Abstracts

As little as 15 minutes of exercise each day may prolong life

A study from Taiwan examined the association between physical activity and mortality. In this study, people who did as little as 90 minutes of exercise each week, who would ordinarily be considered physically inactive, were looked at as a separate group. Around 12.5% (28 311/226 493) of those who exercised at all did so for about 15 minutes on 6 days a week. It turns out that even such low levels of exercise improve survival. The study followed up for an average of 8 years more than 400 000 people who underwent regular health check-ups.

Compared with people who exercised very little, those who did not exercise at all had a 17% higher risk of dying from any cause, and an 11% higher risk of dying from cancer. Each extra 15 minutes of daily exercise was linked with a 4% reduction in the risk of dying from any cause, and a 1% lower risk of cancer-related death. The results held in both sexes, regardless of age, smoking and drinking habits, and overall risk of cardiovascular disease.

At age 30, men who exercised for 15 minutes each day on average could expect to live 2.6 years longer than their peers who did not exercise at all. This was 3.1 years for women. Among 30-year-olds who met the recommendations for physical activity (30 minutes' exercise on 5 days a week) men could expect to live 4.2 years longer and women 3.7 years longer, compared with their physically inactive peers.

Wen CP, et al. Lancet 2011; doi:10.1016/S0140-6736(11)60749-6

Development of Prognosis in Palliative care Study (PiPS) predictor models to improve prognostication in advanced cancer: prospective cohort study

The authors of this study intended to develop a novel prognostic indicator for use in patients with advanced cancer that is significantly better than clinicians' estimates of survival, using a prospective multicentre observational cohort study.

The setting was 18 palliative care services in the UK (including hospices, hospital support teams, and community teams).

Participants were 1 018 patients with locally advanced or metastatic cancer, no longer being treated for cancer, and recently referred to palliative care services.

The main outcome measures were performance of a composite model to predict whether patients were likely to survive for 'days' (0 - 13 days), 'weeks' (14 - 55 days), or 'months+' (>55 days), compared with actual survival and clinicians' predictions.

On multivariate analysis, 11 core variables (pulse rate, general health status, mental test score, performance status, presence of anorexia, presence of any site of metastatic disease, presence of liver metastases, C-reactive protein, white blood count, platelet count, and urea) independently predicted both 2-week and 2-month survival. Four variables had prognostic significance only for 2-week survival (dyspnoea, dysphagia, bone metastases, and alanine transaminase), and eight variables had prognostic significance only for 2-month survival (primary breast cancer, male genital cancer, tiredness, loss of weight, lymphocyte count, neutrophil count, alkaline phosphatase and albumin). Separate prognostic models were created for patients without (PiPS-A) or with (PiPS-B) blood results. The area under the curve for all models varied between 0.79 and 0.86. Absolute agreement between actual survival and PiPS predictions was 57.3% (after correction for over-optimism). The median survival across the PiPS-A categories was 5, 33, and 92 days and survival across PiPS-B categories was 7, 32, and 100.5 days. All models performed as well as, or better than, clinicians' estimates of survival.

In patients with advanced cancer no longer being treated, a combination of clinical and laboratory variables can reliably predict 2-week and 2-month survival.

Gwilliam B, et al. BMJ 2011;343:d4920.

Vitamin A supplements for preventing mortality, illness and blindness in children aged under 5: systematic review and meta-analysis

The authors of this paper in the *British Medical Journal* set out to determine if vitamin A supplementation is associated with reductions in mortality and morbidity in children aged 6 months - 5 years.

Two reviewers independently assessed studies for inclusion. Data were double extracted and discrepancies were resolved by discussion. Meta-analyses were performed for mortality, illness, vision, and side-effects.

Data sources were the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, Medline, Embase, Global Health, Latin American and Caribbean Health Sciences, MetaRegister of Controlled Trials, and African Index Medicus. Databases were searched to April 2010 without restriction by language or publication status.

Eligibility criteria for selecting studies were randomised trials of synthetic oral vitamin A supplements in children aged 6 months - 5 years. Studies of children with current illness (such as diarrhoea, measles and HIV), studies of children in hospital and studies of food fortification or β carotene were excluded.

