

Evidence in Practice

There are just not enough hours in the day to read all the research journals, even if you wanted to. This section of the *BJPCN* – Evidence in Practice – will keep you on top of relevant research without having to spend hours in the library.

Each journal review gives you a bite-size summary of new research, pulling out key points for primary care and recommending the action that you might consider taking.

WALKING AND CYCLING REDUCES COPD EXACERBATIONS

Patients with chronic obstructive pulmonary disease (COPD) who take regular physical activity are less likely to be admitted to hospital and have a lower risk of death than those who are more sedentary.

A 20-year follow-up study of more than 15,000 Danish people found 2,386 individuals with COPD. After adjusting for confounders, including severity of disease, those with the disease who walked or cycled for two hours a week or more had a 30-40% lower risk of hospital admission for their condition and of respiratory mortality. Low, moderate and high levels of regular physical activity were associated with an adjusted lower risk of all-cause mortality (hazard ratio (HR) 0.76, 95% CI 0.65 to 0.90) and respiratory mortality (HR 0.70, 95% CI 0.48 to 1.02). There was no dose-response relationship.

ACTION

People with COPD who perform some level of regular physical activity have a lower risk of both COPD admissions and mortality. Patients with COPD should be encouraged to maintain or increase their levels of regular physical activity.

Thorax 2006; 61: 772-8.



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SMOKERS HAVE A 25% CHANCE OF DEVELOPING COPD



Smokers have a 25% chance of developing chronic obstructive pulmonary disease (COPD), according to a major long-term follow-up study.

The study followed up 8,000 people over a 25-year period. They were aged 30-60 at baseline. Two-thirds of the study group (5,280; 66%) were smokers, 1,252 used to smoke, while the remaining 1,513 had never smoked.

At the end of the 25 years, the researchers found that 40% of smokers had some signs of COPD. One-quarter (25%) of smokers who had no signs of COPD at the beginning of the period had clinically significant COPD. A total of 2,900 people had died, including 109 who had died from COPD, of whom only 2 were non-smokers and 7 were ex-smokers. 90% of those who died were smokers at the start of the study.

Of the ex-smokers, none developed severe COPD. Almost 100% of male non-smokers continued to have good lung function. Far fewer smokers – 60% – continued to have good lung function throughout the study.

ACTION

Yet more evidence for us to encourage patients to stop smoking. In patients who find it impossible to stop, it is important to monitor lung function to detect deterioration promptly.

Thorax 2006; 61: 935-939.



SMOKING CESSATION CENTRAL TO IMPROVING PROGNOSIS OF PATIENTS WITH RESPIRATORY DISEASE

Smoking cessation should be a high priority and an integral component in the management of all patients with respiratory diseases, recommended European Respiratory Society Task Force guidelines published recently.

The task force reviewed currently available evidence and recommended that patients with respiratory disease have a greater and more urgent need to stop smoking than the average smoker, so it is important to take a proactive and continuing role with motivating them to stop and in providing treatment to aid smoking cessation.

Smoking cessation treatment should be integrated into the management of the patient's respiratory condition. Therapies should include pharmacological treatment (nicotine replacement therapy, bupropion or varenicline) combined with behavioural support. Health professionals managing patients with respiratory diseases should have appropriate training in smoking cessation.



Sheila Terry/Science Photo Library

ACTION

Encouraging smoking cessation is important for all of our patients but these guidelines emphasise the particular and pressing need to encourage patients with respiratory conditions to stop smoking. We should always check whether or not patients smoke and for those who do, integrate a smoking cessation strategy into their treatment.

Eur Respir J 2007; **29**: 390-417.

STATINS ASSOCIATED WITH REDUCED MORTALITY IN COPD

Treatment with statins was associated with improved survival after a COPD exacerbation, while inhaled corticosteroids appeared to further increase the survival benefit, according to a study.

The retrospective study followed up 854 consecutive patients (mean age 70.8 yrs; 51.5% female) with a diagnosis of COPD exacerbation after discharge from a Norwegian teaching hospital. During a median follow-up of 1.9 yrs, during which 333 patients died, the crude mortality rate was 110 per 1,000 person-years in patients treated with statins compared to 191 in patients not treated with statins.

Statin treatment was associated with a 43% reduction in mortality, with a hazard ratio for statin users versus statin nonusers of 0.57 (95% confidence interval 0.38–0.87) after adjusting for sex, age, smoking, pulmonary function and co-morbidities. The risk of death was lower in patients taking both statins and inhaled corticosteroids (HR 0.39 (0.22–0.67) for the combined treatment with statins and ICS compared with neither of these treatments) compared to 0.75 (0.58–0.98) for ICS only and 0.69 (0.36–1.3) for statins only.

The Norwegian researchers believe the reason for the benefit they saw with statins could be the presence of undiagnosed ischaemic heart disease, which is common in people with COPD.

