these reviews are listed in the evidence table but were not critically appraised. Studies identified in addition to those included in the systematic review were included in the appraisal process.

The study populations considered varied between clinical questions. At times evidence was not available from studies that were specific to a chronic obstructive pulmonary disease population; therefore, it was necessary to consider studies in either a heterogeneous respiratory disease population or other chronic conditions.

Study quality, although formally assessed, was not used as a basis for informing the evidence level assigned to evidence statements. Descriptive limitations of studies are included in the evidence statements as appropriate.

Expert Papers

On occasion the GDG identified a clinical question that could not be appropriately answered through undertaking a systematic review (where the evidence was scarce or where the question could not usefully be answered with the largely dichotomous output of a review). These questions were addressed via an expert-drafted discussion paper, subject to consideration by the GDG. In these instances Medline and Cochrane databases were searched together with a review of frequently cited papers and key review articles but there was no formal assessment of the studies cited. These review papers were developed and used as a basis for discussion by the GDG as a whole.

Finally, national and international evidence based guidelines were referred to during the development process. These were not formally appraised owing to the inherent difficulties of such a process, in that the consistency of process and of evidence base can be difficult to ascertain across such documents.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus
Expert Consensus (Nominal Group Technique)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The National Collaborating Centre for Chronic Conditions is housed by the Royal College of Physicians (RCP) but governed by a multi-professional partners board inclusive of patient groups and National Health Service management. The Collaborating Centre was set up in 2001, to undertake commissions from the National Institute for Clinical Excellence (NICE), to develop clinical guidelines for the National Health Service.

The technical team consisted of an information scientist, a systematic reviewer, a lead clinical advisor, and a health economist, supported by project management and administrative personnel. The clinical advisor also acted as the appointed Chair of the Guidelines Development Group (GDG). The technical team met monthly in addition to partaking in the meetings of the GDG.

The GDG met twelve times at monthly intervals to review the evidence identified by the technical team, to comment on its completeness, and to develop and refine clinical recommendations based on that evidence and other considerations.

Editorial responsibility for the guideline rested solely with the GDG, which also developed the audit criteria.

An extension of the GDG, the larger Consensus Reference Group, met three times throughout the process, once early in the development to ensure the aims and clinical questions were appropriate, once after three meetings of the GDG to confirm an operational definition of chronic obstructive pulmonary disease (COPD) and agree recommendations on diagnosis. Finally, at the end of the process to review the validity of the recommendations drafted by the GDG. The group employed formal consensus techniques.

Involvement of People with COPD

As part of the development process, the National Collaborating Centre for Chronic Conditions was keen to ensure that the guideline development process was informed by the views of people with COPD and their carers. This was achieved in two ways:

- by securing patient organisation representation on the guideline development group
- by having a patient with COPD on the guideline development group

The patient and a representative of the British Lung Foundations Breathe Easy patient support groups were present at every meeting of the GDG and Consensus Reference Group. They were therefore involved at every stage of the guideline development process and were able to consult with their wider constituencies throughout the process.

Drafting Recommendations

Evidence for each topic was extracted into tables and summarised in evidence statements. The Guideline Development Group reviewed the evidence tables and statements at each meeting and reached a group opinion. Recommendations were explicitly linked to the evidence supporting them and graded according to the level of the evidence upon which they were based, using the grading system detailed in section 3 of the original guideline document (full version) and in the section of this summary titled Rating Scheme for the Strength of the Recommendations.

Agreeing Recommendations

Once the evidence review had been completed and an early draft of the guideline produced, a one-day meeting of the Consensus Reference Group was held to finalise the recommendations. This included a premeeting vote on the recommendations and a further vote at the Consensus Reference Group meeting, where the group was asked to consider the draft guideline in 2 stages:

1. Are the evidence-based statements acceptable and is the evidence cited sufficient to justify the grading attached?

2. Are the recommendations derived from the evidence justified and are they sufficiently practical so that those at the clinical front line can implement them prospectively?

There were 3 types of recommendation to be considered:

- a recommendation from the Guideline Development Group based on strong evidence - usually noncontroversial unless there was important evidence that had been missed or misinterpreted
- a recommendation that was based on good evidence but where it was necessary to extrapolate the findings to make it useful in the National Health Service the extrapolation approved by consensus
- recommendations for which no evidence exists but which address important aspects of chronic obstructive pulmonary disease care or management - and for which a consensus on best practice could be reached.

This formal consensus method has been established within the National Collaborating Centre for Chronic Conditions, drawing on the knowledge set out in the Health Technology Appraisal, and practical experience.

Writing the Guideline

The first formal version of the guideline was drawn up by the technical team in accord with the decisions of the Guideline Development Group.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading of Recommendations

Grade A: Based on hierarchy I evidence

Grade B: Based on hierarchy II evidence or extrapolated from hierarchy I evidence

Grade C: Based on hierarchy III evidence or extrapolated from hierarchy I or II evidence

Grade D: Directly based on hierarchy IV evidence or extrapolated from hierarchy I, II, or III evidence

The guideline development group also identifies evidence from the National Institute for Clinical Excellence (NICE) guidelines or Health Technology Appraisal programme and evidence from Health Service Circulars (HSC) as follows:

NICE: Evidence from NICE guidelines or Health Technology Appraisal programme

HSC: Evidence from Health Service Circular

COST ANALYSIS

Identified titles and abstracts from the economics searches were reviewed by the health economist and full papers obtained as appropriate. The full papers were critically appraised by the health economist and the relevant data was conveyed to the Guideline Development Group alongside the clinical evidence for each question. Given that the economics searches were broad and that no standard measure of assessing the quality of economic evidence is available, careful consideration was given to each study design and the applicability of the results to the guideline context. An important issue in this respect is that much of the evidence on costs and benefits comes from the health care systems around the world and is therefore of limited applicability to a guideline for England and Wales.

As well as presenting existing evidence on the costs and benefits of a broad range of interventions to the Guideline Development Group, the issue of opportunistic case finding linked to targeted smoking cessation programmes was identified as an important area for further economic analysis. This choice was made on the grounds that this approach may be associated with:

- potentially large health benefits
- a potentially large effect on National Health Service resources
- uncertainty surrounding the benefits and resources
- a potentially large service impact

Health economic analysis can provide a framework for collating information from a variety of sources in order to estimate and systematically compare costs and benefits. This is a complex and labour intensive process and it does require a level of clinical evidence that is not always readily available. The results of this analysis are discussed briefly in section 15 of the original guideline document (full version).

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was validated through two consultations.

1. The first draft of the guideline (the full guideline, National Institute for Clinical Excellence [NICE] guideline and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation has been allotted a grading which directly reflects the hierarchy of evidence upon which it is based. Readers are asked to note that the hierarchy of evidence and the recommendations gradings relate to the strength of the evidence not to clinical importance.

Levels of evidence (Ia-IV, NICE, HSC) and grading of recommendations (AD, NICE, HSC) are defined at the end of the Major Recommendations field.

