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Primary Care Respiratory **UPDATE**



www.pcrs-uk.org/pcru

HIGHLIGHTS ...

Exacerbations; lessons from the National COPD audit

Preventing exacerbations; new approaches to care

Getting the basic rights - special pull-out feature

Journal round up

npj Primary Care Respiratory Medicine - first 9 months

Delivering excellence locally initiatives from around the UK



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Each single inhalation of FF 200mcg and VI 25mcg provides a delivered dose of 184mcg of FF and 22mcg of VI. **Indications:** *Asthma:* Regular treatment of asthma in patients ≥ 12 years and older not adequately controlled on inhaled corticosteroids and "as needed" short-acting inhaled β_2 -agonists, where a long-acting β_2 -agonist and inhaled corticosteroid combination is appropriate. *COPD:* Symptomatic treatment of adults with COPD with a $FEV_1 < 70\%$ predicted normal (post-bronchodilator) and an exacerbation history despite regular bronchodilator therapy. **Dosage and administration:** Inhalation only. *Asthma:* Adults and adolescents ≥ 12 years: one inhalation once daily of: Relvar 92/22mcg for patients who require a low to mid dose of inhaled corticosteroid in combination with a long-acting beta2-agonist. If patients are inadequately controlled then the dose can be increased to one inhalation once daily Relvar 184/22mcg. Relvar 184/22mcg can also be considered for patients who require a higher dose of inhaled corticosteroid in combination with a long-acting beta2-agonist. Regularly review patients and reduce dose to lowest that maintains effective symptom control. *COPD:* one inhalation once daily of Relvar 92/22mcg. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients (lactose monohydrate & magnesium stearate). **Precautions:** Pulmonary tuberculosis, severe cardiovascular disorders, chronic or untreated infections, diabetes mellitus. Paradoxical bronchospasm – substitute alternative therapy if necessary. In patients with hepatic with moderate to severe impairment 92/22mcg dose should be used. *Acute symptoms:* Not for acute symptoms, use short-acting inhaled bronchodilator. Warn patients to seek medical advice if short-acting inhaled bronchodilator use increases. Therapy should not be abruptly stopped without physician supervision due to risk of symptom recurrence. Asthma-related adverse events and exacerbations may occur during treatment. Patients should continue treatment but seek medical advice if asthma symptoms remain uncontrolled or worsen after initiation of Relvar. *Systemic effects:* Systemic effects of inhaled corticosteroids may occur, particularly at high doses for long periods, but much less likely than with oral corticosteroids. *Possible Systemic effects include:* Cushing's syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, growth retardation in children and adolescents, cataract, glaucoma. More rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). 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Relvar should not be used in conjunction with other long-acting β_2 -adrenergic agonists or medicinal products containing long-acting β_2 -adrenergic agonists. **Pregnancy and breast-feeding:** Experience limited. Balance risks against benefits. **Side effects:** Very Common ($\geq 1/10$): Headache, nasopharyngitis. Common ($\geq 1/100$ to $< 1/10$): Candidiasis of the mouth and throat, dysphonia, pneumonia, bronchitis, upper respiratory tract infection, influenza, oropharyngeal pain, sinusitis, pharyngitis, rhinitis, cough, abdominal pain, arthralgia, back pain, fractures, pyrexia. Uncommon ($\geq 1/1,000$ to $< 1/100$): Extrasystoles. Rare ($\geq 1/10,000$ to $< 1/1,000$): Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria. **Legal category:** POM. **Presentation and Basic NHS cost:** Relvar® Elliпта®. 1 inhaler x 30 doses. Relvar Elliпта 92/22 - £27.80. Relvar Elliпта 184/22 - £38.87. **Marketing authorisation (MA) nos. 92/22mcg 1x30 doses [EU/1/13/886/002]; 184/22mcg 1x30 doses [EU/1/13/886/005]. MA holder:** Glaxo Group Ltd, 980 Great West Road, Brentford, Middlesex TW8 9GS, UK. **Last date of revision:** December 2014. Relvar® and Elliпта® are registered trademarks of the GlaxoSmithKline group of companies. All rights reserved. Relvar® Elliпта® was developed in collaboration with Theravance, Inc.

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1. Relvar Elliпта 92/22 Summary of Product Characteristics. GlaxoSmithKline, December 2014.
2. Relvar Elliпта 184/22 Summary of Product Characteristics, GlaxoSmithKline, December 2014.
3. Svendsater H, Jacques L, Goldfrad C et al. Ease of use of the ELLIPTA dry powder inhaler: data from three randomised controlled trials in patients with asthma npj Primary Care Respiratory Medicine (2014) 24, 14019; doi:10.1038/npcr.2014.19

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with other medicinal products: Interaction studies have only been performed in adults. Avoid β -blockers. Caution is advised when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin, itraconazole, ritonavir, telithromycin). Anoro Ellipta should not be used in conjunction with other long-acting β_2 -adrenergic agonists or medicinal products containing long-acting muscarinic antagonists. Caution is advised with concomitant use with methylxanthine derivatives, steroids or non-potassium-sparing diuretics as it may potentiate possible hypokalaemic effect of β_2 -adrenergic agonists. **Fertility, pregnancy, and breast-feeding:** No available data. Balance risks against benefits. **Side effects:** Common: Urinary tract infection, sinusitis, nasopharyngitis, pharyngitis, upper respiratory tract infection, headache, cough, oropharyngeal pain, constipation and dry mouth. Uncommon: Atrial fibrillation, supraventricular tachycardia, rhythm idioventricular, tachycardia, supraventricular extrasystoles and rash. **Legal category:** POM. **Presentation and Basic NHS cost:** Anoro[®] Ellipta[®]. 1 inhaler x 30 doses. Anoro Ellipta 55/22mcg - £32.50. **Marketing authorisation (MA) nos. 55/22mcg 1x30 doses [EU/1/14/898/002]; MA holder:** Glaxo Group Ltd, 980 Great West Road, Brentford, Middlesex TW8 9GS, UK. **Last date of revision:** October 2014. UK/RESP/0077/14c. Anoro[®] and Ellipta[®] are registered trademarks of the GlaxoSmithKline group of companies. All rights reserved. Anoro[®] Ellipta[®] was developed in collaboration with Theravance, Inc.

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1. Decramer et al. Lancet Resp Med 2014 ; Vol 2 No. 6 pp 472-4486.
2. Maleki-Yazdi et al. Respir Med. 2014;108(12):1752-1760.



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maintenance dose is 2 inhalations per day, given either as one inhalation morning and evening or as 2 inhalations in either the morning or evening. For some patients a maintenance dose of 2 inhalations twice daily may be appropriate. Patients should take 1 additional inhalation as needed in response to symptoms. If symptoms persist after a few minutes, an additional inhalation should be taken. Not more than 6 inhalations should be taken on any single occasion. A total daily dose of up to 12 inhalations could be used for a limited period. Patients using more than 8 inhalations daily should be strongly recommended to seek medical advice. DuoResp[®] Spiromax[®] 320/9: Only to be used as maintenance therapy. **Adults:** 1 inhalation twice daily (maximum of 2 inhalations twice daily). **COPD: Adults:** 1 inhalation twice daily. **Elderly patients (≥ 65 years old):** No special requirements. **Patients with renal or hepatic impairment:** No data available. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Precautions and warnings:** If treatment is ineffective, or exceeds the highest recommended dose, medical attention must be sought. Patients with sudden and progressive deterioration in control of asthma or COPD should undergo urgent medical assessment. Patients should have their rescue inhaler available at all times. The reliever inhalations should be taken in response to symptoms and are not intended for regular prophylactic use e.g. before exercise. For such, a separate rapid-acting bronchodilator should be considered. Patients should not be initiated during an exacerbation. Serious asthma-related adverse events and exacerbations may occur. If asthma symptoms remain uncontrolled or worsen, patients should continue treatment and seek medical advice. If paradoxical bronchospasm occurs, treatment should be discontinued immediately. Paradoxical bronchospasm responds to a rapid-acting inhaled bronchodilator and should be treated straightaway. Systemic effects may occur, particularly at high doses prescribed for long periods. Potential effects on bone density should be considered, particularly in patients on high doses for prolonged periods that have co-existing risk factors for osteoporosis. Prolonged treatment with high doses of inhaled corticosteroids may result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be

considered during periods of stress. Treatment should not be stopped abruptly. Transfer from oral steroid therapy to a budesonide/formoterol fumarate fixed-dose combination may result in the appearance of allergic or arthritic symptoms which will require treatment. In rare cases, tiredness, headache, nausea and vomiting can occur due to insufficient glucocorticosteroid effect and temporary increase in the dose of oral glucocorticosteroids may be necessary. To minimise risk of oropharyngeal Candida infection patients should rinse mouth with water. Administer with caution in patients with thyrotoxicosis, pheochromocytoma, diabetes mellitus, untreated hypokalaemia, or severe cardiovascular disorders. The need for, and dose of inhaled corticosteroids should be re-evaluated in patients with active or quiescent pulmonary tuberculosis, fungal and viral infections in the airways. Additional blood glucose controls should be considered in diabetic patients. Hypokalaemia may occur at high doses. Particular caution is recommended in unstable or acute severe asthma. Serum potassium levels should be monitored in these patients. As with other lactose containing products the small amounts of milk proteins present may cause allergic reactions. **Interactions:** Concomitant treatment with potent CYP3A4 inhibitors should be avoided. If this is not possible the time interval between administration should be as long as possible. Not recommended with β -adrenergic blockers (including eye drops) unless compelling reasons. Concomitant treatment with quinidine, disopyramide, procainamide, phenothiazines, antihistamines (terfenadine), Monoamine Oxidase Inhibitors (MAOIs) and Tricyclic Antidepressants (TCAs) can prolong the QTc-interval and increase the risk of ventricular arrhythmias. L-Dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance. Concomitant treatment with MAOIs, including agents with similar properties, may precipitate hypertensive reactions. Patients receiving anaesthesia with halogenated hydrocarbons have an elevated risk of arrhythmias. Hypokalaemia may increase the disposition towards arrhythmias in patients taking digitalis glycosides. **Pregnancy and lactation:** Use only when benefits outweigh potential risks. Budesonide is excreted in breast milk; of therapeutic doses no effects on infants are anticipated. **Effects on ability to drive and use machines:**

No or negligible influence. **Adverse reactions:** Since DuoResp[®] Spiromax[®] contains both budesonide and formoterol, the same pattern of adverse reactions as reported for these substances may occur. No increased incidence of adverse reactions has been seen following concurrent administration of the two compounds. **Serious:** Immediate and delayed hypersensitivity reactions, e.g. exanthema, urticaria, pruritus, dermatitis, angioedema and anaphylactic reaction, Cushing's syndrome, adrenal suppression, growth retardation, decrease in bone mineral density, hypokalaemia, hyperglycaemia, aggression, psychomotor hyperactivity, anxiety, sleep disorders, depression, behavioural changes, cataract and glaucoma, tachycardia, cardiac arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia and extrasystoles, angina pectoris, prolongation of QTc-interval, variations in blood pressure, bronchospasm and paradoxical bronchospasm. **Common:** Candida infections in the oropharynx, headache, tremor, palpitations, mild irritation in the throat, coughing and hoarseness. See the Summary of Product Characteristics in relation to other side effects. **Overdose:** An overdose of formoterol may lead to: tremor, headache, palpitations. Symptoms reported from isolated cases are tachycardia, hyperglycaemia, hypokalaemia, prolonged QTc-interval, arrhythmia, nausea and vomiting. Supportive and symptomatic treatment may be indicated. **Price per pack:** DuoResp[®] Spiromax[®] 160/4.5 and DuoResp[®] Spiromax[®] 320/9: £29.97. **Legal Category:** POM. **Marketing Authorisation Numbers:** DuoResp[®] Spiromax[®] 160/4.5: EU/1/14/920/001. DuoResp[®] Spiromax[®] 320/9: EU/1/14/920/004. **Marketing Authorisation Holder:** Teva Pharma BV, Computerweg 10, 3542 DR Utrecht, The Netherlands. **Date of Preparation:** May 2014. **Job Code:** UK/MED/14/0019. **References:** 1. Rychlik R, Kreimendahl F. Presented at the 7th IPCRG World Conference, 2014. 2. Plusa T, Bijos P. Poster 2805 presented at the European Respiratory Society International Congress, 2014. 3. Plusa T, Bijos P. Poster 2807 presented at the European Respiratory Society International Congress, 2014. Teva Pharmaceuticals Europe BV, Piet Heinkade 107, 1019 GM Amsterdam, The Netherlands.

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Primary Care Respiratory **UPDATE**



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SPECIAL PULL-OUT FEATURE

Getting the Basics Right Your essential guide to the management of COPD

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Reference: 1. Hubbard GP *et al. Clin Nutr* 2012;31;293-312.

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Editor's Round-up

Hilary Pinnock, *Editor*



This edition of *Primary Care Respiratory Update* has a focus on chronic obstructive pulmonary disease (COPD) – a particularly important topic at this time of year, which sees the peak in emergency admissions largely driven by respiratory infections many of which will have COPD as an underlying cause.

The National COPD audit shows that our care of people with COPD, like the curate's egg, is good in parts. A reduction in lengths of stay and fewer in-hospital deaths are balanced against an increased number of admissions with wide variations in care throughout the UK. It is particularly disappointing that less than half the respiratory units are able to provide post-discharge pulmonary rehabilitation – an intervention known to improve exercise tolerance, quality of life, and if delivered within 4 weeks of discharge, reduces readmissions. Would this situation be tolerated if the context were cardiac rehabilitation post-myocardial infarction?

In a round-up of initiatives associated with a fall in admission rates, Francesca Robinson, PCRS-UK Communications Consultant, highlights schemes in Southampton, Tower Hamlets and in hospitals throughout the UK. The common thread is the commitment of the organisation to change: thinking outside the box, breaking down historical divides and creating new partnerships within which change can flourish. The sociological theory of 'social capital' reminds us of the

resources of knowledge and experience we all have within our practices and wider communities of care. Mobilising these resources requires leadership and organisational commitment – but the message from these initiatives is that it can be done.

Leadership is something in which the PCRS-UK has invested time and resources, and the policy changes outlined by Bronwen Wagstaff offer respiratory leaders opportunities to improve integrated care for people with respiratory conditions. The section on the initiatives of the Regional Respiratory leads makes inspiring reading: an asthma and COPD improvement programme in Portsmouth (including PCRS-UK membership for all the practices), a new respiratory network covering ten clinical commissioning groups (CCGs) in West Yorkshire, and an established network of Local Nurse Groups in Oxfordshire described enthusiastically as a 'lifeline'. If all this inspires you to leadership, you will want to note the days of the 2015 Respiratory Leaders Meetings (5th and 6th June and 6th and 7th November).

Finally, take a look at the report of the first nine months of the *npjPrimary Care Respiratory Journal*. What an amazing success story!

It all makes one very proud to be a member of the PCRS-UK.

Chair's perspective: Lessons on preventing exacerbations from the National COPD Audit Programme

Stephen Gaduzo, *PCRS-UK Executive Chair*



COPD care is improving but it is a sobering thought that hospital admissions as a result of exacerbations have risen by 13% since 2008.

The figure comes from a clinical audit of the management of COPD exacerbations admitted to acute units in England and Wales during 2014 led by the Royal College of Physicians. Called 'COPD: Who cares matters',¹ this is the second report from the secondary care workstream of the National COPD audit programme.² The first report, 'COPD: who cares',³ which covered the organisation of care in acute units, was published in November 2014.

The data show that hospital care for patients with COPD has improved since the last audit in 2008.

The key improvements in the management of exacerbations are:¹

- The percentage of patients dying during the admission has reduced from 7.8% to 4.3%
- The median length of stay has reduced from 5 to 4 days
- The number of patients able to leave hospital early due to supported discharge schemes has risen from 18% to 40%

However, some aspects of care are still not good enough:

- Hospital admissions have risen by 13% since 2008¹
- There are considerable variations in standards of care around the UK¹
- 1 in 5 patients was not seen by a respiratory expert during their admission¹
- The proportion of patients seen by the respiratory team within 24 hours of admission was significantly less for those patients admitted at the weekend compared with during the week¹
- Nearly a third of units do not deploy discharge care bundles³

- Only 38% of units have access to pulmonary rehabilitation for patients within four weeks of discharge³
- There is room for improvement in inpatient care in five key clinical areas: oxygen prescribing, smoking cessation support, recording of MRC dyspnoea score, recording of spirometry, and recording of body mass index¹

In primary care we are in a good position to influence these data. I would recommend that everyone in primary care reads at least the executive summary of both these reports.^{1,3} The improvements in hospital care are very welcome but there is a lot more that we can all do to support our hospital colleagues (for example in the immediate post-discharge period) to improve outcomes for our patients.

The message for us in primary care is that we should all take a good look at the routine care we provide and see if there are any areas that we could improve. Good, basic care not only helps to identify patients at risk of exacerbations and prevent emergency admissions but it also helps patients to stay out of hospital once they have been discharged. Using structured, planned reviews and supporting patients to self-manage their condition can lead to improved quality of life, fewer exacerbations and better management of unscheduled events.

We should all ensure that we: give patients annual reviews; check they have received their 'flu and pneumococcal vaccinations; give smokers advice and support on quitting; check breathlessness scores, encourage physical activity, refer for pulmonary rehabilitation (and encourage our patients to attend), review patients' medication and check that they know how to use their inhalers correctly. All these elements of care ensure the patient gets

the best out of their treatment and empowers them to do all they can to protect themselves.

PCRS-UK has a wealth of evidence based practice improvement tools that can help you to assess whether you are providing first-rate care. Based on national guidelines, these tools provide clinicians with a structured, systematic way of reviewing the respiratory care they deliver and can help to identify areas that can be improved. PCRS-UK improvement tools can also be used to check whether there are any gaps in care across multiple practices.

Two Improvement Worksheets relevant to preventing exacerbations are *Identifying high impact COPD* and *Post acute COPD care bundle*. They are easy to use and available to all members; find them on the website and see for yourself: <https://www.pcrs-uk.org>

Our recently updated COPD Quick Guide is now also available on the PCRS-UK website. It simplifies and demystifies guidelines and describes management of COPD in practical everyday terms, with its excellent colour coded centrefold reminding us of how to improve care and outcomes at every stage of COPD. I am delighted that our COPD Quick Guide is supported by the RCGP. Please take this opportunity to read the revised version and show your colleagues; why not use it as

What we can do in primary care:

- Offer patients structured annual reviews
- Remind patients to have their 'flu and pneumococcal vaccinations
- Give smokers advice and offer support on quitting
- Check patients' breathlessness scores (and act on the result)
- Encourage physical activity; refer and encourage people to attend for pulmonary rehabilitation.
- Ensure patients are on the right medication
- Check patients know how to use their inhalers correctly

part of an educational update for your clinical team?

