



Report of the COPD7 Conference 2010

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OVERVIEW

This year's biennial COPD (Chronic Obstructive Pulmonary Disease) conference, COPD7, was held at the International Convention Centre, Birmingham, from 30th June to 2nd July. The event attracted over 600 delegates including respiratory specialists and other healthcare professionals (HCPs), and representatives from the pharmaceutical industry. The extensive programme, delivered by over 70 speakers, included a mixture of plenary sessions, company symposia, intimate Meet-the-Experts sessions, mini-symposia and posters. The presentations were varied and covered the latest information on the burden of COPD and approaches to treatment. In this COPD7 report, we focus on highlights from the conference.



Burden of COPD

'We are entering a brave new world' (P Calverley, UK)

The burden of COPD continues to increase, with recent statistics reporting that COPD affects the lives of 210 million people and contributes to 5% of deaths globally. (WHO 2009) Further evidence suggests that by 2030, COPD will become the 3rd leading cause of death worldwide. Despite these statistics, many of the presentations at COPD7 suggested a move away from the therapeutic nihilism felt by many HCPs treating patients with COPD, towards a more optimistic and promising approach to the future. The experienced panel of speakers hinted that approaches to treating COPD are changing, moving away from the current focus on FEV₁ towards an approach that considers the range of patient symptoms suffered by COPD patients, and encompasses refreshing new holistic treatment strategies.

The recession of 2008 continues to have significant consequences for many countries' economies, and the long-term implications on healthcare spending remain to be seen. This is concerning for HCPs and patients alike, particularly in light of recent data which show that countries that spend less on healthcare suffer from higher rates of mortality than countries that are able to invest more funds. (Stuckler et al, 2010) Professor Peter Calverley, UK reported that the annual costs for treating patients with COPD in the UK are £801–930 million, and COPD is responsible for an estimated 9% of certified sickness absence. Moreover, Professor Leonardo Fabbri from Italy added that 68.4% of patients with COPD suffer from co-morbidities, which adds significantly to the financial burden of the disease.

While COPD is known to significantly impact older age groups, it also affects people of working age. Recent data report that 26% of people with COPD in the UK aged 45–65 gave up work because of their condition, and of those remaining in work, 22.9% felt that having COPD lowered their productivity. (Fletcher et al, 2010) The COPD Uncovered survey reported that the total annual healthcare costs associated with UK COPD patients aged 45–64 was £277.7 million, and annual impaired productivity costs within this patient group were £366.2 million (Figure 1). (Baldwin et al, 2010)

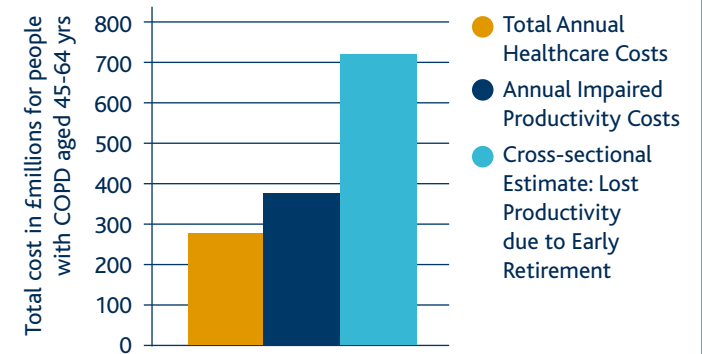


Figure 1. Total annual healthcare and impaired productivity costs in people with COPD aged 45-64 yrs, UK. Adapted from Baldwin et al, 2010.

Finding new and effective ways of managing COPD is particularly challenging in this time of limited healthcare budgets. Professor Calverley (UK) proposed that a holistic approach to COPD management, including treating each patient's symptoms with a range of targeted therapies, would be necessary to manage the disease in a more successful and cost-effective way. This was echoed by Dr Jean Borbeau (Canada) who proposed that encouraging patients to make good choices and sustain healthy behaviour would lead to cost savings.





