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This alert service highlights some of the key health care conclusions and their implications for practice publishing in The Cochrane Library, 2005, Issue 3.

To receive a full copy of the reviews highlighted in this newsletter, or to arrange an interview with an author, contact Polly Young (+44 (0)1243 770633 or by email [pyoung@wiley.co.uk](mailto:pyoung@wiley.co.uk)).

Reviews highlighted in this newsletter:

**Obesity interventions in children have limited effect**

Many diet and exercise interventions aimed at preventing childhood obesity promote healthy diets and increased physical activity, but do not appear to have radical impacts on reducing overweight and obesity gain.

**Metformin works well in type 2 diabetes especially where patients are overweight or obese**

People with type 2 diabetes who are overweight or obese are at increased risk of cardiovascular diseases like strokes and heart attacks. Metformin can help tackle their diabetes while also protecting against diabetes-related organ damage.

**Bisphosphonates - a successful treatment for metastatic bone disease associated with breast cancer**

Secondary tumours in bone cause a lot of pain and tissue damage in half the women who have advanced breast cancer, but bisphosphonates can reduce the risk of bone disease in women already undergoing cancer therapy.

**Inhale magnesium sulphate along with beta-2-agonists during asthma attacks**

Severe asthma attacks can be life threatening and intravenous magnesium sulphate is known to help, but inhaling nebulised magnesium sulphate can also improve lung function.

**Combined injectable contraceptives find high early acceptance**

Providing safe and effective contraception by injecting a mixture of progestins and oestrogens causes fewer side-effects than injecting progesterone-like chemicals alone.

**Oral contraceptives are well tolerated when taken continuously**

Traditionally, oral contraceptives are taken for 21 days followed by a placebo week. This placebo week causes an artificial withdrawal bleed that gives the appearance of a normal monthly menstrual cycle, but now evidence shows that women tolerate contraceptives well if they skip this bleed.

## **Pain generated by damage to the nervous system can be treated with antidepressants**

Antidepressant drugs such as amitriptyline are effective against a variety of neuropathic pains.

## **Biologic drug adalimumab is effective in treating rheumatoid arthritis**

There is good evidence that adding adalimumab (Humira) to the treatment of people with long-standing rheumatoid arthritis is more effective than using oral methotrexate alone.

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## **Obesity interventions in children have limited effect**

### **Many diet and exercise interventions aimed at preventing childhood obesity promote healthy diets and increased physical activity, but do not appear to have radical impacts on reducing overweight and obesity gain.**

The epidemic of child obesity demands serious action, and around the world many people have looked at ways of helping children eat less and exercise more. In preparing this review, the Cochrane Review Authors identified 22 studies that between them tested a variety of different approaches involving changes to diet, exercise, or diet and exercise. By pooling data, the review drew on findings from about 10,000 participants who were under 18 years old and came from Asia, South America, Europe and North America.

While the authors were unable to identify one particular program that could prevent obesity in children lead-author, Carolyn Summerbell, a Professor of Human Nutrition who works at the University of Teesside, England, believes that any intervention that leads to a better lifestyle will reduce obesity if it is kept up for long enough.

Summerbell believes that the most effective programmes are the ones that put fun into fitness and good food. This means that features like dance and martial arts should be included alongside traditional sports and physical exercise in the school curriculum.

Despite the importance of childhood obesity, the review was only able to find a limited number of studies to draw findings from and some of these were pilot projects that showed great promise but were not designed to be able to measure changes in body weight.

“It is becoming increasingly clear that decision-makers need much more information on which to base policy and program decisions,” says Professor Elizabeth Waters, who is a professor of Public Health based at Deakin University, Melbourne, Australia.

The authors note that there are many different programmes underway at the moment, and look forward to seeing the outcomes. "We believe that programmes aimed at creating environments that enable and support long-term behaviour change are likely to make more of a positive impact than the interventions that people have studied so far," Waters adds.

"This review made a central contribution to the WHO Expert Consultation on childhood obesity at Kobe, Japan, in June 2005, and the report of this consultation will be published in June 2006. As one of a number of reviews where a controlled evaluation has been used it makes a valuable contribution to our understanding of childhood obesity. But given the importance of tackling childhood obesity it is clear that there is a need for much more research in the area, and research that is thoroughly designed so that it generates useful data," says Summerbell

Review Title: Summerbell et al: Interventions for preventing obesity in children. *The Cochrane Database of Systematic Reviews* 2005 Issue 3

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## **Metformin works well in type 2 diabetes especially where patients are overweight or obese**

**People with type 2 diabetes who are overweight or obese are at increased risk of cardiovascular diseases like strokes and heart attacks. Metformin can help tackle their diabetes while also protecting against diabetes-related organ damage.**

In diabetes, either the body fails to produce enough insulin or the cells ignore the insulin. Without this hormonal signal working properly glucose increases in the blood stream, but still can't be used by the body. The number of people with type 2 diabetes is rising because it is linked to overweight or obesity.

Metformin increases peripheral and liver sensitivity to insulin. It therefore reduces the amount of glucose released from the liver and increases the amount taken up and used by the rest of the body. It also reduces the level of fats in blood and helps people stabilise or reduce their weight. Taken together, these help reduce damage to blood vessels throughout the body.