If you are active in your Clinical Commissioning Group (CCG) or as a PCRS-UK affiliated group lead, please raise the flag about improving care. Talk to your CCG long term conditions lead or table the issue for discussion at your next local group respiratory network meeting. We can all do more at every level to improve care for our COPD patients.

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Special Feature - New approaches to care which help to prevent exacerbations

Francesca Robinson, *PCRS-UK Communications Consultant*



Acute exacerbations of COPD are one of the most common reasons for emergency hospital admission in the UK.

It is a concern that COPD admissions continue to rise year on year and that as many as one in three patients with COPD are likely to be readmitted within 28 days of a hospital admission for an exacerbation.¹

However some of the latest research shows that there is considerable potential for clinicians in primary care to improve on these statistics.

The following selection of studies, all published in the last year, demonstrate that adopting a new approach to care can have a significant impact on preventing exacerbations.

A 12 month service improvement project in Southampton²

A two pronged approach focusing on improving early diagnosis and interventions to prevent hospitalisation has helped to reduce hospital admissions for acute exacerbations of COPD in Southampton.

At the time of the study Southampton had the highest at-risk population for future admissions for an acute exacerbation of COPD on the South Coast. This was due to a high smoking prevalence and higher than average deprivation levels within the city. There was also a lower than expected recorded prevalence of COPD, suggesting that diagnostic processes were not working effectively.

Dr Simon Bourne and colleagues at University Hospital Southampton found that 34 patients with acute exacerbations were responsible for 176 admissions, more than fifth (22%) of total COPD admissions.

They also discovered that increasingly patients were coming directly to the emergency department, often out of hours, without first consulting with their GPs.

This group of 34 "frequent fliers" had very severe disease and the vast majority were smokers. For the duration of the study this group was looked after by respiratory teams. They were reviewed in their homes by a consultant and respiratory specialist nurse to evaluate any causes underlying the multiple admissions, optimise treatment and put interventions in place to reduce future admissions. The interventions included pharmacological optimisation, increased level of care provision, home non-invasive ventilation and priority access to pulmonary rehabilitation.

In addition a package of education and screening measures was introduced in 34 GP practices to improve the identification, diagnosis and management of COPD. Patients were encouraged to adhere to prescribed medication and GP practices were encouraged to follow national guidelines including referral to pulmonary rehabilitation if appropriate.

At the end of the project, hospital admissions for acute exacerbations among the frequent attendees reduced and the 30-day readmission rate dropped from 13.4% to 1.9%. Prior to the project, the prevalence of COPD (as registered by the Quality and Outcomes Framework) within the city was 1.5%; after just one year, the prevalence had increased from 1.5% to 2.27%.

Dr Bourne says: "We present a new way of working in a vertically integrated fashion across both primary and secondary care, led by respiratory consultants who subspecialise in COPD and a COPD specialist nurse team. By first identifying the key factors

driving hospital admissions, as well as defining key deficiencies across the whole care pathway, we have presented a model that can reduce admissions from acute exacerbations and improve the diagnostic processes in the community."

GPs improve COPD outcomes through practice networks³

Historically high emergency COPD admissions were reduced in the London borough of Tower Hamlets after 36 practices grouped together in eight networks of four to five practices to deliver collectively a care package for COPD.

Marked improvements in clinically important indicators of COPD management were achieved between 2010 and 2013 by the eight networks.

Practices increased the number of patients on the COPD register by more than 20%. They achieved this through a range of initiatives including offering spirometry to smokers within target age groups, reviewing asthma diagnoses among persistent smokers and giving new patients brief questionnaires on COPD.

The networks also managed to increase the proportion of patients with COPD with a completed annual review, from 53% to 87%. Pulmonary rehabilitation referrals rose from 45% to 70% and rates of 'flu immunisation rose from 81% to 83%.

Although emergency admission rates currently remain higher than the London average, the introduction of an outreach team for admission avoidance may have contributed to a decline since 2011.

The study, led by Dr Sally Hull at Queen Mary University London, concludes: "Investment of financial, organisational and educational resource into general practice networks was associated with clinically important improvements in COPD care in socially deprived, ethnically diverse communities. Key behav-

our change included collaborative working between practices driven by high-quality information to support performance review, shared financial incentives, and engagement between primary and secondary care clinicians."

Self-management can be an effective tool⁴

Effective self-management has the potential to reduce hospital admissions and improve outcomes in COPD, claim the authors of a study which looked at patients' experience of identifying and managing exacerbations.

As patients are first to notice a change in their condition, it is crucial that they understand what constitutes an exacerbation, recognise deteriorating symptoms and react appropriately, says lead author Dr Veronika Williams of the Nuffield Department of Primary Care Health Sciences, University of Oxford.

To explore patients' current understanding and experience of managing and identifying COPD exacerbations at home the researchers interviewed 44 patients aged 55 to 85 years with moderate to very severe COPD.

Patients identified exacerbations on the basis of the classic measurable, "visible" symptoms, such as cough and sputum as well as a range of "invisible" symptoms, such as chest sensations and bodily knowledge. Most patients used a combination of visible and invisible symptoms when identifying exacerbations, according to the symptoms that had the most impact on their well-being. Patients used additional self-management strategies during an exacerbation, such as self-medication (antibiotics and steroids) and monitored their recovery. Contact with health-care professionals usually occurred when patients felt no longer able to manage themselves.

Dr Williams concludes: "Patients use both assessment of objective biomarkers, which are aligned with medical knowledge, and subjective symptoms based on their

experience, to identify and manage exacerbations of COPD. Healthcare professionals and clinicians should acknowledge this "expert patient" knowledge and integrate this into patients' care plans to facilitate early recognition and treatment of exacerbations."

A cognitive behavioural manual can help to reduce emergency admissions⁵

A self-help manual, underpinned by a cognitive behavioural component, can reduce accident and emergency (A&E) attendances for COPD in addition to improving patients' mood and health status, say researchers.

Called the COPD Manual, this guided self-help intervention applies cognitive behavioural techniques within a self-management framework and specifically targets aspects of breathlessness and panic.

For this study 222 patients with COPD were randomly allocated to receive either the COPD Manual or a series of British Lung Foundation COPD information booklets.

They were instructed to work through their programme at home, over five weeks. Guidance from a facilitator was provided at an initial home visit plus two telephone call follow-ups.

After 12 months, total A&E visits had reduced by 42% in the COPD Manual group, compared with a 16% rise in the information booklet group. The odds of people in the information booklet group attending A&E 12 months post-intervention was 1.9 times higher than for the COPD Manual group. Reduction in hospital admissions and bed days were greater in the COPD Manual group. At six months, there were significantly greater improvements in anxiety, depression and dyspnoea in the COPD Manual group. Estimated savings at 12 months were larger in this group, amounting to £30,000 or £270 per participant.

The authors conclude: "The COPD Manual, which addresses physical and mental health, is a straightforward cost-effective intervention that is worth offering to COPD patients within primary or secondary care."

COPD care bundles improve quality of care⁶

COPD care bundles have the potential to impact on processes of care and on measurable clinical outcomes according to a study by the British Thoracic Society (BTS).

Data on processes and outcomes of care were collected on 3,266 admissions with an acute exacerbation of COPD to 21 NHS Trusts and Health Boards in England and Wales. In total, 1,438 care bundles were delivered to these patients.

Use of a care bundle was associated with a reduction in 30-day in-patient mortality from community acquired pneumonia from 13.6% to 8.8%. There was also a reduction in mortality from acute exacerbations of COPD as the care bundle promoted timely provision of care, including safe use of oxygen.

This is the first time that use of a COPD bundle has been associated with a reduction in in-hospital mortality, comments Dr James

Calvert, Consultant Respiratory Physician at North Bristol Lung Centre and chair of the BTS Professional and Organisational Standards Committee. He also commented that care bundles could improve standards and reduce unwarranted variability.

Although particularly applicable in clinical contexts in which there is a clearly defined aim, care bundles have some messages for the less clearly delineated world of primary care. The concept of focussing on key, measurable evidence-based actions may be a useful tool in improving the quality of care in specific clinical conditions or contexts.

A practice improvement worksheet, called Identifying High Impact COPD,⁸ equips primary care clinicians to identify patients at risk of exacerbations. The PCRS-UK website contains many other evidence based tools to help its members improve respiratory care.

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Policy Round-Up

Bronwen Thompson, PCRS-UK Policy Advisor

A summary of the latest developments in the UK health services, including any major new reports, guidelines and other documents relevant to primary care respiratory medicine

Emergency admissions – a policy overview

The start of 2015 has seen a number of hospitals declare 'major incidents' as they find themselves overwhelmed with dealing with urgent cases in Accident and Emergency (A&E) departments across the country, and A&E performance is deemed to be at an all time low. There has been an increase in emergency admissions of 45.7% in the 11 years between 2001/2 and 2012/13, and this is expected to go on rising for the next 5 years. Coping with the hospital admissions that can result from emergencies is putting significant pressure on the whole system, as hospitals take a range of measures to address the increased demand for emergency care.

The number of bed days arising from emergency admissions is actually falling as length of stays are getting shorter. However, there have been rises in the number of longer (2 or more days) spells for various conditions, including respiratory conditions. In the over 85s, respiratory conditions account for 17% of all emergency bed days.

We know that older people feature highly in any discussions about the burden on A&E and resulting admissions. Two reports on frail older people concluded that better social and community care may be able to delay the need for acute hospital care, but will not be able to reduce the need for acute beds. Older and frail people are likely to need care in hospital at some stage. The Better care fund, introduced in June 2013 to ensure transformation of integrated health and social care, has always expected to be able to make efficiency savings on the premise that improving community services would reduce the demand for and cost of hospital care, but it is increasingly recognised that this is unlikely as more is understood about the drivers of increasing admissions.

However, this does not mean it is not worthwhile for primary and community care to examine their management of older people, and particularly those with respiratory disease. Sources such as the National COPD audit and BTS audits indicate that there is considerable scope for improvement in the management of respiratory disease both in the community and in hospitals. Improving the standard of care of respiratory disease in older people will impact positively on the overall outcomes of many frail older people, and could contribute to improving the picture on admissions in this age group.

In brief

The Kings Fund hosted an event at which Sir Bruce Keogh outlined his views on urgent and emergency care. See a 6 minute video of his talk (www.kingsfund.org.uk/audio-video/sir-bruce-keogh-future-urgent-and-emergency-care-services-england)

Sources:

Understanding emergency admissions in older people - the Centre for Health Service Economics and Organisation <http://www.hsj.co.uk/acute-care/emergency-care-demand-for-older-people-predicted-to-rise/5077787.article#.VLSWryusXsY>

Commission on hospital care for frail older people - Health Service Journal and SERCO <http://www.hsj.co.uk/comment/frail-older-people/commission-on-hospital-care-for-frail-older-people-main-report/5076859.article#.VL5XbiusXsY>

Fit for Frailty - The British Geriatric Society in association with RCGP and Age UK <http://www.hsj.co.uk/comment/the-guidance-you-can-swear-by-for-the-f-word-frailty/5078028.article#.VLSV7iusXsY>

Co-commissioning of primary care

At present it is the Area Teams, as local offices of NHS England, which hold GMS/PMS/APMS* contracts with local practices, although CCGs are responsible for primary care 'development'. Many CCGs have been calling for more involvement in the planning and commissioning of primary care services. They argue that if they are to bring down hospital admissions, then they need more flexibility to organise their resources and manpower in a way that might achieve this, for example, by exercising more control over what their own GPs and nurses provide. In autumn 2014, NHS England announced an intention to invite CCGs to adopt one of three models of co-commissioning, so that CCGs are more involved with Area teams in exploring the best ways to configure primary care services to improve them and ensure they meet the needs of the population. The three models offer varying levels of involvement for CCGs:

- greater CCG involvement in NHS England decision making

* GMS – General medical services; PMS – Personal medical services; APMS – Alternative provider medical services

- joint decision making by NHS England and CCGs
- CCGs taking on delegated responsibilities for NHS England

In respiratory care, this could mean the development of different services or creation of new roles within primary care. CCGs could decide to employ some nurses to provide a bridge between hospital and home, by in-reaching to patients while in hospital, who then provide continuity as a named care coordinator, by home visiting them on discharge, providing proactive follow up and ensuring appropriate support such as oxygen and pulmonary rehabilitation, until they have had their treatments optimised and can resume normal daily activities without support. By weakening the traditional divide between primary and secondary care, a more tailored and responsive service could be designed.

In brief

Dr Stephen Gaduzo has outlined the key learning from the National COPD audit to date in the Chair's perspective on page 8. The primary care part of the National COPD audit is due to start in spring 2015. Keep a lookout for announcements from PCRS-UK and Royal College of Physicians to find out how to sign up for this audit, which involves contributing data automatically with no additional work for the practice. In return, you will receive tailored feedback for your practice.

NHS England's five year forward view

This is an important strategy that puts forward proposals for a managed transition to new ways of working within a framework of new models of care. In October 2014, NHS England published this strategic planning document which has significant implications for primary care. It sets out the challenges and potential solutions to the issues in the current NHS. It also recognises a range of important issues for primary care: the need for innovation and testing new models of care, the importance of clustering smaller practices into larger groups, the challenges of adequate and appropriate staffing, improving access for patients and the need for a significant shift towards prevention of ill health.

It confirms that list-based primary care will continue to be a cornerstone of the NHS and one attracting increasing investment. Primary care is to be supported with resources and training so that it can provide a more comprehensive range of out-of-hospital services.

There is an opportunity for respiratory disease to benefit from some of the 'testbed' work that will be undertaken to evaluate new models of care. These might allow, for example:

- A 'multispecialty community provider' to develop an integrated service involving respiratory specialists and respiratory physiologists and physios to work alongside specialist respiratory nurses in hospital and the community. They would work as part of a community based MDT providing proactive care in line with individual care plans, ideally in the community and the patient's home wherever possible.
- 'Primary and acute care systems' will allow vertical integration of care providers so that a coordinated package of care including acute care can be provided to a list of patients. For respiratory patients this could mean more responsive and coordinated care, with joined up IT systems, especially in areas where primary care is under-provided and under-developed

It is recognised that in future it is systems and networks of care that need to be planned and managed – not just organisations. Out of hospital care needs to be a much larger part of what the NHS does, and services need to be properly organised and integrated around the patient, who may have a range of health and social care needs.

Journal Round-Up

npj Primary Care Respiratory Medicine Key Summaries

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Respiratory Medicine

A selection of short summaries of original research articles published in *npj Primary Care Respiratory Medicine*. The articles featured have been selected by the Primary Care Respiratory Update editorial board as being the most relevant and useful to primary care respiratory clinical practice in the UK. You can download freely any articles of interest from the website <http://www.nature.com/npjpcrm/>

npj Primary Care Respiratory Medicine is the only fully indexed scientific journal devoted to the management of respiratory diseases in primary care. It is an international, online, open access journal and is part of the Nature Partner Journal series.

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** RECOMMENDED MANUSCRIPT **

Improving outcomes for people with COPD by developing networks of general practices: evaluation of a quality improvement project in east London

Sally Hull, Rohini Mathur, Simon Lloyd-Owen, Thomas Round & John Robson. *npj Primary Care Respiratory Medicine* 24, Article number: 14082 (2014) doi:10.1038/npjpcrm.2014.82 Published online 16 October 2014

Chronic obstructive pulmonary disease: Creating quality care through GP networks.

Investing in management and education to develop primary care networks in deprived areas improves the lives of patients with lung disease. Chronic obstructive pulmonary disease (COPD) puts immense pressure on the National Health Service (NHS) in the UK, and the disease is particularly problematic in deprived, ethnically diverse urban areas. Sally Hull at the University of London and colleagues evaluated a new initiative aimed at

improving COPD care in an area of inner London between 2010 and 2013. The project aimed to create networks of GP surgeries, combining different care methods and investing in new managerial staff and education budgets for each network. These restructured, carefully managed networks resulted in significant behavioural changes in primary care, culminating in a decrease in hospital admissions and a significant rise in completed care plans and COPD rehabilitation referrals.

'The COPD breathlessness manual': a randomised controlled trial to test a cognitive-behavioural manual versus information booklets on health service use, mood and health status, in patients with chronic obstructive pulmonary disease

Claire Howard & Simon Dupont. *npj Primary Care Respiratory Medicine* 24, Article number: 14076 (2014) doi:10.1038/npjpcrm.2014.76 Published online 16 October 2014

Chronic obstructive pulmonary disease: Managing mood helps patients manage breathlessness.

A cognitive-behavioural manual that helps patients manage their breathlessness significantly reduces visits to emergency departments. Up to 60% of patients with chronic obstructive pulmonary disease (COPD) also suffer from anxiety, panic and depression due to their shortness of breath. To assess the effect of a cognitive-behavioural therapy approach on health service use and the mental health of patients with COPD, Claire Howard at The Hillingdon

Hospital in Uxbridge, UK, and colleague Simon Dupont, randomly allocated either information booklets about the disease or The COPD Breathlessness Manual (CM) to over 200 patients. The manual was developed by psychologists to help patients self-manage their condition. After 12 months, the researchers found a reduction in anxiety and depression in the CM group and a significant drop in visits to emergency departments, indicating that the manual represents a cost-effective intervention.

Inhaler device technique can be improved in older adults through tailored education: findings from a randomised controlled trial

Melanie A Crane, Christine R Jenkins, Dianne P Goeman & Jo A Douglass. *npj Primary Care Respiratory Medicine* 24, Article number: 14034 (2014) doi:10.1038/npjpcrm.2014.34 Published online 04 September 2014

Asthma: Improving inhaler technique in older adults.

Individual coaching rather than written information is important to improve the inhaler technique of older adults with asthma. Management of asthma symptoms requires the correct use of inhalers to administer drugs effectively but many people with asthma, particularly those who are older, do not use their inhalers properly. In an Australian study, Melanie Crane and colleagues showed that in 123 adults with asthma over age 55, most did not demonstrate correct inhaler technique. Participants who then received one-on-one coaching on proper inhaler use improved their technique while those who received only passive education via an instructional booklet showed no improvement in technique. The findings suggest that active teaching of inhaler use is necessary to achieve proper inhaler technique in older adults.

