

# 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.

## STERIOD PLUS BETA<sub>2</sub> AGONIST REDUCES MORTALITY IN COPD



The three-year multicentre study randomised 6,112 patients with moderate-to-severe COPD to inhaled fluticasone propionate (500 microgram) alone, salmeterol (50 microgram) alone, a combination of the two drugs (Advair 500/50 Diskus) twice daily, or placebo. The mean age of the study population was 65 years. There was a higher proportion of men (76%) than women and 43% of the study population were current smokers.

Results showed a statistically significant reduction in mortality (the primary endpoint) with combination therapy (12.6%) compared to placebo (15.2%) ( $p=0.031$ ). The two immunotherapy groups did not show a significant reduction in mortality.

### ACTION

The results of this study were eagerly awaited as treatment that reduces mortality is the 'holy grail' of COPD management. They indicate that a combination of inhaled fluticasone and salmeterol significantly reduces mortality compared to placebo. It must be noted that the TORCH investigators used high doses of fluticasone and salmeterol. This may raise some concern about side-effects. Side-effect data have not yet been reported, but there was a report of "some hoarseness, some oral thrush because of the high level of immunosuppression and a higher incidence of pneumonia, but no increase in deaths from pneumonia."

*American College of Chest Physicians annual meeting; Salt Lake City, Utah, USA, 21–24 October 2006.*

Combination treatment with a corticosteroid (fluticasone) and a long-acting beta<sub>2</sub> agonist (salmeterol) reduces mortality risk in patients with chronic obstructive pulmonary disease (COPD), according to results from the TORCH (Towards a Revolution in COPD Health) study, reported at the annual meeting of the American College of Chest Physicians.

## HIGH-DOSE INHALED STEROID MAY CAUSE ADRENAL INSUFFICIENCY IN CHILDREN

Adrenal insufficiency has been found in children with asthma taking high-dose ( $\geq 500$  µg daily) inhaled fluticasone propionate (FP). Following two cases of serious adrenal insufficiency (one fatal) attributed to FP, a Glasgow research group evaluated adrenal function in nearly 200 children recorded as prescribed FP  $\geq 500$  µg/day who were invited to attend for assessment.

Adrenal function was measured using the low dose Synacthen test (500 ng/1.73 m<sup>2</sup> intravenously) and was categorised as: biochemically normal (peak cortisol response  $>500$  nmol/L); impaired (peak cortisol 500 nmol/L); or flat (peak cortisol  $<500$  nmol/L with increment of  $<200$  nmol/L and basal morning cortisol  $<200$  nmol/L).

Of 194 children receiving FP  $\geq 500$  µg/day, six had flat responses, 82 impaired responses, 104 were normal, and in 2 the test was unsuccessful. Apart from the index child, the other five with flat responses were asymptomatic; a further child with impairment (peak cortisol 296 nmol/L)

had encephalopathic symptoms with borderline hypoglycaemia during an intercurrent illness.

Overall, flat adrenal responses in association with FP occurred in 2.8% of children tested, all receiving  $\geq 1000$  µg/day, while impaired responses were seen in 39.6%.

### ACTION

Children on doses of FP above the licensed dose (400 µg/day) should have their adrenal function monitored; should carry a steroid card; and should have specific written advice for emergency steroid replacement at the time of any severe illness. In line with current guidelines, doses of inhaled steroid should be "stepped down" once control has been achieved.

*Archives of Disease in Childhood 2006; 91: 808-813.*



NEWS FROM THE EUROPEAN RESPIRATORY SOCIETY ANNUAL CONGRESS (2 – 6 SEPTEMBER 2006, MUNICH)



Samuel Ashfield/Science Photo Library

## Vaccinating babies might protect against developing asthma

**R**esults of a five-year study in almost 9,000 children showed that routine childhood vaccination – far from increasing the risk of asthma as has sometimes been suggested – may reduce their risk of developing asthma.

The study included 8,700 children aged one to four years randomly selected from the population of Leicestershire. They were followed up prospectively for five years, by which time the children were aged between six and nine.

Data on vaccination status were collected from the local NHS database and from information provided by families. The children's parents were approached four times, at intervals of between 12 and 24 months, to ask whether, during the past year, the child had suffered any wheezing.

The results showed that 14% of children aged from six to nine had wheezing symptoms even though they were fully vaccinated according to the UK schedule, but this increased by half as much again – to 21% – among children who had not completed the vaccination schedule or who were not vaccinated at all.

There were twice as many children with chronic wheezing in the incompletely vaccinated/unvaccinated group compared to children fully vaccinated (15% compared to 8%).

Delaying vaccination beyond the seventh month increased the risk of wheezing by 56%, rising to 84% for the six to nine age group.

All figures were adjusted for factors that could impact on wheezing and on compliance with the vaccination schedule, including socioeconomic status, number of siblings, family history of allergy and atopy, respiratory infections, parental smoking, duration of breastfeeding, age of the mother when the child was born, and number of medical consultations.

