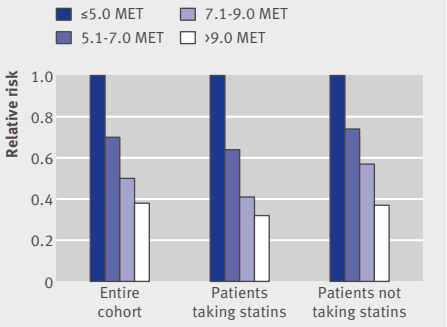
All you need to read in the other general medical journals

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

Prescribe exercise for men with dyslipidaemia

Relative mortality risk by fitness category



Adapted from *Lancet* 2012; doi :10.1016/S0140-6736(12)61426-3

Statins reduce mortality in middle aged men with dyslipidaemia. Physical fitness is also associated with longer survival in this group, say researchers. We should be prescribing both.

In a cohort of 10 043 adults from the US (mostly men), statins and fitness had independent effects on risk of death from all causes over 10 years. Mortality fell steadily with increasing physical fitness in men who took statins and in those who didn't. The two treatments are clearly complementary, says a linked comment (doi:10.1016/S0140-6736(12)61804-2). Among men treated with statins, the most fit were 70% less likely to die than the least fit (hazard ratio 0.30, 95% CI 0.21 to 0.41). The comparable hazard ratio was 0.53 (0.44 to 0.65) in men not treated with statins.

This cohort had an average age close to 60 years when recruited. Roughly half the participants had hypertension, a fifth were smokers, and more than a third had diabetes. Cardiovascular disease was common. They had high concentrations of total cholesterol (6.1 and 6.0 mmol/L in the two statin groups) and low density lipoprotein cholesterol (4.2 and 4.0 mmol/L) at baseline. Associations were adjusted for age, sex, body mass index, other treatments for cardiovascular disease, cardiovascular history, and risk factors. The authors did further analyses to try to account for the fact that sick men don't exercise (reverse causation).

They defined fitness using metabolic equivalents or METS, where one MET is energy expenditure at rest. Any fitness level above 5 METS was linked to lower mortality in this study, regardless of statin treatment. Men can achieve this level of fitness through moderate exercise such as light cycling, says the comment. Exercise is cheap, easy, and safe within reasonable limits. Exercise prescriptions should be the rule not the exception.

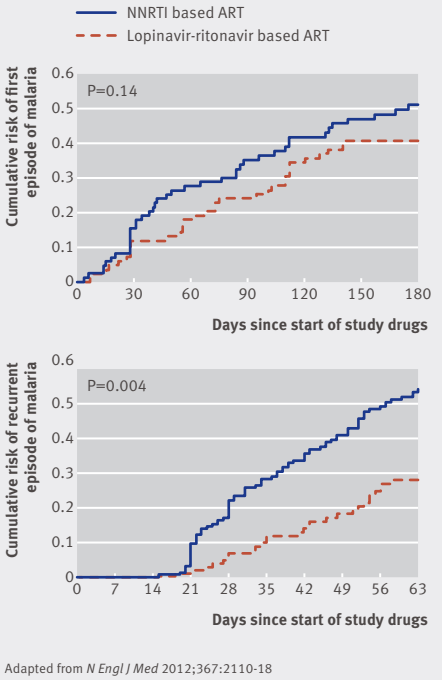
Lancet 2012; doi:10.1016/S0140-6736(12)61426-3

Cite this as: *BMJ* 2012;345:e8209

ART regimen protects children from malaria

A preliminary trial from Uganda suggests that some antiretroviral treatments (ART) for HIV can also help prevent malaria in children. Children treated for HIV with a regimen based on lopinavir and ritonavir had significantly fewer episodes of falciparum malaria than controls treated with a plan based on non-nucleoside reverse transcriptase inhibitors (NNRTIs) (1.32 *v* 2.25 episodes per person year; incidence rate ratio 0.59, 95% CI 0.36 to 0.97). The difference was driven by a large decrease in recurrences among children given lopinavir and ritanovir.