Exploring the role of quantitative feedback in inhaler technique education: a cluster-randomised, two-arm, parallel-group, repeated-measures study

Mariam Toumas-Shehata, David Price, Iman Amin Basheti & Sinthia Bosnic-Anticevich. *npj Primary Care Respiratory Medicine* 24, Article number: 14071 (2014) doi:10.1038/npjpcrm.2014. Published online 13 November 2014

Asthma inhaler technique: Improving education.

Combining methods to educate patients on correct inhaler use improves their technique long-term, an international research team states. Over half of asthma sufferers use their inhalers incorrectly, with many not retaining the training given at the start of treatment. Mariam Toumas-Shehata and co-workers at the University of Sydney, together with researchers in the UK and Jordan, studied two groups of patients trained by pharmacists in order to determine the best methods for improving inhaler technique. Both groups were given individual verbal feedback on technique and a physical demonstration of correct use. One group was also taught using an Inhalation Manager machine, which allowed patients to see their breathing patterns and visualize mistakes. Patients in both groups improved their inhaler technique, with significantly greater improvement in the group also taught using the Inhalation Manager.

General practitioners' home visit tendency and readmission-free survival after COPD hospitalisation: a Danish nationwide cohort study

Jesper Lykkegaard, Pia V Larsen, Maja S Paulsen & Jens Søndergaard *npj Primary Care Respiratory Medicine* 24, Article number: 14100 (2014) doi:10.1038/npjpcrm.2014.100 Published online 27 November 2014

Chronic obstructive pulmonary disease: Home visits by general practitioners.

Hospital readmission rates for patients with chronic lung disease are moderately affected by whether or not doctors make home visits. Chronic obstructive pulmonary disease (COPD), a serious lung condition particularly affecting the elderly, is one of the most common reasons for repeated hospitalisations. To determine whether home visits by general practitioners (GPs) lower COPD hospital readmission and patient survival rates, Jesper Lykkegaard at the University of Southern Denmark and co-workers analysed data from 14,425 COPD patients aged over 45 from 1,389 GP surgeries, who were first admitted to Danish hospitals between 2006 and 2008.

Compared with patients from surgeries where GPs made home visits to 20-30% of their COPD patients, patients from surgeries where GPs made either more or fewer home visits had up to 20% higher risk of readmission or death.

A prospective cohort study of the use of domiciliary intravenous antibiotics in bronchiectasis

Pallavi Bedi, Manjit K Sidhu, Lucienne S Donaldson, James D Chalmers, Maeve P Smith, Kim Turnbull, Joanna L Pentland, Jenny Scott & Adam T Hill. *npj Primary Care Respiratory Medicine* 24, Article number: 14090 (2014) doi:10.1038/npjpcrm.2014.90 Published online 23 October 2014

Bronchiectasis: At home with intravenous antibiotics

Safe and effective antibiotic therapy for bronchiectasis can be provided at home, improving patients' quality of life. Bronchiectasis is a chronic respiratory condition in which inflamed airways trigger excess mucus and frequent chest infections. Flare-ups often lead to hospitalization and antibiotic treatment. In order to reduce pressure on hospitals and improve patients' quality of life, Pallavi Bedi at Queen's Medical Research Institute, Edinburgh, UK, and colleagues conducted a study into the feasibility of providing intravenous antibiotic treatment at home. Over five years, the team monitored 116 patients whenever they required antibiotics. Those patients capable of correctly self-medicating were taught how to administer antibiotics at home. Of 196 courses of antibiotics, 84 were delivered at home. The team found that home-based treatment was as safe and effective as hospital treatment, saving 1,443 hospital bed days.

Assessment of five different guideline indication criteria for spirometry, including modified GOLD criteria, in order to detect COPD: data from 5,315 subjects in the PLATINO study

Ana P Luize, Ana Maria B Menezes, Rogelio Perez-Padilla, Adriana Muiño, Maria Victorina López, Gonzalo Valdivia, Carmem Lisboa, Maria Montes de Oca, Carlos Tálamo, Bartolomé Celli, Oliver A Nascimento, Mariana R Gazzotti & José R Jardim for the PLATINO Team. *npj Primary Care Respiratory Medicine* 24, Article number: 14075 (2014) doi:10.1038/npjpcrm.2014.75 Published online 30 October 2014

Chronic obstructive pulmonary disease: Criteria for indicating diagnostic testing.

A new study reveals the most useful criteria for indicating spirometry testing in patients with chronic obstructive pulmonary disease (COPD). Spirometry, which assesses lung function by measuring how much air is inhaled and how quickly it is exhaled, is the most accurate diagnostic test for COPD but there are different criteria indicating its use. An international group of researchers led by José R. Jardim, Universidade Federal de São Paulo, Brasil, evaluated the proportion of individuals from a 5,315-patient study carried out in Latin America that met criteria for spirometry testing according to five different guidelines. They found that the modified GOLD (Global Initiative for COPD) criteria, which consider symptoms and history of flare-ups as well as the degree of airflow obstruction, are the most sensitive and specific for diagnosing COPD.

Depression and heart failure associated with clinical COPD questionnaire outcome in primary care COPD patients: a cross-sectional study

Manon Urff, Jan-Willem K van den Berg, Steven M Uil, Niels H Chavannes & Roger AMJ Damoiseaux. *npj Primary Care Respiratory Medicine* 24, Article number: 14066 (2014) doi:10.1038/npjpcrm.2014.66 Published online 18 September 2014

Chronic obstructive pulmonary disease: Considering co-existing illnesses for better treatment.

Tailored holistic treatments could benefit patients who suffer from chronic obstructive pulmonary disease (COPD) and other health problems. Efforts by doctors to improve quality of life for patients with COPD can be complicated by the presence of accompanying illnesses, or comorbidity, such as heart problems. Manon Urff at the University Medical Center in Utrecht, together with co-workers across The Netherlands, completed a cross-sectional study examining the influence of COPD and comorbidity on quality of life in 341 patients in primary care. The team carried out statistical analyses on data from a COPD-specific questionnaire completed by patients. They found that having heart failure and depression alongside COPD significantly reduced patients' quality of life, and call for a more holistic approach to treating and managing the complexities of the disease.

Prediction of COPD-specific health-related quality of life in primary care COPD patients: a prospective cohort study

Lara Siebeling, Jammbe Z Musoro, Ronald B Geskus, Marco Zoller, Patrick Muggensturm, Anja Frei, Milo A Puhan & Gerben ter Riet *npj Primary Care Respiratory Medicine* 24, Article number: 14060 (2014) doi:10.1038/npjpcrm.2014.60 Published online 28 August 2014

Chronic obstructive pulmonary disease: Predicting health-related quality of life

Previous health-related quality of life (HRQL) is the best predictor of future HRQL in patients with chronic obstructive pulmonary disease. Gerben ter Riet and colleagues at the University of Amsterdam, with collaborators at the University of Zurich, recruited 409 primary care patients from Switzerland and the Netherlands into a prospective cohort study. Patients were assessed on entry to the study and again by HRQL questionnaire after 6 and 24 months. The results indicated that asking patients explicitly about dyspnea, fatigue, depression and how they are coping with the disease can provide GPs with additional important information about future HRQL. Fatigue and dyspnea scores were the best predictors. Other commonly used predictors such as Forced Expiratory Volume in one second (FEV1) and exercise capacity add little to the prediction of HRQL.

A retrospective study of the impact of a telephone alert service (Healthy Outlook) on hospital admissions for patients with chronic obstructive pulmonary disease

Christophe Sarran, David Halpin, Mark L Levy, Samantha Prigmore & Patrick Sachon. *npj Primary Care Respiratory Medicine* 24, Article number: 14080 (2014) doi:10.1038/npjpcrm.2014.80 Published online 23 October 2014

Chronic obstructive pulmonary disease: Weather alerts make a difference.

A telephone service giving advanced warning of weather conditions that exacerbate lung disease may help reduce hospital admissions. Atmospheric conditions such as cold temperatures and excess humidity can adversely affect the respiratory health of patients with chronic obstructive pulmonary disease (COPD). The 'Healthy Outlook' phone service, run by the Met Office in England from 2006 to 2013, gave advanced warning of difficult weather conditions accompanied by medical advice, aiming to improve COPD patients' quality of life. Christophe Sarran at the Met Office, Exeter, together with scientists across the UK, analysed data on hospital admissions for over 31,000 COPD patients from 661 GP practices who received Healthy Outlook calls. Sarran's team found an average reduction of 16% in hospital admissions in the first year of operation of the call.

Influence of lung function on course of disease and response to antibiotic therapy in adult primary care patients with acute cough: a post hoc analysis of patients enrolled in a prospective multicentre study

Nicole van Erp, Paul Little, Beth Stuart, Michael Moore, Mike Thomas, Chris C Butler, Kerenza Hood, Samuel Coenen, Herman Goossens, Margareta Leven & Theo J M Verheij on behalf of the GRACE consortium. *npj Primary Care Respiratory Medicine* 24, Article number: 14067 (2014) doi:10.1038/npjpcrm.2014.67 Published online 25 September 2014

Lung function: Negligible effect on acute cough

Impaired lung function does not significantly affect the course of acute coughing episodes nor response to antibiotics. An international study led by Nicole van Erp at the University Medical Centre Utrecht, The Netherlands, examined the influence of decreased lung function due to conditions such as asthma and chronic obstructive pulmonary disease on the resolution of coughing episodes lasting less than three weeks in 2,427 adult patients. Such episodes are normally associated with mild lower respiratory tract infections and were thought to be worse in patients with underlying lung disease. Symptom severity increased moderately 2–4 days after initial consultation in patients with severe airway obstruction or who were using inhaled corticosteroids. However, after 4 weeks, there were no significant differences in the recovery and response to antibiotics between patients with lung function abnormalities and those without.

Cost-effectiveness of initiating extrafine- or standard size-particle inhaled corticosteroid for asthma in two health-care systems: a retrospective matched cohort study

Richard J Martin, David Price, Nicolas Roche, Elliot Israel, Willem MC van Aalderen, Jonathan Grigg, Dirkje S Postma, Theresa W Guilbert, Elizabeth V Hillyer, Anne Burden, Julie von Ziegenweid & Gene Colice. *npj Primary Care Respiratory Medicine* 24, Article number: 14081 (2014) doi:10.1038/npjpcrm.2014.81 Published online 09 October 2014

Asthma: The finer the better

A retrospective matched cohort study shows that extrafine inhaled corticosteroid therapy is a cost-effective option for treating asthma. Current treatment guidelines recommend the use of inhaled corticosteroids as a first-line therapy for patients with asthma but such therapy can be expensive. An international team led by David Price

at the University of Aberdeen in the UK compared the cost and effectiveness of extrafine inhaled corticosteroids with those of standard inhaled corticosteroids using data from two large, well-established cohort, one from the UK and the other from the USA. They showed that patients in both countries who used

extrafine inhaled corticosteroids achieved better overall control of their asthma. The annual costs of standard inhaled corticosteroids were significantly higher in both countries, suggesting the use of extrafine inhaled corticosteroids is probably the preferred treatment option.

Best of the rest

These reviews were prepared by Dr Basil Penney and published by Doctors.net.uk Journal Watch. They have been selected and edited for inclusion into *Primary Care Respiratory Update* by editor Dr Hilary Pinnock.



The Doctors.net.uk Journal Watch service covers other specialities as well as respiratory medicine. Doctors.net.uk is the largest network of GMC-registered doctors in the UK. To find out more about membership visit <http://www.doctors.net.uk>

Abbreviations used in these reviews are:

Guidelines

NICE	National Institute for Health and Care Excellence
GOLD	Global Initiative for Chronic Obstructive Lung Disease

Diagnoses and clinical investigations

COPD	chronic obstructive pulmonary disease
OSAS	obstructive sleep apnoea syndrome
MRC	Medical Research Council dyspnoea score
CAT	COPD Assessment Tool
CXR	chest X-ray
FEV1	forced expiratory volume in 1 second

Management and drug treatments

PR	pulmonary rehabilitation
CPAP	Continuous Positive Airway Pressure
LABA	long-acting β -agonist
ICS	inhaled corticosteroid
LAMA	Long-acting muscarinic antagonists
MDT	Multidisciplinary team

Outcome measures, study design and statistics

RCT	randomised controlled trials
HRQoL	Health-related quality of life
HR	Hazard ratio
SD	standard deviation
95% CI	95% confidence interval
MCID	Minimum Clinically Important Difference

Combination long-acting β -agonists and inhaled corticosteroids in older adults with COPD



Gershon AS *et al*; *JAMA* 2014;312(11):1114-1121
doi:10.1001/jama.2014.11432
<http://jama.jamanetwork.com/article.aspx?articleid=1904829>

Combination therapy consisting of LABAs and ICSs has been shown to decrease exacerbations and possibly decrease mortality compared with placebo. However, results of RCTs may not be generalisable to older, frailer COPD patients with co-morbidities.

This real world observational retrospective cohort study from Ontario, examined the association of LABA-ICS combination therapy compared with LABAs alone and the composite outcome of mortality and COPD hospitalisations in older COPD patients with naturally occurring comorbidities, including asthma.

Using multiple linked population healthcare databases, subjects aged 66 years or older with physician-diagnosed COPD and who were new users of LABAs or LABA-ICS combination therapy between 2003 and 2011, were included. There were 8,712 new users

of LABA-ICS combination therapy and 3,160 new users of LABAs alone who were followed up for median times of 2.7 years and 2.5 years, respectively.

Among older adults with COPD, people newly prescribed LABA-ICS combination therapy, compared with newly prescribed LABAs alone, had a significantly lower risk of the composite outcome of death or COPD hospitalisation (HR, 0.92; 95% CI, 0.88-0.96). The greatest difference was among COPD patients with a co-diagnosis of asthma (HR, 0.84; 95% CI, 0.77-0.91) and those who were not receiving inhaled long-acting anticholinergic medication (HR, 0.79; 95% CI, 0.73-0.86). Similarly lower risks were also observed for mortality and COPD hospitalisations analysed separately. There was no significant difference in the risk of pneumonia or fracture hospitalisation.

Limitations of the study design, include potential misclassification of individuals with COPD in health administrative dataset and the effect of unrecognised confounders. Strengths include its population, real-world relevance, and power to examine the relative effects of LABAs compared with LABAs-ICSs in various subgroups. These findings should be confirmed in RCTs.

**** RECOMMENDED PUBLICATION ****

Effectiveness of integrated disease management for primary care COPD patients

Kruis AL *et al.* *BMJ* 2014;349:g5392 doi: 10.1136/bmj.g5392
<http://www.bmj.com/content/349/bmj.g5392>



Management of COPD patients requires a patient-centered approach that identifies and treats all aspects of the disease, with collaborative interaction between actively involved patients and a proactive multidisciplinary team. Integrated disease management programmes promote such interaction. This large 24-month pragmatic cluster RCT ('RECODE') investigated whether integrated disease management implemented in primary care was effective in improving the quality of life of COPD patients.

40 general practices in the western part of the Netherlands were randomly assigned to the intervention (integrated disease management) or usual care. Eligible patients had a diagnosis of COPD, excluding those with terminal illness, cognitive impairment, hard drug or alcohol misuse, and inability to fill in questionnaires. General practitioners, practice nurses, and specialised physiotherapists in the intervention group received a 2-day training course on COPD management, and incorporating integrated care into practice. At the end of the second day, each practice team had a group discussion to plan how they would implement integrated disease management into their daily practice. The control group continued usual care (based on international guidelines).

The primary outcome was difference in health status at 12 months, measured by the Clinical COPD Questionnaire (CCQ); quality of life, Medical Research Council dyspnoea, exacerbation related outcomes, self management, physical activity, and level of integrated care (PACIC) were also assessed as secondary outcomes.

Of a total of 1,086 patients from 40 clusters, 20 practices (554 patients) were randomly assigned to the intervention group and 20 clusters (532 patients) to the usual care group.

No difference was seen between groups in the CCQ at 12 months (mean difference -0.01, 95% confidence interval, -0.10 to 0.08; P=0.8). After 24 months, no differences were seen in outcomes, except for the PACIC follow-up/ coordination domain suggesting that the intervention had succeeded in its aim of improving integration of care. Exacerbation rates as well as number of days in hospital did not differ between groups.

In this study, integrated disease management incorporated in primary care was not effective in improving quality of life. The contradictory findings to earlier positive studies could be explained by differences between interventions (provider-versus patient targeted), selective reporting of positive trials, or little room for improvement in the well developed Dutch healthcare system.

Lung cancer in never-smokers: a case-control study in a radon-prone area (Galicia, Spain)



Torres-Durán *et al.* *Eur Respir J* 2014; 44: 994–1001
 doi: 10.1183/09031936.00017114
<http://erj.ersjournals.com/content/44/4/850.full>

Tobacco consumption is the most important risk factor for lung cancer; however, between 15 and 25% of all lung cancer cases occur in never-smokers. Compared to smokers, never-smokers have better survival, a different age of onset and have mainly adenocarcinomas.

Residential radon exposure is the second risk factor of lung cancer after tobacco consumption and the first risk factor for never-smokers. This multicentre hospital-based case-control study in the north-west of Spain investigated the effect of residential radon exposure on the risk of lung cancer in never-smokers and to ascertain if Environmental Tobacco Smoke (ETS) exposure modifies the effect of residential radon.

Cases and controls (aged >30 years with no previous history of malignancy) were recruited between January 2011 and June 2013. All participants were never-smokers. 21% were males. A never-smoker was defined as: 1) an individual reporting <100 cigarettes in a lifetime and 2) had not smoked for 6 months. Cases (n=192) were identified by pneumonologists as having confirmed lung cancer. Controls (n=329) were recruited from ambulatory individuals undergoing minor, non-oncological surgery. Participants were asked

about different aspects of their lifestyle and occupation with special emphasis on ETS exposure, leisure time exposures, diet, and alcohol consumption. Participants were given a radon detector to take home and position in their bedroom for up to 3 months.

The investigators observed an odds ratio of 2.42 (95% CI, 1.45-4.06) for individuals exposed to ≥ 200 Bq.m⁻³ compared with those exposed to <100 Bq.m⁻³. ETS exposure at home increased lung cancer risk in individuals with radon exposure >200 Bq.m⁻³, and conversely exposure to radon concentrations >200 Bq.m⁻³ increased risk of lung cancer in those exposed to ETS.

Residential radon is confirmed as a risk factor for lung cancer in never-smokers. There seems to be a joint effect of residential radon with ETS exposure, with individuals with both exposures having the highest risk of lung cancer. These results clarify public health messages related to residential radon and ETS.