By looking at data contained in 29 separate trials, the Cochrane Review Authors concluded that metformin works well as a single-drug therapy for many people with type 2 diabetes. In addition to helping control diabetes, people who were overweight, had type 2 diabetes and were on intensive

metformin were also less likely to be affected by stroke, heart attacks, and are less likely to die.

The authors could not compare metformin with newer drugs, because trials of more recently available drugs such as new sulphonylureas, thiazolidinediones, meglitinides and alpha glucosidase inhibitors did not show any direct comparisons with metformin for these primary outcomes.

They could, however, determine that metformin was as good as, or better than these other drugs at controlling blood glucose and lipids, and body weight.

"Our review of literature suggests that metformin is a good first line therapy for overweight or obese people with type 2 diabetes," says lead author Antonio Saenz, who works as a family physician in Madrid, Spain.

Review Title: Saenz et al: Metformin monotherapy for type 2 diabetes mellitus. *The Cochrane Database of Systematic Reviews* 2005 Issue 3

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## **Bisphosphonates - a successful treatment for metastatic bone disease associated with breast cancer**

**Secondary tumours in bone cause a lot of pain and tissue damage in half the women who have advanced breast cancer, but bisphosphonates can reduce the risk of bone disease in women already undergoing cancer therapy.**

Worldwide, breast cancer is the most common cause of cancer-related death in women. In these women, bone is the most common site for secondary tumours to take hold and develop. In healthy bones, the structure is constantly being broken down and rebuilt, but bone tumours influence the rate and balance of this cycle. Bisphosphonates slow the process that breaks down bone material.

By searching the world's databases, the Cochrane Review Authors identified 21 high-quality studies that looked at the use of bisphosphonates and met stringent selection criteria. Having pooled the data they concluded that bisphosphonates can reduce the incidence and rate of skeletal damage in women with advanced breast cancer. There was still, however, uncertainty about the best time to start giving these drugs.

"Our research confirms the general feeling that bisphosphonates are important in reducing bone complications in women with breast cancer and

bone involvement" says lead author Nick Pavlakis who works in the Royal North Shore Hospital, Sydney, Australia.

Review Title: Pavakis et al: Bisphosphonates for breast cancer. *The Cochrane Database of Systematic Reviews* 2005 Issue 3

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## **Inhale magnesium sulphate along with beta-2-agonists during asthma attacks**

**Severe asthma attacks can be life threatening and intravenous magnesium sulphate is known to help, but inhaling nebulised magnesium sulphate can also improve lung function.**

Asthma is a chronic disease of the lungs where people have periods where their breathing is stable, and other periods where it is restricted. These 'exacerbations' or 'attacks' can be mild or so severe that the person needs hospital treatment.

During most episodes people use inhaled beta-2-agonists, but in more severe cases these alone may not be enough to restore breathing to normal. The Cochrane Review Authors therefore searched the literature to examine the evidence regarding the use of inhaled magnesium sulphate as an additional therapeutic option.

They concluded that there was good evidence that nebulised magnesium sulphate was safe and effective and that it should be considered as an additional therapy along with beta-2-agonists.

"We also found that magnesium sulphate was most useful in situations where the exacerbation was severe," says lead author Maurice Blitz, who works in the Division of General Surgery, at the University of Alberta, Canada.

Review Title: Blitz et al: Inhaled magnesium sulphate in the treatment of acute asthma. *The Cochrane Database of Systematic Reviews* 2005 Issue 3

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## **Combined injectable contraceptives find high early acceptance**

**Providing safe and effective contraception by injecting a mixture of progestins and oestrogens causes fewer side-effects than injecting progesterone-like chemicals alone.**

Some women prefer not to take a contraceptive pill every day. For this reason researchers have created contraceptive options in which hormones are injected. These hormones are slowly released into the body, providing long-term contraception. One problem is that the constant supply of additional hormone can stop a woman experiencing monthly menstrual bleeding, and some women are disturbed by this lack of scheduled bleeding.

The Cochrane Review Authors found that injectable contraceptives that include medroxyprogesterone acetate (DMPA) and estradiol cypionate (E<sub>2</sub>C) were better tolerated than those containing DMPA alone. Both forms of contraception were highly effective at preventing pregnancy.

Along with the difference in composition, the two contraceptives have different patterns of use. While the combined injectable contraceptives are given once a month, the single-hormone version is injected every two or three months. In contrast with the single-hormone version in which women frequently have no menstrual bleeding, the monthly dosing with combined contraceptives causes levels of hormones to rise and fall in a monthly cycle, which in turn induces mild bleeding each month. This element of cyclical bleeding could be one of the reasons for its higher initial acceptance.

Over time, however, more people discontinue using the combined version than discontinue the single one.

It could be that the inconvenience of visiting a clinic every month for the next injection causes women to stop using combined injectable contraceptives. "Healthcare providers may need to think of other ways of providing the service to get over this problem," says lead author Maria Gallo, who works at Ipas in Chapel Hill, North Carolina.