ACTION

The study reminds us of the importance of checking all aspects of a patient's health – including signs of CVD in patients with COPD – and treating all risk factors appropriately. However, this was a cohort study, so randomised studies are needed to confirm the finding.

Eur Respir J 2007; **29**: 279-283.

ALLERGIC RHINITIS IMPAIRS QUALITY OF SLEEP

Allergic rhinitis (AR) – both intermittent and persistent – can significantly impair quality of sleep, warns a nation-wide study.

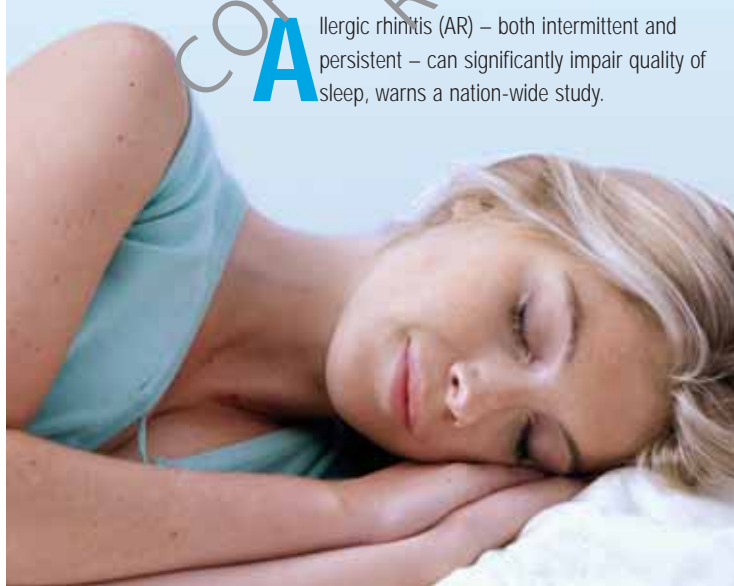
In the study, a representative sample of 260 French ear, nose and throat and allergy specialists enrolled 591 patients with AR of at least one year's duration. Sleep disorders, sleep quality, and AR were assessed using validated tools (Sleep Disorders Questionnaire, Epworth Sleepiness Scale, and Score for Allergic Rhinitis). The severity of AR was assessed using the Allergic Rhinitis and its Impact on Asthma classification.

The results showed that all dimensions of sleep were impaired by AR, particularly by severe AR. Both intermittent and persistent AR had similar effects on sleep.

ACTION

These data underline the impact that AR can have on sleep and highlight the need for healthcare professionals to ask patients about how they sleep and to provide treatment that improves AR symptoms sufficiently to improve sleep quality.

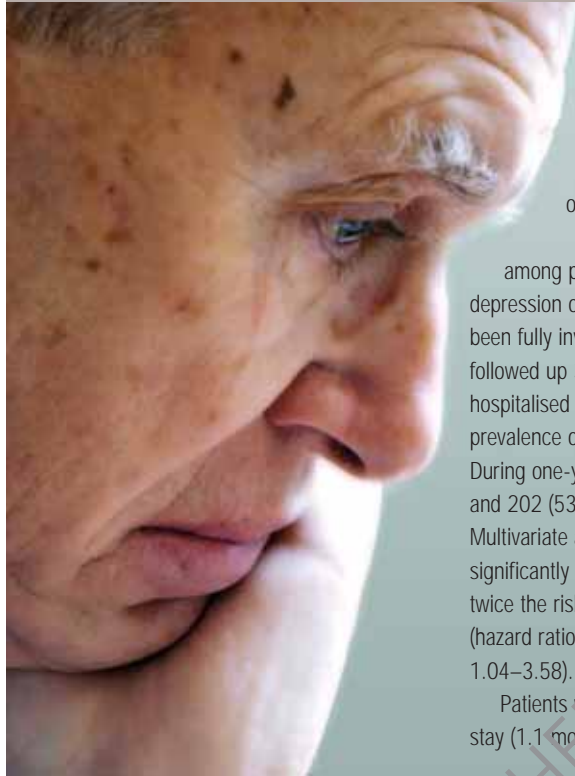
Arch Intern Med 2006; **166**: 1744–1748.



AI Photo/Science Photo Library



DEPRESSION IS ASSOCIATED WITH POORER SURVIVAL IN COPD



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Patients with COPD who also suffer from depression have poorer survival, suggesting that interventions designed to reduce depressive symptoms may improve outcomes.

Depression is, not surprisingly, common among patients with COPD, but the impact of depression on COPD outcomes has not previously been fully investigated. A prospective cohort study followed up 376 consecutive patients with COPD hospitalised for acute exacerbations for one year. The prevalence of depression at admission was 14.1%. During one-year follow-up 57 patients (15.2%) died, and 202 (53.7%) were readmitted at least once. Multivariate analyses showed that depression was significantly associated with mortality, with nearly twice the risk of death in patients who were depressed (hazard ratio, 1.93; 95% confidence interval, 1.04–3.58).

