



National Prescribing Service Limited



Case study 53 report: Maximising benefits with inhaled therapy

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Inside

Case study 53: Maximising benefits with inhaled therapy

Scenario and questions page 3

Summary of results page 5

Results in detail

Managing acute exacerbation of COPD/ asthma page 7

Managing stable COPD/ asthma page 8

Choosing smoking-cessation therapies page 8

Use of inhaled corticosteroids in COPD page 10

Commentaries

Associate Professor David McKenzie page 11

Dr Julia Walters page 13

Appendix

Commonly used inhaled medications in asthma and/or COPD page 15

References page 16

Case study 53

Maximising benefits with inhaled therapy

Scenario

Jane, a 60-year-old primary school teacher with stable COPD (diagnosed 2 years ago) presents with a wheeze and increased breathlessness, especially at night, several times over the past week following a viral infection.

On examination, PEF is 60% of her previous best normal value. Spirometry results today reveal mild COPD with a reversible component; FEV₁ 77% of predicted (> 12% improvement from pre-bronchodilator result) and FEV₁/FVC 60%. Blood pressure is 135/86 mmHg, pulse 76, mildly distressed respiratory rate 22 and she is afebrile. Auscultation of the chest reveals widespread expiratory wheeze. Chest X-ray shows a hyper-inflated chest with no acute changes. Her body mass index is 18 kg/m².

There is a family history of atopy and an uncle has asthma. She has no pets. She smokes about 20 cigarettes per day and has done so for the last 20 years. Past attempts to quit smoking 'cold turkey' have been unsuccessful. She has a medical history of hypertension, stable ischaemic heart disease and eczema. Her regular respiratory medications include tiotropium 18 micrograms daily and salbutamol inhaler 200 micrograms every 4–6 hours when required. Prior therapy with ipratropium bromide did not relieve her symptoms. She is also taking enalapril 20 mg, amlodipine 10 mg, isosorbide mononitrate 120 mg and aspirin 150 mg (all once daily). She uses glyceryl trinitrate spray when required and mometasone cream during eczema flare-ups.

Abbreviations: FEV₁ = forced expiratory volume in 1 second (post bronchodilator), FEV₁/FVC = ratio of FEV₁ to forced vital capacity, PEF = peak expiratory flow.

1a) Given Jane's symptoms, would you recommend any changes to her COPD/ asthma medications to manage the exacerbation?

Yes No

b) If yes, please list Jane's COPD/ asthma regimen during the exacerbation (include tiotropium and salbutamol if continuing)

Drug	Dose	Frequency	Duration
_____	_____	_____	_____

2a) What would you prescribe for stable COPD/ asthma management after this exacerbation? (include tiotropium and salbutamol if continuing)

Drug	Dose	Frequency	Duration
_____	_____	_____	_____

3 Jane asks for some advice on smoking cessation. What are the advantages/disadvantages?

	Advantages	Disadvantages
a) Bupropion	_____	_____
b) Nicotine replacement	_____	_____
c) Varenicline	_____	_____

4a) If Jane had moderate COPD without asthma (FEV₁ 45% predicted post bronchodilator with no reversible component) and 2 exacerbations that required treatment with antibiotics this year, would you recommend an inhaled corticosteroid?

Yes No

b) Why/ Why not?

c) If yes, how long would you trial an inhaled corticosteroid before assessing for benefit?

_____ weeks

Summary of results

At the time of publication, 804 responses had been received. This report summarises responses from 200 general practitioners.

Case synopsis

Jane, a 60-year-old primary school teacher with stable COPD, presented with a wheeze and increased breathlessness, especially at night, several times over the past week following a viral infection. She smokes 20 cigarettes per day and has a medical history of hypertension, stable ischaemic heart disease and eczema. Her respiratory medications include tiotropium 18 micrograms daily and salbutamol inhaler 200 micrograms every 4–6 hours when required. Spirometry results today reveal mild COPD with a reversible component; FEV₁ 77% of predicted (> 12% improvement from pre-bronchodilator result) and FEV₁/FVC 60%. (See page 3 for more details.)