Review Title: Gallo et al: Combination injectable contraceptives for contraception. *The Cochrane Database of Systematic Reviews* 2005 Issue 3

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**Oral contraceptives are well tolerated when taken continuously**

**Traditionally, oral contraceptives are taken for 21 days followed by a placebo week. This placebo week causes an artificial withdrawal bleed that gives the appearance of a normal monthly menstrual**

**cycle, but now evidence shows that women tolerate contraceptives well if they skip this bleed.**

An increasing number of women take oral contraceptives that combine oestrogen and progesterone (combined oral contraceptives - COC) continuously. Continuously-dosed COCs treat conditions like endometriosis, dysmenorrhoea and symptoms associated with monthly menstruation. Many women, however, simply want to avoid menstruation, leading to less interference in daily life, and fewer menstruation-related days off from work or school.

The Cochrane Review Authors set out to see if women experienced any differences when taking COC's in the standard pattern versus continuously.

Their conclusion was that the two dosing regimens have similar participant satisfaction and similar discontinuation rates. They also found evidence suggesting that menstrual-associated symptoms were reduced in continuous regimens. There was, however, not enough data to draw any conclusions about differences in the long-term safety or contraceptive effectiveness between the two dosing regimens.

"Overall, oral contraceptives are safe and effective, and continuous pill-use is a reasonable approach to oral contraception," says lead-author Alison Edelman who works at Oregon Health & Science University, Portland, Oregon, USA.

Review Title: Edelman et al: Continuous or extended cycle vs. cyclic use of combined contraceptives for contraception. *The Cochrane Database of Systematic Reviews* 2005 Issue 3

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**Pain generated by damage to the nervous system can be treated with antidepressants**

**Antidepressant drugs such as amitriptyline are effective against a variety of neuropathic pains.**

Neuropathic pains result when injury or disease causes damage to the nervous system. These pains can last for months or years after any injury has healed. The damage may be in peripheral nerves that run through the body and limbs, or within the central nervous system in the spine or brain. Patients with this form of pain are frequently given antidepressant drugs, and researchers who have assessed the findings of 50 trials conducted around the

world conclude that there is good evidence that at least some of them work well.

The most convincing evidence was for amitriptyline in doses up to 150mg per day, which achieved at least moderate pain relief. It was difficult to assess the value of selective serotonin reuptake inhibitors (SSRIs) as there are few trials in neuropathic pain. The Cochrane Review Authors also found that there was insufficient high quality evidence for them to draw any conclusions about St John's Wort, venlafaxine and L-tryptophan.

"The clinical impression is that antidepressants are effective and this review confirms this belief," said lead author Tiina Saarto who works in Helsinki University Central Hospital, Helsinki, Finland. "If the drug is going to be effective, it normally starts to reduce pain within a few days of starting to take it."

Antidepressants had most effect treating diabetic neuropathy and post-herpetic neuralgia. There was limited evidence that they could also help people with central pain, atypical facial pain and pain after breast cancer treatment. There was a lack of evidence that they helped people with HIV-related neuropathic pain or 'burning mouth syndrome'.

Review Title: Saarto et al: Antidepressants for neuropathic pain. *The Cochrane Database of Systematic Reviews* 2005 Issue 3

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## **Biologic drug adalimumab is effective in treating rheumatoid arthritis**

**There is good evidence that adding adalimumab (Humira) to the treatment of people with long-standing rheumatoid arthritis is more effective than using oral methotrexate alone.**

Adalimumab is a relatively new antibody-based therapy. Patients given 24 weeks of therapy with adalimumab and methotrexate had decreased pain and swelling and an increased ability to perform normal daily activities compared with those given methotrexate alone or no disease modifying anti-rheumatic drugs (DMARDs). X-ray damage to the joints is also slowed. Side effects in the short-term are well-tolerated. Rare and long-term side effects are not yet known.

"The drug is relatively new and so it is not surprising that there is little data from long-term studies, but the evidence so far is encouraging," says lead

author Federico Navarro-Sarabia, Chair of Rheumatology at the Hospital Universitario Virgen Macarena, Seville, Spain.

In the UK, the National Institute for Health and Clinical Excellence (NICE) is currently assessing adalimumab for use in rheumatoid arthritis.

Review Title: Navarro-Sarabia et al: Adalimumab for treating rheumatoid arthritis. *The Cochrane Database of Systematic Reviews* 2005 Issue 3

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#### Notes to the Editor

1. The Cochrane Library contains high quality health care information, including Systematic Reviews from The Cochrane Collaboration. These reviews bring together research on the effects of health care and are considered the gold standard for determining the relative effectiveness of different interventions. The Cochrane Collaboration (<http://www.cochrane.org>) is a UK registered international charity and the world's leading producer of systematic reviews. It has been demonstrated that Cochrane Systematic Reviews are of comparable or better quality and are updated more often than the reviews published in print journals<sup>a</sup>.
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<sup>a</sup> Jadad AR, Cook DJ, Jones A, Klassen TP, Tugwell P, Moher M, et al. Methodology and reports of systematic reviews and meta-analyses: a comparison of Cochrane reviews with articles published in paper-based journal.