Patients who were depressed also had longer index stay (1.1 more days; $p = 0.02$) and total hospital stay

(3.0 more days; $p = 0.047$), were more than twice as likely to be still smoking at 6 months (odds ratio 2.30; 95% confidence interval, 1.17–4.52), and had 12% to 37% worse symptoms, activities, and impact scores at the index hospitalisation and one year later, even after controlling for chronicity and severity of COPD, co-morbidities, and behavioural, psychosocial, and socioeconomic variables.

ACTION

This study demonstrates that depression may affect a range of outcomes in COPD. Interventions that reduce depressive symptoms may potentially be beneficial. Trials of antidepressant and psychological interventions should provide conclusive evidence of improved survival, quality of life, and self-management behaviour and reduced health care utilisation.

Arch Intern Med 2007; **167**: 60-67.

SALMETEROL/FLUTICASONE COMBINATION REDUCES EXACERBATIONS IN SEVERE COPD

Salmeterol/fluticasone combination therapy reduces exacerbations in patients with severe COPD more than salmeterol alone, according to the results of a large study. However, patients given combination therapy experienced significantly more pneumonia.

Prevention of exacerbations is an important goal in the treatment of COPD. After a four-week run-in period, 994 clinically stable patients were randomised to one of two treatments: salmeterol/fluticasone combination (50/500 mcg twice daily) or salmeterol (50 mcg twice daily) for 44 weeks.

The number of exacerbations was significantly lower with combination therapy than with salmeterol alone (334 vs 464; $p < 0.0001$). The annualised rate of moderate and severe exacerbations per patient was 0.92 with combination therapy and 1.4 with salmeterol, corresponding to a 35% decrease.

The mean time to first exacerbation was significantly longer in the combination therapy group compared with that of the salmeterol group (128 vs 93 days, $p < 0.0001$). Other endpoints, including health-related quality of life, peak expiratory flow, and



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use of rescue medication, were also significantly improved in the combination therapy group. Both treatments were well tolerated, but there was disparity regarding cases of suspected pneumonia (7 in the salmeterol group vs 23 cases in the salmeterol/fluticasone group).

ACTION

This study demonstrates that combination therapy with salmeterol/fluticasone compared with salmeterol monotherapy significantly reduces the frequency of moderate/severe exacerbations in patients with severe COPD. An editorial accompanying this paper noted that only a small minority of patients with COPD had a clinically noticeable improvement in health status with inhaled steroids. It suggested that decisions to initiate an inhaled steroid with a long-acting beta-agonist should focus on severely symptomatic and exacerbation-prone patients.

Am J Respir Crit Care Med 2007; **175**: 144-149.



WAIST CIRCUMFERENCE IS BETTER PREDICTOR OF LUNG FUNCTION THAN BMI



Ian Hooton/Science Photo Library

Waist circumference was consistently associated with pulmonary function across all BMI categories in a recent cross-sectional study of normal-weight, overweight and obese adults.

Obesity is becoming a serious public health issue and is related to lung dysfunction. The objective of this study was to determine the predictability of waist circumference and BMI for pulmonary function in adults with and without excess body weight. It included 1,674 adults aged 18 years and over.

Results showed that waist circumference was negatively associated with forced vital capacity and forced expiratory volume in 1 second (FEV₁) – so as waist circumference increased, these measures of lung function decreased. These associations were consistent across sex, age, and BMI categories. On average, a 1 cm increase in waist circumference was associated with a 13 ml reduction in forced vital capacity and an 11 ml reduction in FEV₁.

The association between waist circumference and pulmonary function was consistent in subjects with normal weight, overweight and obesity. In subjects with normal weight, BMI was positively associated with forced vital capacity and FEV₁.

ACTION

Waist circumference is a better predictor of pulmonary dysfunction than BMI in adults. With the growing emphasis on management of obesity, we should be measuring patients' waist circumference routinely. The association with lung function is yet another reason to record waist measurement and advise patients on achieving a healthy waist circumference (<37 inches for men; <32 inches for women, with lower measurements in South Asians).

Am J Clin Nutr 2007; **85**: 35-39.

INHALED STEROID MONOTHERAPY MOST EFFECTIVE IN MILD-MODERATE PAEDIATRIC ASTHMA

Inhaled fluticasone monotherapy twice a day was the most effective treatment in controlling symptoms in a comparison of three treatment regimens for school-aged children with mild-to-moderate persistent asthma in the Pediatric Asthma Controller Trial (PACT) reported recently.