Managing acute exacerbation of COPD/ asthma

- Given Jane's symptoms, all respondents would recommend changes to her COPD/ asthma medications: 82.0% would continue using tiotropium 18 micrograms daily, while 79.0% would continue the salbutamol inhaler at different doses and frequencies.
- Main drugs added to Jane's current medications included:

Oral corticosteroids

— prednisolone (35.5%)

Inhaled corticosteroids (ICS)

— fluticasone (20.0%)

— budesonide (5.5%)

ICS/long-acting beta₂ agonist (LABA) fixed-dose combination

— fluticasone/salmeterol (*Seretide*) (35.0%)

— budesonide/eformoterol (*Symbicort*) (17.5%)

Inhaled LABA

— salmeterol (6.0%)

Other

— oral antibiotics (7.5%).

Managing stable COPD/ asthma

- After Jane's COPD/ asthma had been stabilised, 87.0% would continue using tiotropium and 66.0% salbutamol inhaler. The main treatment regimen selected by respondents were:
 - fluticasone/salmeterol (*Seretide*) (41.5%)
 - fluticasone (20.0%)
 - budesonide/eformoterol (*Symbicort*) (18.0%)
 - budesonide (5.5%)
 - salmeterol (5.0%).

Choosing smoking-cessation therapies

- More than 20% of all respondents recognised the effectiveness of smoking-cessation therapies, more than 14.0% found that they were easy to use, and more than 6.5% reported that they reduced withdrawal symptoms associated with smoking cessation. Pharmaceutical Benefits Scheme (PBS) listing was considered an advantage for bupropion and varenicline, while over-the-counter availability of nicotine replacement therapy (NRT) was considered a bonus. 17.5% acknowledged that varenicline was the most effective smoking-cessation therapy available, although it is unclear how it compares with nicotine-replacement therapy or whether its benefits persist beyond 12 months.
- The most commonly reported disadvantage for bupropion was risk of central nervous system disturbances (insomnia, nightmares, headache) (61.0%). For NRT, the most commonly reported disadvantage was risk of skin irritation with patches (29.5%), while for varenicline it was the risk of psychiatric adverse effects (38.0%).

Use of inhaled corticosteroids in COPD

- If Jane had moderate COPD without asthma, and 2 exacerbations that required treatment with antibiotics in the year, 86.0% of respondents would recommend using an ICS as consistent with guidelines.^{1,2}
- Main reasons for using an ICS were:
 - to reduce further exacerbations (61.6%)
 - to reduce the inflammatory component of the condition (20.3%)
 - FEV₁ < 50% (19.2%)
 - proven efficacy (14.0%).
- Main reasons for not using an ICS were:
 - no proven benefit (53.6%)
 - indicated for later stages of COPD only (17.9%)
 - increased risk of pneumonia (10.7%).
- Of those who would recommend an ICS, 64.0% would trial this for 4–8 weeks before assessing benefit.

Results in detail

Managing acute exacerbation of COPD/ asthma

- Given Jane's symptoms, all respondents would recommend changes to her medications. 82.0% would continue using tiotropium 18 micrograms daily, while 79.0% would continue the salbutamol inhaler, altering the dose and frequency.
- 1.6% of those who would use a salbutamol inhaler recommended use with a spacer.

Additional medications and doses recommended by respondents

Medication	% of respondents* (n = 200)
Prednisolone (mostly 25–50 mg daily; duration of treatment 3–10 days) oral	35.5
Fluticasone/salmeterol (<i>Seretide</i>) (mostly 500/50 micrograms twice daily) inhaled	35.0
Fluticasone (mostly 250–500 micrograms twice daily) inhaled	20.0
Budesonide/eformoterol (<i>Symbicort</i>) (mostly 400/12 micrograms twice daily) inhaled	17.5
Antibiotics (mostly amoxicillin 500 mg three times daily) oral	7.5
Salmeterol (mostly 50 micrograms twice daily) inhaled	6.0
Budesonide (mostly 200 micrograms twice daily) inhaled	5.5
Other (eformoterol, smoking-cessation therapy, ciclesonide, ipratropium, beclomethasone)	4.0