Risk of new malaria and risk of recurrence



Adapted from *N Engl J Med* 2012;367:2110-18

All episodes of malaria were treated with artemether and lumefantrine. Children taking lopinavir and ritonavir had significantly higher serum concentrations of lumefantrine than controls. The likeliest explanation is that their antiretroviral regimen inhibited metabolism of lumefantrine, boosting exposure and preventing recurrences of malaria, say the authors. Higher concentrations of lumefantrine were associated with significantly more pruritis in this group (5.6% *v* 1.2%; P=0.04). The authors report 10 serious adverse events overall and judge that just three were linked to study drugs: one child taking the NNRTI regimen developed Stevens-Johnson syndrome and two children taking lopinavir and ritonavir developed neutropenia.

The trial wasn't big enough to establish the safety of the antimalarial ART regimen and further trials should now be done, say the authors. Not least to see if these promising results extrapolate to areas with a lower incidence of malaria. The 176 children in this study had 285 new episodes of malaria during an average follow-up of one year.

N Engl J Med 2012;367:2110-8

Cite this as: *BMJ* 2012;345:e8214

Automated calls and letters encourage adults to fill first prescriptions

Many patients stop taking their prescribed drugs and many more don't even start. In a pretrial audit from the US, almost one in five adults failed to fill their first prescription for a statin. Automated telephone calls and letters helped reduce primary non-adherence in the subsequent trial, but even then more than half the intervention group failed to pick up their tablets at a pharmacy (42.3% (1102/2606) of the intervention group filled a first prescription *v* 26.0% (679/2610) of controls; P<0.001). Adherence to subsequent prescriptions was even lower.

Automated telephone calls and letters are relatively cheap. These authors computed marginal costs of $1.70 (£1.05; €1.3) per person, although they were operating within a single well organised health plan, with integrated medical and pharmacy services. Patients could be tracked easily from clinic to pharmacy and prompted when they didn't make it.

"A cream cheese spread, a smooth orchestral sound, the birthplace of the American constitution, brotherly love, and a chromosome of evil repute: what do they all have in common? Why, yes, it is the name Philadelphia"
Richard Lehman's blog at www.bmj.com/blogs

Most healthcare in the US isn't that well integrated, says a link comment (doi:10.1001/jamainternmed.2013.1821). We aren't yet ready for this kind of intervention on a large scale, although we may be heading in the right direction. Primary non-adherence is likely to remain a serious problem until we find ways to engage all patients at the point of prescription, instead of waiting until they have failed to collect their drugs.

Arch Intern Med 2012; doi:10.1001/2013.jamainternmed.717

Cite this as: *BMJ* 2012;345:e8215

Maltreated neglected children are more likely be troubled adults

A meta-analysis of 124 observational studies has found a strong and consistent association between non-sexual maltreatment of children and mental health problems, drug use, risky sexual behaviour, and sexually transmitted infections later in life.

The authors focused on physical abuse, emotional abuse, and neglect of children. All three were significantly associated with poor mental health later, including depression, anxiety, eating disorders, and suicide. Risks were increased twofold to threefold in adults who reported abuse as children, relative to those who did not. Most of the studies were cross sectional or retrospective, but 16 prospective cohorts were able to establish that adverse outcomes followed abuse, rather than the reverse.