Nocturnal hypoxia predicts prevalent hypertension in the European Sleep Apnoea Database study



Tkacova R *et al* on behalf of the European Sleep Apnoea Database study collaborators. *Eur Respir J* 2014; 44: 931–941
 doi: 10.1183/09031936.00225113
<http://erj.ersjournals.com/content/44/4/931.short?cited-by=yes&legend=erj;44/4/931>

Cardiovascular diseases represent an important co-morbidity of obstructive sleep apnoea syndrome (OSAS). Effective treatment for

OSAS with continuous positive airway pressure (CPAP) is associated with considerable benefits in cardiovascular co-morbidity, particularly hypertension. Potential mechanisms of hypertension in OSAS include intermittent hypoxia which stimulates systemic inflammation, oxidative stress and endothelial dysfunction, as well as recurring arousals, which contribute to sympathetic activation. However, the respective contribution of these mechanisms to established hypertension is unclear.

A collaborative European network of 24 sleep centres established a European Sleep Apnoea Database (ESADA) to evaluate cardiovascular morbidity associated with OSAS. The present report describes the relationship of OSAS with systemic hypertension in the ESADA cohort and examines the role of various consequences of OSAS in this relationship.

A total of 11,911 adults referred with suspected OSAS between March 2007 and September 2013 underwent overnight sleep studies, either cardiorespiratory polygraphy or polysomnography. The investigators compared the predictive value of the apnoea-hypopnoea index (AHI) and 4% oxygen desaturation index (ODI) for prevalent hypertension, adjusting for relevant covariates including age, smoking, obesity, dyslipidaemia and diabetes.

Among patients (70% male, mean (SD) age: 52 (12) years), 78% had AHI > 5 events and 41% systemic hypertension. Both AHI and ODI independently related to prevalent hypertension after adjustment for relevant covariates ($p < 0.0001$ for linear trend across quartiles of severity for both variables). However, in multiple regression analysis with both ODI and AHI in the model, ODI was, whereas AHI was not, independently associated with prevalent hypertension.

The present findings confirm previous population-based hallmark studies showing that OSAS is independently associated with prevalent systemic hypertension. The data show that not only measures of intermittent hypoxaemia predict OSA related hypertension but also suggest that intermittent hypoxia is an important mechanism in the pathogenesis of hypertension in OSAS.

The COPD assessment test: a systematic review

Gupta N *et al.* *Eur Respir J* 2014; 44: 873–884

doi: 10.1183/09031936.00025214

<http://erj.ersjournals.com/content/early/2014/07/03/09031936.00025214.abstract>



The international GOLD guideline advocates that individualised management decisions on COPD should be based on a multidimensional assessment including HRQoL. The COPD Assessment Tool (CAT) is a self-administered eight item questionnaire that provides a simple measure of HRQoL. This review systematically searched the literature to evaluate and summarise the psychometric properties of the CAT (reliability, validity, responsiveness and minimum clinically important difference (MCID)) as a HRQoL instrument used in patients with COPD.

The 36 articles (45 to 6,469 participants) included in the review encompassed patients (aged 56 to 73 years) with a range of severity (FEV1 39% to 98% of predicted). Internal consistency (reliability) was 0.85–0.98, and test-retest reliability was 0.80–0.96. External validity, as assessed by correlation with other validated measures of

HRQoL was good, and scores differed with GOLD stages, exacerbations and mMRC grades. Mean scores improved with pulmonary rehabilitation (2.2–3 units) and worsened at exacerbation onset (4.7 units). One study reported that the minimum clinically important difference (MCID) was 2 units and 3.3–3.8 units using the anchor-based approach and distribution-based approach, respectively.

This supports the reliability and validity of the CAT and that the tool is responsive to interventions, although the MCID remains uncertain. Since the CAT demonstrates good performance and is a simple and quick tool that assesses the HRQoL in patients with COPD, there is a growing interest in its use in clinical practice. Further studies are needed to clarify the use of this questionnaire for the symptomatic assessment of patients with COPD in the new GOLD classification, and to assess performance in sub-groups of patients (e.g. younger/older, very mild) and in real-life clinical practice.

The efficacy of a brief motivational enhancement education program on CPAP adherence in OSA

Lai AYK *et al.* *Chest* 2014; 146(3): 600–610.

doi:10.1378/chest.13-2228

<http://journal.publications.chestnet.org/article.aspx?articleid=1868825>



Continuous positive airway pressure (CPAP) is an effective treatment for OSAS but this is often limited by poor adherence to therapy. Psychological factors have been recognised as playing an important role in the determination of CPAP adherence.

This RCT, from Hong Kong, examined the efficacy of a brief motivational enhancement education program in improving adherence to CPAP treatment in subjects with OSAS. Inclusion criteria were the following: (1) age ≥ 18 years old with newly diagnosed OSAS (apnea-hypopnea index ≥ 5), (2) receiving in-laboratory auto-CPAP titration for the first time, and (3) no prior OSAS or CPAP education classes.

A total of 100 subjects were recruited and randomised to either control group (usual care) ($n=51$) or intervention group (brief motivational enhancement education plus usual care) ($n=49$). Two patients dropped out of the study.

The control group received usual advice on the importance of CPAP therapy and its care. The intervention group received usual care plus a brief motivational educational program directed at enhancing the subjects' knowledge, motivation, and self-efficacy to use CPAP through the use of a 25-minute video, a 20-minute patient-centred interview, and a 10-minute telephone follow-up. Self-reported daytime sleepiness, adherence-related cognitions and quality of life were assessed at 1 month and 3 months. CPAP usage data were downloaded at the completion of this 3-month study.

The intervention group had better CPAP use (higher daily CPAP usage by 2 hours/day ($P < 0.001$), a fourfold increase in the number using CPAP for at least 4h/day on 70% or more days ($P < 0.001$)), and greater improvements in daytime sleepiness (Epworth Sleepiness Score) by 2.2 units ($P = 0.001$) and treatment self-efficacy by 0.2 units ($P = 0.012$) compared with the control group.

Subjects with OSAS who received motivational enhancement education in addition to usual care were more likely to show better

adherence to CPAP treatment, with greater improvements in treatment self-efficacy and daytime sleepiness.

An evaluation of factors associated with completion and benefit from pulmonary rehabilitation in COPD

BMJ Open Respiratory Research

Afroditi K Boutou, Rebecca J Tanner, Victoria M Lord, Lauren Hogg, Jane Nolan, Helen Jefford, Evelyn J Corner, Christine Falzon, Cassandra Lee, Rachel Garrod, Michael I Polkey and Nicholas S Hopkinson. *BMJ Open Resp Res* 2014;1:e000051
doi:10.1136/bmjresp-2014-000051
<http://bmjopenrespres.bmj.com/content/1/1/e000051.abstract>

Pulmonary rehabilitation (PR) programmes improve exercise capacity, reduce dyspnoea, anxiety and depression, while improving quality of life, among patients with COPD. Drop-out rates for those who attend PR are high, with up to 50-75% of people offered PR declining to take part or failing to complete the programme. It is important to be able to identify patients who may need additional support to complete a PR programme or additional input to achieve useful improvement. This UK multicentre study aimed to identify whether there is an optimal tool or universal measure that could independently predict: (1) the completion of the PR programme and (2) achievement of the accepted MCID in terms of exercise capacity and quality of life.

Data were collected prospectively from 787 patients with COPD (68.1 (SD 10.5) years old; 50% males) who attended the initial assessment visit of an outpatient PR programme in one of eight centres between March 2012 and March 2013. Patients were included in the study when baseline characteristics and spirometry had been recorded, along with at least one outcome measure (exercise capacity, dyspnoea score or a HRQoL questionnaire). Specific instruments used varied according to the clinical practice of the site, and their significance assessed using published MCID. Patients with a clinical diagnosis of asthma or significant heart failure were excluded. "Completion" was defined as attending at least 75% of the designated PR visits and returning for the follow up evaluation.

Mean FEV₁ predicted was 49.7% (SD 19.7). Most patients (42%) presented with GOLD stage II or 32.4% with GOLD stage III: 6.8% presented with GOLD stage I, and 18.8% with GOLD stage IV.

Patients who completed PR (n=449, 57.1%) were significantly older with less severe airflow obstruction, lower anxiety and depression scores, less dyspnoea and better HRQoL. CAT score was the only independent predictor of PR completion, with completers having lower baseline CAT scores, indicating a better health status. Patients with the lowest baseline walking distance were most likely to achieve the MCID for exercise capacity.

Patients with better HRQoL are more likely to complete PR, while worse baseline exercise performance makes the achievement of a positive MCID in exercise capacity more likely. No baseline parameter could predict who would benefit the most in terms of HRQoL.

Changes in physical activity and all-cause mortality in COPD

EUROPEAN RESPIRATORY JOURNAL
OFFICIAL SCIENTIFIC JOURNAL OF THE ERS

Anouk W. Vaes, Judith Garcia-Aymerich, Jacob L. Marott, Marta Benet, Miriam T.J. Groenen, Peter Schnohr, Frits M.E. Franssen, Jørgen Vestbo, Emiel F.M. Wouters, Peter Lange and Martijn A. Spruit *Eur Respir J* 2014 44:5, 1107-1109
<http://erj.ersjournals.com/content/early/2014/07/25/09031936.00023214.abstract>

People with COPD have lower levels of regular physical activity compared to subjects without COPD, even in mild-to-moderate disease. This is associated with accelerated lung function decline, exercise intolerance, lower limb muscle weakness, lower muscle mass and hospitalisations. COPD patients with very low levels of regular physical activity have the worst prognosis. In subjects with and without COPD, this study sought to: 1) compare the longitudinal changes in the level of self-reported regular physical activity; 2) identify baseline determinants of changes in physical activity; and 3) identify the association between the changes in the level of self-reported regular physical activity and all-cause mortality.

A total of 10,004 subjects, from the Copenhagen City Heart Study, were analysed; 1,270 subjects with COPD and 8,734 subjects without COPD who had had at least two consecutive examinations. The median time between the baseline examination and follow up examination was 9 (5-11) years. Each examination included a clinical examination and a questionnaire regarding: socioeconomic factors (sex, age, education, marital status and cohabitation); current smoking; and self-reported co-morbidities. Physical activity was measured at each examination using a validated questionnaire, and was classified into "low", "moderate" or "high". Spirometry was used to assess lung function.

This study has three major findings: 1) a decline in self-reported regular physical activity is significantly more common in subjects with COPD compared to subjects without COPD; 2) changes in physical activity in subjects without COPD are determined by a large variety of socio-demographic and clinical factors (including the presence of co-morbidities), whereas in subjects with COPD the variables with the highest likelihood for changes in physical activity are sex, the degree of airflow obstruction and smoking status; and 3) a substantial reduction in physical activity (i.e. from moderate or high at baseline to low level at follow up) had the highest risk of mortality (HR1.73 and 2.35, respectively; both p<0.001). In COPD subjects with low baseline physical activity, increased physical activity at follow up did not confer survival benefit. In addition, subjects without COPD with low physical activity at follow up had the highest mortality, irrespective of baseline physical activity level (p≤0.05).

These observational data suggest that it is important to assess and encourage physical activity in the earliest stages of COPD in order to maintain a physical activity level that is as high as possible, as this is associated with better prognosis.

Improving care for patients with idiopathic pulmonary fibrosis (IPF) in the UK: a round table discussion

Thorax

David R Thickett, Clare Kendall, Lisa G Spencer, Nick Screaton, William A Wallace, Hilary Pinnock, Julia Bott, Lucy Pigram, Sarah Watson, Ann B Millar. *Thorax* 2014;0:2014 thoraxjnl-2014-206598v1-thoraxjnl-2014-206598
Thorax doi:10.1136/thoraxjnl-2014-206284

Idiopathic pulmonary fibrosis (IPF) is a chronic progressive fibrotic interstitial lung disease (ILD) of unknown origin. It is a rare condition with only 5,000 new cases diagnosed each year in the UK, and a mean survival of only three years after diagnosis. With the emergence of new, potentially disease modifying therapies for patients with IPF, it is clear that prompt diagnosis and specialist assessment of patients with IPF are increasingly important. This paper reports an advisory round-table discussion convened by Thorax to highlight problem areas and agree recommendations to improve future care.

A patient with IPF typically presents to their GP with breathlessness or cough. These symptoms are extremely common in primary care consultations, whereas a full-time GP might expect to identify one new case of IPF every seven years. Symptom-based algorithms could help GPs identify which patients warrant further investigation and subsequent referral to a respiratory specialist.

Diagnostic and management decisions should be taken by regional specialist ILD multidisciplinary teams (MDTs) according to local referral pathways. A balance needs to be struck between centralisation and access to practical community care; virtual MDTs may have a role.

IPF is a disease that patients struggle to understand, which can heighten their anxiety. From the very start, patients need to be given clear and consistent information on its course, management and care, in line with the British Lung Foundation's IPF patient charter. Patients should have rapid access to pulmonary rehabilitation, occupational therapy and physiotherapy with availability of ambulatory oxygen and long-term oxygen therapy if required. A register of services, such as Macmillan nurses, respiratory nurses and community matrons available in each area would be helpful to assist ILD specialist nurses with interdisciplinary liaison. GPs will need updated information on the likely disease course and the role of new treatment modalities so that they can support patients.

All patients with IPF are likely to have palliative care needs at some point, which will again involve primary care. It can be challenging for professionals to judge the optimum timing of referral but it is important to get it right because there is a growing body of evidence showing unmet palliative needs in the ILD patient group. Although the NICE guideline on IPF, which recommends that discussion about end of life should begin at diagnosis, is controversial, it is important to start explanations about the disease course and management from the outset so that patients can begin to prepare themselves.

Characteristics of primary care and patients associated with early death from lung cancer

<http://www.doctors.net.uk/journalwatch/ReviewsExpand.aspx?reviewid=5881#a16557>
<http://www.ncbi.nlm.nih.gov/pubmed/25074705>

The UK has poor lung cancer survival rates compared to other countries and this is partly explained by differences in mortality in

the early months after diagnosis. This study aimed to identify the individual risk factors for early death from lung cancer in the UK, and any primary care features which may contribute to this. All cases of lung cancer diagnosed between 2000 and 2013 were extracted from The Health Improvement Network (THIN) database. Patients who died within 90 days of diagnosis were compared with those who survived longer. Standardised chest X-ray (CXR) and lung cancer rates were calculated for each practice.

Of 20,142 people with lung cancer, 30% of patients died within 90 days of their diagnosis. Increasing age (OR 1.80; 95% CI 1.62 to 1.99 for age \geq 80 years compared to 65-69 years), male sex (OR 1.17; 95% CI 1.10 to 1.24), socioeconomic deprivation (OR 1.16; 95% CI 1.04 to 1.30 for Townsend quintile 5 vs 1), rural versus urban location (OR 1.22; 95% CI 1.06 to 1.41) and current smoking (OR 1.43; 95% CI 1.28 to 1.61), were all strongly and independently associated with early death, although early death was less likely in ex-smokers compared with never-smokers. Those who died early consulted their GP more frequently than those who did not, and were less likely to have had a CXR performed by primary care. Variation in the quality and timeliness of CXR reporting which could have influenced this unexpected finding, were not assessed.

At a practice level, a higher CXR rate was not associated with a reduction in early deaths; in fact, patients seen at practices with a high CXR rate were more likely to have died early than those seen at practices with lower CXR rates. Practices with higher background lung cancer rates do not seem to be any more likely to diagnose their patients at an early enough point in the disease process to impact on early mortality. The performance of secondary care may have affected primary care outcomes but was not assessed.

The assumption is that patients die early from lung cancer because primary care misses the opportunity for prompt diagnosis. This study emphasises the complexity of making an early diagnosis of lung cancer in primary care. A general increase in CXR requests potentially reflecting increased awareness, was not associated with improved survival. Factors such as quality and timeliness of CXR services, awareness of the risk of false negatives, and as well as primary care access to investigations such as CT scanning for high risk patients needs further assessment.

Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD

 THE NEW ENGLAND JOURNAL OF MEDICINE

Helgo Magnussen, M.D., Bernd Disse, M.D., Ph.D., Roberto Rodriguez-Roisin, M.D., Anne Kirsten, M.D., Henrik Watz, M.D., Kay Tetzlaff, M.D., Lesley Towse, B.Sc., Helen Finnigan, M.Sc., Ronald Dahl, M.D., Marc Decramer, M.D., Ph.D., Pascal Chanez, M.D., Ph.D., Emiel F.M. Wouters, M.D., Ph.D., and Peter M.A. Calverley, M.D. for the WISDOM Investigators.

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<http://www.nejm.org/doi/full/10.1056/NEJMoa1407154>

Treatment with ICS reduces the exacerbation rate, especially when used in combination with a LABA. Consequently, combination therapy with an ICS/LABA combination is recommended in patients with severe COPD and a history of frequent exacerbations. LAMAs have also been shown to prevent exacerbations. However, the benefit of ICS in a regimen that includes both LABA and LAMA has not yet been determined in an adequately powered study.

This 12-month, multinational, double-blind, parallel-group WISDOM (Withdrawal of Inhaled Steroids during Optimized Bronchodilator Management) RCT, was designed to determine whether patients with COPD who were receiving both LAMA and LABA therapy with ICS would have similar outcomes regardless of whether the glucocorticoids were withdrawn or continued.

A total of 2,485 patients with severe or very severe COPD and a history of exacerbations received triple therapy consisting of tiotropium (18 mcg once daily), salmeterol (50 mcg twice daily) and fluticasone propionate (500 mcg twice daily) during a 6-week run in period. Patients were then randomly assigned to continued triple therapy or withdrawal of fluticasone in three steps over a 12-week period. The primary end point was the time to the first moderate or severe COPD exacerbation. Spirometric findings, health status and dyspnoea were also monitored. 82.5% of the patients were men; the mean age was 63.8 years, and the mean FEV₁ after bronchodilation was 32.8% of the predicted value. Of the 2,485 patients, 2,027 completed the study.

Compared with continued ICS use, fluticasone withdrawal met the pre-specified non-inferiority criterion of 1.20 for the upper limit of the 95% CI with respect to the first moderate or severe COPD exacerbation (HR: 1.06; 95% CI, 0.94 to 1.19). At week 18, when glucocorticoid withdrawal was complete, the adjusted mean reduction from baseline in the trough FEV₁ was 38 ml greater in the ICS-withdrawal group than in the ICS-continuation group ($p < 0.001$). A similar between-group difference was seen at week 52 ($p = 0.001$). Minor changes in health status but no change in dyspnoea occurred in the glucocorticoid-withdrawal group. Adverse events were similar in both groups.