*Respondents may have more than one response



Practice points

- The diagnosis of asthma in patients with COPD relies on patient history and reversibility of airflow limitation. If airflow limitation is fully or substantially reversible, the patient with COPD should be treated as for asthma.¹ However, the definition of 'fully or substantially reversible' airflow limitation varies between guidelines.
 - COPD-X guidelines suggest that an increase in FEV₁ > 12% and 200 mL is greater than average day-to-day variability and unlikely to occur by chance.¹
 - UK guidelines suggest a diagnosis of asthma when serial peak expiratory flow (PEF) measurement shows ≥ 20% diurnal or day-to-day variability, or a large (> 400 mL) FEV₁ response to either bronchodilators or 30 mg prednisolone daily for 2 weeks.³
 - Asthma guidelines define airflow limitation as reversible if either baseline FEV₁ is > 1.7 L and post-bronchodilator FEV₁ at least 12% higher than baseline, or baseline FEV₁ is ≤ 1.7 L and post-bronchodilator FEV₁ at least 200 mL higher than baseline.⁴
- Treatment for acute exacerbations of asthma and COPD are similar and rely on oral corticosteroids and short-acting beta₂ agonists.
 - For asthma exacerbations, the dose of prednisolone is 0.5-1.0 mg/kg up to 60 mg daily for 7–10 days.⁴
 - For COPD exacerbations, up to 2 weeks' therapy with prednisolone (40–50 mg daily) is sufficient.¹
- In asthma exacerbations there may be a role for high-dose inhaled corticosteroids for 1–2 weeks, but it is unknown how they compare with oral corticosteroids.⁴ The role of ICS and LABA in the acute phase of COPD is more uncertain.
- Antibiotics are rarely indicated in the treatment of asthma exacerbations. For COPD exacerbations, antibiotics are recommended if there are clinical signs of infection (increased volume *and* change in colour of sputum and/or fever, leukocytosis).¹ In Jane's case, her viral infection would not benefit from antibiotic use.
- During asthma and COPD exacerbations, short-acting beta₂-agonists should be administered via metered-dose inhaler (MDI) and spacer.^{1,4}

Managing stable COPD/ asthma

- After Jane's asthma/COPD has been stabilised, 87.0% would continue using tiotropium and 66.0% salbutamol inhaler.

Additional medications and doses recommended by respondents

Medication	% of respondents* (n = 200)
Fluticasone/salmeterol (<i>Seretide</i>) (mostly 250/25 or 250/50 or 500/50 micrograms twice daily)	41.5
Fluticasone (mostly 250–500 micrograms twice daily)	20.0
Budesonide/eformoterol (<i>Symbicort</i>) (mostly 400/12 micrograms twice daily)	18.0
Budesonide (mostly 200 micrograms twice daily)	5.5
Salmeterol (mostly 50 micrograms twice daily)	5.0
Other (eformoterol, ciclesonide, pneumococcal or influenza vaccination, beclomethasone, smoking-cessation therapy)	8.0

*Respondents may have more than one response



Practice points

- If Jane was treated as per asthma guidelines, she would be classified with moderate persistent asthma and would require low-dose ICS (80–160 micrograms ciclesonide daily, 100–200 micrograms fluticasone/beclomethasone or 200–400 micrograms budesonide daily) plus a LABA. Consider step-down of medications once asthma is controlled for 6–12 weeks by decreasing dose by 25–50%.⁴
- Conversely, in COPD, ICS should only be considered for the later stages of disease but LABAs may be used earlier in therapy.¹

Choosing smoking-cessation therapies

Advantages and disadvantages identified for bupropion

- In general, more than 59.0% of respondents agreed that bupropion was beneficial in smoking cessation.
- The major adverse effects for bupropion were central nervous system (CNS) disturbances and seizures, as described by respondents and outlined in the product information.⁵

Advantages of bupropion	% of respondents (n = 200)*	Disadvantages of bupropion	% of respondents (n = 200)*
Good evidence of efficacy	59.0	CNS disturbances	61.0
Easy to administer	20.5	Seizures	27.0
PBS listed	19.5	General adverse effects	22.5
Milder withdrawal symptoms	10.0	Drug interactions	16.5
		PBS authority requirements	14.0
		Gastrointestinal adverse effects	13.5
		Expensive	6.5
		Dry mouth	6.5

*Respondents may have more than one response

Advantages and disadvantages identified for nicotine-replacement therapy (NRT)

- In general, the major advantage of NRT reported by respondents was accessibility.
- Skin irritation (patches) and cost to patient were the most frequently described disadvantages.