Diagnosing Chronic Obstructive Pulmonary Disease (COPD)

The diagnosis of COPD depends on thinking of it as a cause of breathlessness or cough. The diagnosis is suspected on the basis of symptoms and signs and supported by spirometry.

Symptoms

Grade D - A diagnosis of COPD should be considered in patients over the age of 35 who have a risk factor (generally smoking) and who present with one or more of the following symptoms:

- Exertional breathlessness
- Chronic cough
- Regular sputum production
- Frequent winter "bronchitis"
- Wheeze

Grade D - Patients in whom a diagnosis of COPD is considered should also be asked about the presence of the following factors:

- Weight loss
- Effort intolerance
- Waking at night
- Ankle swelling
- Fatigue
- Occupational hazards
- Chest pain
- Haemoptysis

Note: These last two symptoms are uncommon in COPD and raise the possibility of an alternative diagnosis.

Grade D - One of the primary symptoms of COPD is breathlessness. The Medical Research Council (MRC) dyspnoea scale (for an adaptation of the scale, see Table 3 below and in the original guideline document [full version]) should be used to grade the breathlessness according to the level of exertion required to elicit it.

Table 3: MRC Dyspnoea Scale	
Grade	**Degree of Breathlessness Related to Activities**

Table 3: MRC Dyspnoea Scale	
Grade	**Degree of Breathlessness Related to Activities**
Grade 1	Not troubled by breathlessness except on strenuous exercise
Grade 2	Short of breath when hurrying or walking up a slight hill
Grade 3	Walks slower than contemporaries on level ground because of breathlessness or has to stop for breath when walking at own pace
Grade 4	Stops for breath after walking about 100 meters or after a few minutes on level ground
Grade 5	Too breathless to leave the house or breathless when dressing or undressing

Adapted from Fletcher CM, Elmes PC, Fairbairn MB et al. (1959) the significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. *British Medical Journal* 2:257-66.

Spirometry

Grade D - Spirometry should be performed:

- At the time of diagnosis
- To reconsider the diagnosis if patients show an exceptionally good response to treatment

Grade D - All health professionals managing patients with COPD should have access to spirometry and be competent in the interpretation of the results.

Grade D - Spirometry can be performed by any health-care worker who has undergone appropriate training and who keeps his or her skills up to date.

Grade D - Spirometry services should be supported by quality control processes.

Grade D - It is recommended that European Respiratory Society (ERS) 1993 reference values* are used but it is recognised that these values may lead to under-diagnosis in the elderly and are not applicable in black and Asian populations.

*Quanjer PH, Tammeling GJ, Cotes JE et al. (1993) Lung volumes and forced ventilator flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *European Respiratory Journal* (Suppl) 16:5-40.

Further Investigations

Grade D - At the time of their initial diagnostic evaluation, in addition to spirometry all patients should have:

- A chest radiograph to exclude other pathologies
- A full blood count to identify anaemia or polycythaemia
- Body mass index (BMI) calculated

Grade D - Additional investigations should be performed to aid management in some circumstances (see Table 5 below and in the original guideline document (full version)).

Table 5: Additional Investigations

Investigation	Role
Serial domiciliary peak flow instruments	To exclude asthma if diagnostic doubt remains
Alpha-1 antitrypsin	If early onset, minimal smoking history, or family history
Transfer factor for carbon monoxide (T_LCO)	To investigate symptoms that seem disproportionate to the spirometric impairment
Computed tomography (CT) scan of the thorax	To investigate symptoms that seem disproportionate to the spirometric impairment To investigate abnormalities seen on a chest radiograph To assess suitability for surgery
Electrocardiography (ECG)	To assess cardiac status if features of cor pulmonale
Echocardiogram	To assess cardiac status if features of cor pulmonale
Pulse oximetry	To assess need for oxygen therapy; if cyanosis or cor pulmonale present, or if forced expiratory volume in 1 second (FEV_1) < 50% predicted
Sputum culture	To identify organisms if sputum is persistently present and purulent

Grade D - Patients identified as having alpha-1 antitrypsin deficiency should be offered the opportunity to be referred to a specialist centre to discuss the clinical management of this condition.

Reversibility Testing

Grade D - In most patients, routine spirometric reversibility testing is not necessary as a part of the diagnostic process or to plan initial therapy with bronchodilators or corticosteroids. It may be unhelpful or misleading because:

- Grade B - Repeated FEV_1 measurements can show small spontaneous fluctuations.
- Grade B - The results of a reversibility test performed on different occasions can be inconsistent and not reproducible.
- Grade B - Over-reliance on a single reversibility test may be misleading unless the change in FEV_1 is greater than 400 ml.
- Grade B - The definition of the magnitude of a significant change is purely arbitrary.
- Grade A - Response to long-term therapy is not predicted by acute reversibility testing.

Grade D - COPD and asthma are frequently distinguishable on the basis of history (and examination) in untreated patients presenting for the first time. Features from the history and examination should be used to differentiate COPD from asthma whenever possible. (See Table 6 in the original guideline document [full version] [see "Companion Documents" field]).

Grade D - Longitudinal observation of patients (whether using spirometry, peak flow, or symptoms) should also be used to help differentiate COPD from asthma.

Grade D - To help resolve cases where diagnostic doubt remains, or both COPD and asthma are present, the following findings should be used to help identify asthma:

- A large (greater than 400 ml) response to bronchodilators
- A large (greater than 400 ml) response to 30 mg oral prednisolone daily for 2 weeks
- Serial peak flow measurements showing 20% or greater diurnal or day-to-day variability

Clinically significant COPD is not present if the FEV_1 and FEV_1/forced vital capacity (FVC) ratio return to normal with drug therapy.

Grade D - If diagnostic uncertainty remains, referral for more detailed investigations, including imaging and measurement of T_LCO, should be considered.

Grade D - If patients report a marked improvement in symptoms in response to inhaled therapy, the diagnosis of COPD should be reconsidered.

Assessment of Severity

COPD is heterogeneous, so no single measure can give an adequate assessment of the true severity of the disease in an individual patient. Severity assessment is, nevertheless, important because it has implications for therapy and relates to prognosis.

Grade D - Mild airflow obstruction can be associated with significant disability in patients with COPD. A true assessment of severity should include assessment of the degree of airflow obstruction and disability, the frequency of exacerbations and the following known prognostic factors:

- FEV_1
- T_LCO
- Breathlessness (MRC scale)
- Health status
- Exercise capacity
- Body mass index (BMI)
- Partial pressure of oxygen in arterial blood (PaO_2)
- Cor pulmonale

Grade D - The severity of airflow obstruction should be assessed according to the reduction in FEV_1 as follows and as shown in Table 7 of the original guideline document (full version):

- Mild airflow obstruction: 50-80% predicted FEV_1
- Moderate airflow obstruction: 30-49% predicted FEV_1
- Severe airflow obstruction: <30% predicted FEV_1

Identification of Early Disease

Grade D - Spirometry should be performed in patients who are over 35, current or ex-smokers, and have a chronic cough.