In patients with severe but stable COPD who were receiving combination therapy with tiotropium, salmeterol, and fluticasone, the stepwise withdrawal of ICS was non-inferior to the continuation of such therapy, with respect to the risk of moderate or severe exacerbations. The effect of withdrawal on symptoms and lung function also needs to be considered when making decisions regarding maintenance therapy in patients with severe but stable COPD.

SABRE: a multicentre randomised control trial of nebulised hypertonic saline in infants hospitalised with acute bronchiolitis

Thorax

Mark L Everard, Daniel Hind, Kelechi Ugona, Jennifer Freeman, Mike Bradburn, Cindy L Cooper, Elizabeth Cross, Chin Maguire, Hannah Cantrill, John Alexander, Paul S McNamara on behalf of The SABRE Study Team. *Thorax* 2014; 69: 1105-1112, doi:10.1136/thoraxjnl-2014-205953 http://thorax.bmj.com/content/69/12/1105.short?g=w_thorax_top10_tab

Acute bronchiolitis is the commonest cause for hospitalisation in infancy. The disease is caused by a number of common respiratory viruses, with respiratory syncytial virus (RSV) the most commonly identified, and is associated with the characteristic winter peaks in admissions.

Supportive care, with supplemental oxygen to correct hypoxia, minimal handling to reduce the risk of exhaustion and the provision of fluids, remains the cornerstone of management. Antiviral agents, oral and inhaled steroids and a variety of bronchodilators have neither decreased lengths of inpatient stay (typically 3 days) nor impacted on the course of the acute illness, while an effective vaccine

still appears somewhat off. A Cochrane review, however, concluded that nebulised saline may have clinical benefit.

The Hypertonic Saline in Acute Bronchiolitis RCT and Economic evaluation (SABRE) trial was a multicentre, randomised, open, pragmatic study where infants under 1 year requiring oxygen therapy for acute bronchiolitis were randomised to receive usual care ($n=141$) or 4 ml nebulised 3% saline 6-hourly in addition to usual care ($n=149$) until they were fit for discharge. Participants were recruited from the assessment units and paediatric wards of 10 participating centres in England and Wales between October 2011 and December 2013.

The primary outcome was the time until the infant was assessed as being 'fit for discharge'. The following were exclusion criteria: a history of wheezy bronchitis or asthma; gastro-oesophageal reflux; previous lower respiratory tract infections; risk factors for severe disease; carers lacking fluent English in the absence of translational services and patients requiring admission to high dependency or intensive care units at presentation.

There was no difference between the two arms in time to being declared fit for discharge (hazard ratio: 0–95, 95% CI: 0.75–1.20) nor to actual discharge (hazard ratio: 0.97, 95% CI: 0.76–1.23). There was no difference in adverse events. One infant in the hypertonic saline group developed bradycardia with desaturation.

This study does not support the use of nebulised hypertonic saline in the treatment of acute bronchiolitis over usual care.

Expert opinion on the cough hypersensitivity syndrome in respiratory medicine

EUROPEAN RESPIRATORY JOURNAL
OFFICIAL JOURNAL OF THE ERS

Morice AH, Millqvist E, Belvisi MG, Bieksiene K, Biring SS, Chung KF, Dal Negro RW, Diczpinigaitis P, Kantar A, McGarvey LP, Pacheco A, Sakalauskas R, Smith JA. *Eur Respir J* 2014; 44: 1132–1148 doi: 10.1183/09031936.00218613

Chronic cough is a common presentation to both primary and secondary care. The management of these patients is often problematic, with relatively few therapeutic options. Many suffer long-term illness with a marked adverse effect on quality of life and major medical and socio-economic consequences. Understanding of chronic cough has traditionally revolved around three diagnostic categories: a form of asthma, rhinitis, or reflux disease, though few patients fit easily into these conventional categories. More recently, a unifying hypothesis, that chronic cough arises from a hypersensitivity of airway sensory nerves, has been proposed.

In 2011, a European Respiratory Society Task Force embarked on a process to determine the position and clinical relevance of the cough hypersensitivity syndrome (CHS). An iterative process supported by a literature review developed a 21-component questionnaire. A total of 44 opinion leaders from 14 countries participated in the survey.

There was a high degree of agreement among opinion leaders as to the concept that cough hypersensitivity underlies the aetiology of chronic cough in the majority of patients. The CHS was considered as an overarching diagnosis, with different phenotypes associated with distinct presentations in individual patients.

The classic stratification of cough into asthmatic, rhinitic and reflux-related phenotypes was supported. Significant disparity of opinion was seen in the response to two questions concerning the therapy of chronic cough. First, the role of acid suppression in reflux cough was questioned. Secondly, the opinion leaders were split as to whether a trial of oral steroids was indicated to establish a diagnosis of eosinophilic cough.

The cough hypersensitivity syndrome was clearly endorsed by the opinion leaders as a valid and useful concept. They considered that support of patients with chronic cough was inadequate and the Task Force recommends that further work is urgently required in this neglected area.

A worldwide survey of chronic cough: a manifestation of enhanced somatosensory response



Morice AH, Jakes AD, Faruqi S, Birring SS, McGarvey L, Canning B, Smith JA, Parker SM, Chung KF, Lai K, Pavord ID, van den Berg J, Song WJ, Millqvist E, Farrell MJ, Mazzone SB, Dicpinigaitis P; Chronic Cough Registry. *Eur Respir J* 2014 Nov; 44(5): 1149-55. doi: 10.1183/09031936.00217813. Epub 2014 Sep 3.

Cough is the most common complaint leading patients to seek medical attention. While the majority of these consultations reflect acute viral illnesses, a substantial degree of morbidity is associated with chronic cough; arbitrarily defined in the American College of Chest Physicians' (ACCP) guidelines as a predominant symptom of cough lasting for at least 8 weeks, with no radiographic evidence of lung disease. Chronic cough may be present in conditions such as asthma, pulmonary fibrosis, lung cancer, or COPD. However the majority of patients presenting with chronic cough do not easily fit into these diagnostic labels, and indeed frequently the underlying diagnosis is not clear.

Reports from individual centres suggest a preponderance of females with chronic cough. Females also have heightened cough reflex sensitivity.

In 2013 the members of the International Cough Registry performed a retrospective review of patients attending 11 specialist cough centres in Europe, North America and Asia. Of the 10,032 patients presenting with chronic cough, two-thirds (6,591) were female and the most common age for presentation was 60–69 years. This patient profile was largely uniform across centres.

To examine neuro-anatomical divergence as an explanation for the striking preponderance in women, male and female healthy volunteers underwent an inhalation cough challenge with capsaicin. 10 males with a mean (interquartile range) age of 28.7 (19–47) years and 10 females aged 27.3 (21–33) years underwent capsaicin cough challenge. The maximum tolerable dose of inhaled capsaicin was significantly lower in females when compared to males. Functional magnetic resonance imaging of central-cough neural networks showed significantly larger regional responses in the primary somatosensory cortices of females compared to males despite the lower mean challenge dose of capsaicin used in females.

Patients presenting with chronic cough from diverse racial and geographic backgrounds have a strikingly homogeneous demographic profile, suggesting a distinct clinical entity. The preponder-

ance of females may be explained by sex-related differences in the central processing of cough sensations.

Characterisation and impact of reported and unreported exacerbations: results from ATTAIN



Paul W. Jones, Rosa Lamarca, Ferran Chuecos, Dave Singh, Alvar Agustí, Eric D. Bateman, Gonzalo de Miquel, Cynthia Caracta and Esther Garcia Gil. *Eur Respir J* 2014; 44: 1156–1165 doi: 10.1183/09031936.00038814

Acute exacerbations of COPD worsen health status, accelerate the decline of lung function, and are associated with increased mortality risk and considerable economic cost. In clinical studies, exacerbations are generally assessed based on healthcare resource utilisation (HCRU), with the degree of therapeutic intervention required to define severity. This approach does not capture exacerbations experienced by the patient but not reported to the clinician and therefore not treated. To address this, the EXacerbations of Chronic pulmonary disease Tool (EXACT) was developed as a standardised patient-reported outcome instrument that evaluates the frequency, severity and duration of exacerbation events, based on changes in symptoms reported directly by the patient.

This study used data from the 24-week, randomised, placebo-controlled Acclidinium To Treat Airway obstruction IN COPD patients (ATTAIN) study to examine reported exacerbation events and those that were not reported but were captured by the EXACT questionnaire. The aims were to: 1) compare the incidence, characteristics and degree of concordance of exacerbation events identified using healthcare resource criteria or the EXACT; 2) assess the effect of maintenance bronchodilator treatment with acclidinium on both types of event; and 3) investigate the impact of reported (HCRU) and unreported (identified only by the EXACT) events on health status and trough forced expiratory volume in 1 s (FEV₁) in these patients.

Patients with moderate-to-severe COPD received twice-daily acclidinium 200 mcg, acclidinium 400 mcg or placebo. "EXACT-identified" events were categorised as "EXACT-reported" (detected by EXACT and reported to the physician) and "EXACT unreported" (detected but not reported). Health status was measured using the St George's Respiratory Questionnaire (SGRQ).

EXACT-identified event rates were more than twice the HSRU events in all study arms. For example, in placebo-treated patients, annualised rates of EXACT-identified events and HCRU events were 1.39 and 0.60 per patient per year, respectively. Concordance between HSRU and EXACT-identified rates was low (κ 0.16). Acclidinium reduced EXACT-identified events (rate ratio versus placebo: acclidinium 200 mcg 0.72 and acclidinium 400 mcg 0.71; both p , <0.05); HCRU events were similarly reduced.

At week 24, SGRQ scores improved (-6.6 versus baseline) in patients with no event during weeks 1–12. The improvements were still significant, though less than the minimum clinically important difference, in patients with HCRU events (-3.4; p =0.036) or EXACT unreported events (-3.0; p =0.002).

Unreported events were more frequent than reported events. Both had similar negative impact on health status. Acclidinium reduced the frequency of both types of event.

PCRS-UK News Round-Up

RESPIRATORY AMBASSADOR MONICA FLETCHER IS HONOURED BY NURSING CHARITY

Education for Health Chief Executive Monica Fletcher has been named as a Fellow of The Queen's Nursing Institute (QNI), a prestigious accolade which recognises her work in nurse respiratory education.



Monica receives her fellowship from Kate Billingham, Chair of QNI Council

Monica has joined a select group of only 51 QNI Fellows in the country, recognised for their significant contribution to community nursing or primary care.

The citation for Monica's fellowship said: "Monica is passionate about the contribution of nurses working in primary care and the need for evidence based, professional development opportunities and robust programmes of education. Her personal clinical and academic expertise is in respiratory care, including asthma and COPD and she is a prolific writer and researcher, influencing clinical nursing and GP practice with dozens of publications in journals and books over the last decade."

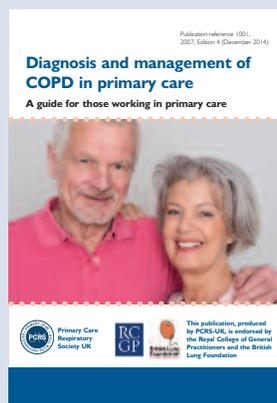
Monica is committed to engaging patients in their own personal health care and supporting them to influence how health services are delivered.

Education for Health says that Monica's ambition for the charity has always been to promote the role of practice nursing and to provide high quality education to enable practice nurses to extend their roles.

NEW PCRS-UK PUBLICATION - TABLE OF INHALED DRUGS

With the ever increasing number of inhaler device types and different inhaled combinations available to treat asthma and COPD, Anna Murphy, Consultant Respiratory Pharmacist at University Hospitals of Leicester NHS Trust, has developed a table for the PCRS-UK to provide succinct information on each drug device, its use, dose, costs and its roles within national recommended guidance. Nowhere else will you find such concise clear summary of this increasingly complicated information. We hope you will find the guide useful in demystifying the range of available medications. You can access the table at <https://www.pcrs-uk.org/resource/Guidelines-and-guidance/table-inhaled-drugs>

GUIDE TO THE DIAGNOSIS AND MANAGEMENT OF COPD IN PRIMARY CARE - NEW 2015 EDITION



Recognising that COPD is a multi-system disease requiring a multi-dimensional assessment and that multimorbidity is the norm, the latest edition of this ever popular PCRS-UK publication, emphasises a holistic patient-centred approach to management.

Primary care healthcare professionals are at the forefront of the provision of care for people with COPD. At different stages, people with COPD may benefit from the specialist skills of respiratory physicians, respiratory physiotherapists, respiratory nurses, occupational therapists, district nurses, dieticians, pharmacists, palliative care specialists and social services (and some of these will be replicated for other co-morbid conditions). The role of primary care, however, is pivotal, providing continuity of care and a generalist oversight to ensure that the patient's individual needs remain the central focus.

Practical and easy to read, the Quick Guide is based on NICE COPD Guidelines and quality standards. It also draws on other relevant national guidance for oxygen, pulmonary rehabilitation and spirometry. Endorsed by the BLF and RCGP, it is an excellent, succinct, patient-centred summary to the diagnosis and management of COPD for the generalist primary care health professional.

It is freely available for you and your colleagues to download from the PCRS-UK website, <https://www.pcrs-uk.org/resource/Guidelines-and-guidance/QGCOPD>

PCRS-UK COMMITTEE RESTRUCTURE

Following a detailed consultation process in 2014 the PCRS-UK Committee structure has been streamlined to facilitate synergies across the organisation and avoid duplication of effort.

Two new sub-committees to the Executive have been created; Education, chaired by Dr Steve Holmes and Service Delivery, chaired by Dr Noel Baxter, in place of the previous Education, Nurse and regional development committees and the Quality



Education Committee Chair, Dr Steve Holmes



Service Delivery Chair, Dr Noel Baxter

PCRS-UK News Round-Up

Award Development Group. Each will be comprised of representatives from PCRS-UK Executive and PCRS-UK membership with additional co-opted experts as appropriate. The membership of each committee will ensure it includes representation from each of the main constituent groups: GPs, practice nurses, respiratory nurse specialists & other health professionals.

The Conference Organising Committee and a respiratory leaders' event organising committee (formerly RLMT) will continue as supporting committees, accountable directly to PCRS-UK Executive but working closely with the two main sub committees.

The Executive will also be supported by key lead roles including the research lead, national policy lead, executive practice nurse lead and Primary Care Respiratory Update editor.

The number of elected members on PCRS-UK Executive has been increased from 8 to 12. Lead roles, previously ex officio positions will be selected from the elected members of PCRS-UK Executive.

PCRS-UK ELECTIONS TO PCRS-UK EXECUTIVE

The committee re-structuring created an unusually large number of vacancies at the end 2014 for the PCRS-UK Executive. Seven applications were received for the seven available vacancies. PCRS-UK is delighted to announce the election of Carol Stonham, Steve Holmes, Rupert Jones, Duncan Keeley, Sandy Walmsley (previously co-opted members) and Sally Harris to the PCRS-UK Executive and the re-election of Andy Whittamore.

FUNDING FOR QUALITY IMPROVEMENT PROJECT SECURED IN PORTSMOUTH



*PCRS-UK
Regional Lead,
South Central,
Andrew Whittamore*

Dr Andrew Whittamore, PCRS-UK Regional Lead, South Central, has successfully secured funding on behalf of PCRS-UK from NHS Portsmouth CCG for an asthma and COPD improvement programme. The funding includes PCRS-UK membership for each of the 28 practices in the CCG - allowing them to access the EQUIP improvement modules and practice improvement worksheets. Resource has also been allocated for a nurse to co-ordinate the programme, working across the local practices. The programme aligns with the CCG's strategic priorities and will be supported by a primary care incentive scheme. You may find some of the arguments that Andy has been putting forward in Portsmouth, useful in discussions with your CCG...

"CCGs are needing support to improved outcomes for patients while reducing the costs due to respiratory disease. The cost for an entire CCG of providing access to PCRS-UK tools to enhance our quality improvement and patient safety agendas, is comparable to that of one uncomplicated admission to hospital. The cost of one PCRS-UK membership for one year is less than the cost of some inhalers so by using EQUIP we are expecting to see significant return on that investment by influencing the care that our patients receive"

STANDARD PACKAGING FOR CIGARETTES

The Public Health Minister has recently announced that the Government will press ahead with standard packaging for cigarettes. Many thanks to all our members who have contributed to the campaign and helped to bring about this victory for the health of future generations.



Credit: British Lung Foundation

There is, however, no room for complacency and there is still much work to be done before the regulations can be implemented. There will be a free vote on the regulations before the election and the tobacco industry will be lobbying hard to prevent this. It is therefore critical to maintain pressure on our MPs. If the regulations are passed this will make the UK only the second country in the world to implement such a measure, demonstrating again that we are world leaders on tackling the issues of tobacco addiction.

Delivering Excellence Locally

Featuring initiatives led by PCRS-UK members around the UK, supported by PCRS-UK programmes and tools

New respiratory network is sharing good practice in West Yorkshire



Francesca Robinson talks to **Dr Anuj Handa**, *PCRS-UK Regional Respiratory Lead, Yorks and Humber*

A new respiratory network covering ten clinical commissioning groups (CCGs) in West Yorkshire is working to build strong relationships across all clinical disciplines, share good practice and improve patient outcomes.

Launched by Dr Anuj Handa, a Huddersfield GP and PCRS-UK Regional Lead, the network's quarterly meetings bring together clinical respiratory leads from primary, community and secondary care and public health with key personnel from CCG and commissioning support units.

The group's aim is to provide commissioners with evidence of what works in practice to enable them to achieve their objectives of commissioning effective respiratory care and reducing variations in care.

The five-year strategic plan for each CCG has been used to identify the common respiratory themes for the next five years. These have formed the basis of the network's programme of work which addresses the priority services that commissioners want to commission. Each CCG is sent a service map to enable them to see what respiratory services they have in each area. This helps them to identify any gaps in services and can be used to inform their commissioning plans for the future.

The network's meetings each have a specific theme and are addressed by speakers from both primary and secondary care. A workshop is then held to tease out what is important, what is relevant and what is working, so that each attendee can take that information back to their

CCG or secondary care trust and address the key issues at a strategic level.

"What is really rich about meetings is that we have the primary, community, secondary and nursing care perspectives aired in one room with people arguing for or against different ideas. There is a lot of sharing among the disciplines. In addition we are working with healthcare outcomes consultants and have charts and data to enable each CCG to drill down to see what is going on at practice level," says Dr Handa.

He adds: "The role of the network is to identify and embrace innovation and be the vehicle for presenting best practice backed up by evidence from the data and service map. Commissioners can see what should be a priority for them and they can then implement the recommendations from our network."