Advantages of NRT	% of respondents (n = 200)*	Disadvantages of NRT	% of respondents (n = 200)*
Over-the-counter product	36.0	Skin irritation (patches)	29.5
Variety of forms and doses	26.5	Cost to patient	25.0
Good evidence	20.0	Less/least effective method	16.0
Fewer adverse effects	15.5	Risk of addiction to nicotine	14.0
Easy to use	14.0	Sleep disturbances	13.0
Cheap	9.0	Gastrointestinal adverse effects	7.0
Reduces withdrawal symptoms	6.5	CNS adverse effects	6.0
		Requires dose titration	5.0
		Ineffective	5.0

*Respondents may have more than one response

Advantages and disadvantages identified for varenicline

- In general, most respondents felt that varenicline had good evidence for in smoking cessation.
- The most common disadvantage of varenicline is nausea, as reported by 33.5% of respondents.⁶ Post-marketing surveillance have included reports of psychiatric adverse effects⁷, as recognised by 38.0% of respondents.

Advantages of varenicline	% of respondents (n = 200)*	Disadvantages of varenicline	% of respondents (n = 200)*
Good evidence	42.5	Psychiatric adverse effects	38.0
More/most effective method	17.5	Gastrointestinal adverse effects	33.5
Easy to use	15.5	Sleep disturbances	18.0
PBS listed	11.5	General adverse effects	15.5
Reduces withdrawal symptoms	8.0	Expensive	11.0
		PBS authority requirements	10.0
		Lack of long-term safety data	7.5
		CNS adverse effects	6.5

*Respondents may have more than one response

Practice points

- Bupropion, NRT or varenicline are all useful aids to assist smoking cessation.⁸ Select therapy according to clinical indication and patient preference.
- Varenicline achieved higher quit and continuous abstinence rates than bupropion users but it is unclear how it compares with NRT or whether its benefits would persist beyond 12 months.⁹
- Ask all patients about changes in mood or behaviour after starting varenicline, during the 2–3-week follow-up visit and after treatment is completed.



Use of inhaled corticosteroids in COPD

- If Jane had moderate COPD without asthma and 2 exacerbations that required treatment with antibiotics, 86.0% of respondents would recommend using an ICS and 14.0% would not.
- Of those who would recommend an ICS, 64.0% would trial this for 4–8 weeks before assessing for benefit.

Reason for adding an ICS	% of respondents (n = 172)*	Reason for not adding an ICS	% of respondents (n = 28)*
To reduce further exacerbations	61.6	No proven benefit	53.6
Anti-inflammatory	20.3	Indicated for later stages of COPD only	17.9
FEV ₁ <50%	19.2	Increase risk of pneumonia	10.7
Good evidence	14.0	Require LABA first	7.1
Recommended in moderate COPD	7.6		

*Respondents may have more than one response



Practice points

- Inhaled corticosteroid therapy is indicated in patients with a documented response or those who have severe COPD with frequent exacerbations.¹
- Fluticasone/salmeterol (*Seretide* 250/25 MDI and *Seretide* 500/50 dry powder inhaler only) is PBS listed for COPD in people with FEV₁ < 50% predicted who have a history of repeated exacerbations despite regular beta₂ agonist treatment. Budesonide/efformoterol (*Symbicort*) is neither TGA registered nor PBS listed for COPD.

Commentary 1

Overview

This 60-year-old woman has been given a diagnosis of stable COPD but she presents with an acute exacerbation after a viral infection, which has many features to suggest asthma. There is a positive family history of asthma and atopy and she is known to have eczema, suggesting an atopic diathesis.

Breathlessness that is worse at night, widespread wheeze and the significant reduction in peak expiratory flow to only 60% of her previous best, together with significant reversibility, are more consistent with asthma than COPD. Her FEV₁ shows only mild airflow obstruction post bronchodilator, at 77% of predicted, indicating only mild COPD.¹

The fact that Jane is underweight means that a nutritional history should be obtained. Low BMI is a poor prognostic feature in patients with advanced COPD. The possibility of occupational asthma should always be considered. In this case the patient is a primary schoolteacher but it is possible that she has a hobby that could be exposing her to chemicals, wood dusts or epoxies.

