

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.

BEING OVERWEIGHT INCREASES ASTHMA RISK BY 50%



Being overweight or obese increases the risk of asthma by up to 50%, warns a US study.

The study searched for prospective studies evaluating body mass index (BMI) and incidence of asthma in adults. The researchers found seven studies including more than 330,000 adults. Compared with normal weight, overweight and obesity (BMI > 25kg/m²) increased the risk of incident asthma by 50%, with an odds ratio (OR) of 1.51 (95% confidence interval [CI], 1.27–1.80).

The risk of asthma increased with BMI. Overweight subjects were nearly 40% more likely to have asthma than those of normal weight (OR 1.38). Those who were obese (BMI > 30kg/m²) had a 90% higher risk of asthma (normal weight versus obesity OR 1.92). A similar increase in the risk of incident asthma due to overweight and obesity was observed in

men (OR, 1.46; 95% CI, 1.05–2.02) and women (OR, 1.65; 95% CI, 1.45–1.94).

ACTION

Obesity is a well-established risk factor for diabetes and heart disease. This study suggests that overweight and obesity are also associated with an increase in risk of asthma in both men and women, suggesting the potential for the incidence of asthma to be reduced by interventions to help people achieve normal weight for their height. The reason for the link between asthma and obesity is not clear (the researchers controlled for obesity making people breathless), but efforts to reduce overweight are good for health generally, so should obviously be encouraged.

American Journal of Respiratory and Critical Care Medicine 2007; 175: 661–666.

PATIENTS CONTROLLED WITH TWICE-DAILY FLUTICASONE CAN STEP DOWN TO ONCE DAILY TREATMENT

Patients whose asthma is well controlled with twice-daily fluticasone can safely step down to treatment with once-daily fluticasone plus salmeterol, according to a large US study. Further results showed that oral montelukast was not as effective, although it provided good asthma control for most patients.

The study randomly assigned 500 patients with asthma that was well controlled by inhaled fluticasone (100mcg) twice daily to continue with the same treatment, or to step down to fluticasone (100mcg) plus salmeterol (50mcg) each night or to montelukast (5 or 10mg each night). Treatment was administered for 16 weeks in a double-blind manner. The primary outcome was the time to treatment failure.

Approximately 20% of patients assigned to receive continued fluticasone or switched to treatment with fluticasone plus salmeterol had treatment failure, compared to 30.3% of those



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switched to montelukast. The hazard ratio for both comparisons was 1.6 (95% confidence interval, 1.1 to 2.6; p=0.03). The percentage of days on which patients were free of asthma symptoms was similar across the three groups (78.7 to 85.8%).

ACTION

Patients with asthma that is well controlled with the use of twice-daily inhaled fluticasone can be switched to once-daily fluticasone plus salmeterol without increased rates of treatment failure. Switching to montelukast results in an increased rate of treatment failure and decreased asthma control, although patients will remain free of symptoms on more than three-quarters of treatment days.

N Engl J Med 2007; 356: 2027–39.



BRONCHIAL HYPERRESPONSIVENESS ASSOCIATED WITH PHYSICAL INACTIVITY

Bronchial hyperresponsiveness is strongly and independently associated with decreased physical activity, according to latest results from the European Community Respiratory Health Survey II.

The study assessed the relationship between physical activity and bronchial hyperresponsiveness in 5,158 men and women aged 28.0–56.5 years randomly selected from 24 centres in 11 countries. Participants were asked about the frequency and duration of usual weekly exercise resulting in breathlessness or sweating. Bronchial hyperresponsiveness was defined as a decrease in forced expiratory volume in 1 second of at least 20% of its post-saline value for a maximum methacholine dose of 2mg.

Results revealed that both the frequency and duration of physical activity were inversely related to bronchial hyperresponsiveness. The prevalence of hyperresponsiveness in subjects exercising 1, 2–3 and 4 times a week was 14.5%, 11.6% and 10.9%, respectively ($p < 0.001$). The corresponding odds ratios were 1.00, 0.78 (95% CI 0.62 to 0.99) and 0.69 (95% CI 0.50 to 0.94) after controlling for potential confounding factors. The frequency of bronchial hyperresponsiveness in subjects exercising <1 hour, 1–3 hours and 4 hours a week was 15.9%, 10.9% and 10.7%, respectively ($p < 0.001$).



ACTION

These results suggest that bronchial hyperresponsiveness is strongly and independently associated with decreased physical activity. Although further studies are needed to determine the mechanisms underlying this association, the results provide yet more reason to encourage people to keep physically active.

Thorax 2007; 62: 403-410.

SYMPTOMS OF ASTHMA AND RHINITIS IMPROVE AFTER REMOVAL OF INDOOR MOULD



Mike Abrahams/Alamy

Symptoms of asthma and rhinitis improved and medication use was reduced following removal of indoor mould, according to results from a randomised controlled trial.