Grade B - Spirometry should be considered in patients with chronic bronchitis. A significant proportion of these will go on to develop airflow limitation. (Jonsson et al., 1998)

Referral for Specialist Advice

Grade D - It is recommended that referrals for specialist advice are made when clinically indicated. Referral may be appropriate at all stages of the disease and not solely in the most severely disabled patients. (See Table 8 in the original guideline document [full version]).

Grade D - Patients who are referred do not always have to be seen by a respiratory physician. In some cases they may be seen by members of the COPD team who have appropriate training and expertise (see Table 8 in the original guideline document [full version] for reasons for referral).

Managing Stable COPD

Smoking Cessation

Grade D - An up-to-date smoking history, including pack years smoked (number of cigarettes smoked per day, divided by 20, multiplied by the number of years smoked), should be documented for everyone with COPD.

Grade A - All COPD patents still smoking, regardless of age, should be encouraged to stop, and offered help to do so, at every opportunity.

Grade B - Unless contraindicated, bupropion or nicotine replacement therapy (NRT) combined with an appropriate support programme should be used to optimise smoking quit rates for people with COPD.

NICE - *"If a smoker's attempt to quit is unsuccessful with treatment using either nicotine replacement therapy (NRT) or bupropion, the National Health Service (NHS) should normally fund no further attempts within 6 months. However, if external factors interfere with a person's initial attempt to stop smoking, it may be reasonable to try again sooner."* (NICE Technology Appraisal Guidance No 39. 2002)

Inhaled Bronchodilator Therapy

Grade B - Short-acting bronchodilators, as necessary, should be the initial empirical treatment for the relief of breathlessness and exercise limitation.

Grade D - The effectiveness of bronchodilator therapy should not be assessed by lung function alone but should include a variety of other measures such as improvement in symptoms, activities of daily living, exercise capacity, and rapidity of symptom relief.

Grade A - Patients who remain symptomatic should have their inhaled treatment intensified to include long-acting bronchodilators or combined therapy with a short-acting beta$_2$-agonist and a short-acting anticholinergic.

Grade A - Long-acting bronchodilators should be used in patients who remain symptomatic despite treatment with short-acting bronchodilators, because these drugs appear to have additional benefits over combinations of short-acting drugs.

Grade D - Long-acting bronchodilators should also be used in patients who have two or more exacerbations per year.

Grade D - The choice of drug(s) should take into account the patient's response to a trial of the drug, the drug's side effects, patient preference, and cost.

Theophylline

In this section of the guideline, the term theophylline is used to mean slow-release formulations of this drug.

Grade D - Theophylline should only be used after a trial of short-acting bronchodilators and long-acting bronchodilators, or in patients who are unable to use inhaled therapy, as there is a need to monitor plasma levels and interactions.

Grade D - Particular caution needs to be taken with the use of theophylline in elderly patients because of differences in pharmacokinetics, the increased likelihood of comorbidities, and the use of other medications.

Grade D - The effectiveness of the treatment with theophylline should be assessed by improvements in symptoms, activities of daily living, exercise capacity, and lung function.

Grade D - The dose of theophylline prescribed should be reduced at the time of an exacerbation if macrolide or fluoroquinolone antibiotics (or other drugs known to interact) are prescribed.

Corticosteroids

Inhaled Corticosteroids

None of the inhaled corticosteroids currently available are licensed for use alone in the treatment of COPD. The following recommendations therefore include usage outside licensed indications, and prescribers need to remember that responsibility for such prescribing lies with them.

Grade A - Oral corticosteroid reversibility tests do not predict response to inhaled corticosteroid therapy and should not be used to identify which patients should be prescribed inhaled corticosteroids.

Grade B - Inhaled corticosteroids should be prescribed for patients with an FEV_1 less than or equal to 50% predicted, who are having two or more exacerbations requiring treatment with antibiotics or oral corticosteroids in a 12-month period. The aim of treatment is to reduce exacerbation rates and slow the decline in health status and not to improve lung function per se.

Grade D - Clinicians should be aware of the potential risk of developing osteoporosis and other side effects in patients treated with high-dose inhaled corticosteroids (especially in the presence of other risk factors), and should discuss the risk with patients.

Oral Corticosteroids

Grade D - Maintenance use of oral corticosteroid therapy in COPD is not normally recommended. Some patients with advanced COPD may require maintenance oral corticosteroids when these cannot be withdrawn following an exacerbation. In these cases, the dose of oral corticosteroids should be kept as low as possible.

Grade D - Patients treated with long-term oral corticosteroid therapy should be monitored for the development of osteoporosis and given appropriate prophylaxis. Patients over the age of 65 should be started on prophylactic treatment, without monitoring.

Combination Therapy

Grade A - If patients remain symptomatic on monotherapy, their treatment should be intensified by combining therapies from different drug classes. Effective combinations include:

- $Beta_2$-agonist and anticholinergic
- $Beta_2$-agonist and theophylline
- Anticholinergic and theophylline
- Long-acting $beta_2$-agonist and inhaled corticosteroids

Grade D - The clinical effectiveness of combined treatments can be assessed by improvements in symptoms, activities of daily living, exercise capacity, and lung function. Combination treatment should be discontinued if there is no benefit after 4 weeks.

Delivery Systems Used to Treat Patients with Stable COPD

Most patients whatever their age are able to acquire and maintain adequate inhaler technique given adequate instruction. The exception to this is that those with significant cognitive impairment (as a guideline, those with a Hodkinson Abbreviated Mental Test Score of 4 or less) are unable to use any form of inhaler device. In most patients, however, a pragmatic approach guided by individual patient assessment is needed in choosing a device.

Inhalers

Grade D - In most cases bronchodilator therapy is best administered using a hand-held inhaler device (including a spacer device if appropriate).

Grade D - If the patient is unable to use a particular device satisfactorily, it is not suitable for him or her and an alternative should be found.

Grade D - Inhalers should be prescribed only after patients have received training in the use of the device and have demonstrated satisfactory technique.

Grade D - Patients should have their ability to use an inhaler device regularly assessed by a competent health-care professional and, if necessary, should be retaught the correct technique.

Grade D - To ensure optimum efficacy for each patient with COPD, the dose of medication should be titrated according to individual clinical response.

Spacers

Grade D - The spacer should be compatible with the patient's metered-dose inhaler.

Grade D - It is recommended that spacers are used in the following way.

- The drug is administered by repeated single actuations of the metered dose inhaler into the spacer, with each followed by inhalation.
- There should be minimal delay between inhaler actuation and inhalation.

- Tidal breathing can be used as it is as effective as single breaths.

Grade D - Spacers should be cleaned no more than monthly, as more frequent cleaning affects their performance (due to build up of static). They should be cleaned with water and washing-up liquid and allowed to air dry. The mouthpiece should be wiped clean of detergent before use.