There is considerable overlap between COPD, ischaemic heart disease (IHD) and peripheral vascular and cerebrovascular disease because of their common association with cigarette smoking. Patients with intercurrent IHD are at considerably increased risk of adverse cardiac events during exacerbations of COPD. The widespread reluctance to prescribe beta blockers to patients with COPD is not justified by the literature¹⁰ Beta blockers were associated with a significant reduction in the risk of adverse cardiac events and mortality related to exacerbations. Cardioselective beta blockers may be the most appropriate choice for patients with significant reversibility.

Summary

The patient has mild COPD with an exacerbation precipitated by a viral infection, which has several features suggestive of acute asthma. The severity of the episode is mild, based on the symptoms and clinical findings, but moderate according to the reduction in peak expiratory flow. The risk of an adverse cardiac event in a patient with coexistent IHD should be kept in mind.

Management of acute exacerbation of COPD/asthma

Most respondents recommended increased doses of inhaled salbutamol but very few recommended use of a spacer with the MDI. Spacers improve the dose delivered to the lungs and reduce oropharyngeal deposition. A reasonably effective alternative to the spacer is the autohaler. The non-CFC propellants have a soft plume with a slow velocity, making this device effective.

Respondents were divided on whether to recommend oral or inhaled corticosteroids. This is understandable because the exacerbation appears to be relatively mild on clinical criteria¹ and, although there was a 40% reduction in PEF, the post-bronchodilator FEV₁ was only mildly reduced, at 77% of predicted. Thus, if treating acute asthma, either oral corticosteroids or high-dose inhaled steroids would be effective and appropriate in this case.⁴ There are few data on the use of either oral or inhaled corticosteroids in the management of acute exacerbations of mild COPD. You would be justified in concluding that this was a case of COPD with substantial reversibility and, as such, should treat as if it were an episode of acute asthma.

Most respondents appropriately agreed that antibiotics were not indicated for a viral infection.

Management of stable COPD/asthma

Decisions regarding ongoing management depend on whether the diagnosis of asthma has been established. As discussed above, the implications are that there is substantial reversibility here and it is therefore justifiable to treat as for asthma. If the reversibility criteria have not been met, a bronchial challenge test with hypertonic saline, mannitol or methacholine should be arranged. Allergy skin tests would be useful to document an atopic status.

Most respondents appear to have concluded that the diagnosis is asthma, with about 85% prescribing an inhaled steroid either alone or in combination. Although we have no information about whether the patient complained of persistent wheeze or nocturnal wheeze after the exacerbation, about 65% of respondents prescribed a LABA, either alone or in combination.

Most respondents seemed to take an each-way bet with COPD and asthma and continued tiotropium. We are not given an FEV₁ value after the exacerbation but it is likely to be greater than 77% of predicted. It is unlikely that a patient with such mild COPD would need both tiotropium and a LABA. If the diagnosis was COPD without significant asthma, then, arguably, the only treatment required would be smoking cessation.

Choosing smoking-cessation therapies

Overall the respondents had a good grasp of the advantages and disadvantages of the various

therapies available to assist smoking cessation. The level of awareness of the effectiveness of NRT was disappointingly low. The combination of a patch and one of the self-administered forms of NRT is probably the most effective means of using this therapy, with good evidence to support it.¹¹

The respondents were less well informed about varenicline than about bupropion, with fewer respondents convinced of its effectiveness. The most commonly reported side effects of varenicline were listed as a disadvantage by fewer than half of the respondents. This may reflect a view that the side effects are uncommon or not severe, rather than a lack of knowledge, but it is recommended that patients should be warned about mood disturbances and asked about them during follow-up visits.

Use of inhaled corticosteroids in moderate COPD with frequent exacerbations

The benefits of inhaled corticosteroids in moderate COPD with frequent exacerbations are well documented, and 86% of respondents recommended them. Inhaled corticosteroids have been shown to reduce the frequency of exacerbations, and improve quality of life. More recent reports have also shown a reduced rate of decline of airway function.

Although the studies have shown an increased incidence of pneumonia, there appeared to be a reduction in mortality in the inhaled steroid groups. This suggests that the preservation of airway function has a more important survival impact than the increased incidence of pneumonia, which is usually non-fatal.