The study randomly allocated 164 homes of asthmatic patients into two groups. In one group, indoor mould was removed, fungicide was applied, and a fan was installed in the loft. In the control group, these interventions were delayed for 12 months.

Results showed that peak expiratory flow rate (PEFR) variability declined in both groups, with no significant differences between them. However, significantly more of the intervention group reported a net improvement in wheeze affecting activities (a difference of 25% between groups, 95% CI 3, 47; $p = 0.028$) at six months. They also showed perceived improvement of breathing (52%, 95% CI 30, 74; $p < 0.0001$) and perceived reduction in medication (59%, 95% CI 35, 81; $p < 0.0001$). By 12 months, the intervention group showed significantly greater reductions than the controls in use of preventer and reliever therapies.

ACTION

The results of this trial are not entirely conclusive, in view of the absence of objective evidence of benefit in peak flow. However, the improvement in wheeze affecting activities suggests that it may be worth recommending that patients with asthma and rhinitis remove mould from their homes. This may be particularly beneficial in more severe asthma, where fungal sensitivity is a powerful risk factor. Mould removal and the application of a fungicide wash would need to be repeated regularly as mould tends to reappear at new sites within 12 months.

Thorax. Published Online First: 27 March 2007.

doi:10.1136/thx.2006.070847.

A NEW TOOL TO PREDICT PROGNOSIS OF ELDERLY PATIENTS WITH LOWER RESPIRATORY TRACT INFECTIONS



Medical-on-Line/Alamy

Dutch researchers have devised a prediction rule for elderly patients with acute lower respiratory tract infections in the community, to estimate the risk of 30-day hospitalisation or death.

The prediction rule includes the following items which all represent a certain score: increasing age, previous hospitalisation, heart failure, diabetes, use of oral glucocorticoids, previous use of antibiotics and a diagnosis of pneumonia or exacerbation of chronic obstructive pulmonary disease. Patients with a low score have a risk of less than 3% of being hospitalised or dying within the next 30 days, compared to more than 30% if their score is high.

ACTION

This simple prediction rule can help primary care professionals to differentiate between high- and low-risk patients. It may be possible to determine low-risk patients who could be suitable for home treatment while high-risk patients might need to be monitored more closely in a homecare or hospital setting.

Eur Respir J 2007; 29: 969-975.

COCHRANE REVIEW SUPPORTS VARENICLINE FOR SMOKING CESSATION

People taking varenicline were three times more likely to achieve successful long-term smoking cessation than those trying to give up without drug treatment, according to a Cochrane review.

The review assessed the efficacy and tolerability of the nicotine receptor partial agonist varenicline in smoking cessation by searching the Cochrane Tobacco Addiction Group's specialised register for trials. The main outcome measured was abstinence from smoking after at least six months from the beginning of treatment.

Five trials of varenicline compared with placebo for smoking cessation, three including a bupropion experimental arm, and one relapse prevention trial comparing varenicline with placebo. The six trials included 4,924 participants, 2,451 of whom used varenicline. People taking varenicline were more than three times more likely to have achieved continuous abstinence at 12 months compared to those given placebo (pooled odds ratio 3.22; 95% confidence interval [CI] 2.43 to 4.27). The pooled (OR) for varenicline versus bupropion was 1.66 (95% CI 1.28 to 2.16).

The main adverse effect of varenicline was nausea, which was mostly mild to moderate and usually subsided over time. The two trials testing the use of varenicline beyond the 12-week standard regimen found the drug to be well-tolerated and effective during long-term use.

The authors suggested that nicotine receptor partial agonists might help smokers to quit by a combination of maintaining moderate levels of dopamine to counteract withdrawal symptoms (acting as an agonist) and reducing smoking satisfaction (acting as an antagonist).

ACTION

There is no doubt about the importance of helping patients to stop smoking. This review suggested that varenicline increased the chances of people quitting successfully and that it may be more effective than bupropion.

Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. The Cochrane Collaboration.

www.thecochranelibrary.com

MEDITERRANEAN DIET COULD HALVE THE RISK OF COPD

Men eating a diet containing high levels of fruit, vegetables, whole grains and fish have half the rates of COPD compared to those eating a more refined diet, according to the US Health Professionals Follow-up Study.



The study compared two dietary patterns: a prudent pattern (high intake of fruits, vegetables, fish and whole grain products) and a Western pattern (high intake of refined grains, cured and red meats, desserts and French fries). These dietary patterns were categorised into quintiles and results were adjusted for age, smoking, race/ethnicity, physician visits, US region, body mass index, physical activity, multivitamin use and energy intake.

