SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

Alison Tonks, associate editor, *BMJ* atonks@bmj.com

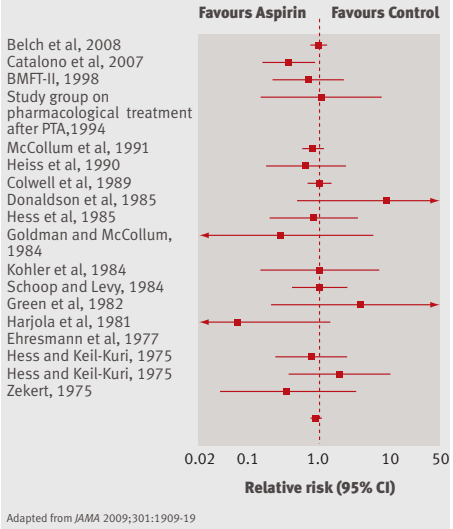
Uncertainty continues over aspirin in peripheral arterial disease

US guidelines recommend low dose aspirin for people with peripheral arterial disease, although the evidence supporting this recommendation is patchy and unconvincing. The latest meta-analysis was ultimately unsatisfying too, reporting a non-significant decrease in cardiovascular events of 12% among patients taking aspirin relative to controls (relative risk 0.88, 95% CI 0.76 to 1.04). The new analysis included 18 randomised controlled trials and 5269 patients with asymptomatic or symptomatic peripheral arterial disease. More than a quarter of the patients came from two trials that recruited only individuals with diabetes. Aspirin appeared to reduce the risk of non-fatal stroke (0.66; 0.47 to 0.94), but had no effect on any other outcome, including death.

These trials had the usual shortcomings: they were relatively small; many were old; and several tested higher doses of aspirin than doctors prescribe today. Some trials combined aspirin and dipyridamole. When all the trials were assessed together, the analysis had just enough power to exclude a 25% reduction in cardiovascular events. Aspirin could, however, be associated with a clinically useful reduction of less than 25%. Doctors should, therefore, continue to prescribe low dose aspirin while waiting for better evidence, says an accompanying editorial (pp 1927-8). At least one large trial is on the way and others must be done. Peripheral arterial disease is an important but long neglected aspect of cardiovascular medicine.

JAMA 2009;30:1909-19

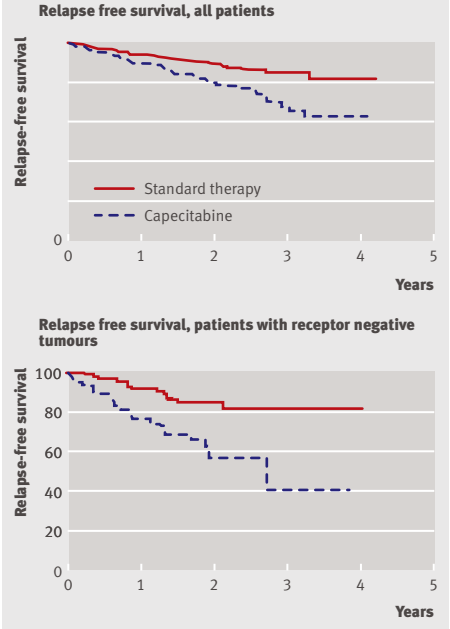
CLINICAL TRIALS ASSESSING ASPIRIN IN PERIPHERAL ARTERIAL DISEASE



Adapted from *JAMA* 2009;301:1909-19

Standard chemotherapy prolongs survival in older women with breast cancer

CHEMOTHERAPY IN OLDER WOMEN WITH BREAST CANCER



Adapted from *N Engl J Med* 2009;360:2055-65

Older women are more likely than younger women to have breast cancer, but much less likely to be included in clinical trials of chemotherapy. To redress the imbalance, researchers from the US recruited only women over 65 years of age for a trial comparing standard chemotherapy with the oral prodrug capecitabine. Standard chemotherapy was clearly better overall, despite being more toxic. Women given capecitabine were more likely to relapse (hazard ratio 2.09, 95% CI 1.38 to 3.17) and more likely to die (1.85, 1.11 to 3.08) than controls given either cyclophosphamide, methotrexate, and fluorouracil or cyclophosphamide and doxorubicin.