The results, from Mike Silverman (University of Leicester) and colleagues, focused mainly on whooping cough vaccination, which had been the subject of the strongest allegations of links with asthma. However, he emphasised that the findings can also be applied to other vaccinations traditionally offered to infants, including tetanus, diphtheria, measles, rubella and mumps.

### ACTION

These results will be useful to reassure parents who think that vaccinations may represent a cause of asthma. They suggest that giving vaccinations according to the schedule might even offer protection against asthma in the future, providing even more reason for following the childhood vaccination schedule.

## Heart disease deaths in snorers reduced by treating sleep apnoea

**T**hree studies reported at the ERS Congress showed that the standard treatment for sleep apnoea – continuous positive airway pressure (CPAP) – reduced mortality.

A prospective study of 739 patients (average age 52 years) with an average apnoea/hypopnoea index of 38.7 interruptions to breathing per hour compared the 523 patients regularly treated by CPAP to the 216 patients who had either chosen to stop the treatment or used it for less than two hours a night (non-CPAP group).

Results showed seven times as many deaths or disabling cardiovascular events in the non-CPAP group than in the CPAP group over the three years of follow-up (6.4% vs 0.9%). There were ten cardiovascular deaths in the non-CPAP group and two in the CPAP group.

A second study monitored 638 patients with sleep apnoea over an average of seven years. Of these, 499 were being treated (mainly with CPAP) and 139 had declined treatment. Over a ten-year period, the proportion of treated patients who remained free of cardiovascular events was 78.5% compared to 54.2% in the untreated group. Multivariate analysis of the results showed that treating sleep apnoea reduces the cardiovascular risk by 64%.

A third study in 939 patients suffering either from obstructive sleep apnoea or from upper airway resistance syndrome demonstrated that although the CPAP-treated patients had a much higher apnoea/hypopnoea index than those who were untreated (average of 44.3 hourly interruptions to breathing compared to 24.7) and a higher body mass index (BMI), they suffered fewer cardiovascular events. There were only 1.9 cardiovascular events per 100 person-years in the CPAP group, compared to 2.96 in the untreated group.

### ACTION

These three studies demonstrate the importance of effective treatment of sleep apnoea for preventing cardiovascular events. CPAP should potentially be part of primary and secondary cardiovascular prevention, even in cases of relatively mild sleep apnoea.



## ANNUAL INFLUENZA VACCINATION REDUCES LOWER RESPIRATORY TRACT INFECTIONS IN ELDERLY PEOPLE LIVING IN THE COMMUNITY



Alain Dex Publiphoto Diffusion/Science Photo Library

**A**nnual influenza revaccination is associated with a reduction in lower respiratory tract infections (LRTI) in elderly people living in the community, a Dutch study has shown.

The population-based cohort study used the computerised Integrated Primary Care Information database in the Netherlands to identify people living in the community who were 65 years or older on January 1 of the year of study entry. For each year from 1996 to 2002, the individual cumulative exposure to influenza vaccination was calculated. The risk of LRTI after a first vaccination or revaccination was compared with the risk for no vaccination, adjusting for age, sex, smoking, and underlying disease.

Results for the study population of 26,071 subjects showed that 3,412 developed LRTIs during follow-up. During the influenza epidemic periods, a first vaccination did not reduce risk for LRTI. In the total population, the hazard ratio following a first vaccination was 0.86. During epidemic periods, revaccination reduced risk of LRTI by 33% (95% CI, 8% to 52%) in individuals without comorbidity. In individuals with comorbidity, the risk reduction of 5% was nonsignificant (95% CI, -10% to 18%).

### ACTION

Influenza vaccination has previously been associated with a reduction in the number of hospital admissions for respiratory conditions in elderly people but little was known about its effect on respiratory tract infections of different severity. This study reinforces our policy of giving annual influenza revaccination to people over 65 years living in the community, in addition to other high-risk groups, demonstrating that it is associated with a reduction in LRTI.

*Ann Intern Med* 2006; **166**: 1980–1985.

## CHILDHOOD ASTHMA ADMISSIONS PEAK WITH RETURN TO SCHOOL

**A**dmissions of children to hospital with asthma peak in the first few days of school after the summer holidays, an Australian study has shown.

The study investigated the seasonal pattern of hospital admissions for asthma in the metropolitan area of Sydney in children aged up to 14 years. During the seven-year study, 20,334 children aged 1–4 years and 13,284 aged 5–14 years were admitted to emergency departments with asthma.

The results showed an increased risk of admission beginning soon after the first day of school of each term for schoolchildren aged 5–14 years old but not in preschool children aged 1–4 years. The risk of admission because of asthma in children aged 5–14 years generally decreased in the long summer holiday and increased steeply after the start of term.

Risk of hospital admission because of asthma increased to a peak between two and four weeks after the first day of school in each term and was 1.5–3 times higher than the risk before return to school for both age groups.