They included 43 trials with 215 633 children. Seventeen trials including 194 483 participants reported a 24% reduction in all-cause mortality (rate ratio=0.76, 95% confidence interval 0.69 - 0.83). Seven trials reported a 28% reduction in mortality

associated with diarrhoea (0.72, 0.57 - 0.91). Vitamin A supplementation was associated with a reduced incidence of diarrhoea (0.85, 0.82 - 0.87) and measles (0.50, 0.37 - 0.67) and a reduced prevalence of vision problems, including night blindness (0.32, 0.21 - 0.50) and xerophthalmia (0.31, 0.22 - 0.45). Three trials reported an increased risk of vomiting within the first 48 hours of supplementation (2.75, 1.81 - 4.19).

They concluded that vitamin A supplementation is associated with large reductions in mortality, morbidity and vision problems in a range of settings, and these results cannot be explained by bias. Further placebo-controlled trials of vitamin A supplementation in children between 6 and 59 months of age are not required. However, there is a need for further studies comparing different doses and delivery mechanisms (for example, fortification). Until other sources are available, vitamin A supplements should be given to all children at risk of deficiency, particularly in low- and middle-income countries.

Mayo-Wilson E, et al. BMJ 2011;343:d5094.

Modern cigarettes linked with more bladder cancer

We've long known that smoking is the most important modifiable risk factor for bladder cancer. A new study quantifies the excess risks in contemporary populations. Nearly half a million US citizens in the National Institutes of Health Diet and Health Study cohort reported their smoking habits and were then followed up over 11 years. During that period new bladder cancer was recorded in about 4 500 participants.

Compared with people who had never smoked, those who had reported smoking regularly had a fourfold increased risk of bladder cancer, with a number needed to harm of 727. The risk was doubled in former smokers compared with never smokers; for every 1 250 former smokers, one extra bladder cancer was diagnosed.

About half of all bladder cancers could be avoided among both men and women if everyone stopped smoking. This contrasts with earlier studies, where the population attributable risk of bladder cancer for tobacco smoking was estimated at 50 - 65% in men and 20 -30% in women. As these studies

had found weaker associations between smoking and bladder cancer, the researchers hypothesise that changes in cigarette design may account for the differences. Modern cigarettes contain less nicotine and tar, but are richer in some known bladder carcinogens, such as β-naphthylamine. Better detection efforts among smokers could also explain the stronger association.

The US Preventive Services Task Force recently reviewed the evidence on screening for bladder cancer in asymptomatic adults (*Ann Intern Med* 2011;155:246-251). The evidence was deemed insufficient to assess the balance of benefits and harms.

Freedman ND, et al. JAMA 2011;306:737-745.

BRIDGET FARHAM

SINGLE SUTURE

Cause found for ambiguous genitalia

A sexual development disorder in baby boys may be due to the absence of a hormone-production pathway identified in wallabies. The finding could help to diagnose cases of ambiguous genitalia.

One in 4 500 babies has gene mutations that disrupt normal development of testes or ovaries in the womb. These children can be born with external genitalia that do not look typically female or male.

In humans, normal development of the testes relies on testosterone and dihydrotestosterone (DHT). The latter is the more potent and is produced when testosterone is broken down.

Wallabies and some rodents are known to be able to make DHT via two different routes, one of which bypasses testosterone completely. The process works by converting cholesterol, the precursor to testosterone, directly into DHT.

To find out whether a similar 'back door' pathway exists in humans, Anna Biason-Lauber and her colleagues at the University Children's Hospital Zurich in Switzerland investigated the genetic make-up of a family, three of whom have ambiguous genitalia. As these individuals were all able to produce DHT from testosterone, multiple attempts to diagnose the cause of their symptoms had failed.

Biason-Lauber's team screened all the family members for mutations in four genes – *AKR1C1* to *AKR1C4* – known to be involved in producing DHT from cholesterol in the wallaby. They found that two of the genes were mutated only in the three affected individuals, suggesting that they were unable to make DHT using this pathway.

Further screening of 34 people with similar disorders revealed a mutation in one of these genes in four of them.

'This unique, newly described form of developmental sexual disorders establishes that the back door pathway is essential for normal male sexual development,' says Biason-Lauber.

'It certainly could explain some of the undiagnosed patients,' says Jacky Hewitt at the Murdoch Children's Research Institute in Melbourne, Australia, who recently found that 43% of people with sex disorders do not receive a definitive diagnosis.

New Scientist 27 August 2011, p.10.