The researchers identified 111 self-reported cases of newly diagnosed COPD between 1986 and 1998 in the total cohort of 42,917 men. Results showed that men eating the prudent pattern had half the risk of newly diagnosed COPD (relative risk for highest vs. lowest quintile [95%CI] = 0.50 [0.25-0.98], p for trend = 0.02). By contrast, eating the Western diet was associated with nearly five times higher risk of COPD (RR for highest vs. lowest quintile [95%CI] = 4.56 [1.95-10.69], p for trend < 0.001).

ACTION

A diet rich in fruits, vegetables and fish may reduce risk of COPD, whereas a diet rich in refined grains, cured and red meats, desserts and French fries may increase risk of COPD.

Thorax. Published Online First: 15 May 2007. doi:10.1136/thx.2006.074534.

TRIPLE THERAPY IMPROVES LUNG FUNCTION IN COPD



PHOTO TAKE Inc./Alamy

Adding fluticasone/salmeterol to tiotropium therapy in patients with moderate to severe COPD improved lung function, quality of life, and hospitalisation rates but did not statistically influence exacerbation rates, a study has shown.

A total of 449 patients with moderate or severe COPD were randomised to one year's treatment with tiotropium plus placebo, tiotropium plus salmeterol, or tiotropium plus fluticasone/salmeterol.

Results showed that nearly two-thirds (62.8%) of patients treated with tiotropium plus placebo experienced an exacerbation, which was similar to the rate in patients given tiotropium plus salmeterol (64.8%) or tiotropium plus fluticasone/salmeterol (60.0%).

Further results demonstrated that tiotropium plus fluticasone/salmeterol improved lung function ($p < 0.049$) and disease-specific quality of life ($p < 0.01$) and reduced the number of hospital admissions for COPD exacerbation (incidence rate ratio, 0.53 [CI, 0.33 to 0.86]) and all cause hospitalisations (incidence rate ratio, 0.67 [CI, 0.45 to 0.99]) compared with tiotropium plus placebo.

In contrast, tiotropium plus salmeterol did not statistically improve lung function or hospitalization rates compared with tiotropium plus placebo.

ACTION

Addition of fluticasone/salmeterol to tiotropium therapy may improve lung function, quality of life, and hospitalisation rates in patients with moderate to severe COPD but will not influence rates of COPD exacerbation.

Ann Intern Med 2007; **146**: 545-555.



Evidence in Practice compiled by:
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The purpose of this series is to help you to understand research concepts by breaking them down into 'bite-sized chunks'.

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DOUBLE BLIND RANDOMISED CONTROLLED TRIAL

The phrase 'double blind randomised controlled trial' is common in research journals but what does it mean?

• What is a 'trial'?

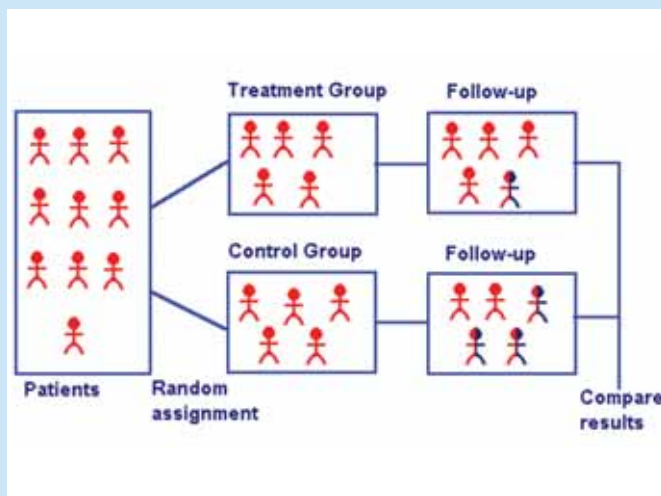
In order for the effectiveness of new interventions (e.g. drugs, treatments or diagnostic methods) to be evaluated they need to be tried out or 'tried'. Research designed to test an intervention is therefore called a trial.

• Why is a trial 'controlled'?

Trials evaluate whether the effects of new interventions on patients differ from usual care or placebo (an inactive substance). The usual care or placebo is the control: the standard against which the new intervention is checked.

• Why is the controlled trial 'randomised'?

Imagine you wish to run a controlled trial to test the effectiveness of a new drug treatment. The intervention and control groups should be as similar as possible at the start so that any differences at the end of the trial can be attributed to the new treatment. The best way of doing this is to randomly allocate patients to receive either the new drug or usual care.



• Why is it the randomised controlled trial 'double blind'?

This means that the patients included in the trial and the researchers handling the data do not know (are blind to) which group patients are in. You might like to ponder why this might be, and whether it is always possible to achieve in clinical trials. These questions will be addressed in the next article.

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