The study randomised 285 children (aged 6-14 years) with mild-to-moderate symptoms of persistent asthma to inhaled fluticasone (100 mcg twice a day), inhaled fluticasone (100 mcg) plus inhaled salmeterol (50 mcg in the morning and salmeterol 50 mcg in the evening), or montelukast (5 mg in the evening). They were treated for 48 weeks.

Fluticasone monotherapy and fluticasone plus salmeterol achieved similar results in many patient-measured outcomes, including the number of asthma control days. However, fluticasone monotherapy was superior in terms of clinic-measured FEV₁/forced vital capacity (p = 0.015), maximum bronchodilator response (p = 0.009), exhaled nitric oxide (p <0.001), and airway responsiveness as measured by PC20 (p <0.001). Fluticasone monotherapy was superior to montelukast for asthma control days (64.2% vs 52.5%; p = 0.004) and for all other control outcomes. Growth over 48 weeks showed no statistical difference (fluticasone, 5.3 cm; PACT combination, 5.3 cm; montelukast, 5.7 cm).

ACTION

Fluticasone monotherapy may be useful in treating children with mild-moderate persistent asthma with FEV₁ >80% predicted. Results of this study showed that fluticasone monotherapy achieved more effective asthma control than montelukast or fluticasone plus salmeterol and without significant side-effects.

J Allergy Clin Immunol 2007; **119**: 64-72.



Adam Gault/Science Photo Library

INFLUENZA VACCINATION REDUCES DEATHS IN COMMUNITY-ACQUIRED PNEUMONIA



Lea Paterson/Science Photo Library

Prior influenza vaccination significantly reduces deaths in people admitted to hospital with community-acquired pneumonia (CAP).

A US study followed consecutive individuals hospitalised with CAP during the 'influenza season' (November to April, 1999-2003). Among the 17,393 adults studied, 1,590 (19% of those with recorded vaccine status) had a history of influenza vaccination in the current or most recent influenza season.

Results showed that people who had been vaccinated were less likely to die in hospital of any cause than those who had not been vaccinated (odds ratio, 0.30; 95% confidence interval, 0.22-0.41). These effects remained significant after adjusting for the co-morbid illnesses and pneumococcal vaccination (adjusted odds ratio for death, 0.61; 95% confidence interval, 0.43-0.87).

ACTION

This observation suggests that ensuring at-risk groups receive an annual influenza vaccination may provide additional benefit in reducing deaths due to community-acquired pneumonia on top of reducing illness associated with influenza.

Arch Intern Med 2007; **167**: 53-59.



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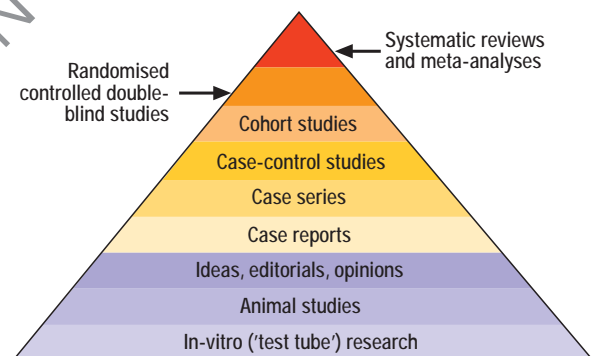
This series aims to demystify research by breaking research concepts down into 'bite-sized' chunks.

Jane Upton

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LEVELS OF EVIDENCE

Research studies that collect quantitative data (see previous article in this series¹) are based on the notion that there is an objective truth waiting to be discovered. For example, that one drug may be better than another for the alleviation of headaches. The task of the researcher is therefore to design and conduct a study that will reveal this truth. Some types of quantitative research designs are better at doing this than others. For example, an experiment to investigate if drug A is more beneficial for patients than drug B (known as a randomised controlled trial; RCT) is more likely to provide 'true' findings than if the researcher were to record and compare case notes. This is represented by the 'evidence pyramid' shown below. Each slice of the pyramid represents a type of research design; the longer slices at the bottom illustrate that these types of studies are more numerous. However, the types of studies at the top of the pyramid provide research findings (evidence) which are nearer to the objective truth.



Clinical guidelines help clinicians to base their practice on the best available research evidence and expert opinion. These guidelines use a grading system to enable clinicians to know the level of evidence on which each part of the guideline is based. Although the way that studies are graded varies slightly between guidelines, the BTS/SIGN guideline for the management of asthma provides a good example². In these guidelines each piece of evidence is labelled from 1++ (systematic reviews of RCTs) to 4 (expert opinion). In the next article in this series the randomised controlled trial will be discussed in more detail.



¹ Upton J, Walker S. Research Made Easy. *The Cochrane Database of Systematic Reviews*. 2006.

² British Thoracic Society (BTS), Scottish Intercollegiate Guidelines Network. *British Guidelines on the Management of Asthma*. 2005. www.brit-thoracic.org.uk