Nebulisers

Grade D - Patients with distressing or disabling breathlessness despite maximal therapy using inhalers should be considered for nebuliser therapy.

Grade D - Nebulised therapy should not continue to be prescribed without assessing and confirming that one or more of the following occurs:

- A reduction in symptoms
- An increase in the ability to undertake activities of daily living
- An increase in exercise capacity
- An improvement in lung function

Grade D - Nebulised therapy should not be prescribed without an assessment of the patient's and/or carer's ability to use it.

Grade D - A nebuliser system that is known to be efficient should be used. Once available, Comit Europeen de Normalisation (European Committee for Standardisation, CEN) data should be used to assess efficiency.

Grade D - Patients should be offered a choice between a facemask and a mouthpiece to administer their nebulised therapy, unless the drug specifically requires a mouthpiece (for example, anticholinergic drugs).

Grade D - If nebuliser therapy is prescribed, the patient should be provided with equipment, servicing, advice, and support.

Oxygen

Long-term Oxygen Therapy (LTOT)

Grade C - Clinicians should be aware that inappropriate oxygen therapy in people with COPD may cause respiratory depression.

Grade A - LTOT is indicated in patients with COPD who have a PaO_2 less than 7.3 kPa when stable or a PaO_2 greater than 7.3 and less than 8 kPa when stable and one of: secondary polycythaemia, nocturnal hypoxaemia (oxygen saturation of arterial blood [SaO_2] less than 90% for more than 30% of time), peripheral oedema, or pulmonary hypertension.

Grade A - To get the benefits of LTOT patients should breathe supplemental oxygen for at least 15 hours per day. Greater benefits are seen in patients receiving oxygen for 20 hours per day.

Grade D - The need for oxygen therapy should be assessed in:

- All patients with severe airflow obstruction (FEV_1 less than 30% predicted)
- Patients with cyanosis
- Patients with polycythaemia
- Patients with peripheral oedema
- Patients with a raised jugular venous pressure
- Patients with oxygen saturations less than or equal to 92% breathing air

Assessment should also be considered in patients with moderate airflow obstruction (FEV_1 30-49% predicted).

Grade D - To ensure all patients eligible for LTOT are identified, pulse oximetry should be available in all health-care settings.

Grade D - The assessment of patients for LTOT should comprise the measurement of arterial blood gasses on two occasions at least 3 weeks apart in patients who have a confident diagnosis of COPD, who are receiving optimum medical management, and whose COPD is stable.

Grade D - Patients receiving LTOT should be reviewed at least once per year by practitioners familiar with LTOT, and this review should include pulse oximetry.

Grade D - Oxygen concentrators should be used to provide the fixed supply at home for long-term oxygen therapy.

Grade D - Patients should be warned about the risks of fire and explosion if they continue to smoke when prescribed oxygen.

Ambulatory Oxygen Therapy

Grade D - People who are already on LTOT who wish to continue with oxygen therapy outside the home, and who are prepared to use it, should have ambulatory oxygen prescribed.

Grade D - Ambulatory oxygen therapy should be considered in patients who have exercise desaturation, are shown to have an improvement in exercise capacity and/or dyspnoea with oxygen, and have the motivation to use oxygen.

Grade D - Ambulatory oxygen therapy is not recommended in COPD if PaO_2 is greater than 7.3 kPa and there is no exercise desaturation.

Grade D - Ambulatory oxygen therapy should only be prescribed after an appropriate assessment has been performed by a specialist. The purpose of the assessment is to assess the extent of desaturation, the improvement in exercise capacity with supplemental oxygen, and the oxygen flow rate required to correct desaturation, aiming to keep the SaO_2 above 90%.

Grade D - Small light-weight cylinders, oxygen-conserving devices, and portable liquid oxygen systems should be available for the treatment of patients with COPD.

Grade D - A choice about the nature of equipment prescribed should take account of the hours of ambulatory oxygen use required by the patient and the oxygen flow rate required. (See Table 12 in the original guideline document [full version] for a list of appropriate equipment for ambulatory oxygen therapy.)

Short-burst Oxygen Therapy

Grade C - Short-burst oxygen therapy should only be considered for episodes of severe breathlessness in patients with COPD not relieved by other treatments.

Grade D - Short-burst oxygen therapy should only continue to be prescribed if an improvement in breathlessness following therapy has been documented.

Grade D - When indicated, short-burst oxygen should be provided from cylinders.

Noninvasive Ventilation (NIV)

Grade D - Adequately treated patients with chronic hypercapnic ventilatory failure who have required assisted ventilation (whether invasive or noninvasive) during an exacerbation or who are hypercapnic or acidotic on LTOT should be referred to a specialist centre for consideration of long-term NIV.

Management of Pulmonary Hypertension and Cor Pulmonale

Diagnosis of Pulmonary Hypertension and Cor Pulmonale

In the context of this guideline, the term "cor pulmonale" has been adopted to define a clinical condition that is identified and managed on the basis of clinical features. This clinical syndrome of cor pulmonale includes patients who have right heart failure secondary to lung disease and those in whom the primary pathology is retention of salt and water, leading to the development of peripheral oedema.

Grade D - A diagnosis of cor pulmonale should be considered if patients have:

- Peripheral oedema
- A raised venous pressure
- A systolic parasternal heave
- A loud pulmonary second heart sound

Grade D - It is recommended that the diagnosis of cor pulmonale is made clinically and that this process should involve excluding other causes of peripheral oedema.

Treatment of Cor Pulmonale

Grade A - Patients presenting with cor pulmonale should be assessed for the need for long-term oxygen therapy.

Grade D - Oedema associated with cor pulmonale can usually be controlled symptomatically with diuretic therapy.

Grade C - The following are not recommended for the treatment of cor pulmonale:

- Angiotensin-converting enzyme inhibitors
- Calcium channel blockers
- Alpha-blockers
- Digoxin (unless there is atrial fibrillation)

Pulmonary Rehabilitation

Pulmonary rehabilitation is defined as a multidisciplinary programme of care for patients with chronic respiratory impairment that is individually tailored and designed to optimise each patient's physical and social performance and autonomy.

Grade A - Pulmonary rehabilitation should be made available to all appropriate patients with COPD.

Grade D - Pulmonary rehabilitation should be offered to all patients who consider themselves functionally disabled by COPD (usually MRC grade 3 and above). Pulmonary rehabilitation is not suitable for patients who are unable to walk, who have unstable angina, or who have had a recent myocardial infarction.

Grade D - For pulmonary rehabilitation programmes to be effective, and to improve concordance, they should be held at times that suit patients and in buildings that are easy for patients to get to and have good access for people with disabilities. Places should be available within a reasonable time of referral.

Grade A - Pulmonary rehabilitation programmes should include multicomponent, multidisciplinary interventions, which are tailored to the individual patient's needs. The rehabilitation process should incorporate a programme of physical training, disease education, and nutritional, psychological, and behavioural intervention.

Grade D - Patients should be made aware of the benefits of pulmonary rehabilitation and the commitment required to gain these.