I can't think of any better repetitive injury than smoking 20 cigarettes a day'
(J Hogg, Canada)

Key points

- COPD affects millions of people and the global burden of the disease is increasing
- COPD costs millions of pounds in terms of lost productivity and healthcare costs
- The struggling worldwide economy will make the management of COPD increasingly challenging in future years and HCPs must adopt more efficient and cost-effective management practices

References

Baldwin M, Williams P, Fletcher M, et al. A novel method to estimate the economic impact of COPD in patients of working age. COPD7 2010: Poster number 8.

Fletcher M, Upton J, Taylor-Fishwick JC, et al. COPD has significant social and economic impact on a working-age population of COPD sufferers; an international survey. Am J Res Crit Care Med. 2010;181:A4060.

Stuckler D, Basu S, McKee M. Budget crises, health, and social welfare programmes. BMJ 2010;340:c3311.

World Health Organization. COPD Fact Sheet No 315. 2009.
<http://www.who.int/mediacentre/factsheets/fs315/en/index.html>

Current challenges in COPD management

'COPD is under-diagnosed, under-treated, under-perceived' (B. Celli, USA)

Despite these alarming statistics on COPD prevalence, evidence suggests that this is not the whole story, as many cases of COPD are never diagnosed by a HCP. Recent data on prevalence modelling in one region of the UK suggests that as few as 25% of patients with COPD have been clinically diagnosed. (Benge et al, 2010)

Diagnosis of COPD

Several COPD7 presentations, including the Boehringer Ingelheim/Pfizer-sponsored symposium, suggested that under-diagnosis of COPD remains a major barrier to effective disease management. The diagnosis of COPD relies upon spirometry measurement. (GOLD 2009) In the UK, spirometry is one of the Quality and Outcomes Framework measurements for which primary care practices receive credit. Additionally, NICE

guidelines (NICE 2010) recommend spirometry for all, smokers and ex-smokers, who are aged >35 years and have a chronic cough. Despite these incentives and recommendations, many patients are never tested by spirometry. A recent study showed that the percentage of patients whose COPD was diagnosed using spirometry and regular FEV₁ measurements in 2007/2008 was as low as 14% in some primary care trusts in the UK. (Benge et al, 2010)

Part of the problem, according to Professor Bart Celli (USA), is that awareness of COPD guidelines and treatment recommendations is falling among HCPs. (Barr et al, 2005) In addition, he suggested it was important to overcome HCPs' reluctance to diagnose the disease simply because they felt nothing could be done.

In particular, mild-to-moderate COPD is poorly diagnosed, although data suggest that many patients with COPD around the world exhibit 'mild' disease. (Buist et al, 2007) In a lively symposium sponsored by Allen & Hanbury's (the specialist respiratory division of GSK), Professor Paul Jones (UK) described the development of a simple patient questionnaire (the COPD Assessment Tool, or

CAT), (Jones, et al 2009) and members of the COPD7 audience described that its use in clinical practice has confirmed that even patients with 'mild' COPD report that it can significantly affect their everyday life and mental health. Dr David Halpin (UK) suggested that closer examination of groups of patients who are typically not referred for spirometry, i.e. those who are young, female, have a low pack history of smoking, and moderately impaired lung function and quality of life, would help to improve rates of diagnosis.

Despite the evidence that treatment of COPD at an early stage is advantageous, many HCPs believe that treatment of mild COPD is unnecessary or ineffectual. However, data from the landmark UPLIFT* study have shown that even patients with moderate COPD benefitted from improved FEV₁, health status, and time to exacerbation when treated using tiotropium. (Decramer et al, 2009) If patients present at an early stage when symptomatic, HCPs are able to initiate early intervention practices such as smoking cessation advice, education, self-management, treatment of symptoms and opportunities for disease modification.

Limitations of current treatments

Even after diagnosis, the correct treatment choices must be made. While many current treatments for COPD are effective at reducing the symptoms of the disease, there remains an urgent need for new treatments that impact long-term management



*UPLIFT: Understanding Potential Long-term Impacts on Function with Tiotropium

of COPD and reduce its debilitating consequences.

