



JOURNAL CLUB

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Prediction of mortality in patients with chronic obstructive pulmonary disease with the new Global Initiative for Chronic Obstructive Lung Disease 2017 classification: a cohort study

Anne Gedebjerg, Szimonetta Komjáthiné Szépligeti, Laura-Maria Holm Wackerhausen, et al.

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Since 2007, chronic obstructive pulmonary disease (COPD) has been classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification system, based on patients' FEV₁ thresholds compared with predicted normal values.

To address the complexity of the disease, and improve understanding of its effect on patients, the 2011 GOLD revision presented an ABCD classification system, combining respiratory symptoms, risk of exacerbation, and airflow limitations as indicated by FEV₁.

While guiding treatment, the 2011 classification does not predict mortality of respiratory outcomes any better than the GOLD 2007 classification.

GOLD 2017 further subdivided its main ABCD groups according to spirometric 1-4 staging. In this Danish cohort study of 33,765 patients with COPD, Gedebjerg and colleagues sought to evaluate the predictive ability of the new GOLD 2017 ABCD classification for all-cause and respiratory mortality compared to the GOLD systems of 2007 and 2011.

The paper concluded that the GOLD 2017 classification based on ABCD groups did not predict all-cause and respiratory mortality better than the 2007 and 2011 GOLD classifications. However, when 16 subgroups (1A to 4D) were defined, the new classification predicted mortality more accurately than the previous systems. None of the GOLD classifications appeared to have sufficient discriminatory power to be used as a standalone tool for risk classification of mortality in patients with COPD.

Quadrupling inhaled glucocorticoid dose to abort asthma exacerbations

Tricia McKeever, Kevin Mortimer, Andrew Wilson, et al.

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Acute exacerbations of asthma can be alarming for patients, cause illness, can be fatal, and account for a large proportion of costs related to asthma.

While asthma control has been shown to improve in patients with self-management plans, a previously recommended step of doubling the dose of inhaled glucocorticoids has been shown to be ineffective at preventing acute exacerbations. In 2016 a Cochrane review concluded that it is unlikely that increasing the dose of inhaled glucocorticoids reduces the odds of systemic glucocorticoid use or hospitalisation or shortens recovery time.

A randomised, unblinded, pragmatic, multicentre trial comprising 1,922 participants (adults and adolescents) was commissioned by the Health Technology Assessment Programme of the National Institute for Health Research in the UK. McKeever, Mortimer and colleagues tested the hypothesis that, when asthma control started to deteriorate, a temporary increase in the dose of inhaled glucocorticoids by a factor of four would reduce the use of oral glucocorticoids for asthma compared with a plan that did not include this step.

The quadrupling group showed (1) fewer severe asthma exacerbations (2) a higher frequency of treatment-related adverse events, such as oral candidiasis, but (3) no significant between-group differences in the incidence of pneumonia.

Given the potential benefit with regard to preventing exacerbations and considering the established toxicity associated with inhaled glucocorticoids as well as the biases that may have been introduced in this study by the absence of blinding, the authors urge that individual

practitioners, patients and guideline committees consider whether the magnitude of the reduction achieved is clinically meaningful.

Guidelines for the diagnosis and management of asthma: a look at the key differences between BTS/SIGN and NICE

John White, James Y Paton, Robert Niven, Hilary Pinnock, on behalf of the British Thoracic Society.

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doi: 10.1136/thoraxjnl-2017-211189

There are at least two national guidelines for the diagnosis and monitoring, and management of asthma in England: the British Thoracic Society/Scottish Intercollegiate Guideline Network (BTS/SIGN) guidelines, last published in 2016, and the National Institute for Health and Care Excellence (NICE) guideline on asthma diagnosis and monitoring and chronic asthma management, published in 2017.

While the evidence base used by both guideline development groups is broadly the same, the recommendations are based on significantly different methodology. BTS/SIGN and NICE methodology both employ robust critical appraisal of the literature, but methodologies diverge after that: BTS/SIGN considers pragmatic studies to ensure their guidelines provide clinically robust recommendations, while NICE employs health economic modelling, with interpretation supported by advice from a multidisciplinary Guideline Development Group.