Most of the women in this trial were between 65 and 80 years old. They had cancers larger than 1 cm in diameter with clear surgical margins, and around 70% had lymph node involvement. The patients were well and active before the trial, which stopped recruiting earlier than planned because the results were so clear cut. The researchers analysed data from 633 women followed up for a median of 2.4 years. The superiority of standard chemotherapy was particularly marked for women with cancers that tested negative for hormone receptors. Both standard chemotherapy regimens were associated with more serious adverse effects than was capecitabine, although the only two treatment related deaths were in the capecitabine group.

Adjuvant chemotherapy is important for older women, say the authors. These relatively fit older women tolerated the more aggressive regimes and lived longer as a result.

N Engl J Med 2009;360:2055-65

New antivenom for children stung by neurotoxic scorpions

The sting of the *Centruroides sculpturatus* scorpion can cause a neurotoxic syndrome that includes thrashing limbs, abnormal eye movements, and severe respiratory distress. About 200 children are affected every year in Arizona in the US, where they are usually treated with intensive supportive care. No federally licensed antivenoms are available against *C sculpturatus* or any other species of scorpion, although a neutralising agent specific to *C sculpturatus* has recently been developed. A preliminary evaluation suggests that this agent is effective. In a small randomised trial, all eight children given three vials of the new antivenom got completely better within four hours, compared with one of the seven children given a matching placebo. Children given the active drug needed significantly less midazolam to control their symptoms, and their serum concentrations of scorpion venom fell to zero within an hour of treatment.

Most of the children in this trial were under 6 years old and all presented to one of two hospitals in Arizona with neurotoxic symptoms following a sting from a scorpion. All participants got better and went home within two days.

The Mexican biotechnology company Instituto Bioclon sponsored and monitored the trial, and provided the antivenom, which is already available commercially in Mexico.

N Engl J Med 2009;360:2090-8

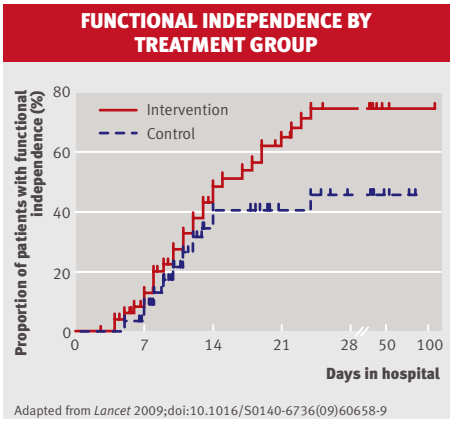
DASH diet helps prevent heart failure

The dietary approaches to stop hypertension (DASH) diet is rich in whole grains, pulses, fruit, and vegetables. It is low fat, high fibre, and increases intakes of potassium, magnesium, and calcium. As its name implies, the DASH diet reduces blood pressure. It might also help prevent heart failure, according to an observational study in more than 36 000 Swedish women.

The participants filled in food frequency questionnaires in 1997 and 1998—when they were at least 48—at the start of a cohort study of mammography. Researchers translated their answers into scores indicating degree of similarity with the DASH diet. Those women with the highest (most consistent) scores were significantly less likely to develop heart failure than those with lowest (least consistent) scores (rate ratio comparing top to bottom quartiles 0.63, 95% CI 0.48 to 0.81). The association between DASH diet components and a lower risk of heart failure was not affected by adjustments for age; activity; energy intake; body mass index; education; heart attack and family history of heart attack; cigarette smoking; use of hormonal therapy; hypertension; and cholesterol concentration. The researchers tracked the women through Sweden's comprehensive hospital admission and death registers for 7 years. Overall, 443 developed heart failure serious enough to require hospital admission, a rate of 18.1 per 10 000 women per year.

Arch Intern Med 2009;169:851-7

Early physical and occupational therapy aids recovery in some ICU patients



A randomised trial in two intensive care units suggests that physiotherapy and occupational therapy during daily interruptions in sedation can help critically ill patients recover functional ability. By the time patients were discharged from hospital, 59% (29/49) of those given daily therapy sessions were completely independent, compared with 35% (19/55) of controls who had standard care, including regular interruptions in sedation (odds ratio 2.7, 95% CI 1.2 to 6.1).