Pneumonia is a co-morbidity associated with COPD. Professor Calverley (UK) presented recent data supporting that pneumonia is reported more often in patients receiving inhaled corticosteroids (ICS) than in the general COPD patient population. (Calverley et al, 2010) Data from INSPIRE* illustrated that pneumonia was more likely following an unresolved exacerbation in patients receiving the ICS fluticasone, than in patients receiving tiotropium alone. This association correlated with increased risk of hospitalisation but not mortality. Professor Calverley suggested that although HCPs should be aware of the side effects associated with ICSs, the relatively small risk of developing pneumonia should be balanced against the benefit of reduced exacerbations achieved by these drugs. He also dispelled other 'myths' regarding ICSs, citing evidence that fail to support a link with osteoporosis, (Ferguson et al, 2009) but confirming that they reduce inflammation, exacerbations and impact disease progression.

Key points

- COPD is poorly diagnosed, particularly among certain patient subgroups and in the mild to moderate stages
- Early diagnosis of COPD presents the best opportunities for successful management of the disease, and even mild to moderate cases can benefit from treatment
- Current treatments for COPD are effective, but there remains an urgent unmet need for new treatment options

*INSPIRE: Investigating New Standards for Prophylaxis in Reduction of Exacerbations

References

- Barr RG, Celli BR, Martinez FJ, et al. Physician and patient perceptions in COPD: the COPD resource network needs assessment survey. *Am J Med* 2005;118:1415.
- Benge N, Bull A, Docherty A et al. Identification and prioritisation of chronic obstructive pulmonary disease management within general practice. COPD7 2010: Poster number 9.
- Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet* 2007;370:741-750.
- Calverley PM, Stockley RA, Seemungal TA, et al. Reported pneumonia in COPD: Findings from the INSPIRE study. *Chest* 2010; Epub ahead of print.
- Decramer M, Celli B, Kesten S, et al. Effect of tiotropium on outcomes in patients with moderate chronic obstructive pulmonary disease (UPLIFT): a prespecified subgroup analysis of a randomised controlled trial. *Lancet* 2009;374:1171-1178.

Ferguson GT, Calverley PM, Anderson JA, et al. Prevalence and progression of osteoporosis in patients with COPD: results from the Towards a Revolution in COPD Health study. *Chest* 2009;136:1456-1465.

Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of COPD. 2009. www.goldcopd.com

Jones P, Harding G, Wiklund I, et al. Improving the process and outcome of care in COPD: development of a standardised assessment tool. *Prim Care Res J* 2009;18:208-215.

National Clinical Guideline Centre (NICE). Chronic obstructive pulmonary disease: Management of chronic obstructive pulmonary disease in adults in primary and secondary care. 2010. <http://guidance.nice.org.uk/CG101>

Overcoming challenges in COPD

'We have more than one element to measure this disease' (B Celli, USA)

Current FEV₁- focused guidelines

The plenary session 'Phenotypes of COPD – same FEV₁, different diseases' set the scene for a major topic of COPD7, examining whether the current FEV₁-based guidelines as defined by GOLD (Global Initiative for Chronic Obstructive Lung Disease) are sufficient to characterise this complex disease. GOLD categorises COPD into four stages according to FEV₁ measurements, and recommends treatment on a stage-specific basis (Figure 2).