Overview

COPD and asthma are common respiratory diseases and may coexist.¹ It is difficult, particularly in older people, to differentiate between them on the basis of common symptoms of breathlessness, cough and wheeze. Airflow obstruction persisting after bronchodilator administration, indicated by a ratio of FEV₁ to FVC < 0.7, confirms a diagnosis of COPD.¹

However, in people with COPD without a history of asthma there is variability in the reversible component of airflow limitation. In an Australian cohort of smokers and ex-smokers with COPD, 47% had significant bronchodilator reversibility using the criteria of $\geq 12\%$ plus 200 mL of baseline FEV₁ or forced vital capacity.¹²

Smoking cessation remains the most effective treatment to prevent progression of COPD. Exacerbations of COPD are common even in mild COPD, with a mean yearly exacerbation rate of 2.2 (95% confidence interval 1.9 to 2.7) found in patients in primary care.¹³

This case study

This 60-year-old woman, a current smoker with a history of smoking 20 cigarettes a day for 20 years, has risk factors for asthma and a positive family history of asthma and atopy, although no personal history of previous asthma symptoms or atopy is given. Her PEF is 60% of previous best, and her post-bronchodilator FEV₁ is 77% of predicted normal.

On spirometry at presentation Jane's condition demonstrates some reversibility, with FEV₁ improvement of more than 12% with bronchodilator; however, there is persistent airflow obstruction consistent with mild COPD by the Australian COPD-X guidelines.¹

Jane has symptoms of a COPD exacerbation (increased breathlessness and wheeze) that would be classified as mild using a symptom-based definition¹⁴ and also using a definition based on healthcare use (increased need for

medication that can be managed in the patient's own environment).¹⁵ However, there are no systemic indicators of bacterial infection, chest X-ray is consistent with COPD and Jane does not show signs of pneumonia. She is normotensive but underweight with a BMI of 18.

For the immediate management of her presentation with a mild exacerbation of COPD, she requires additional treatment with adequate doses of short-acting bronchodilators to relieve her symptoms, salbutamol (100 micrograms up to 10 puffs via MDI and spacer) and oral glucocorticoids at the recommended dose of 40–50 mg prednisolone for 10–14 days.

When she is symptomatically stable, Jane's longer-term management is based on deciding if she has asthma in addition to COPD. There is no total agreement on the interpretation of what constitutes 'substantial reversibility of airflow limitation' in the guidelines¹ and in Jane's case a personal history of atopy and diurnal airflow variability is lacking.⁴ Thus, treatment for mild COPD with short-acting bronchodilator salbutamol 200 micrograms 4-hourly as required and tiotropium 18 micrograms once daily are indicated. If asthma is also diagnosed, she should be treated with inhaled glucocorticoids, to which a LABA can be added if there are persistent symptoms using a fixed-dose combination inhaler.⁴

Effective smoking-cessation advice and assistance and should be the highest priority target for management, with a multifaceted approach including counselling and pharmacotherapy. Self-management support should not be forgotten even in mild COPD, as this can improve quality of life and promote positive health behaviours.

Comments on responses

Managing acute exacerbation of COPD/ asthma

One-third of respondents indicated that they would start treatment with oral glucocorticoids, after the recommendations for an exacerbation

of COPD¹⁶, while others would start treatment with inhaled glucocorticoids, possibly deciding to treat as if an acute exacerbation of asthma.

Most respondents would increase the dose and frequency of short-acting bronchodilator (salbutamol) but only a small minority recommended use of a spacer to assist patient convenience and increase effectiveness.¹⁷

A small number of respondents would start a LABA (salmeterol or eformoterol alone), most in a fixed-dose combination inhaler with an inhaled glucocorticoid. Assessment of appropriate clinical indications for use of a LABA in this patient needs to be made at a later stage, as they are not recommended for use in an exacerbation of COPD.

Most respondents recognised that antibiotics were not indicated in a mild exacerbation without an increase in amount and purulence of sputum.¹⁴

Managing stable COPD/asthma

Respondents to this question were not given information about past symptoms, presence of atopy or diurnal variability of airflow limitation in this patient that would assist assessment of whether to treat ongoing asthma with inhaled glucocorticoids. However, many respondents appeared to follow this path and indicated that they would treat asthma using fluticasone or budesonide in different forms.

Most respondents would continue to treat Jane's COPD with tiotropium, but fewer continued the short-acting beta agonist salbutamol for symptom relief. This may be related to the large proportion of respondents who treated asthma with a LABA alone or in a fixed-dose combination inhaler with an inhaled glucocorticoid.