Dr Handa says setting up the network was a steep learning curve but he was helped with support from PCRS-UK and Lisa Chandler a former strategic health authority respiratory manager who was able to provide contacts, practical advice and help with getting the network off the ground. PCRS-UK Regional Lead colleagues have supported Dr Handa by identifying key themes, sharing experience and providing speakers for meetings.

The next meeting on the theme of admission avoidance is being held on February 13 at Broad Lea House, Dyson Wood Way, Bradley, Huddersfield HD2 1GZ. For further information email: westyorkshire.respiratorynetwork@nhs.net

PCRS-UK Affiliated Local Nurse Groups form a lifeline for practice nurses in Oxfordshire



Dr Robin Carr PCRS-UK Affiliated Group Lead, Oxfordshire

It is cold and we are all being encouraged to dig deep and look out for all those vulnerable respiratory patients so as to avoid any more admissions.

The responsibility for people's health can be a daunting one and the seemingly endless number of targets and achievements we are exhorted to reach can produce a degree of "snow blindness".

Here in Oxfordshire CCG we have found that the local nurse groups, which now run in all the localities and are affiliated to PCRS-UK, have provided a lifeline for the hard pressed practice nurse with an interest in respiratory illness. Meeting regularly, 3-4 times a year, they provide a welcome opportunity for nurses to talk with colleagues and discover that they are not the only one who struggles with preschool wheeze or end stage breathlessness in COPD. It can be a lonely job in the consulting room but the knowledge that we all face similar challenges can be very reassuring.

Keeping up to date can be really hard, and the last thing you want to do at the end of an 11 hour day when it is dark and cold, is go out again; but educational events are as much entertaining as they are informative. The camaraderie also contributes to the educational content, with each person chipping in with their own experience and how they managed a situation. There are many of ways of doing some parts of our jobs, and sometimes no evidence to provide guidance. So having lots of tried and tested examples can really help; something that only comes from getting together with

your fellow practice nurses. It's a hard job but it is massively rewarding and made all the better by some mutual support.

We have an informal mentoring scheme which has been helpful, and has meant, for example, that Association for Respiratory Technology & Physiology trained nurses can either teach spirometry, or help interpret results or symptoms, when asked by fellow nursing staff. This collaboration helps those asking, and enables them to learn as well as empowering those who have the skills and wish to use them. In short we all win.

Our network of networks also means that when we were organising a couple of study days we were able quickly and efficiently to contact the majority of the local respiratory nurses to tell them when it was and what was on. We have also had the opportunity to ask the nurse groups what they wanted to learn about this year, how far people were prepared to travel, and when during the day would be convenient. We then produce a table of what is on, when and where it is to be held, which encourages nurses from one group to meet colleagues in other groups and the learning and bonding continues to build.

If you have a group, do keep going, it is worth it, IN SPADES...

..and If you don't have a group, do consider setting one up. If you want any help or some enthusiastic support, please ask, we have enthusiasm and advice to spare, even in these cold and dark winter times.

PCRS-UK is here to help you deliver excellence locally!



If you are keen to follow any of the examples highlighted in this section or have other ideas about how you want to improve care locally, but are not sure what to do as the next step, then please contact info@pcrs-uk or call **Tel: +44 (0)1675 477600**. We will put you in touch with someone who can help you .

PCRS-UK improvement tools in practice

Simply EQUIPPed to Practice



**Jane Scullion, Anna Murphy,
Darren Jackson, Jake Cooke**

Respiratory problems in primary care account for around 17% of total general practice workload¹ and whilst a proportion of this is children and upper respiratory tract infections, much of this workload is chronic respiratory disease management. With this in mind, and thinking about value, outcomes and cost, as with other commissioning groups, West Leicestershire CCG (WLCCG) identified respiratory as an area amenable to improving health outcomes for its population. WLCCG currently plans and purchases NHS services for a population of 366,000 and has a commissioning budget of £362 million. It covers three district council areas and 50 GP practices and has affluent areas, deprived areas, rural poverty, gypsies, a transient travelling population and black and ethnic minorities (www.westleicestershireccg.nhs.uk).

The following article looks how our CCG plans to use the very practical, clinically focused PCRS-UK improvement tools (Table 1) linked with a modular based approach to education (Table 2) (www.simplestepseducation.co.uk). All practices have been provided with membership of PCRS-UK so they can use the PCRS-UK improvement tools including EQUIP, a modular-based approach using audit and practical tips on how to make a positive change (<https://www.pcrs-uk.org/equip>). A practical booklet and online resource has been produced incorporating the SIMPLE steps approach linked to PCRS-UK resources and with further reading (Table 3).

Prior to attendance the participants filled in a practice profile, with details of their asthma and COPD registers, and current list size, prevalence figures, Quality and Outcome Framework (QoF) achievement and exception reporting. Additional information was the number of patients referred to smoking cessation services and the number of respiratory patients who had received flu vaccination. Free text was available to add what was currently working well within the practice with regard to respiratory care, what was not working as well, and three areas for improvement.

87 participants, predominantly general practitioners but also practice nurses and the community teams, signed up for the modules repeated on two evenings to allow for maximal atten-

Module 1	<ul style="list-style-type: none"> • Outcomes and Value • Diagnosis • Breathlessness assessment • Case Studies
Module 2	<ul style="list-style-type: none"> • Smoking Cessation • Inhaler techniques
Module 3	<ul style="list-style-type: none"> • Monitoring • Pharmacotherapy • Lifestyle • Education
Module 4	<ul style="list-style-type: none"> • Advanced COPD • Palliation and EOL • Case studies
Evaluation	

Diagnosis	
S	Stop Smoking
I	Inhaler Technique
M	Monitoring
P	Pharmacotherapy
L	Lifestyle
E	Education

dance. Pre course evaluation through an on-line survey and a 'mop up' session prior to the first modules included an asthma questionnaire and the Bristol Knowledge Questionnaire.²

Changing behaviour in practice involves more than telling people what needs to be done; to facilitate change teaching and discussion need to link with practice routines and practical help needs to be available. Change needs to be owned by the people undertaking the care. We look forward to reporting on the overall uptake and evaluation of the modules.

References

1. Simpson CR, Helms PJ, Taylor MW, Baxter-Jones AD. Respiratory morbidity in primary care. A population based study, using practices from the Scottish Continuous Morbidity Recording Research Database. www.thepcrj.org/journ/vol10_2/0034_0036_simpson.pdf
2. White R, Walker P, Roberts S et al 2006 Bristol COPD Knowledge Questionnaire (BCKQ): testing what we teach patients about COPD Chronic Respiratory Disease 2006;3:123-131

Table 3: Example of linking modules and PCRS-UK resources (Diagnosis)

	<p>PCRS Equip: Module 2 Prevalence, early and accurate diagnosis</p>	
<p>https://www.pcrs-uk.org/resource/Improvement-tools/equip-module-2-prevalence-and-diagnosis</p>	<p>Practice Improvement Worksheet - Reviewing asthma diagnosis in children PCRS (2014).</p>	
<p>https://www.pcrs-uk.org/resource/Improvement-tools/reviewing-asthma-diagnosis-children-improvement-worksheet</p>	<p>Opinion Sheet - Management of asthma in children PCRS Opinion Sheet (2011)</p>	<p>(www.simplestepseducation.co.uk)</p>

East Kent Prescribing Group using PCRS-UK 'stepping down triple therapy' worksheet

Tricia Bryant, PCRS-UK Operations Director

East Kent Prescribing Group has developed a decision support tool to help healthcare professionals with the treatment of inhaled COPD therapy. The tool provides step-by-step guidance on assessing and reviewing patients on COPD and also recommends the use of the PCRS-UK Practice Improvement Worksheet – Stepping Down Triple Therapy in COPD (available to members of the PCRS-

UK via <https://www.pcrs-uk.org/worksheets>) as a pragmatic and concise way of reviewing patients on triple therapy.

Participants are being asked to feed back on the results of their work via an online survey that we hope to bring to you in due course.

Respiratory Leaders Programme

Top tips for setting up a successful project



Francesca Robinson, Reporting from the last PCRS-UK Respiratory Leaders Meeting

The key to delivering a project, which brings about a change in practice is to adopt a structured approach, Catherine Blackaby, Senior Improvement Manager with NHS Improving Quality, told the November meeting of the Respiratory Leaders Network. Held at Studley Castle, Warwickshire, the interactive skills based workshop focused on practical tips for making a project happen.

The sessions were aimed at clinicians interested in all types of projects – from small practice-based initiatives such as implementing an audit, or organising an educational update, to much larger projects across a whole locality such as bringing about service delivery change or setting up a local group or network. Delegates were given the opportunity to learn from experts and to practise the necessary skills in a supportive and safe environment.

"The first step to take when setting up a project is to understand where you are starting from", said Catherine Blackaby. You need to understand how the system works now: i.e. what services currently exist, how do they interact to create a system, who are the local stakeholders, where are the bottlenecks, what might get in the way, in which areas is care below expectations and what is affecting outcomes?

Then you need to consider what different stakeholders will want to achieve in this area. Who has power and influence, will they be interested in the topic covered by your project, what motivates patient, public and staff behaviour, how do people behave and what resistance or support for change is likely?

The next stage is to consider what you know about the need for your project. What national evidence is available, what do you think works and why, what ideas for change exist locally and what are the theories behind them? Also think about what might be causing any local problems, what untested assumptions do you have about how or why things currently work and why does this matter?

A fourth set of questions to ask is how and where do things differ? For example: do different groups (e.g. ethnic groups, diagnostic groups) have different needs, are services provided or used differently by different localities or groups, what do you know about

trends in outcomes or processes over time, do you understand why things are evolving and what measures do you have and what do they tell you?

Then you need to devise a project plan, work out what tasks must be prioritised and create a "to do" list. Next, draw up a communication plan which should include a list of project reports, team meetings, events, health and safety issues, staffing issues, task reminders that need to be organised. Work out who is the target audience for your project; this could be the project team, sponsor, NHS Improvement, steering group, stakeholders and patients. Plan how often you need to contact them and how – through meetings, presentations, events, emails or hand-outs.

Other experienced members from the PCRS-UK leader faculty gave presentations on the leadership skills that are required to make a project successful. Topics ranged from how to get noticed and be heard at the right events, how to use policy to your advantage, and how to communicate effectively. Delegates were given a review of recent published evidence and developments which can be used to drive improvements and an update on the PCRS-UK resources that are available to support respiratory leaders.

Table workshop sessions provided advice on how to build on success and learn for the future, how to improve written communication skills and top tips for presentations and getting across your unique selling point.

Presentations from the event can be accessed at:
<https://www.pcrs-uk.org/feedback-last-meeting>

SAVE THE DATES

2015 PCRS-UK Respiratory Leadership Development Workshops

5th and 6th June 2015

6th and 7th November 2015

LOCATION:
Midlands

Full details to be announced shortly



npj | Primary Care Respiratory Medicine

Celebrating a successful first 9 months**Joe Bennett**, Senior Publishing Manager, Nature Publishing Group**Emma Hedington**, Marketing Manager, Nature Publishing Group

In April 2014, PCRS-UK and the IPCRG entered in to a new partnership with Nature Publishing Group, re-launching Primary Care Respiratory Journal as *npj Primary Care Respiratory Medicine*, an online-only, open access journal, and the inaugural title in the Nature Partner Journals series.

Under the editorial leadership of Professor Aziz Sheikh and Dr Paul Stephenson, the journal continues to publish high-quality research in all areas of the primary care management of respiratory and respiratory-related allergic diseases.

The first nine months of publication has been a great success. With over 75,000 new visitors so far, *npj Primary Care Respiratory Medicine* now has a readership of researchers from the primary care and respiratory community from over 140 countries worldwide.

What can readers expect from *npj Primary Care Respiratory Medicine*?

The only fully-indexed scientific journal devoted to the management of respiratory diseases in primary care, *npj Primary Care Respiratory Medicine* publishes papers representing significant advances to specialists within the field of primary care and respiratory medicine. Receiving an increased Impact Factor of 2.909* in July 2014, the journal further cemented its place as a leading journal in the fields of both primary care and respiratory systems.

npj Primary Care Respiratory Medicine publishes articles, review articles, editorials, brief communications, protocols and case reports. As part of the Nature Partner Journals (npj) series, the journal publishes a professionally written editorial summary to accompany each article, summarising the key issue addressed in the article - the summaries of the most relevant articles are included in Primary Care Respiratory Update. Each article published displays article metrics, including total citations, online attention (including news coverage and social media mentions), and total page views for the articles.

Open access: allowing the widest dissemination of your research

All articles published in *npj Primary Care Respiratory Medicine* are open access: freely and universally available online for all to read, use, and cite without restriction. Open access publication allows a number of benefits, including compliance with open access funder and policy mandates (including RCUK and the recently announced Wellcome Trust Charity Open Access Fund (COAF)), and studies indicate that it may result in increased visibility and citation of research**.

The journal is funded through the payment of an article processing charge (APC) for articles accepted for publication. In instances where the author genuinely cannot pay the full amount charged for publication, the journal considers applications for the APC to be sponsored for publication. We encourage authors to contact the journal to find out whether they are eligible.

As *npj Primary Care Respiratory Medicine* is now online-only and open access, PCRS-UK members do not receive a print issue. Visit the journal website for the full content listing – you do not require a password or membership number to access content published in the journal. We also encourage you to sign up to receive free monthly Table of Contents alerts through the link on the journal homepage.

Looking ahead to 2015

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REVIEW ARTICLE OPEN

When should acute exacerbations of COPD be treated with systemic corticosteroids and antibiotics in primary care: a systematic review of current COPD guidelines

Johanna Laue¹, Eirik Reiherth² and Hasse Melbye¹

Not all patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) benefit from treatment with systemic corticosteroids and antibiotics. The aim of the study was to identify criteria recommended in current COPD guidelines for treating acute exacerbations with systemic corticosteroids and antibiotics and to assess the underlying evidence. Current COPD guidelines were identified by a systematic literature search. The most recent guidelines as per country/organisation containing recommendations about treating acute exacerbations of COPD were included. Guideline development and criteria for treating acute exacerbations with systemic corticosteroids and antibiotics were appraised. Randomised controlled trials directly referred to in context with the recommendations were evaluated in terms of study design, setting, and study population. A total of 19 COPD guidelines were included. Systemic corticosteroids were often universally recommended to all patients with acute exacerbations. Criteria for treatment with antibiotics were mainly an increase in respiratory symptoms. Objective diagnostic tests or clinical examination were only rarely recommended. Only few criteria were directly linked to underlying evidence, and the trial patients represented a highly specific group of COPD patients. Current COPD guidelines are of little help in primary care to identify patients with acute exacerbations probably benefitting from treatment with systemic corticosteroids and antibiotics in primary care, and might contribute to overuse or inappropriate use of either treatment.

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INTRODUCTION

Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) occur frequently in the course of COPD.¹ They can differ in severity and many require hospitalisation, but the majority of mild to moderate AECOPD can be managed in primary care.² Antibiotics and systemic corticosteroids are beneficial treatment options that are often used.^{3,4} However, the benefit of antibiotics in mild to moderate AECOPD remains controversial,⁵ and their overuse can contribute to the development of bacterial resistance.⁶ Systemic corticosteroids bear the risk of adverse side effects,³ especially in patients with co-morbidities.⁷ Inappropriate use of either treatment should be avoided, and targeting patient treatment requires careful patient assessment. Clinical practice guidelines are intended to assist treatment decisions, based on the best available evidence.⁸ A critical appraisal of 15 COPD guidelines found variations in the content and between recommendations on several management strategies for COPD, and concluded that these were rather a result of 'selective experience' than based on scientific evidence.⁹ Consequently, we designed this study to identify recommended assessment strategies for treating AECOPD patients with systemic corticosteroids and antibiotics in COPD guidelines. Furthermore, we aimed to evaluate the quality of guideline development and the applicability of underlying evidence to primary care.

METHODS

A systematic literature review was conducted in Web of Science, SCOPUS, SveMed+, PubMed, Embase, Cihnal (EBSCO) and Ovid MD

to identify COPD guidelines. Throughout the entire search, 'COPD' as Mesh-term was used whenever applicable. If a database did not support Mesh-terms, 'COPD' was searched in keywords, abstract and title. 'COPD' was combined with the search phrases 'guideline' and 'recommendation'. The search string used throughout the search was as follows:

- Chronic Obstructive Pulmonary Disease AND (Guideline OR Recommendation).

Our initial search was performed with a time limit set for publications between 2003 and 2013. It was then extended to 8 May 2014 to ensure the inclusion of any new publications during our work on this project. Eligibility assessment was conducted by the first and the last author, and the approach from the preferred reporting items for systematic reviews and meta-analyses statement was followed¹⁰ (Figure 1). To avoid overlooking documents that were published elsewhere than in the searched databases, a supplemental search was conducted in the guideline databases UpToDate, Best Practice, National Guideline Clearinghouse, Cochrane Library, Guidelines International Network and websites of the Canadian Medical Association, and American College of Physicians. Furthermore, websites of national health authorities (Germany, Denmark, Sweden, Norway, Austria, Switzerland, and Netherlands) were searched for eligible guidelines. This search was not repeated after 2013. Only guidelines and published documents with recommendations on adults with AECOPD and/or infectious diseases of the lungs when containing AECOPD were

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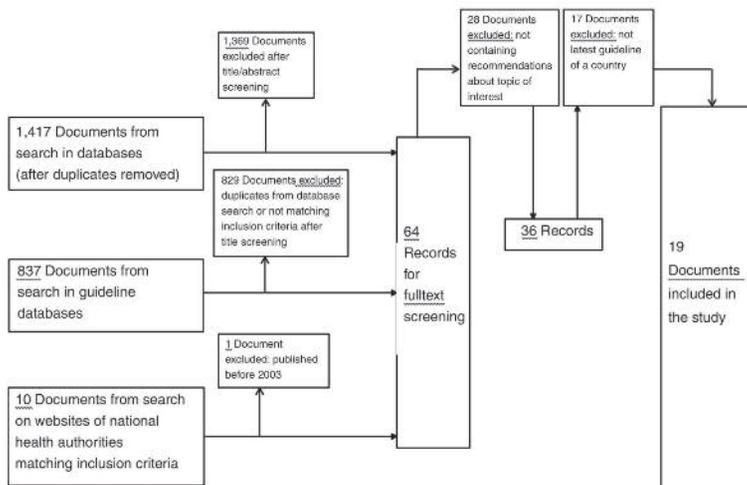


Figure 1. Flowchart describing the systematic search and eligibility assessment.

included in this study. They also had to be published in English, German, Dutch, or a Scandinavian language. The most recent guideline from each country was included. The included guidelines were analysed in terms of guideline development by applying criteria from the AGREE II tool (Appraisal of guidelines for research and evaluation II).¹¹ The criteria applied belonged to the domains 2 (stakeholder involvement), 3 (rigor of development), and 6 (editorial independence). We extracted recommendations about patient assessment for treatment with systemic corticosteroids and antibiotics. If recommendations were given separately for inpatients and outpatients, only those for outpatients were considered. Evidence explicitly linked to the recommendations, as described in domain 3 of the AGREE II tool,¹¹ was obtained, and randomised controlled trials published in scientific medical journals were assessed in terms of study setting, study design, and inclusion and exclusion criteria. Furthermore, we decided to add the trials included in the latest versions of the Cochrane reviews about treating AECOPD with systemic corticosteroids³ and antibiotics,⁴ although not directly referred to in the guidelines.