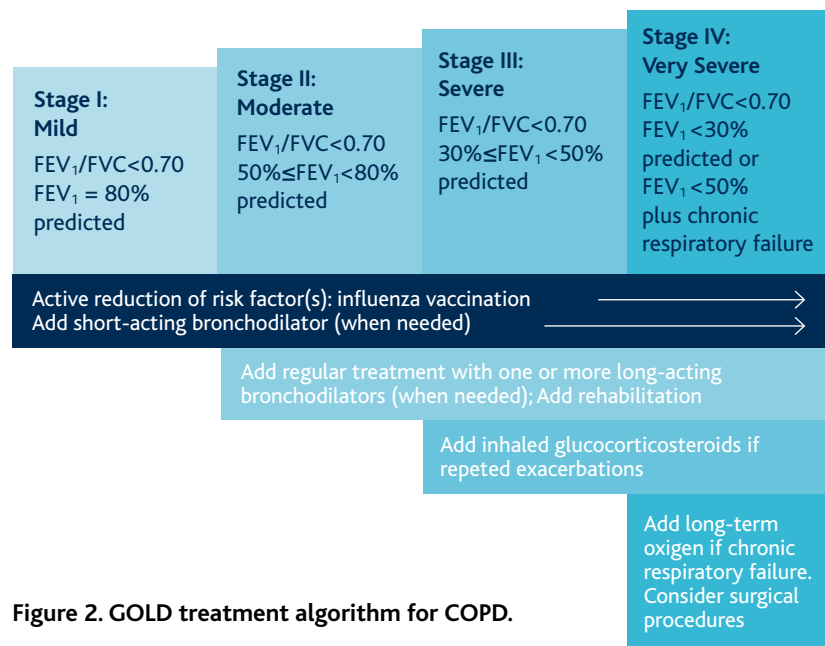


Figure 2. GOLD treatment algorithm for COPD.

Adapted with permission from the Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of COPD. 2009.

Several speakers suggested that categorising COPD based on FEV₁ alone excludes some patients from receiving the best treatment for their needs. Dr Halpin (UK) presented data showing that a sub-group of patients with FEV₁ < 50% predicted suffer from frequent exacerbations, while others do not exacerbate frequently. At the other end of the disease continuum, patients with COPD in GOLD stages I and II (mild to moderate COPD) display signs of elevated chronic inflammation. (Hogg et al, 2004) Professor Bart Celli (USA)

described that studies have shown that women with COPD generally report more breathlessness, depression and frequent exacerbations than men, even when their FEV₁ is the same.

The categorisation of COPD by FEV₁ therefore clearly has its limitations, and COPD7 delegates were interested to hear that the next update of GOLD guidelines would be moving away from strict separation of stages based on FEV₁, to allow for more fluid categorisation and treatment algorithms.

FEV₁-independent COPD phenotypes

Several speakers highlighted that within the FEV₁-defined GOLD stages of COPD, there is a huge variation in the range of symptoms and severity of COPD displayed by each patient. Recognition of different COPD phenotypes – where phenotype refers to 'a single or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes' (Han et al, 2010) – may be more useful than relying on measurements of lung function, which focus on only one aspect of the disease. Such an approach would allow for the classification of patients into distinct prognostic and therapeutic subgroups, with individuals of the same phenotype having similar underlying biologic or physiologic mechanisms. The concept of a biomarker fingerprint for identifying different COPD phenotypes was proposed, with ongoing research suggesting the markers of chronic inflammation are likely to be good indicators of disease severity and progression. (Cazzola et al, 2010)

Thus, different 'therapeutic phenotypes' could be used to drive appropriate treatment strategies. This approach is already used in clinical practice, for example recommending smoking cessation to smokers but not non-smokers, or recommending oxygen therapy for patients with hypoxia. In addition, the sub-group of patients with chronic cough and sputum have been identified as having an elevated exacerbation risk (Figure 3, Burgel et al, 2009) suggesting they could benefit from tailored treatment that reduces exacerbations.

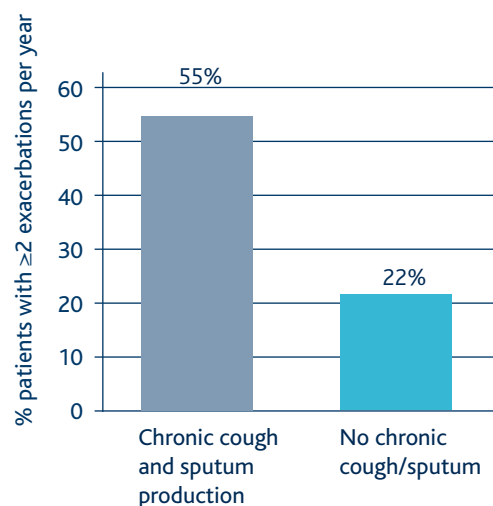


Figure 3. Elevated exacerbation risk associated with chronic cough and sputum. Adapted from Burgel PR, et al, 2009.