Vaccination and Antiviral Therapy

HSC - Pneumococcal vaccination and an annual influenza vaccination should be offered to all patients with COPD as recommended by the Chief Medical Officer.

NICE - *"Within their licensed indications, zanamivir and oseltamivir are recommended for the treatment of at-risk adults who present with influenza-like illness and who can start therapy within 48 hours of the onset of symptoms*." (NICE technology appraisal guidance- No. 58. 2003)

The technology appraisal also notes that zanamivir should be used with caution in people with COPD because of risk of bronchospasm. If people with COPD are prescribed zanamivir, they should be made aware of the risks and have a fast-acting bronchodilator available.

Lung Surgery

Grade C - Patients who are breathless and have a single large bulla on a computed tomography (CT) scan and an FEV_1 less than 50% predicted should be referred for consideration of bullectomy.

Grade A - Patients with severe COPD who remain breathless with marked restrictions of their activities of daily living, despite maximal medical therapy (including rehabilitation), should be referred for consideration of lung volume reduction surgery if they meet all of the following criteria:

- FEV_1 more than 20% predicted
- $PaCO_2$ less than 7.3 kPa
- Upper lobe predominant emphysema
- T_LCO more than 20% predicted

Grade C - Patients with severe COPD who remain breathless with marked restrictions of their activities of daily living despite maximal medical therapy should be considered for referral for assessment for lung transplantation, bearing in mind comorbidities and local surgical protocols. Considerations include:

- Age
- FEV_1
- $PaCO_2$
- Homogeneously distributed emphysema on CT scan
- Elevated pulmonary artery pressures with progressive deterioration

Alpha-1 Antitrypsin Replacement Therapy

Grade D - Alpha-1 antitrypsin replacement therapy is not recommended in the management of patients with alpha-1 antitrypsin deficiency (see also Table 5 in the original guideline document [full version])

Mucolytic Therapy

Grade B - Mucolytic drug therapy should be considered in patients with a chronic cough productive of sputum.

Grade D - Mucolytic therapy should be continued if there is symptomatic improvement (for example, reduction in frequency of cough and sputum production).

Antioxidant Therapy

Grade A - Treatment with alpha-tocopherol and beta-carotene supplements, alone or in combination, is not recommended.

Antitussive Therapy

Grade D - Antitussive therapy should not be used in the management of stable COPD.

Prophylactic Antibiotic Therapy

Grade D - There is insufficient evidence to recommend prophylactic antibiotic therapy in the management of stable COPD.

Multidisciplinary Management

Multidisciplinary working is breaking down historic demarcation of roles, and many of the activities in managing COPD can be undertaken by individuals from different professional backgrounds. Many of these activities may be undertaken in the clinic or in the practice as part of routine care by the practitioner seeing the patient, but in certain circumstances it may be necessary for the patient to be referred to a specialist department, such as physiotherapy.

Grade D - COPD care should be delivered by a multidisciplinary team.

Grade D - The following functions should be considered when defining the activity of the multidisciplinary team:

- Assessing patients (including performing spirometry and assessing the need for oxygen, the need for aids for daily living, and the appropriateness of delivery systems for inhaled therapy)
- Managing patients (including noninvasive ventilation, pulmonary rehabilitation, hospital-at-home/early discharge schemes, providing palliative care, identifying and managing anxiety and depression, advising patients on relaxation techniques, dietary issues, exercise, social security benefits, and travel)
- Advising patients on self-management strategies
- Identifying and monitoring patients at high risk of exacerbations and undertaking activities which aim to avoid emergency admissions
- Advising patients on exercise
- Education of patients and other health professionals

Respiratory Nurse Specialists

Grade D - It is recommended that respiratory nurse specialists form part of the multidisciplinary COPD team.

Physiotherapy

If patients have excessive sputum, they should be taught:

- **Grade B** - The use of Positive Expiratory Pressure masks
- **Grade D** - Active cycle of breathing techniques

Identifying and Managing Anxiety and Depression

Grade D - Health-care professionals should be alert to the presence of depression in patients with COPD. The presence of anxiety and depression should be considered in patients:

- Who are hypoxic (SaO_2 less than 92%)
- Who have severe dyspnoea
- Who have been seen at or admitted to a hospital with an exacerbation of COPD

Grade D - The presence of anxiety and depression in patients with COPD can be identified using validated assessment tools.

Grade A - Patients found to be depressed or anxious should be treated with conventional pharmacotherapy.

Grade C - For antidepressant treatment to be successful, it needs to be supplemented by spending time with the patient explaining why depression needs to be treated alongside the physical disorder.

Nutritional Factors

Grade D - BMI should be calculated in patients with COPD (see Section 6.6 in the original guideline document [full version]).

- The normal range for BMI is 20 to less than 25. (Wrenn et al., 1991)
- If the BMI is abnormal (high or low) or changing over time, the patient should be referred for dietetic advice.
- If the BMI is low, patients should also be given nutritional supplements to increase their total calorific intake, and be encouraged to take exercise to augment the effects of nutritional supplementation.

The NICE guideline *Nutritional support in adults: oral supplements, enteral and parenteral feeding*, can be referred to when it is available (scheduled for publication in December 2005).

Grade D - In older patients, attention should also be paid to changes in weight, particularly if the change is more than 3 kg.

Palliative Care

Grade D - Opioids should be used when appropriate to palliate breathlessness in patients with end-stage COPD which is unresponsive to other medical therapy.

Grade D - Benzodiazepines, tricyclic antidepressants, major tranquillisers, and oxygen should also be used when appropriate for breathlessness in patients with end-stage COPD unresponsive to other medical therapy.

Grade D - Patients with end-stage COPD and their family and carers should have access to the full range of services offered by multidisciplinary palliative care teams, including admission to hospices.

Assessment for Occupational Therapy

Grade D - Patients should be regularly asked about their ability to undertake activities of daily living and how breathless they become when doing these.

Grade D - Clinicians managing patients with COPD should assess their need for occupational therapy using validated tools.

Social Services

Grade D - Patients disabled by COPD should be considered for referral for assessment by a social services department.

Advice on Travel

Grade D - All patients on LTOT planning air travel should be assessed in line with the British Thoracic Society (BTS) recommendations (Managing passengers with respiratory disease planning air travel: British Thoracic Society recommendations [2002] *Thorax* 57(4):289304).

Grade D - All patients with an FEV_1 less than 50% predicted who are planning air travel should be assessed in line with the BTS recommendations.

Grade D - All patients known to have bullous disease should be warned that they are at a theoretically increased risk of developing a pneumothorax during air travel.

Advice on Diving

Grade D - Scuba diving is not recommended for patients with COPD.

Education

Grade A - There are significant differences in the response of patients with COPD and asthma to education programmes. Programmes designed for asthma should not be used in COPD.

Grade D - Specific educational packages should be developed for patients with COPD.

- Suggested topics for inclusion are listed in Appendix C of the original guideline document (full version).
- The packages should take account of the different needs of patients at different stages of their disease.