The largest increase in asthma risk occurred in the first term after the long summer holiday. The risk for children aged 5–14 years increased significantly by a factor of 3.05 (95% confidence interval 2.37 to 3.93), peaking at 23 days after the first day of school.

It is likely that children returning to school have greater exposure to viral respiratory infections after school holidays and are therefore more likely to be admitted to hospital with an acute asthma exacerbation.



Martin Rea/Science Photo Library

### ACTION

Returning to school, even after a short break, substantially increases the risk of a child experiencing an asthma attack requiring medical attention, according to this study. It is worth warning children with asthma and their parents to be alert to this problem and to plan treatment accordingly.

*Public Health* published online 10 Aug 2006, doi:10.1016/j.puhe.2006.05.015.

## WOMEN WITH OXYGEN-DEPENDENT COPD HAVE HIGHER MORTALITY



**W**omen with severe COPD who are on long-term oxygen therapy (LTOT) have higher mortality than men, warns a large study.

The prevalence of COPD is rising among women and is approaching that of men, but it has previously been unclear as to whether sex affects survival. A seven-year prospective cohort study compared survival in 435 outpatients with COPD – 184 women, 251 men – referred for

long-term oxygen therapy at two respiratory clinics in Sao Paulo, Brazil. Baseline data were collected on enrolment into oxygen therapy, when patients were clinically stable.

The researchers analysed the effect of gender on survival using Kaplan-Meier survival curves, and then used Cox proportional hazards models to control for potential confounders. Results showed that women were at more than 50% higher risk of death compared to men (hazard ratio, 1.54; 95% confidence interval, 1.15–2.07;  $p = 0.004$ ) after adjusting for potential confounders (age, pack-years smoked, PaO<sub>2</sub>, FEV<sub>1</sub> and body mass index). Other independent predictors of death were lower PaO<sub>2</sub> ( $p < 0.001$ ) and lower body mass index ( $p < 0.05$ ).

### ACTION

The study demonstrates that women with COPD who are on long-term oxygen therapy are at higher risk of dying than men. The observed survival difference could have occurred if women were less likely to use their oxygen as prescribed than men – as has been seen in previous studies, making it worth taking efforts to encourage adherence. Another explanation for worse survival among women might be that some of the systemic complications of COPD, such as muscle dysfunction or depression, are more common in women and that these lead to worse outcomes. Management of women with COPD should obviously aim to treat these complications as effectively as possible.

*American Journal of Respiratory and Critical Care Medicine* 2006; **174**: 524–529.



Evidence in Practice compiled by:  
**Susan Mayor**  
Managing editor of *BJPCN*

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

One of the most basic concepts is the difference between qualitative and quantitative research methods, so this is where we will start.

**Jane Upton**

Research Project Manager, Education for Health

**Samantha Walker**

Director of Research, Education for Health

**T**he choice between qualitative and quantitative methods is one of the first decisions that researchers make when embarking on a study. The simplest way of explaining the difference between them is that qualitative research generally deals with words while quantitative research deals with numbers. Which method is chosen depends entirely on the research question being asked.

Research questions that ask 'why?' are often best answered using qualitative research methods. This is because the best way to explore why a person or group of people holds certain views, or acts in a certain way, is to observe or listen to them. For example, if the question is "Why are there differences in hospital admission rates for asthma between different ethnic groups?", this might best be answered by interviewing staff and patients. Alternatively, it may sometimes be preferable to listen to participants discuss the topic with one another. This may help participants explore their views through discussion with others. As an example, in a study that asked health professionals and patients about their views on guided self-management plans for asthma, the researchers ran focus groups.

Research questions that ask 'how much?' are often best answered using quantitative research methods. In research terms, quantitative (or numerical) methods are often used to investigate the relationship between two or more factors, *ie* does a change in one thing result in a change in something else?

If a researcher were to ask: "Is there a relationship between shoe size and height?", this could not be found out by asking people what they thought of their feet and their height! Rather, the researcher would measure subjects' shoe sizes and height and analyse whether people with bigger feet were taller. This is also true for studies asking questions such as 'Is there a relationship between antihypertensive medications and the risk of type 2 diabetes?', or 'between commercial diet programmes and weight loss?'. In recent studies asking these questions, relevant factors (such as social, physiological and behavioural characteristics) were measured objectively by collecting numerical data. These data were then analysed to reveal the strength of the relationship between the factors.

**i** Griffiths C, Kaur F, Gantley M, *et al*. Influences on hospital admission for asthma in south Asian and white adults: qualitative interview study. *BMJ* 2001; **323**: 1–8.

Kitzinger J. Qualitative Research: Introducing focus groups. *BMJ* 1995; **311**: 299–302.

Jones A, Pill R, Adams S. Qualitative study of views of health professionals and patients on guided self management plans for asthma. *BMJ* 2000; **321**: 1507–1510.