Treatment by phenotype

The Nycomed symposium 'Thinking Differently in COPD' clearly illustrated the concept of treatment by phenotype. The symposium focused on roflumilast, the first in a new class of phosphodiesterase 4 (PDE4) inhibitors targeted at COPD-specific inflammation. In his presentation entitled 'COPD treatments: building blocks for a different future' Professor Klaus Rabe (The Netherlands) discussed the unique mode of action of roflumilast and results from pivotal phase III clinical studies. (Fabbri et al, 2009; Calverley et al, 2009) Roflumilast is in late-stage development for the treatment of patients with severe COPD, with a history of frequent exacerbations and symptoms of chronic cough and sputum. Patients of this phenotype are known to experience more exacerbations, and therefore might benefit from treatment with drugs that reduce the frequency of exacerbations.

In phase III clinical studies, roflumilast did not significantly reduce exacerbations in an unselected population of COPD patients with severe airway obstruction. (Calverley et al, 2007) However, clinical studies in a carefully selected subgroup of patients with an increased risk of exacerbations reported that roflumilast was particularly effective at reducing moderate-to-severe exacerbations in patients with severe COPD and a history of chronic cough and sputum according to the ATS/ERS criteria for chronic bronchitis, with or without emphysema. (Figure 4, Calverley et al, 2010) Data reported in several posters at COPD7 showed that roflumilast significantly reduced exacerbations in patients of this subgroup, independent of concomitant LABA (long-acting β_2 -agonists), SAMA (short-acting muscarinic antagonist) (Small et al, 2010) or salmeterol use (McNee et al, 2010), or the use of ICS prior to randomisation. (Shale D et al, 2010) This highlights the potential for treatments to be effectively used on a phenotype-basis.

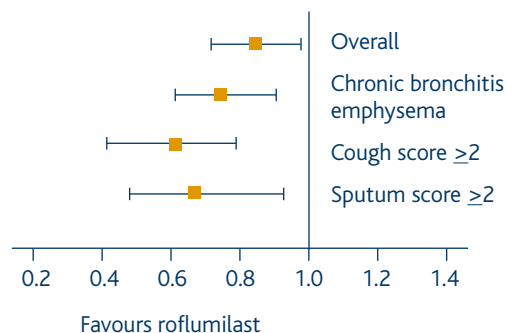
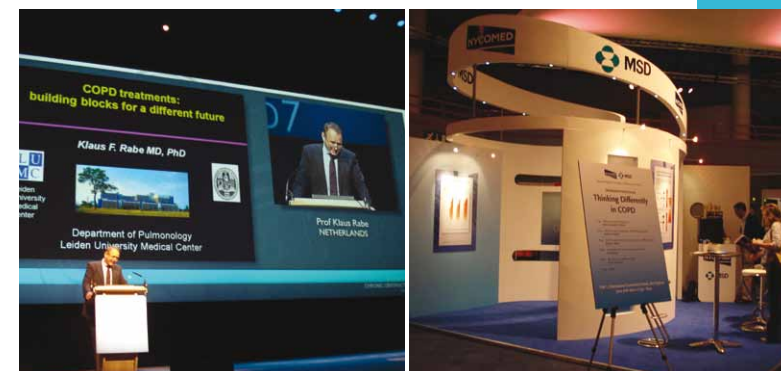