Grade D - Patients with moderate and severe COPD should be made aware of the technique of NIV. Its benefits and limitations should be explained so that, if it is ever necessary in the future, they will be aware of these issues (see below under "Non-invasive ventilation and COPD exacerbations" and in section 8.13 of the original guideline document [full version]).

Self-management

Grade A - Patients at risk of having an exacerbation of COPD should be given self-management advice that encourages them to respond promptly to the symptoms of an exacerbation.

Grade D - Patients should be encouraged to respond promptly to the symptoms of an exacerbation by:

- Starting oral corticosteroid therapy if their increased breathlessness interferes with activities of daily living (unless contraindicated)
- Starting antibiotic therapy if their sputum is purulent
- Adjusting their bronchodilator therapy to control their symptoms

Grade D - Patients at risk of having an exacerbation of COPD should be given a course of antibiotic and corticosteroid tablets to keep at home for use as part of a self-management strategy (see recommendation 150 of the original guideline document [full version]).

Grade D - The appropriate use of these tablets should be monitored.

Grade D - Patients given self-management plans should be advised to contact a health-care professional if they do not improve.

Fitness for General Surgery

Grade D - The ultimate clinical decision about whether or not to proceed with surgery should rest with a consultant anaesthetist and consultant surgeon taking account of the presence of comorbidities, the functional status of the patient, and the necessity of the surgery.

Grade D - It is recommended that lung function should not be the only criterion used to assess patients with COPD before surgery. Composite assessment tools such as the American Society of Anaesthesiologists (ASA) scoring system are the best predictors of risk.

Grade D - If time permits, the medical management of the patient should be optimised prior to surgery, and this might include undertaking a course of pulmonary rehabilitation.

Follow-up of Patients with COPD

Grade D Follow-up of all patients with COPD should include:

- Highlighting the diagnosis of COPD in the case record and recording this using Read codes on a computer database
- Recording the values of spirometric tests performed at diagnosis (both absolute and percent predicted)
- Offering smoking cessation advice
- Recording the opportunistic measurement of spirometric parameters (a loss of 500 ml or more over 5 years will select out those patients with rapidly progressing disease who may need specialist referral and investigation)

Grade D - Patients with mild or moderate COPD should be reviewed at least once per year, or more frequently if indicated, and the review should cover the issues listed below in Table 14.

Table 14: Summary of Follow up of Patients with COPD in Primary Care

	Mild/Moderate	Severe
Frequency	**At least annual**	**At least twice per year**

Clinical Assessments	• smoking status & desire to quit
	• adequacy of symptom control
	  • breathlessness
	  • exercise tolerance
	  • estimated exacerbation frequency
	• presence of complications
	• effects of each drug treatment
	• inhaler technique
	• need for referral to specialist and therapy services
	• need for pulmonary rehabilitation
		• smoking status & desire to quit
		• adequacy of symptom control
		  • breathlessness
		  • exercise tolerance
		  • estimated exacerbation frequency
		• presence of cor pulmonale
		• need for long-term oxygen therapy
		• patient's nutritional state
		• presence of depression
		• effects of each drug treatment
		• inhaler technique
		• need for Social Services & Occupational Therapy input
		• need for referral to specialist and therapy services
		• need for pulmonary rehabilitation

Measurements to Make	• FEV_1 & FVC • calculate BMI • MRC dyspnoea score	• FEV_1 & FVC • calculate BMI • MRC dyspnoea score • SaO_2

Grade D - For most patients with stable severe disease, regular hospital review is not necessary, but there should be locally agreed mechanisms to allow rapid access to hospital assessment when necessary

Grade D - When patients with severe COPD are reviewed in primary care, they should be seen at least twice a year, and specific attention should be paid to the issues listed above in Table 14.

Grade D - Patients with severe disease requiring interventions such as long-term noninvasive ventilation should be reviewed regularly by specialists.

Management of Exacerbations of COPD

Definition of an exacerbation: An exacerbation is a sustained worsening of the patient's symptoms from their 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.

Assessment of Need for Hospital Treatment

Grade D - Factors that should be used to assess the need to treat patients in hospital are listed in Table 15 of the original guideline document (full version).

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.

Primary Care

Grade D - In patients with an exacerbation managed in primary care:

- 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

Patients Referred to a Hospital

Grade D - In all patients with an exacerbation referred to hospital:

- A chest radiograph should be obtained
- Arterial blood gas tensions should be measured and the inspired oxygen concentration recorded
- An electrocardiogram (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

Hospital-at-home and Assisted Discharge Schemes

Grade A - 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 D - The multi-professional team required to operate these schemes should include allied heath professionals with experience in managing patients with COPD, and may include nurses, physiotherapists, occupational therapists, and generic health workers.

Grade D - 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 - Patient's preferences about treatment at home or in hospital should be considered.

Pharmacological Management

Increased breathlessness is a common feature of an exacerbation of COPD. This is usually managed by taking increased doses of short-acting bronchodilators, and these drugs may be given using different delivery systems.

Delivery Systems for Inhaled Therapy During Exacerbations

Grade A - Both nebulisers and hand-held inhalers can be used to administer inhaled therapy during exacerbations of COPD.

Grade D - 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 - 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 - 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 - The driving gas for nebulised therapy should always be specified in the prescription.

Systemic Corticosteroids

Grade A - 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 B - 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 D - Patients requiring corticosteroid therapy should be encouraged to present early to get maximum benefits (see recommendations 122-126 in the original guideline document [full version]).

Grade D - Prednisolone 30 mg orally should be prescribed for 7 to 14 days.

Grade A - 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 D - For guidance on stopping oral corticosteroid therapy it is recommended that clinicians refer to the *British National Formulary* section 6.3.2.

Grade D - Osteoporosis prophylaxis should be considered in patients requiring frequent courses of oral corticosteroids.

Grade D - Patients should be made aware of the optimum duration of treatment and the adverse effects of prolonged therapy.

Grade D - Patients, particularly those discharged from hospital, should be given clear instructions about why, when, and how to stop their corticosteroid treatment.

Antibiotics

Grade A - Antibiotics should be used to treat exacerbations of COPD associated with a history of more purulent sputum.

Grade B - 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 D - 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 - When sputum has been sent for culture, the appropriateness of antibiotic treatment should be checked against laboratory culture and sensitivities when they become available.

Theophylline and Other Methylxanthines

Grade D - Intravenous theophylline should only be used as an adjunct to the management of exacerbations of COPD if there is an inadequate response to nebulised bronchodilators.

Grade D - 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 - Theophylline levels should be monitored within 24 hours of starting treatment and subsequently as frequently as indicated by the clinical circumstances.

Respiratory Stimulants

Grade D - It is recommended that doxapram is used only when noninvasive ventilation is either unavailable or considered inappropriate.

Oxygen Therapy during Exacerbations of COPD

Grade D - The oxygen saturation should be measured in patients with an exacerbation of COPD, if there are no facilities to measure arterial blood gases.