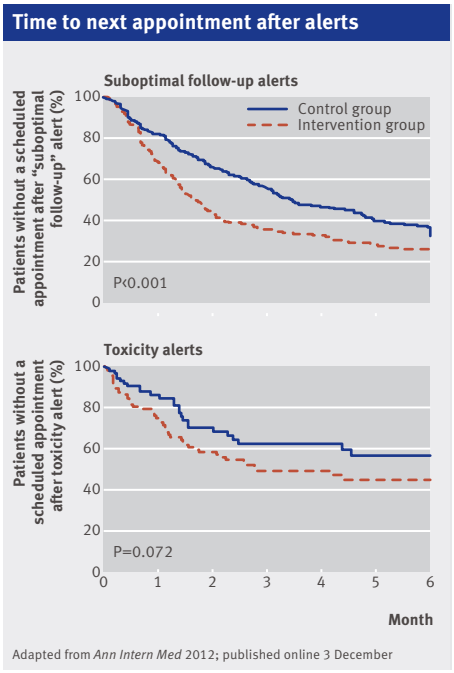
Many studies made some attempt to control for the confounding effect of social and demographic factors and a shared family environment, but few were able to account for inheritance of poor mental health. Methods, definitions, and populations were heterogeneous, and the authors found hints of publication bias—the tendency for studies reporting positive associations to be published, while negative studies are not.

Despite these limitations, combined results give a strong signal that non-sexual abuse of children is at least an important risk factor for poor mental and sexual health in adulthood, say the authors. Causality is impossible to prove but looks plausible.

PLoS Med 2012;9:e1001349

Cite this as: *BMJ* 2012;345:e8216

Interactive alerts improve immune status of patients with HIV



Adapted from *Ann Intern Med* 2012; published online 3 December

In 2007, informatics experts at one US hospital developed and began testing a new clinical decision support system (CDSS) to streamline the management of outpatients with HIV. The system was embedded in the electronic medical record, and it alerted health professionals when patients needed an appointment because of new drug toxicity, virological failure, or suboptimal follow-up. The alerts were interactive and included short cuts to encourage appropriate action. They were emailed to providers twice a week, as well as appearing prominently on home pages in electronic medical records.

The new CDSS was popular and seemed to work. In a randomised trial, patients in the new system had greater increases in CD4 cell counts than controls managed with straightforward static alerts (0.0053 *v* 0.0032×10^9 cells/L/month; difference 0.0021×10^9 cells/L/month; 95% CI 0.0001 to 0.004). They were seen more quickly after abnormal laboratory tests or an alert about poor follow-up. They had lower rates of suboptimal follow-up after six months (20.6 *v* 30.1 events per 100 patient years; P=0.022).

The authors tested their system, called FastTrack, in 1011 patients at the clinic, managed by 33 healthcare providers, mostly doctors. Training took just five minutes. The trial wasn't perfect and took place in a single clinic with strong informatics infrastructure and back-up. But the results do suggest that well designed decision support can make a clinically relevant difference to patients with HIV, say the authors.

Ann Intern Med 2012; published online 3 December

Cite this as: *BMJ* 2012;345:e8217

Protected sleep time for US interns

In 2009 general medical interns at two US hospitals had to work one night in four. They began work at 7 am one morning and went home about 1 pm the following day, an overnight shift of roughly 30 hours. They got little sleep during shifts, so researchers conducted trials (one at each hospital) to test a new schedule that gave on-call interns five hours of protected sleep between 12.30 am and 5.30 am. Interns slept about one hour longer during protected nights than they did during control nights (2.86 *v* 1.98 hours at one hospital and 3.04 *v* 2.04 hours at the other; P<0.001 for both comparisons). They had significantly fewer nights with no sleep, did better than controls on tests of vigilance in the morning, and were less sleepy during the day. The authors couldn't tell if protected sleep helped interns make fewer mistakes. It had no discernible effect on patient outcomes, including deaths.

Protecting interns' sleep proved feasible in both hospitals, although one had to employ an extra resident to cover protected nights. Both hospitals had to pay incumbent residents extra for holding interns' mobile phones between 12.30 am and 5.30 am.

In 2011, the US regulator of graduate medical education had to decide how to tackle harmful long shifts for doctors in the first year of training. The accreditation council chose shorter shifts (16 hours maximum) over protected sleep time. This new evidence justifies a head to head trial comparing the two, say the authors, and it must be big enough to establish which option is better for patients, as well as doctors.

JAMA 2012;308:2208-17

Cite this as: *BMJ* 2012;345:e8224