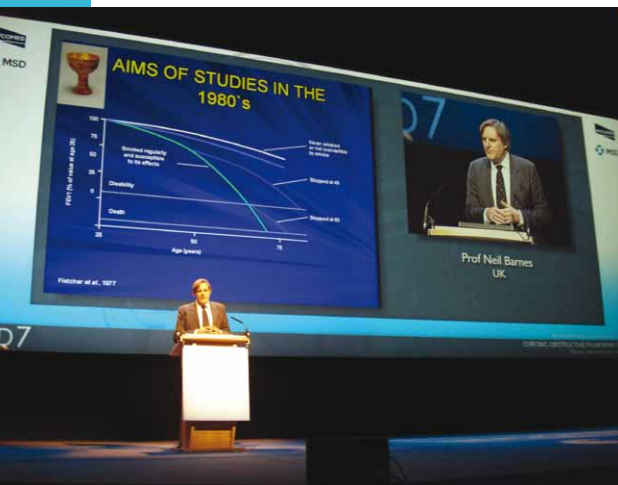
Figure 4. Effect of roflumilast treatment according to rate ratios for reduction in moderate-to-severe COPD exacerbations in patients with: chronic bronchitis with or without emphysema; cough score 2; or sputum score 2. Error bars represent 95% confidence intervals. Adapted from Calverley et al, 2010.

Treating the whole patient

In summary, several speakers at COPD7 highlighted the importance of treating the patient as a whole, targeting the right therapies to the right patient. Professor Neil Barnes (UK) suggested that pulmonologists could benefit from taking a similar approach to that of cardiologists, by treating patients with a range of medications from diagnosis of chronic illness. Professor William MacNee (UK) discussed how COPD and its co-morbidities should be treated simultaneously and described how statins were currently being assessed in clinical trials for COPD.



'Our challenge is to find out what works in each of our individual patients' (C Jenkins, Australia)



'We need to get away from thinking about individual drugs' (N Barnes, UK)

Key points

- COPD phenotypes can be identified that are not FEV₁ specific
- Tailoring treatments based on patient phenotypes may promote effective and cost-effective management of COPD
- The benefits of treating specific patient phenotypes with therapies targeted at their symptoms has been illustrated by the use of roflumilast to reduce exacerbations in patients with increased risk of exacerbations
- HCPs should consider the whole patient when devising a treatment plan, including the use of complementary therapies

References

Burgel PR, Nesme-Meyer P, Chanez P et al. Cough and sputum production are associated with frequent exacerbations and hospitalizations in COPD subjects. *Chest* 2009;135:975-982.

Calverley PM, Sanchez-Toril F, Mclvot A et al. Effect of 1-yr treatment with roflumilast in severe chronic obstructive pulmonary disease. *Am J Crit Care Med* 2007;176:154-161.

Calverley PMA, Rabe KF, Goehring UM et al. Roflumilast in symptomatic chronic obstructive pulmonary disease: two randomised clinical trials. *Lancet* 2009;374:685-694.

Calverley PMA, Martinez FJ, Goehring UM et al. Defining patient populations in COPD: experience with roflumilast. *COPD* 2010;48.

Cazzola M, Novelli G. Biomarkers in COPD. *Pulm Pharmacol Ther* 2010;Epub ahead of print.

Fabbri LM, Calverley PMA, Izquierdo-Alonso JL et al. Roflumilast in moderate-to-severe chronic obstructive pulmonary disease treated with longacting bronchodilators: two randomised clinical trials. *Lancet* 2009;374:695-703.

Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of COPD. 2009. www.goldcopd.com

Han MK, Agusti A, Calverley PM et al. COPD phenotype: The future of COPD. *Am*

J Crit Care Med 2010. Epub ahead of print.

Hogg JC, Chu F, Utokaparch S. The nature of small airway obstruction in Chronic Obstructive Pulmonary Disease. *N Engl J Med* 2004;350:2645-2653.

MacNee W, Brose M, Goehring UM et al. Roflumilast as an add-on to salmeterol – efficacy in patients with chronic bronchitis. *COPD* 2010: Poster 44.

Shale D, Calverley P. Efficacy of roflumilast in patients receiving concomitant treatments for COPD over 12 months. *COPD* 2010: Poster 46.

Small I, Freeman D, Kaplan A. Potential of roflumilast for COPD – which patients would benefit? *COPD* 2010: Poster 47.