Grade C - If necessary, oxygen should be given to keep the SaO_2 greater than 90%.

Grade D - 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 - 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 - During the transfer to hospital the following points should be considered.

- 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 - 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 - The aim of supplemental oxygen therapy in exacerbations of COPD is to maintain adequate levels of oxygenation (SaO_2 greater than 90%), without precipitating respiratory acidosis or worsening hypercapnia. Patients with pH less than 7.35 should be considered for ventilatory support.

Noninvasive Ventilation (NIV) and COPD Exacerbations

Grade A - NIV should be used as the treatment of choice for persistent hypercapnic ventilatory failure during exacerbations despite optimal medical therapy.

Grade D - 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 - 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.

Invasive Ventilation and Intensive Care

Grade C - Patients with exacerbations of COPD should receive treatment on intensive care units, including invasive ventilation when this is thought to be necessary.

Grade D - During exacerbations of COPD, functional status, BMI, requirement for oxygen when stable, comorbidities, 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 A - NIV should be considered for patients who are slow to wean from invasive ventilation.

Respiratory Physiotherapy and Exacerbations

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

Monitoring Recovery from an Exacerbation

Grade D - Patient's recovery should be monitored by regular clinical assessment of their symptoms and observation of their functional capacity.

Grade D - Pulse oximetry should be used to monitor the recovery of patients with nonhypercapnic, nonacidotic respiratory failure.

Grade D - 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 - Daily monitoring of peak expiratory flow (PEF) or FEV_1 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.

Discharge Planning

Grade D - Spirometry should be measured in all patients before discharge.

Grade D - Patients should be reestablished on their optimal maintenance bronchodilator therapy before discharge.

Grade D - Patients who have had an episode of respiratory failure should have satisfactory oximetry or arterial blood gas results before discharge.

Grade D - All aspects of the routine care that patients receive (including appropriateness and risk of side effects) should be assessed before discharge.

Grade D - 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 - Arrangements for follow-up and home care (e.g., visiting nurse, oxygen delivery, referral for other support) should be made before discharge.

Grade D - 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.

Definitions

Hierarchy of Evidence

Levels of Evidence

Ia: Evidence from systematic reviews or meta-analysis of randomised controlled trials

Ib: Evidence from at least one randomised controlled trial

IIa: Evidence from at least one controlled study without randomisation

IIb: Evidence from at least one other type of quasi-experimental study

III: Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies and case-control studies

IV: Evidence from expert committee reports or opinions and/or clinical experience of respected authorities

The guideline development group also identifies evidence from the National Institute for Clinical Excellence (NICE) guidelines or Health Technology Appraisal programme and evidence from Health Service Circulars (HSC) as follows:

NICE: Evidence from NICE guidelines or Health Technology Appraisal programme

HSC: Evidence from Health Service Circulars

Grading of Recommendations

Grade A: Based on hierarchy I evidence

Grade B: Based on hierarchy II evidence or extrapolated from hierarchy I evidence

Grade C: Based on hierarchy III evidence or extrapolated from hierarchy I or II evidence

Grade D: Directly based on hierarchy IV evidence or extrapolated from hierarchy I, II, or III evidence

NICE: Evidence from NICE guidelines or Health Technology Appraisal programme

HSC: Evidence from Health Service Circulars

CLINICAL ALGORITHM(S)

Clinical algorithms were provided in the original guideline document (full version) for the diagnosis of chronic obstructive pulmonary disease, the management of stable chronic obstructive pulmonary disease, and the management of exacerbations of chronic obstructive pulmonary disease.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

If adopted, these guideline recommendations should lead to better standards of care and thus better outcomes from chronic obstructive pulmonary disease.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the National Institute for Clinical Excellence (NICE) and the National Collaborating Centre for Chronic Conditions, which was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of health professionals to make decisions

appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

- The document and recommendations are subject to various limitations. The commissioning authority, National Institute for Clinical Evidence (NICE), is primarily concerned with Health Services, and so these recommendations only indirectly refer to Social Services and the voluntary sector. Nonetheless the importance of other agencies cannot be overstated, and in each locality the aim should be to integrate chronic obstructive pulmonary disease (COPD) care across all relevant sectors. A systematic approach was used to locate and appraise the evidence, and explicit inclusion criteria were applied. Due to the magnitude of the literature potentially relevant to COPD, the inclusion criteria aimed to limit the included studies to those of a higher quality conducted primarily in people with COPD. Where these were not available, well-conducted studies outside COPD or lower level studies in people with COPD were included. The guideline usually recommends within medication licence indications. Exceptionally, where there was clear supporting evidence, recommendations outside the licence indications have been included. As far as possible where this is the case it is indicated.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation in the National Health Service

Local health communities should review their existing practice for the management of chronic obstructive pulmonary disease (COPD) against this guideline as they develop their Local Delivery Plans. The review should consider the resources required to implement the recommendations detailed below and in Section 1 of the National Institute for Clinical Excellence (NICE) version (short version) of the guideline document (see "Companion Documents" field), the people and processes involved, and the timeline over which full implementation is envisaged. It is in the interests of patients that the implementation timeline is as rapid as possible.

Relevant local clinical guidelines, care pathways, and protocols should be reviewed in the light of this guidance and revised accordingly.

This guideline should be used in conjunction with the National Institute for Clinical Excellence (NICE) technology appraisals listed in Section 6 of the NICE version (short version) of the guideline document (see "Companion Documents" field), and with the National Service Framework for Older People, which is available from www.doh.gov.uk/nsf/olderpeople/index.htm.

Suggested audit criteria are listed in Appendix D of the NICE version (short version) of the guideline. These can be used as the basis for local clinical audit, at the discretion of those in practice.

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation. (Note that the order of the key priorities given here is arbitrary and does not reflect their relative importance. The reader should refer to the original recommendations for further detail.)

Diagnose COPD

- A diagnosis of COPD should be considered in patients over the age of 35 who have a risk factor (generally smoking) and who present with exertional breathlessness, chronic cough, regular sputum production, frequent winter bronchitis, or wheeze. The presence of airflow obstruction should be confirmed by performing spirometry.
- All health professionals managing patients with COPD should have access to spirometry and be competent in the interpretation of the results.

Stop Smoking

- Encouraging patients with COPD to stop smoking is one of the most important components of their management. All COPD patients still smoking, regardless of age should be encouraged to stop and offered help to do so at every opportunity.

Effective Inhaled Therapy

- Long-acting inhaled bronchodilators (beta$_2$-agonists and / or anticholinergics) should be used to control symptoms and improve exercise capacity in patients who continue to experience problems despite the use of short-acting drugs.
- Inhaled corticosteroids should be added to long-acting bronchodilators to decrease exacerbation frequency in patients with an FEV_1 less than or equal to 50% predicted who have had two or more exacerbations requiring treatment with antibiotics or oral corticosteroids in a 12-month period.

