

RESEARCH

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RESEARCH NEWS All you need to read in the other general medical journals Kristina Fišter, associate editor, *BMJ* kfister@bmj.com

Miravirsen works against hepatitis C virus

Hepatitis C virus is dependant for growth on microRNA-122 in the liver of infected people. A new drug, miravirsen, binds to microRNA-122, disabling the binding and growth of the virus.

A phase IIa study tested three doses (3 mg, 5 mg, and 7 mg/kg body weight) against placebo in 36 people with previously untreated chronic hepatitis C infection. The drug was injected weekly for a month.

Over the four and a half months of the study, a dose dependent reduction was seen in plasma levels of viral RNA. Compared with baseline, the mean maximum reduction in viral RNA (\log_{10} IU per mL) was 1.2 with 3 mg, 2.9 with 5 mg, and 3.0 with 7 mg. In the placebo group, this figure was 0.4 \log_{10} IU per mL.

Four of nine patients randomised to the maximum dose were clear of the virus at the end of treatment. Still, once the drug was stopped, levels of viral RNA rebounded in participants who were not taking interferon and ribavirin.

The drug was well tolerated and no signs of drug resistance were noted. A linked editorial notes that miravirsen could become part of a future drug cocktail that can control hepatitis C virus (doi:10.1056/NEJMe1301348).

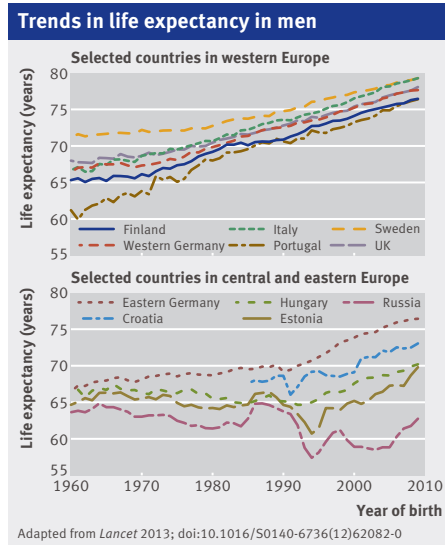
N Engl J Med 2013; doi:10.1056/NEJMoa1209026

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Shorter life expectancies in eastern versus western Europe

The gap in life expectancy between eastern and western Europe is 12 years for men and eight years for women, and it is greater today for men than it was four decades ago. Whereas life expectancy has continuously improved in the west over that time, patterns have been inconsistent in the east.

The rise in the west is thought to be linked with economic growth and improvements in healthcare and policy. Success was seen in relation to perinatal and maternal health, immunisations, detection and treatment of hypertension, screening for cancer, and more effective treatment of many diseases. Policies such as tobacco control, road traffic safety, and



reductions in air pollution have also contributed to better health, although success has varied between countries.

In the east—in this study, central and eastern Europe as well as the whole of the former Soviet Union—economic problems coupled with the lack of effective health policies have led to poorer health. Before the fall of the Berlin Wall, tobacco and alcohol control were almost non-existent in large parts of the region, as was awareness of the role of nutrition in prevention of chronic diseases. Smoking rates are still high, especially in young women. In some countries surrogate alcohols—sold as aftershaves and medicinal tinctures and containing 70-90% ethanol—are consumed widely. Control of infectious diseases broke down in some countries, with re-emergence of diphtheria and tuberculosis.

Care may have improved in central and eastern Europe since the fall of communism, but it has worsened in the former Soviet Union, where the newly introduced formal and informal payments now mean many people don't get the care they need.

Also of concern are rising health inequalities within countries, and common challenges remain in both eastern and western Europe, such as policies on food and alcohol.

This is the first time the *Lancet* has published a series of papers on health in Europe (www.thelancet.com/series/health-in-europe).

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Chelation therapy may improve cardiovascular health

Chelation has been used by alternative therapists to treat atherosclerosis for over half a century, with little evidence to back it. Usually given with a vitamin infusion, disodium EDTA binds divalent and trivalent cations such as calcium, magnesium, lead, zinc, and aluminum to facilitate their excretion in urine. More than 100 000 adults undergo this treatment annually in the US.

A study used a 2×2 factorial design to test 40 infusions of a 500 mL chelation solution (containing disodium EDTA, ascorbate, B vitamins, electrolytes, procaine, and heparin) against an infusion placebo, as well as an oral regimen of vitamins and minerals against oral placebo. The 1708 participants, recruited from 134 US and Canadian centres, were people over 50 years who had experienced myocardial infarction and had a serum creatinine of 2 mg/dL (1 mg/dL=88.4 μ mol/L) or less.

During a median follow-up of more than four years, an effect was seen on the composite outcome of death, recurrent heart attack, stroke, coronary revascularisation, or admission to hospital for angina. This outcome was seen in 222 (26%) people randomised to chelation versus 261 (30%) of those who received placebo (hazard ratio 0.82, 95% CI 0.69 to 0.99). A similar effect was seen for the individual components of the composite outcome, although not for deaths (10% v 11% with placebo; 0.93, 0.70 to 1.25).

The authors warn that this evidence does not justify routine use of chelation, as do two linked editorials. In one (p 1291), the journal's editors explain why they decided to publish the paper despite this 10 year, \$31m (£20.5m; €24.2m) trial having been controversial since its inception. The other editorial discusses the study's shortcomings, arguing that its results are not reliable (p 1293). Concerns include marginal statistical significance for the main finding, unbalanced dropout rates—289 (17%) of participants withdrew consent during the trial, 115 of those receiving chelation versus 174 with placebo—as well as unblinding of the sponsors and possibly researchers and participants.

JAMA 2013;309:1241-50

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