RESULTS

The systematic database search resulted in 1,417 documents, and the supplemental search in the guideline databases in 873 documents. Further, 10 documents were retrieved from the websites of national health authorities. A total of 64 documents (47, 8, and 9 documents, respectively) remained for full-text screening after excluding duplicates and those not matching the inclusion criteria. After full-text screening, 36 documents remained, of which 17 outdated versions were excluded. Finally, 19 guidelines were included in the study (Figure 1).

Characteristics of guideline development

The guidelines were published between 2004 and 2014, and 12 of these were updates from earlier versions (Table 1). The time between previous and current editions varied from continuous updating to 15 years between two versions. Four guidelines gave a date for planned revision. A total of 14 guidelines provided information about the development committee, and in 10 committees at least one general practitioner was included. The guidelines from the Netherlands and from the International

Primary Care Respiratory Group were especially targeted towards primary care physicians, and this was reflected in the high number of general practitioners in the development groups (Table 1). Furthermore, eight guidelines gave separate recommendations for inpatients and outpatients. Information about funding or conflict of interests was provided in 11 guidelines, 5 of which were sponsored by pharmaceutical companies (Table 1). A detailed description of important steps in the guideline development process, such as literature review, was only given in six guidelines (Table 1). AECOPD definitions across the guidelines were symptom based including the terms ‘dyspnoea’, ‘cough’, and ‘changes in sputum’ in the majority of cases.

Criteria for initiating treatment with systemic corticosteroids

A total of 17 of the 19 guidelines addressed the treatment option ‘systemic corticosteroids’, with 11 criteria being identified (Table 2). The guidelines from the European Respiratory Society and Germany addressed infectious diseases and did not contain recommendations about systemic corticosteroids. We found that nine guidelines recommended systemic corticosteroids universally to all AECOPD patients, and the Spanish guideline reserved such treatment to all patients with an at least moderate exacerbation (without providing information about different severity grades). One guideline reserved such treatment to patients with severe underlying COPD, and two guidelines to patients with moderate to severe COPD (Table 2). Three guidelines recommended basing treatment decisions on patients’ actual respiratory symptoms, namely a significant increase in dyspnoea and wheezing. The Dutch guideline recommended waiting for the response to increased dosage of bronchodilators, as first-line emergency treatment, and assessing the patients’ general condition before starting a course with systemic corticosteroids in all patients not requiring hospitalisation. The Swedish guideline was the only guideline to suggest objective measures by clinical examination (respiratory rate and heart rate) and to recommend the use of the diagnostic tests pulse oximetry and blood gas analysis (Table 2).

Characteristics of the primary evidence supporting recommendations for systemic corticosteroids

We found 11 randomised controlled trials directly referred to in context with a certain recommendation^{12–22} and two trials in the Cochrane review,³ which were not directly referred to in context

Table 1. Overview of guidelines included in the study and characteristics of the development process

Guidelines ^a (country or organisation and year of publication)	Time (years) between current and previous version	Date for planned revision presented	Comprehensible description of literature search	GPs/all members in development committees (n)	Separate recommendations for inpatients and outpatients	Funding by the pharmaceutical industry
Austria ⁶¹ 2004	15	No	No	NA	No	NA
IPCRG ⁶² 2006	NA	No	No	4/8	For primary care	Yes
Denmark ⁶³ 2007	NA	No	No	1/20	Yes	NA
Netherlands ⁶⁴ 2007	6	No	No	7/9	For primary care	No
Sweden ⁶⁵ 2009	NA	No	No	2/8	Yes	NA
Germany ⁶⁶ 2009	4	Yes	No	0/14	No	No
NICE ⁶⁷ 2010	6	No	Yes	4/31	Yes	No
South Africa ⁶⁸ 2011	2	No	Yes	NA	No	Yes
Canada ⁶⁹ 2011	NA	No	No	NA	No	NA
ERS ⁷⁰ 2011	6	No	Yes	1/12	Yes	No
Australia/New Zealand ⁷¹ 2012	9	No	No	3/45	No	Yes
Norway ⁷² 2012	NA	No	No	2/8	Yes	NA
Switzerland ⁷³ 2013	10	No	No	1/13	Yes	NA
ICSI ⁷⁴ 2013	1	Yes	Yes	0/10	No	No
GOLD ⁷⁵ 2013	1	Yes	Yes	2/25	No	Yes
UpToDate ^{76,77} 2013	Cont.	Yes	No	NA	No	NA
India ⁷⁸ 2013	NA	No	Yes	NA	No	NA
Saudi ⁷⁹ 2014	NA	No	Yes	0/12	Yes	No
Spain ⁴⁶ 2014	4	No	No	0/19	Yes	Yes

Abbreviations: cont., guidelines are continuously updated; GP, general practitioner; NA, information not available or remained unclear.
^aAbbreviations for organisations: ERS, European Respiratory Society; GOLD, Global initiative for chronic obstructive lung disease; IPCRG, International Primary Care Respiratory Group; ICSI, Institute for Clinical Systems Improvement; NICE, National Institute for Health and Care Excellence.

Table 2. Recommendations for assessing outpatients for treatment with systemic corticosteroids and antibiotics

Criteria	No. of guidelines	Countries/organisations applied (ISO codes) ^a
Systemic corticosteroids		
All patients with AECOPD	9	ZA, AU/NZ, IN, NO, SW, ES ^b , ICSI, GOLD, UpToDate
Baseline FEV1% predicted < 50%	1	AT
Stadium III	1	AT
Moderate to severe COPD	2	CA, DK
Significant increase in dyspnoea/wheezing	3	SE, IPCRG, NICE
Impaired general condition	1	NL
Treatment failure of first-line treatment (bronchodilators)	1	NL
Respiratory rate > 25/min, heart rate > 110/min, SpO2 < 90%, PaO2 < 8 kPa	1	SE
Antibiotics		
All patients with AECOPD	2	IN, KSA
Severe underlying COPD	4	DE, NO, ERS, NL
Increase in dyspnoea, cough, sputum volume and purulence	3	CA, IPCRG, NL
Increase in dyspnoea, sputum volume and purulence (2 or 3 of 3 symptoms)	6	ZA, GOLD, ERS, SUI, ICSI, UpToDate
Increase in sputum volume and colour	2	AT, AU/NZ
Change in sputum colour/purulent sputum	6	NO, SE, DK, NICE, DE, ES
Insufficient improvement after 4 days	1	NL
Clinical signs of pneumonia	2	DK, NICE
Fever	5	AU/NZ, AT, NO, DK, NL
Impaired general condition	2	DK, NL
Use of accessory muscles	1	NL
Respiratory rate > 30/min, heart rate > 120/min	1	NL
Leukocytosis	1	AU/NZ
CRP > 50 mg/l	1	NO
Procalcitonin > 0.1 ng/ml	1	DE
Chest radiography	1	NICE

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; PaO2, partial oxygen pressure; SpO2, blood oxygen saturation.
^aISO codes of countries and abbreviations of organisations: AT, Austria; AU/NZ, Australia/New Zealand; CA, Canada; DE, Germany; DK, Denmark; ES, Spain; GOLD, Global initiative for chronic obstructive lung disease; ICSI, Institute for Clinical Systems Improvement; IN, India; IPCRG, International Primary Care Respiratory Group; KSA, Saudi; NICE, National Institute for Health and Care Excellence; NL, Netherlands; NO, Norway; SE, Sweden; SUI, Switzerland; ZA, South Africa.
^bTo all patients with at least moderate exacerbation.

with a certain recommendation in the guidelines (Table 3). Publication dates varied between 1980 and 2011, and 9 of the 11 trials were hospital based. The number of study participants ranged from 27 to 210 patients (Table 3). The majority were male, and one trial had included only male patients (Table 3). The percentage of the patients who were finally randomised among those screened for eligibility varied between 14 and 96% (Table 3). Cardiovascular co-morbidities were explicitly described as exclusion criteria in 7 trials (uncontrolled heart failure in 5 trials, diabetes mellitus in 2 trials, and uncontrolled arterial hypertension in 1 trial). The forced expiratory volume after 1 s (FEV₁% predicted) or FEV₁ in litre at inclusion were provided in 10 trials. Their values ranged between 24.7 and 59.6%, or between 0.5 and 1.3 litre, respectively (Table 3).

Criteria for initiating treatment with antibiotics

All guidelines contained recommendations about treatment with antibiotics, and 12 assessment criteria were identified (Table 2). Two guidelines recommended antibiotics to all patients with AECOPD. All others, apart from the Dutch guideline, recommended basing antibiotic treatment on an increase of the respiratory symptoms 'dyspnoea', 'cough', 'sputum volume', or 'sputum purulence'. A total of eight of these guidelines only recommended changes in sputum (mostly purulent or changes in sputum colour). These guidelines also provided additional criteria (Table 2), which were mostly the severity of underlying COPD or systemic symptoms such as 'fever' and 'impaired general condition'. Only four guidelines recommended conducting additional diagnostic tests: C-reactive protein (CRP), white blood cell count, procalcitonin, and chest radiography (Table 2). The guidelines from India²³ and Saudi²⁴ emphasised that the use of biomarkers has no role in the assessment of AECOPD. The Dutch guideline was exceptional, as they did not recommend any of the respiratory symptoms. Here, the focus was only on the patient's general condition and fever as signs for bacterial infection, in combination with severe underlying COPD and insufficient improvement after 4 days. However, it was stated that a course of antibiotics might be initiated in all patients with a severe exacerbation, characterised by heavy dyspnoea, use of accessory

muscles, respiratory rate >30/min and heart rate >120/min (Table 2).

Characteristics of the primary evidence supporting recommendations for antibiotics

We found 4 randomised controlled trials that were directly referred to in context with a certain recommendation²⁵⁻²⁸ and 11 trials in the Cochrane review⁴ that were not directly referred to in the guidelines²⁸⁻³⁹ (Table 4). They were published between 1960 and 2013. In four trials, patients were excluded owing to both cardiovascular diseases (left ventricular failure in one trial, severe heart disease in two trials, and stroke in one trial) and a broad range of infectious diseases. Almost all trials included significantly more men than women (Table 4). A total of 11 trials provided information about initial exclusion rates before randomisation, which ranged between 56 and 3%. The average baseline FEV₁% predicted or peak expiratory flow of the included study patients was presented in 13 trials, with the FEV₁% predicted ranging from 33.9 to 65% and peak expiratory flow from 63 to 295 l/min (Table 4).

DISCUSSION

Main findings

There was a considerable lack of transparency regarding guideline development, as the literature review was often not documented comprehensively. It is also problematic that a considerable number of guidelines were financed by pharmaceutical companies, or their funding sources were not reported.⁴⁰ Owing to the small number of general practitioners in the guideline development committees, primary care expertise might not be considered sufficiently during guideline development.

Treatment recommendations were mostly universal and unspecific and often recommended for all AECOPD patients or all patients with underlying moderate to severe COPD, or, in terms of antibiotics, patients with certain symptoms. The use of diagnostic tests was only recommended in a few guidelines.

The patients in the trials that the recommendations were based on were a rather selected group of COPD patients. Most trials were conducted in hospitalised patients, the exclusion rates before

Table 3. Characteristics of randomised controlled trials underlying recommendations for treating acute exacerbations of chronic obstructive pulmonary disease with systemic corticosteroids.

Author, year of Publication	No. of patients (m/f)	% Of patients included of those initially screened	Cardiovascular co-morbidities in exclusion criteria	Average baseline lung function (FEV ₁ % predicted or FEV ₁ in litre) of study patients at the time of inclusion	Study setting (hospital or outpatient)
Albert <i>et al.</i> ¹²	44 (44/0)	NA	No	0.6 l	H
Thompson <i>et al.</i> ¹³	27 (26/1)	19%	Yes	1.3 l	O
Niewoehner <i>et al.</i> ¹⁴	271 (268/3)	15%	NA	0.8 l	H/O
Davies <i>et al.</i> ¹⁵	50 (34/16)	20%	Yes	24.7%	H
Maltais <i>et al.</i> ¹⁶	199 (162/37)	29%	No	NA	H
Aaron <i>et al.</i> ¹⁷	147 (84/63)	14%	Yes	38.0%	O
DeJong <i>et al.</i> ¹⁸	210 (157/53)	48%	Yes	37.0%	H
Gunen <i>et al.</i> ¹⁹	121 (103/18)	NA	No	37.2%	H
Ställberg <i>et al.</i> ²⁰	109 (56/53)	NA	No	45.0%	H/O
Alia <i>et al.</i> ²¹	83 (66/17)	23%	Yes	NA	H
Leuppi <i>et al.</i> ²²	311 (188/123)	43%	No	31.5	H
<i>Trials from the Cochrane review³</i>					
Emerman ⁷⁹	96 (50/46)	96%	Yes	59.6%	H
Bullard ⁴⁶	113 (97/16)	82%	No	0.5 l	H

Abbreviations: f, female; FEV₁, forced expiratory volume in 1 s; H, hospital-based study; m, male; NA, information not available or unclear; O, study conducted with outpatients.

Table 4. Characteristics of randomised controlled trials underlying recommendations for treating acute exacerbations of chronic obstructive pulmonary disease with antibiotics

Author, year of Publication	No. of patients (m/f)	% Of patients included of those initially screened	Cardiovascular co-morbidities in exclusion criteria	Average baseline lung function (FEV1 % predicted, FEV1 in litre or PEF litre/min) of study patients at the time of inclusion	Study setting (hospital or outpatient)
Anthonisen <i>et al.</i> ²⁵	173 (134/39)	—	Yes	33.9%	O
Seemungal <i>et al.</i> ²⁶	83 (59/24)	—	Yes	41.3%	O
Patel <i>et al.</i> ²⁷	29 (21/8)	—	No	38.7%	O
Nouira <i>et al.</i> ²⁸	93 (84/9)	44%	No	0.7 l	H
<i>Trials from the Cochrane review</i> ⁴					
Berry <i>et al.</i> ²⁹	53 (31/21) ^a	NA	NA	NA	O
Fear <i>et al.</i> ³⁰	62 (NA)	NA	No	NA	O
Elmes <i>et al.</i> ³¹	74 (47/27)	76%	Yes	79.2 l/min	H
Pines <i>et al.</i> ³²	186 (186/0)	No	76.0 l/min	H	H
Pines <i>et al.</i> ³³	259 (259/0)	NA	No	146.0 l/min	H
Manresa <i>et al.</i> ³⁴	19 (NA)	NA	No	172.0 l/min	H
Jørgensen <i>et al.</i> ³⁵	270 (115/278)	97%	Yes	295.0 l/min (circa)	O
Sachs <i>et al.</i> ³⁶	71 (30/41)	NA	No	63 l/min	O
Brusse-Keizer ³⁷	35 (21/14)	56%	No	48.6%	O
Daniels <i>et al.</i> ³⁸	223 (133/90)	70%	No	45.4%	H
Llor <i>et al.</i> ³⁹	310 (251/59)	88%	No	65.0%	O

Abbreviations: f, female; FEV1, forced expiratory volume in 1 s; H, hospital-based study; m, male; NA, information not available or unclear; O, study conducted with outpatients; PEF, peak expiratory flow.

^aOne not recorded.

randomisation were high in many trials, and the patients were often characterised by severely reduced lung function and low prevalence of cardiovascular co-morbidities or diabetes.

Strengths and limitations

We conducted a rigorous and systematic literature search to get hold of the COPD guidelines. However, we might have missed guidelines published in languages other than the ones included.⁴¹ As we did not use the AGREE II tool to its full extent, we are limited in making reliable statements on the guideline quality. Further, we only considered primary studies that were explicitly linked to the recommendations in the appraisal of underlying evidence. Whether studies are cited directly linked to a recommendation or not could be owing to the technical presentation of recommendations, and it does not necessarily reflect the existence of the evidence used. However, according to the AGREE II tool, an explicit link between recommendations and evidence is important for judging the source of a recommendation.¹¹ As we additionally appraised the trials included in the latest Cochrane reviews on treating AECOPD with systemic corticosteroids³ and antibiotics,⁴ we are able to make a valid statement about the evidence that the current treatment recommendations are based on.

Interpretation of findings in relation to previously published work *Relevance of the underlying evidence for primary care patients.* The characteristics of the trial patients of the studies underlying the recommendations were not necessarily comparable to the 'common' COPD patient in primary care, who tend to have milder airflow obstruction⁴² and frequently suffer from co-morbidities.⁴³ When evidence is based on patients without co-morbidities, it could be risky to follow the guidelines in primary care patients who also suffer from heart failure or diabetes. Herland *et al.* expressed similar concerns, questioning whether results of the trials on obstructive lung diseases really can be extrapolated to 'real-life' populations of patients.⁴³ Considering that frequent co-morbidities,⁴³ such as heart failure, can mimic the symptoms of increased cough and dyspnoea,^{44,45} adherence to the current guidelines might lead to over-treatment or inappropriate

treatment with antibiotics and systemic corticosteroids. In addition, the authors of the latest Cochrane reviews about antibiotics⁴ and systemic corticosteroids³ for AECOPD underline that the effect of both treatments in outpatients and patients with mild airflow obstruction still remains unclear. They emphasise the need for diagnostic tests and biomarkers to identify patients who may benefit from the treatment.