Pulmonary Rehabilitation for All Who Need It

- Pulmonary rehabilitation should be made available to all appropriate patients with COPD

Use Noninvasive Ventilation

- Noninvasive ventilation should be used as the treatment of choice for persistent hypercapnic ventilatory failure during exacerbations not responding to medical therapy. It should be delivered by staff trained in its application, experienced in its use, and aware of its limitations
- When patients are started on noninvasive ventilation, there should be a clear plan covering what to do in the event of deterioration and ceilings of therapy should be agreed.

Manage Exacerbations

- The frequency of exacerbations should be reduced by appropriate use of inhaled corticosteroids and bronchodilators and vaccinations

- The impact of exacerbations should be minimised by:
    1. Giving self-management advice on responding promptly to the symptoms of an exacerbation
    2. Starting appropriate treatment with oral steroids and/or antibiotics
    3. Use of non-invasive ventilation when indicated
    4. Use of hospital-at-home or assisted-discharge schemes

Multidisciplinary Working

- COPD care should be delivered by a multi-disciplinary team.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Clinical Algorithm
Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Chronic Conditions. Chronic obstructive pulmonary disease. National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. Thorax 2004 Feb;59 Suppl 1:1-232. [491 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Feb

GUIDELINE DEVELOPER(S)

National Collaborating Centre for Chronic Conditions - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Guideline Development Group
Consensus Reference Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Guideline Development Group Committee Members: Dr David MG Halpin* (Lead and Clinical Advisor), Consultant Physician and Senior Lecturer, Royal Devon & Exeter Hospital; Ms Jill Parnham*, Senior Health Services Research Fellow in Guideline Development, National Collaborating Centre for Chronic Conditions; Dr David Bellamy*, General Practitioner, Bournemouth; Ms Julie Booker*, Respiratory Nurse Specialist, Rotherham General Hospital; Professor Peter Calverley* (seconded from the Consensus Reference Group for three meetings); Professor of Respiratory Medicine, University of Liverpool and Aintree Hospital NHS Trust; Dr Martin Connolly*, Consultant Geriatrician, University of Manchester; Dr Rachel Garrod*, Senior Lecturer, Kingston University; Mr Ashley Green* (deputy for Esther Threlfall), Breathe Easy Assistant Manager, British Lung Foundation; Ms Gwen Haylett*, Patient Representative; Dr Michael ML Morgan* (seconded from the Consensus Reference Group for one meeting), Consultant Physician, University Hospitals of Leicester NHS Trust; Ms Karen Reid*, Information Scientist, National Collaborating Centre for Chronic Conditions; Dr Michael Rudolf*, Consultant Physician, Ealing Hospital NHS Trust; Ms Katherine Stevens*, Research Associate in Health Economics, School of Health and Related Research, University of Sheffield; Ms Esther Threlfall*, UK Breathe Easy Manager, British Lung Foundation; Ms Jane Scullion* (attended two meetings as deputy for Julie Booker), Respiratory Consultant Nurse, University Hospital of Leicester; Ms Teresa Smith (attended five meetings as deputy for Julie Booker), Senior Respiratory Nurse/Chest Clinic Manager, Heatherwood and Wexham Park NHS Trust; Ms Elaine Stevenson (attended one meeting as deputy for Julie Booker), Clinical Practitioner Respiratory Care, Southern Derbyshire Acute Hospitals Trust; Professor Jadwiga Wedzicha*, Professor of Respiratory Medicine, St Bartholomew's and the Royal London School of Medicine

Consensus Reference Group Members: Professor Duncan Geddes (Chair), Professor of Respiratory Medicine, Royal Brompton Hospital NHS Trust; Ms Alison Bent (attended one meeting as deputy for Mary Hickson) Dietitian, Hammersmith Hospitals NHS Trust; Professor Peter Calverley, Professor of Respiratory Medicine, University of Liverpool and Aintree Hospital NHS Trust; Dr Stephen Connellan, Consultant Physician, The Royal Wolverhampton Hospitals NHS Trust; Dr Sujal

Desai (attended one meeting) Radiologist, Kings College Hospital; Dr Gillian Hawksworth, Community Pharmacist; Dr Mary Hickson, Senior Research Dietician, Hammersmith Hospitals NHS Trust; Professor Walter W Holland, Emeritus Professor of Public Health Medicine, Visiting Professor, London School of Economics; Dr Bill Homes (attended one meeting) Group Medical Director, Nestor Healthcare Group Plc; Professor Paul Little, Professor of Primary Care Research, University of Southampton; Dr Michael ML Morgan, Consultant Physician, University Hospitals of Leicester NHS Trust; Ms Louise Sewell, Pulmonary Rehabilitation Specialist, University Hospitals of Leicester NHS Trust; Dr Mangalam Sridhar, Consultant Physician, Hammersmith Hospitals NHS Trust; Dr Mike Thomas (attended one meeting as deputy for David Bellamy) General Practitioner, Minchinhampton, Gloucestershire; Ms Patrician Turner-Lawlor (attended one meeting as deputy for Louise Sewell) Senior Research Occupational Therapist, Cardiff and Vale NHS Trust

* Denotes member of both the Guideline Development Group and the Consensus Reference Group

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All group members made a formal Declaration of Interests at the start of the guideline development and provided updates throughout the process. The National Collaborating Centre for Chronic Conditions (NCC-CC) and the Group Chair monitored these.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- National Collaborating Centre for Chronic Conditions. Chronic obstructive pulmonary disease. Management of chronic obstructive pulmonary disease in adults in primary and secondary care. London (UK): National Institute for Clinical Excellence; 2004 Feb 1. 53 p. (Clinical guideline; no. 12). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Clinical Excellence (NICE) Web site
- Chronic obstructive pulmonary disease. Management of chronic obstructive pulmonary disease in adults in primary and secondary care. Quick reference guide. National Collaborating Centre for Chronic Conditions, 2004 Feb. 11 p. Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455, ref: N0462. 11 Strand, London, WC2N 5HR.

Additionally, Audit Criteria can be found in Section 9 of the original guideline document.

PATIENT RESOURCES

The following is available:

- Chronic obstructive pulmonary disease: Understanding NICE guidance - information for people with chronic obstructive pulmonary disease, their families and carers, and the public. National Institute for Clinical Excellence (NICE), 2004 Feb. 52 p.

Electronic copies: Available from the National Institute for Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS), 11 Strand, London, WC2N 5HR. Response Line 0870 1555 455, ref N0479.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on July 12, 2004. The information was verified by the guideline developer on November 29, 2004. This summary was updated by ECRI on December 5, 2005 following the U.S. Food and Drug Administration (FDA) advisory on long-acting beta2-adrenergic agonists (LABA). This summary was updated by ECRI on November 21, 2006 following the FDA advisory on Tamiflu. This summary was updated by ECRI Institute on November 6, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on March 10, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Tamiflu (oseltamivir phosphate). This summary was updated by ECRI Institute on April 9, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Relenza (zanamivir).

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 10/13/2008