Physiotherapy and occupational therapy were tailored to patient ability; started within two days of admission to the intensive care unit; and ranged from passive movement of limbs to transfers, sitting out, and even walking. All activity milestones were achieved faster by patients having therapy. The intervention also seemed to reduce delirium, even though both groups had daily breaks from sedation. Therapy made no measurable difference to length of stay in the intensive care unit, length of stay in hospital, or survival, but the trial was small and might have been underpowered for these outcomes.

The 104 participants were carefully selected and were functionally well before admission to one of the intensive care units. Most had sepsis, half had acute lung injury, and a third had diabetes. Fewer than one in ten patients screened were suitable for recruitment, so these findings will not apply to everyone in intensive care.

Lancet 2009; doi:10.1016/S0140-6736(09)60658-9

Hospital pharmacists offer lasting benefits to older inpatients

Older inpatients have a high risk of drug related problems including errors, omissions, drug reactions, and poor adherence on discharge, all of which can lead to further hospital visits. In a randomised trial from Sweden, a dedicated pharmacist for patients over 80 years of age reduced hospital visits in the year after discharge by a significant 16% (odds ratio 0.84, 95% CI 0.72 to 0.99). This drop was driven by a 47% reduction in visits to the emergency department (0.53, 0.37 to 0.75).

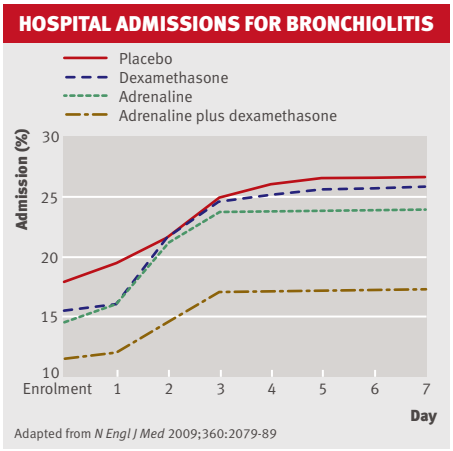
The study included 400 people who were admitted to one of two medical wards in a single hospital. Half of the participants were cared for by a team that included a hospital pharmacist who reviewed drug treatments, advised health professionals, counselled patients, checked discharge prescriptions, liaised with the primary care team, and telephoned patients two months after discharge to encourage adherence and answer questions. The remaining participants had usual care.

The pharmacists seemed particularly effective at preventing drug related readmissions, which were 80% lower in the intervention group (0.20, 0.10 to 0.41). Overprescribing of psychotropic drugs, antihypertensive agents, or diuretics was the commonest cause of drug related readmission.

The patients in this trial were old and frail, with a high prevalence of chronic diseases. They were taking an average of eight different drugs a day.

Arch Intern Med 2009;169:894-900

Combination therapy might reduce hospital admissions for bronchiolitis



Nebulised adrenaline and oral dexamethasone are both potentially useful treatments for babies with bronchiolitis. These treatments seem to work best when given together, according to a randomised trial from Canada. The trial compared dexamethasone alone; nebulised adrenaline alone; both treatments; or neither treatment (a double placebo) in 800 babies attending the emergency department with probable bronchiolitis. Babies given both active treatments were less likely to be admitted (34/199 (17.1%) *v* 53/201 (26.4%); relative risk 0.65, 95% CI 0.45 to 0.95) and were discharged from the emergency department slightly earlier than babies given a double placebo. Neither active treatment alone reduced admissions. The combined treatment and adrenaline alone improved symptoms in the first hour.

The synergistic effect of combining nebulised adrenaline with five days of oral dexamethasone was unexpected, and it's too early to recommend this regimen routinely, says an accompanying editorial (pp 2130-3). The benefit seemed small and became statistically insignificant once the researchers adjusted their admission results to account for the multiple comparisons necessary in a trial with four arms. The researchers, however, believe this drug combination is worth exploring further. The babies in this trial presented during peak season for respiratory syncytial virus with respiratory distress, their first episode of wheeze, and signs of a respiratory tract infection.

N Engl J Med 2009;360:2079-89

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