To help clinicians in the care of people with asthma, the BTS has issued a statement, written by John White, James Paton, Robert Niven and Hilary Pinnock, which considers the similarities and differences.

The statement provides context for these differences in the areas of diagnosis and pharmacological management, with the latter broken down into key areas: treatment at diagnosis, the introduction of leukotriene receptor antagonist after low-dose inhaled corticosteroids, maintenance and reliever therapy, treatment beyond combined inhaler therapy and issues in managing asthma in children.

The statement also highlights recommendations in the BTS/SIGN guidelines regarding aspects of asthma management not addressed in the NICE guidelines, including guidance on inhaler devices, the management of acute asthma attacks in both adults and children, the management of difficult asthma, guidance on asthma in adolescents, in pregnant women and on occupational factors.

Factors influencing treatment escalation from long-acting muscarinic antagonist monotherapy to triple therapy in patients with COPD: a retrospective THIN-database study

John R Hurst, Maria Dilleen, Kevin Morris, Sian Hills, Birol Emir and Rupert Jones

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doi: 10.2147/COPD.S153655

Inappropriate use of inhaled corticosteroids (ICSs) in patients with COPD can have serious clinical implications, and contributes to the economic burden of COPD. In this retrospective non-interventional database study, John Hurst from University College London and colleagues examined the records of 14,866 COPD patients who received long-acting muscarinic antagonist (LAMA) monotherapy as their initial treatment, and recorded the time until treatment was escalated to 'triple therapy', a combination of LAMA plus ICS and a long-acting beta-agonist (LABA).

In total, 6,482 patients (43.6%) received treatment escalation. Of these patients, 85% of escalations occurred within two years of starting LAMA monotherapy, with a median time to escalation of 155 days. In multivariate analysis, an acute COPD exacerbation was the variable most strongly associated with treatment escalation (hazard ratio: 2.11). Other variables positively associated with escalation were a diagnosis of asthma, greater breathlessness according to the MRC Dyspnoea

scale, contact with healthcare services and number of short-acting bronchodilator prescriptions.

Results were analysed according to patients' GOLD grade, based on the 2011/2013 guidelines (which stratified patients based on FEV₁ and MRC score) and 2017 guidelines (derived from MRC score and number of exacerbations). Fewer treatment-escalated patients were classified as groups C or D under the 2017 strategy, compared with the 2011/2013 edition. This suggests that many patients were being overtreated according to the GOLD 2017 strategy; reviewing patients' treatment in the light of the most recent GOLD strategy could reduce inappropriate prescription of these powerful drugs.

Factors associated with appropriate inhaler use in patients with COPD – lessons from the REAL survey

David Price, Dorothy L Keininger, Boomi Viswanad, Matthias Gasser, Susann Walda, and Florian S Gutzwiller
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doi: 10.2147/COPD.S14904

Self-management of COPD is dependent upon patients' ability to self-administer inhaled medication on a daily basis, yet between 28% to 68% of patients may be using their inhalers incorrectly. The Real-life Experience and Accuracy of inhaLer use (REAL) study was a qualitative survey conducted by David Price from the University of Aberdeen (and supported by Novartis), enrolling 764 COPD patients from nine countries. Approximately 30% of respondents reported not receiving any training on inhaler use, but those who did receive training were significantly more confident that they were receiving a full medication dose. Among trained patients, the strongest preference was for technique to be demonstrated personally – 83% said this technique was 'very helpful', compared with 58% for video, 51% for instructions and 34% for leaflets. A total of 29% of patients had not had their inhaler technique checked in the past two years, but those who had been checked were more confident that they received the full doses. When results were stratified by inhaler device, patient confidence was higher with Breezhaler® vs Ellipta® or Respimat® ($p=0.001$ for both), but the difference between Breezhaler and Genuair® did not appear to be significant. This study underlined the importance of teaching inhaler technique in increasing patients' confidence and capacity to self-manage, and provided evidence that this teaching should be delivered in person wherever possible.