Criteria for systemic corticosteroids. According to many guidelines, systemic corticosteroids seemed to be universally useful. Diagnostic tests or clinical examination were rarely recommended, but prescribing a corticosteroid should rather be based on the patient's respiratory symptoms. It is striking that the recommended criteria for treating AECOPD with systemic corticosteroids resemble in most cases the (clinical) definition of an AECOPD, which is an 'acute event characterised by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to change in medication'.⁴⁶ Thus, once the clinical diagnosis of AECOPD is made, most patients would fit the criteria for a course of systemic corticosteroids according to the guidelines. Yet, common adverse side effects, such as hyperglycaemic episodes in patients with diabetes,⁷ call for a rather critical use of systemic corticosteroids. An 'increase in dyspnoea' might be caused by other (non-)respiratory conditions that are not necessarily responsive to systemic corticosteroids.^{44,45} Therefore, a more careful assessment to identify patients with a clear benefit would be of major importance. Yet, no reliable method for further investigation beyond assessment of symptoms has been established, and this is probably the reason for rather speculative recommendations such as those recommended in the Swedish guidelines (pulse oximetry and blood gas analysis). Interestingly, spirometry was explicitly advised against in, for instance, the Global initiative for chronic obstructive lung disease (GOLD) guidelines, as it is 'difficult to perform' and 'measurements are not accurate enough'.⁴⁷ When looking at clinical trials, we find spirometry being a common outcome measure to quantify airflow obstruction and to show the effect of, for instance, systemic corticosteroids.³ Thus, the arguments to abandon spirometry from the assessment of AECOPD do not seem to be thoroughly

deliberated. Further evaluation in primary care might help identify a role for spirometry in the assessment of AECOPD.

Criteria for antibiotic treatment. Most guidelines recommend antibiotic treatment based on respiratory symptoms, and increased purulence in particular. This recommendation rests on the subgroup analyses in Anthonisens landmark study.²⁵ The special weight laid on increased purulence is supported by the increased risk of positive bacterial culture in COPD patients with purulence⁴⁸ and, recently, by Miravittles' study of predictors of treatment failure in AECOPD in patients with mild to moderate disease not treated with antibiotics.⁴⁹ However, sputum colour alone might not be sufficient to identify patients possibly benefiting from antibiotics,⁵⁰ and therefore biomarkers could be very valuable: in the study by Miravittles,⁴⁹ a CRP value >40 mg/l was found to be the strongest predictor of treatment failure. Results from another study emphasise the usefulness of the CRP test in general practice, as it was found that sputum-guided therapy alone resulted in higher prescription rates than when combined with CRP.³⁹ However, by now, CRP is only recommended in the Norwegian guideline. 'Procalcitonin', which was recommended in the German and also mentioned in the Suisse guideline, has also been found to be a promising biomarker for targeting antibiotic treatment.⁵¹ It is, however, not yet available as a point-of-care test for use in primary care. The strict clinical criteria in the Dutch guideline indicating a severe AECOPD are similar to those in the systemic inflammatory response syndrome score⁵² and in the CRB65 score.⁵³ Yet, they do not refer to supporting evidence. Although the CRB65 score can be helpful to identify severe AECOPD with high inpatient mortality,⁵⁴ it might be problematic to apply these criteria as indicators for antibiotic treatment in AECOPD.

Future perspectives and conclusion

Our results lead to the conclusion that current COPD guidelines are of little help in identifying which AECOPD patients might benefit from treatment with systemic corticosteroids and antibiotics in a primary care setting. Increased purulence has been shown to be a useful criterion for antibiotic treatment in patients with severe disease,²⁵ but we still do not know whether reliance on purulence leads to over-treatment in patients with mild to moderate disease. Despite little evidence supporting the usefulness of biomarkers, some guidelines have started to include tests in the diagnostic work-up. However, a better understanding of how COPD/AECOPD interferes with other conditions will probably be as important as establishing a test or biomarker to meet the current challenges, such as differentiation between AECOPD and other diseases. Future guidelines will surely be influenced by currently ongoing research on the use of biomarkers in AECOPD.^{55–59} Further, the new understanding of how COPD should be subclassified into phenotypes⁶⁰ may also lead to a new way of understanding the exacerbations, which may vary by phenotype. Antibiotics may be more frequently needed in a phenotype associated with chronic bronchitis than in those dominated by emphysema or when the patient can be classified as COPD-asthma overlap. We recommend that future research should, to a larger extent, focus on AECOPD in patients with mild to moderate airflow obstruction (FEV₁ predicted >50%), similar to the study by Llor *et al.*,³⁹ and consider the concern of multimorbidity in COPD patients. Moreover, we find it necessary to reconsider the uncritical way in which the use of systemic corticosteroids is presented in current COPD guidelines, and to stress the importance of developing better methods for targeting treatment with systemic corticosteroids. Such moves will be necessary to make future guidelines more helpful in primary care and to improve care for COPD patients.

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CONTRIBUTIONS

JL is the main author as she was primarily engaged in designing and conducting the study. ER performed the systematic literature search and contributed with guidance relevant for the method used in the study. HM supervised the whole work and assisted in the eligibility assessment of the search results.

COMPETING INTERESTS

The authors declare no conflict of interest.

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¹ NHS Health Education England (2014) 'Framework '15: Health Education England Strategic Framework 2014 – 2019'

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Prescribing information for Duaklir Genuair (aclidinium bromide/formoterol)

Duaklir Genuair contains two bronchodilators available as inhalation powder: aclidinium is a long-acting muscarinic antagonist and formoterol is a long-acting β_2 -adrenergic agonist. Each delivered dose (the dose leaving the mouthpiece) contains 396 micrograms of aclidinium bromide (equivalent to 340 micrograms of aclidinium) and 11.8 micrograms of formoterol fumarate dihydrate. This corresponds to a metered dose of 400 micrograms of aclidinium bromide (equivalent to 343 micrograms of aclidinium) and a metered dose of 12 micrograms of formoterol fumarate dihydrate. **Indications:** Duaklir Genuair is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). **Dose and administration:** The recommended dose is one inhalation of Duaklir Genuair 340 micrograms /12 micrograms twice daily. **Contraindications:** Hypersensitivity to the active substances or to the excipient lactose monohydrate. **Warnings and precautions:** **Asthma:** Duaklir Genuair should not be used in asthma; clinical studies of Duaklir Genuair in asthma have not been conducted. **Paradoxical bronchospasm:** In clinical studies, paradoxical bronchospasm was not observed with Duaklir Genuair at its recommended dose. However, paradoxical bronchospasm has been observed with other inhalation therapies. If this occurs, medicinal product should be stopped and other treatment will be considered. **Not for acute use:** Duaklir Genuair is not indicated for the treatment of acute episodes of bronchospasm. **Cardiovascular effects:** Patients with a myocardial infarction during the previous 6 months, unstable angina, newly diagnosed arrhythmia within the previous 3 months, QTc (Bazett's method) above 470 msec, or hospitalisation within the previous 12 months for heart failure functional classes III and IV as per the "New York Heart Association" were excluded from the clinical studies, therefore Duaklir Genuair should be used with caution in these patient groups. β_2 -adrenergic agonists may produce increases in pulse rate and blood pressure, electrocardiogram (ECG) changes such as T wave flattening, ST segment depression and prolongation of the QTc-interval in some patients. In case such effects occur, treatment may need to be discontinued. Long-acting β_2 -adrenergic agonists should be used with caution in patients with history of or known prolongation of the QTc-interval or treated with medicinal products affecting the QTc interval. **Systemic effects:** Duaklir Genuair should be used with caution in patients with severe cardiovascular disorders, convulsive disorders, thyrotoxicosis and pheochromocytoma. Metabolic effects of hyperglycaemia and hypokalaemia may be observed with high doses of β_2 -adrenergic agonists. In Phase III clinical studies, the frequency of notable increases in blood

glucose with Duaklir Genuair was low (0.1%) and similar to placebo. Hypokalaemia is usually transient, not requiring supplementation. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment (see section 4.5). Hypokalaemia increases susceptibility to cardiac arrhythmias. Due to its anticholinergic activity, Duaklir Genuair should be used with caution in patients with symptomatic prostatic hyperplasia, urinary retention or narrow-angle glaucoma (even though direct contact of the product with the eyes is very unlikely). Dry mouth, which has been observed with anticholinergic treatment, may in the long term be associated with dental caries. **Excipients:** Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. **Interactions:** **COPD medicinal products:** Co-administration of Duaklir Genuair with other anticholinergic and/or long-acting β_2 -adrenergic agonist containing medicinal products has not been studied and is not recommended. Although no formal *in vivo* drug interaction studies have been performed with Duaklir Genuair, it has been used concomitantly with other COPD medicinal products including short-acting β_2 -adrenergic bronchodilators, methylxanthines, and oral and inhaled steroids without clinical evidence of drug interactions. **Metabolic interactions:** *In vitro* studies have shown that aclidinium or its metabolites at the therapeutic dose are not expected to cause interactions with P-glycoprotein (P-gp) substrate drugs or drugs metabolised by cytochrome P450 (CYP450) enzymes and esterases. Formoterol does not inhibit the CYP450 enzymes at therapeutically relevant concentrations. **Hypokalaemic treatment:** Concomitant treatment with methylxanthine derivatives, steroids, or non-potassium-sparing diuretics may potentiate the possible hypokalaemic effect of β_2 -adrenergic agonists, therefore caution is advised in their concomitant use. **β -adrenergic blockers:** β -adrenergic blockers may weaken or antagonise the effect of β_2 -adrenergic agonists. If β -adrenergic blockers are required (including eye drops), cardioselective beta-adrenergic blockers are preferred, although they should also be administered with caution. **Other pharmacodynamic interactions:** Duaklir Genuair should be administered with caution to patients being treated with medicinal products known to prolong the QTc interval such as monoamine oxidase inhibitors, tricyclic antidepressants, antihistamines or macrolides because the action of formoterol, a component of Duaklir Genuair, on the cardiovascular system may be potentiated by these medicinal products. Medicinal products that are known to prolong the QTc interval are associated with an increased risk of ventricular arrhythmias. **Fertility, pregnancy, and lactation:** **Pregnancy:** There are no data available on the use of Duaklir Genuair in pregnant women. Studies in animals have shown fetotoxicity only at dose levels much higher than the maximum human exposure to aclidinium and adverse effects in reproduction studies with formoterol at very high systemic exposure levels. Duaklir Genuair should only be used during pregnancy if the expected benefits outweigh

the potential risks. **Breast-feeding:** It is unknown whether aclidinium (and/or its metabolites) or formoterol are excreted in human milk. As studies in rats have shown excretion of small amounts of aclidinium (and/or its metabolites) and formoterol into milk, the use of Duaklir Genuair by breast-feeding women should only be considered if the expected benefit to the woman is greater than any possible risk to the infant. **Fertility:** Studies in rats have shown slight reductions in fertility only at dose levels much higher than the maximum human exposure to aclidinium and formoterol. Nevertheless, it is considered unlikely that Duaklir Genuair administered at the recommended dose will affect fertility in humans. **Effects on ability to drive and use of machines:** Duaklir Genuair has no or negligible influence on the ability to drive and use machines. The occurrence of blurred vision or dizziness may influence the ability to drive or use machines. **Undesirable effects:** The presentation of the safety profile is based on the experience with Duaklir Genuair and the individual components. The safety experience with Duaklir Genuair comprised exposure at the recommended therapeutic dose for up to 12 months. Adverse reactions associated with Duaklir Genuair were similar to those of the individual components. As Duaklir Genuair contains aclidinium and formoterol, the type and severity of adverse reactions associated with each of the components may be expected with Duaklir Genuair. The most frequently reported adverse reactions with Duaklir Genuair were nasopharyngitis (7.9%) and headache (6.8%). Common ($\geq 1/100$ to $< 1/10$) undesirable effects included Nasopharyngitis, Urinary tract infection, Sinusitis, Tooth abscess, Insomnia, Anxiety, Headache, Dizziness, Tremor, Cough, Diarrhoea, Nausea, Dry mouth, Myalgia, Muscle spasms, Oedema peripheral, Blood creatine phosphokinase increased. Uncommon ($\geq 1/1,000$ to $< 1/100$) undesirable effects included Hypokalaemia, Hyperglycaemia, Agitation, Dysgeusia, Blurred vision, Tachycardia, Electrocardiogram QTc prolonged, Palpitations, Dysphonia, Throat irritation, Rash, Pruritus, Urinary retention, Blood pressure increased; rare ($\geq 1/10,000$ to $< 1/1,000$) undesirable effects included Hypersensitivity, Bronchospasm, including paradoxical; not known undesirable effect included Angioedema. **Pack sizes:** Carton containing 1 inhaler with 60 doses. Carton containing 3 inhalers each with 60 doses. Not all pack sizes may be marketed. **Marketing Authorisation Holder:** Almiral, S.A. Ronda General Mitre, 151, 08022 Barcelona, Spain. **Date of last revision:** December 2014. **References:** 1. Duaklir[®] Genuair[®] Summary of Product Characteristics. Barcelona, Spain: Almiral, S.A. 2014. 2. Singh D, Jones P, Bateman E, et al. Efficacy and safety of aclidinium bromide/formoterol fumarate fixed-dose combinations compared with individual components and placebo in patients with COPD (ACLIFORM-COPD): a multicentre, randomised study. *BMC Pulm Med.* 2014;14:178. 3. Singh D, Chapman KR, Make BJ, et al. LAC30-31: Effect of aclidinium bromide/formoterol fumarate fixed-dose combination (FDC) on night-time and early morning symptoms in COPD. *Eur Respir J.* 2014;44(Suppl 58):A2415.



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(▼) This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Prescribing Information for EKLIRA GENUAIR (aclidinium bromide inhalation powder)

Long-acting muscarinic antagonist available as inhalation powder. Each delivered dose (the dose leaving the mouthpiece) contains 375 µg aclidinium bromide equivalent to 322 µg of aclidinium. This corresponds to a metered dose of 400 µg aclidinium bromide equivalent to 343 µg aclidinium. **Indications:** Eklira Genuair is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). **Dose and administration:** The recommended dose is one inhalation of 322 µg aclidinium twice daily. **Contraindications:** Hypersensitivity to aclidinium bromide, atropine or its derivatives, including ipratropium, oxitropium or tiotropium, or to the excipient lactose monohydrate. **Warnings and Precautions:** **Asthma:** Eklira Genuair should not be used in asthma; clinical trials of aclidinium bromide in asthma have not been conducted. **Paradoxical bronchospasm:** As with other inhalation therapies, administration of Eklira Genuair may cause paradoxical bronchospasm. If this occurs, treatment with Eklira Genuair should be stopped and other treatments considered. **Deterioration of disease:** Aclidinium bromide is a maintenance bronchodilator and should not be used for the relief of acute episodes of bronchospasm, i.e. as a rescue therapy. In the event of a change in COPD intensity while the patient is being treated with aclidinium bromide so that the patient considers additional rescue medication is required, a re-evaluation of the patient and the patient's treatment regimen should be conducted. **Cardiovascular effects:** Cardiovascular safety profile is characterized by the anticholinergic effects. Eklira Genuair should be used with caution in patients with a myocardial infarction during the previous

6 months, unstable angina, newly diagnosed arrhythmia within the previous 3 months, or hospitalisation within the previous 12 months for heart failure functional classes III and IV as per the "New York Heart Association." Such patients were excluded from the clinical trials and these conditions may be affected by the anticholinergic mechanism of action. **Anticholinergic activity:** Dry mouth, which has been observed with anticholinergic treatment, may in the long term be associated with dental caries. Consistent with its anticholinergic activity, aclidinium bromide should be used with caution in patients with symptomatic prostatic hyperplasia or bladder-neck obstruction or with narrow-angle glaucoma (even though direct contact of the product with the eyes is very unlikely). **Excipients:** Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. **Interactions:** Co-administration of aclidinium bromide with other anticholinergic-containing medicinal products has not been studied and is not recommended. Although no formal *in vivo* drug interaction studies have been performed, inhaled aclidinium bromide has been used concomitantly with other COPD medicinal products including sympathomimetic bronchodilators, methylxanthines, and oral and inhaled steroids without clinical evidence of drug interactions. **In vitro** studies have shown that aclidinium bromide or the metabolites of aclidinium bromide at the therapeutic dose are not expected to cause interactions with P-glycoprotein (P-gp) substrate drugs or drugs metabolised by cytochrome P450 (CYP450) enzymes and esterases. **Fertility, pregnancy, and lactation:** Pregnancy: There are no data available on the use of aclidinium bromide in pregnant women. Studies in animals have shown fetotoxicity only at dose levels much higher than the maximum human exposure to aclidinium bromide. Aclidinium bromide should only be used during pregnancy if the expected benefits outweigh the potential risks. **Breast-feeding:** It is unknown whether aclidinium bromide and/or its metabolites are excreted in human milk. As animal studies have shown

excretion of small amounts of aclidinium bromide and/or metabolites into milk, a decision must be made whether to discontinue breast-feeding or to discontinue therapy with aclidinium bromide taking into account the benefit of breast-feeding for the child and the benefit of long-term aclidinium bromide therapy to the woman. **Fertility:** Studies in rats have shown slight reductions in fertility only at dose levels much higher than the maximum human exposure to aclidinium bromide. It is considered unlikely that aclidinium bromide administered at the recommended dose will affect fertility in humans. **Effects on ability to drive and use machines:** Aclidinium bromide has no or negligible influence on the ability to drive and use machines. The occurrence of headache or blurred vision may influence the ability to drive or to use machinery. **Undesirable effects:** The most frequently reported adverse reactions with Eklira Genuair were headache (6.6%) and nasopharyngitis (5.5%). Common (≥1/100 to <1/10) undesirable effects included sinusitis, nasopharyngitis, headache, cough, and diarrhoea. Uncommon (≥1/1,000 to <1/100) undesirable effects included blurred vision, tachycardia, dysphonia, dry mouth, and urinary retention. **Pack sizes:** Carton containing 1 inhaler with 30 unit doses. Carton containing 1 inhaler with 60 unit doses. Carton containing 3 inhalers each with 60 unit doses. Not all pack sizes may be marketed. **Marketing Authorisation Holder:** Almirall, S.A. General Mitre, 151, 08022 Barcelona, Spain. **MA numbers:** EU/1/12/778/001-003. Date of preparation of prescribing information: November 2014. Date of EMA approval: 24th July 2012.

References: 1. Jones PW, Singh D, Bateman ED, *et al.* Efficacy and safety of twice-daily aclidinium bromide in COPD patients: the ATTAIN study. *Eur Respir J.* 2012; 40(4):830-6. 2. Kerwin EM, D'Urzo AD, Gelb AF, *et al.* Efficacy and safety of a 12-week treatment with twice-daily aclidinium bromide in COPD patients (ACCORD COPD I). *COPD.* 2012;9(2):90-101. 3. Eklira Genuair Summary of Product Characteristics. Barcelona, Spain: Almirall, S.A.