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RESEARCH NEWS All you need to read in the other general medical journals Alison Tonks, associate editor, *BMJ* atonks@bmj.com

Dabigatran "non-inferior" to warfarin, but only just

New oral anticoagulants offer the prospect of stability and convenience for people needing treatment for a recent deep vein thrombosis or pulmonary embolus. They might also allow longer term treatment to prevent recurrence, and Boehringer Ingelheim recently reported results from a pair of trials that tested extended use of their new agent dabigatran, a direct thrombin inhibitor. Dabigatran looked non-inferior to warfarin in a head to head trial (risk of recurrence 1.8% (26/1430) *v* 1.3% (18/1426); hazard ratio 1.44, 95% CI 0.78 to 2.64) and caused significantly fewer bleeds of any severity (19.4% *v* 26.2%; 0.71, 0.61 to 0.83). All participants had completed treatment for a first unprovoked episode of venous thromboembolism and were judged to be at risk of a second. They took warfarin or dabigatran for an extra six to 36 months. Dabigatran worked better than a placebo in a smaller sister trial and caused more bleeding.

The authors admit they were generous with their non-inferiority margin in the head to head comparison, which allowed a risk increase of nearly threefold (2.85) to be accepted as non-inferior. The upper confidence limit around the main results came close, and the editorial says doubts remain about this and other new oral anticoagulants (p 767). Dabigatran was associated with a significantly higher risk than warfarin of acute coronary syndrome (0.9% *v* 0.2%; P=0.02). Others have reported similar concerns and the association deserves further scrutiny, says the editorial.

N Engl J Med 2013;368:709-18

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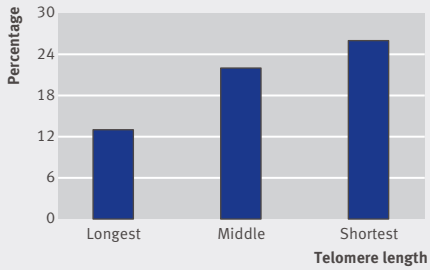
Young adults with shorter telomeres have lower resistance to colds

Researchers from the US recently infected 152 volunteers with the common cold to study the link between acute infections and telomere length in leucocytes. The volunteers, who had a mean age of 30 years, agreed to be given nose drops containing rhinovirus 39 in exchange for a fee of $1000 (£655; €758). After a blood test to measure telomere length, they were isolated for five days while researchers conducted daily nasal lavage to look for viral shedding, weighed nasal mucus, and measured clearance using flavoured dye placed on the inferior turbinates. Further blood tests tracked their immune response.

Incidence of clinical infection by telomere length in CD8CD28 negative lymphocytes



Adapted from *JAMA* 2013;309:699-705

Just over two thirds of the volunteers started shedding virus or developed specific antibodies indicating infection (105; 69%). Just over a fifth also had a cold, defined by the weight of nasal mucus and sluggish mucociliary clearance (33; 22%). Volunteers with the shortest telomeres had the highest odds of infection in adjusted analyses (odds ratio per 1 standard deviation decrease in telomere length, 1.71, 95% CI 1.08 to 2.72). The researchers also found a link between clinical colds and shorter telomeres, but only for the subset of T cells most susceptible to telomere shortening (CD8CD28 negative cells). This subset has an important role in clearing infected cells, say the researchers.

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Worse outcomes for adults given lactated Ringer's solution during resuscitation

In Japan, management of cardiac arrest outside hospital can include an intravenous infusion of lactated Ringer's solution. These infusions, usually around 200 or 300 ml, were associated with lower odds of a good outcome in a large cohort study, and researchers suspect worsening acidosis might be to blame. Lactated Ringer's solution has a mean pH of 6.7.

The researchers analysed routine data collected on more than half a million Japanese adults who had a cardiac arrest outside hospital between 2005 and 2009. A fifth (109 140/531 854) received lactated Ringer's solution before they reached hospital. They were more likely to return to spontaneous circulation than adults managed without the infusions but less likely to survive for one month with no more than moderate disability. The difference was consistent in a series of increasingly rigorous analyses, culminating in a comparison of adults matched using propensity scores, which reported a 25% reduction in the odds of a good neurological outcome at one month for adults given infusions (1.58% *v* 1.79%; odds ratio 0.746, 95% CI 0.573 to 0.971).

Lactated Ringer's solution might be harmful, but it's impossible to prove with this kind of analysis, say the researchers. Future studies should include data on what happened to patients when they reached hospital, an unavoidable omission from these analyses.

PLoS Med 2013;10:e1001394

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Advanced breast cancers increasing in young women

The incidence of advanced breast cancers is rising slowly but steadily among young women in the US, according to national registry data. The absolute increase between 1976 and 2009 looks small but significant say researchers (from 1.53/100 000 to 2.9/100 000) and indicates a rise of 2% a year for the past three decades (2.07%, 95% CI 1.57% to 2.58%). The trend may even be accelerating and seems confined to women aged 25-39 years who have distant spread at diagnosis.

Rates of cancer diagnosed at other stages, and in other age groups, remained steady during the study period, except for a short term increase in early diagnoses after the launch of screening mammography for older women. The study included almost a million women with cancers recorded in registries that covered 28% of the US population by 2009.

The rising trend of late diagnoses in young women was particularly steep for breast cancers that tested positive for hormone receptors. Annual increases for these cancers reached more than 8% a year between 1992 and 2009.

Young women with advanced cancers have the worst prognosis and the most years of life to lose, say the researchers. We don't know why more young women are being diagnosed so late, and researchers from other countries should check their national data for a similar signal.

JAMA 2013;309:800-5

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