Assessing adherence to inhaled medication in asthma: impact of once-daily versus twice-daily dosing frequency. The ATUAD study

Luis Pérez de Llano, Abel Pallares Sanmartin, Francisco Javier González-Barcala, et al.
J Asthma 2018; published online 20 February 2018
doi: 10.1080/02770903.2018.1426769

Adherence to asthma treatment is reported to be around 50%, even in patients with difficult-to-manage asthma. This study by Luis Pérez de Llano (Hospital Lucus Augusti, Lugo, Spain) and colleagues recruited adults with asthma from six outpatient asthma clinics in tertiary hospitals in Spain. A total of 180 patients attended the two study visits, six months apart. Eighty-six followed a once-daily inhaled medication regimen, while 94 followed the more common twice-daily strategy. Adherence, measured by the Test of Adherence to Inhalers (TAI), increased from visit one to visit two in both groups but these differences were insignificant. However, at the second visit 29.8% of patients on once-daily treatment scored <50 points on the TAI (indicating non-adherence), compared with 46.9% in the twice-daily group ($p=0.01$). This was supported by the electronic prescription refill rate, which was <80% (again, indicating non-adherence) in 22.6% of once-daily patients and 37.5% of the twice-daily group. Interestingly, there were no

differences in clinical outcomes between adherent and non-adherent groups. The authors caution that although once-daily treatment may support adherence, missing a single dose means missing a whole day of treatment, which could lead to worse clinical outcomes. Nonetheless, this study seems to indicate that once-daily dosing may lead to increased adherence to asthma maintenance treatment.

Short-term respiratory effects of e-cigarettes in healthy individuals and smokers with asthma

Andreas S Lappas, Anna S Tzortzi, Efstathia M Konstantinidi, et al.
Respirology 2018;23:291-7
doi:10.1111/resp.13180

With electronic cigarettes (e-cigarettes) rising in popularity as effective smoking cessation aids, research has focused on the health effects associated with using these devices. In particular, how they affect the lung function of asthmatic patients is of important consideration. In this study, Andreas S Lappas and colleagues aimed to explore the differences between the respiratory effects of e-cigarette vapour in both healthy and asthmatic patients who smoke. The study exposed 27 healthy smokers (HS) and 27 smokers with mild asthma (MA) to controlled conditions, in which the participant use a third-generation e-cigarette without the coil or e-liquid (meaning vapour was not produced), and experimental conditions (in which the device included all components and vapour was produced) for five minutes. The participants' impulse oscillometry impedance, lung resistance, reactance and fractional exhaled nitric oxide (FeNO) were then measured at 0, 15 and 30 minutes after each condition. Results highlighted that control sessions produced no significant changes in lung function, while experimental sessions induced a significant increase in respiratory system resistance. In addition, the MA group exhibited higher baseline values and a greater respiratory effect after e-cigarette use compared with the HS subjects. This experiment highlighted single sessions of e-cigarette vaping induces mechanical and inflammatory effects on the respiratory system. These were intensified and more prominent in smokers with asthma.

The role of anxiety sensitivity-physical concerns in terms of quit day withdrawal symptoms and cravings: A pilot test among smokers with asthma

Andrienne L Johnson, Emily M O'Bryan, Kristen M Kraemer, et al.
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doi: 10.1080/02770903.2018.1437175.

Compared with their non-asthmatic counterparts, asthmatic patients often experience increased risk of relapse during the first months of their quit attempt due to prolonged withdrawal symptoms and cravings. Such experiences are believed to be linked to anxiety sensitivity (AS), a cognitive-affective vulnerability factor defined as the fear of arousal-related sensations due to perceived negative consequences. In this study, Dr Andrienne L Johnson and colleagues aimed to explore the predictive ability of precessation AS-physical concerns on the likelihood of withdrawal symptoms and cravings during a patient's quit attempt. Controlling for the effects of cognitive and social domains of AS, this study specifically explored the effect of AS physical-concerns on the experience of these symptoms. Results showed that increased AS physical-concerns at precessation significantly predicted greater quit-day withdrawal symptoms and urge to smoke. The researchers concluded that asthmatic smokers are more likely to experience quit-day withdrawal symptoms if they experience AS-physical concerns. Based on this, AS concerns should be targeted as a smoking cessation strategy to help avoid increased withdrawal symptoms and cravings in asthmatic patients. Nicotine replacement therapies should also be optimised to help combat the experience of these symptoms.



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