



# JOURNAL CLUB

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MAY 2018 | KEY PAPER SUMMARIES

## The use of electronic alerts in primary care computer systems to identify the excessive prescription of short-acting beta<sub>2</sub>-agonists for people with asthma: a systematic review

Shauna McKibben, Anna De Simoni, Andy Bush, et al.  
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Asthma is the most common long-term condition in the UK, with a prevalence of 6% in 2016–17. Approximately 5.4 million people currently receive treatment for the condition in the UK, and in 2015–16 there were an estimated 1.4 million asthma-related admissions to hospital in England and Wales.

Of 195 deaths from asthma between 2012 and 2013, the National Review of Asthma Deaths (NRAD) reported that 39% of these patients had been prescribed more than 12 short-acting beta<sub>2</sub>-agonist inhalers (SABAs) in the previous year, and 4% had been prescribed more than 50.

Given that patients with good asthma control have less need for SABAs and require no emergency visits, it was recommended, after the publication of NRAD, that there be an electronic surveillance of SABA-prescription-refill frequency to alert clinicians to overuse. McKibben and colleagues from Asthma UK Centres for Applied Research in London and Southampton undertook a systematic review of MEDLINE, CINAHL, Embase, Cochrane and Scopus databases for randomised controlled trials between 2001 and 2015 using electronic alerts to signal SABA overuse in primary care.

They screened 2,035 articles and four trials involving both adults and children, and only included computer support systems that incorporated an alert initiated by excessive prescribing or dispensing of SABAs for asthma.

The analysis found that electronic alerts, when delivered as a multicomponent intervention in an integrated healthcare system, have the potential to successfully identify and reduce excessive SABA prescribing. Due to variations in healthcare systems, intervention design and outcomes measurements in the studies considered, further research is needed to establish optimal design of alerting systems.

## Chronic airway obstruction in a population-based adult asthma cohort: prevalence, incidence and prognostic factors

Helena Backman, Sven-Arne Jansson, Caroline Stridsman, et al.  
*Respir Med* 2018;138:115–22  
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People with asthma may develop chronic airway obstruction (CAO). Its prevalence in patients recruited from hospitals and primary care ranges from 29% to 60%, and from 19% to 32% in population-based samples. The incidence of CAO has not been recorded, and risk factor patterns for prevalent CAO among asthmatics are conflicting.

Asthma-COPD overlap (ACO), proposed by joint Global Initiative for Asthma and GOLD guidelines, lacks an accepted definition, and it is unclear whether the term is a distinct disease entity or used to describe the co-existence of both asthma and COPD. Whichever it may be, it is important to study the natural history of ACO, so as to better define management and treatment of those affected.

The aims of this study were to estimate prevalence and incidence of CAO in a large population-based adult asthma cohort,

and to study risk factors for both prevalent and incident CAO.

The asthma cohort comprised 2,055 adults aged 19–72 years, and the study was run between 1986 and 2001. CAO was defined as post-bronchodilator FEV<sub>1</sub>/FVC < 0.7. The cohort was invited to a clinical follow-up involving interview, spirometry and blood sampling in 2012–2014, of whom 983 attended.

The study concluded that the prevalence of CAO at study entry level was 11.4%. The incidence rate was 16 per 1,000 per year, meaning the majority did not develop CAO. Those with CAO had higher levels of neutrophils and greater incidence of heart disease. Risk pattern factors for both prevalent and incident CAO were similar, and corresponded to that of general population COPD patients, namely, smoking, older ages and male sex. There was nothing in the findings to suggest ACO is a specific disease entity.

## ‘Exacerbation-free time’ to assess the impact of exacerbations in patients with chronic obstructive pulmonary disease (COPD): a prospective observational study

Lonneke M Boer, Erik W Bischoff, Xandra Borgjink, et al.  
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Exacerbation frequency is a frequently used indicator in COPD studies. However, this may not fairly reflect the effects of every intervention. For example, self-management strategies are often not intended to prevent exacerbations occurring, but to reduce their severity. Boer and colleagues from Nijmegen in the Netherlands therefore propose considering the total amount of time a patient suffers from exacerbations, rather than the simple frequency.

This study was a secondary analysis of two prospective cohort studies, one in primary care and one in an outpatient setting. Data from 166 patients was included. In patients with < 3 exacerbations per year, the correlation between exacerbation frequency and exacerbation-free time was strong, but this was not the case for those with ≥ 3 exacerbations per year.

Medical Research Council (MRC) category was related to exacerbation frequency, and to some extent exacerbation-free time. Patients in MRC category 1 had more exacerbation-free time than those in category 3, but there was no significant difference between patients in categories 2 and 3. Current smokers also had less exacerbation-free time, but not a higher exacerbation frequency, than ex-smokers or never-smokers. Correlation between exacerbation frequency and health-related quality of life scores was weak. However, greater exacerbation-free time was related to a higher quality of life score.