Use of inhaled corticosteroids in COPD

A large majority of respondents recognised the benefit of treatment with an inhaled glucocorticoid in moderate COPD without asthma but with two exacerbations in a year

that required treatment with antibiotics. The main advantages are to reduce further exacerbations and improve quality of life¹⁸, and treatment should be continued long term.

Some respondents cited the increased risk of pneumonia as the reason for not adding an inhaled glucocorticoid. Two studies (a comparison of fluticasone/salmeterol with tiotropium and a comparison of fluticasone and salmeterol separately or in combination with placebo) found a higher probability of having pneumonia reported as an adverse event.^{19,20} Neither study was designed to measure pneumonia incidence as an endpoint, and further investigations are needed.

Choosing smoking-cessation therapies

A systematic review found evidence that a combination of psychosocial interventions and pharmacological interventions is superior to no treatment or to psychosocial interventions alone.²¹ Most respondents rated bupropion as effective in smoking cessation. This is supported by a systematic review indicating that it can about double the odds of quitting.²² Many respondents identified its side effects — insomnia, dry mouth, nausea and seizures. At the dose used for smoking cessation the risk of seizures is estimated to be 1 in 1000.²²

Only a minority of respondents gave good evidence of effectiveness as an advantage for NRT, although a systematic review of NRT (gum, lozenges, sublingual tablets) found that they significantly increased the odds of quitting, with little difference between products but some evidence that a combination of nicotine patch and a form allowing ad-lib dosing increased quit rates.¹¹

Varenicline was reported as effective by nearly half of respondents. The major adverse effects of nausea, mood and sleep disturbances were recognised by some respondents. Varenicline is an option for smokers who have expressed a desire to quit smoking, but should normally be prescribed only as part of a program of behavioural support.²³

Appendix

Commonly used inhaled medications in COPD and/or asthma^{24,25}

Generic name	Device	Brand names	Strength (in micrograms, unless otherwise indicated)
Bronchodilators			
Short-acting beta₂ agonists			
Salbutamol	Autohaler	Airomir Autohaler	100
	MDI	Airomir, Asmol CFC-free, Epaq, Ventolin CFC-free	100
	Nebuliser	Asmol Uni-dose, Butamol, Ventolin Nebules, Ventolin Respirator Solution	2.5mg/2.5mL, 5mg/2.5mL 5mg/1mL
	Rotahaler	Ventolin Rotacaps	200
	Diskhaler	Ventolin Disks	200
Terbutaline	Nebuliser	Bricanyl Respules	5mg/2mL
	Turbuhaler	Bricanyl Turbuhaler	500
Long-acting beta₂ agonists			
Eformoterol	Aeroliser	Foradile	12
	Turbuhaler	Oxis Turbuhaler	6, 12
Salmeterol	Accuhaler	Serevent Accuhaler	50
	MDI	Serevent	25
Anticholinergic bronchodilators			
Ipratropium	MDI	Atrovent CFC-Free	20
	Nebuliser	Aeron, Apoven, Atrovent preparations, Ipratrin, Ipravent	250/mL, 500/mL
Tiotropium	Handihaler	Spiriva	18
Combination bronchodilator			
Salbutamol/ipratropium	MDI	Combivent	100/20
Corticosteroids			
Beclomethasone	Autohaler	Qvar Autohaler	50, 100
	MDI	Qvar	50, 100
Budesonide	Nebuliser	Pulmicort Respules	500/2mL, 1000/2mL
	Turbuhaler	Pulmicort Turbuhaler	100, 200, 400
Ciclesonide	MDI	Alvesco	80, 160
Fluticasone	Accuhaler	Flixotide Accuhaler	100, 250, 500
	MDI	Flixotide	50, 125, 250
	Nebuliser	Flixotide Nebules	500/2mL, 2000/2mL
Combination corticosteroid / long-acting beta₂ agonists			
Budesonide/eformoterol	Turbuhaler	Symbicort Turbuhaler	100/6, 200/6, 400/12
Fluticasone/salmeterol	Accuhaler	Seretide Accuhaler	100/50, 250/50, 500/50
	MDI	Seretide	50/25, 125/25, 250/25

MDI= metered-dose inhaler

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