This suggests that exacerbation-free time and exacerbation frequency are two distinct indicators in COPD, particularly in smokers and frequent exacerbators. The greater correlation of exacerbation-free time with quality of life may indicate this is a more patient-centred outcome than exacerbation frequency, which has relevance for clinical practice as well as research.

## Occupational exposures and 20-year incidence of COPD: the European Community Respiratory Health Survey

Theodore Lytras, Manolis Kogevinas, Hans Kromhout, et al.  
*Thorax* 2018; published online 24 March 2018  
[doi.org/10.1136/thoraxjnl-2017-211158](https://doi.org/10.1136/thoraxjnl-2017-211158)

Smoking is a well-known risk factor for COPD, but the role of occupational exposure to other irritants is less well characterised. Few studies have prospectively assessed the association of occupational exposure with incidence of COPD. The European Community Respiratory Health Survey (ECRHS) is a longitudinal population-based study with a long follow-up duration, and this paper by Theodore Lytras (Barcelona, Spain) and colleagues analysed the ECRHS data to examine the effect of occupational exposure on COPD incidence after 20 years of follow-up.

In total, 3,443 participants were analysed, originating from 24 study centres in 12 countries. Participants were enrolled in 1991–1993, and followed up in 1998–2002 and again in 2010–2012. Anyone reporting current asthma was excluded from the analysis.

After adjusting for covariates, there was a significant association between biological dust exposure and COPD incidence. There was also a significant effect for all pesticides, specifically insecticides; however, these effects were based on a small number of cases. Exposure to 'gases and fumes' was also significant, but there was no significant effect associated with mineral dust or 'vapours, gases, dusts and fumes' overall. There was weak evidence of a dose–response relationship for biological dust, but the intensity of exposure did not affect results for any other irritants.

This was the first study to show a link between occupational exposure to biological dust and increased incidence of spirometrically determined COPD. It also supported previous studies linking pesticide exposure with respiratory disease. As worldwide smoking prevalence declines, the role of occupational exposure may become more important and should be critically re-examined.

Researchers concluded that smoking duration may provide the strongest risk estimate of COPD than other defining parameters of tobacco exposure. This may suggest that smoking duration should be optimised as a defining factor of tobacco exposure in epidemiological studies to accurately represent the association between smoking and COPD. epidemiological studies to accurately represent the association between smoking and COPD.

## Intensified therapy with inhaled corticosteroids and long-acting $\beta_2$ -agonists at the onset of upper respiratory tract infection to prevent chronic obstructive pulmonary disease exacerbations. A multicenter, randomized, double-blind, placebo-controlled trial

Daiana Stolz, Hans H Hirsch, Daniel Schilter, et al.  
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Upper respiratory tract infections (URTI) are strongly associated with COPD exacerbations, resulting in hospital admissions and increasing the risk of mortality. Use of intensified combination therapy, involving inhaled corticosteroids (ICS) and long-acting  $\beta_2$ -agonists (LABA), at the onset of URTI symptoms may help reduce their effect in COPD patients. In this study, researchers explored the efficacy of ICS/LABA therapy at the onset of URTI symptoms in COPD patients by measuring the occurrence of COPD exacerbations. They conducted a multicentre, randomised, double-blind, placebo-controlled trial in which 450 patients with stable, moderate to very severe COPD were tested. Participants were randomised into two conditions in which they were provided either an intensified dose of ICS/LABA or a placebo. They were instructed to take the medication twice daily for 10 days at the onset of URTI symptoms. Findings showed that intensified ICS/LABA therapy did not significantly decrease the incidence of COPD exacerbations when compared with placebo therapy (14.6% vs. 16.2%, respectively). However, the risk of severe exacerbation decreased by 72% in the ICS/LABA group. Researchers therefore concluded that use of intensified combination therapy with ICS/LABA at the onset of URTI symptoms does not decrease the incidence of COPD exacerbations. However, it may help manage the severity of exacerbation experienced.

## Smoking duration alone provides stronger risk estimates of chronic obstructive pulmonary disease than pack-years

Surya P Bhatt, Young-il Kim, Kathy F Harrington, et al.  
*Thorax* 2018;73:414–21  
[doi.org/10.1136/thoraxjnl-2017-210722](https://doi.org/10.1136/thoraxjnl-2017-210722)

Tobacco smoking is known to be one of the greatest risk factors for COPD. When comparing the strength of association between COPD and smoking, the parameters used to define tobacco exposure often explore the amount smoked over a long period of time (i.e. pack-years). However, other factors, such as the duration of tobacco smoking, may provide a more representative depiction of tobacco exposure than those currently used. In this study, Dr Surya Bhatt and colleagues aimed to examine the relative contributions of pack-years, cigarettes smoked per day and duration on the development of COPD, particularly its effect on airflow obstruction. They conducted a cross-sectional study analysing data from a large multicentre cohort, COPDGene, including 10,187 subjects. Findings showed that the parameter most associated with estimates of COPD (e.g. FEV1) was smoking duration. In particular, smoking duration produced the greatest adjusted effect size in airflow obstruction, CT emphysema and respiratory morbidity than cigarettes/day and pack-years.



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