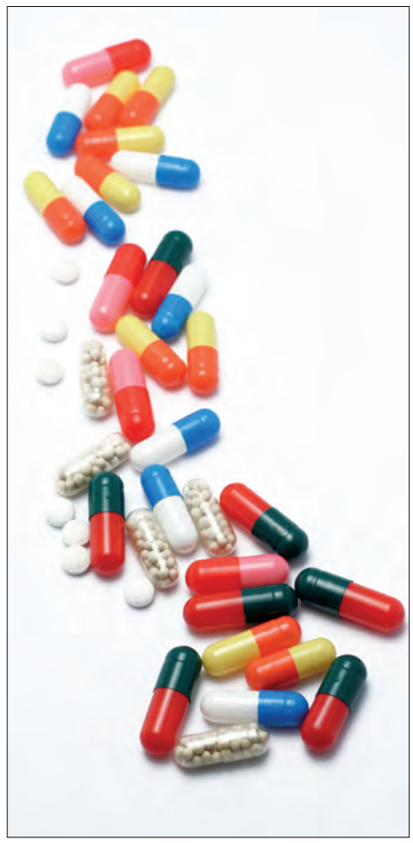
Abstracts

Revisit standards for approving long-term drugs

The European Medicines Agency (EMA) approved 200 brand-new drugs between 2000 and 2010. The 161 standard medicines – not orphans – included 84 destined for long-term use, by patients with asthma, for example. A review of the regulator's public reports found that standard drugs had been tested in a mean of 1 708 volunteers and patients before approval. More than half had been tested in fewer than 2 000 people, and 20 had been tested in 500 or less.



The 84 drugs for long-term use had been tested in a mean of 2 338 volunteers and patients before approval. They weren't tested for long enough to establish safety, say the authors. There are no hard and fast rules, but European and US regulators both follow international guidance recommending that at least 1 000 - 1 500 patients receive drugs for long-term use before approval, including at least 300 treated for 6 months and at least 100 treated for 12 months. Four-fifths of new long-term drugs in the review met these standards (69/84 for 6 months and 67/84 for 12 months), and the authors think the recommendations should be more demanding. The total number of people exposed to drugs before approval has changed little since the 1980s. A re-evaluation is long overdue.

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Life expectancy in eastern Europe shorter than in western Europe

The gap in life expectancy between eastern and western Europe is 12 years for men and 8 years for women, and it is greater today for men than it was 4 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 (http://www.thelancet.com/series/health-in-europe).

BMJ 2013;346 [http://dx.doi.org/10.1136/bmj.f2067] (Published 3 April 2013.)

Lessons from Cuba

As a result of a profound economic crisis in 1990, the population of Cuba has been involved in a massive public health experiment. Variations in the rates prevalence of type 2 diabetes around the world have largely been explained by relative weight or adiposity. Most cohort studies have suggested a 'U-shaped' association between body mass index and mortality, with the lowest point in the index range of 24 - 29. What is not known are the net health impacts of a reduction in body mass index in a population and the time lag between changes in body mass index and the prevalence of non-communicable disease.

In the early 1990s Cuba saw a reduction in the overall amount of food available

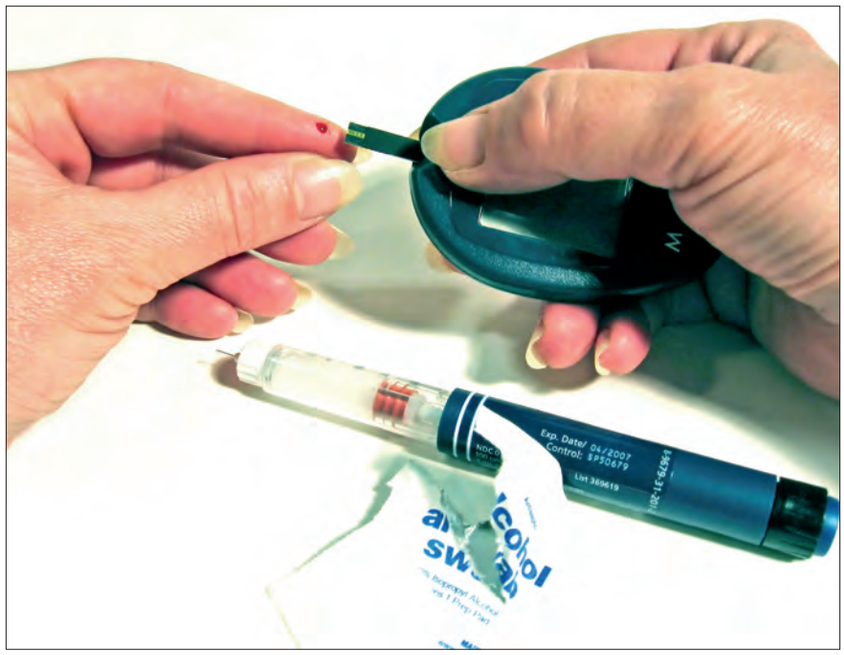
to its population and a simultaneous decrease in the availability of motorised transport, forcing people to walk or cycle. This was a result of the aftermath of the dissolution of the former Soviet Union and a tighter US embargo. The largest effect of this economic crisis took place over about 5 years (1991-1995 – the so-called 'special period'). Normal daily life was largely unaffected – but people ate less and exercised more because they continued to go to work and school and public health surveillance continued.

The authors of a recent paper in the *British Medical Journal* report on repeated cross-sectional surveys and ecological comparison of secular trends to look at the association between population-wide loss and gain in weight and the prevalence of diabetes and cardiovascular and cancer mortality trends over a 30-year interval.

They found rapid declines in diabetes and heart disease, which accompanied an average population-wide loss of 5.5 kg in weight. A rebound in population weight followed in 1995 (33.5% prevalence of overweight and obesity) and exceeded pre-crisis levels by 2010 (52.9% prevalence). The population-wide increase in weight was immediately followed by a 116% increase in diabetes prevalence and 140% increase in diabetes incidence. Six years into the weight rebound phase, diabetes mortality increased by 49% (from 9.3 deaths per 10 000 people in 2002 to 13.9 deaths per 10 000 people in 2010). A deceleration in the rate of decline in mortality from coronary heart disease was also observed.

The conclusions were that a relatively modest 4 - 5 kg loss of weight, in a relatively healthy population, resulted in a reduction by half in diabetes mortality and by a third in coronary heart disease mortality. The rebound in body weight that occurred after 2000 was accompanied by an increase in diabetes incidence and mortality and a reduction in the decline in mortality in coronary heart disease. The authors point out that these findings cannot be compared with other countries since no country or regional population has successfully reduced the distribution of body mass index or reduced the prevalence of obesity through public health campaigns or targeted treatment programmes.

Franco M, et al. BMJ 2013;346 [http://dx.doi.org/10.1136/bmj.f1515] (Published 9 April 2013.)



Melatonin secretion and the incidence of type 2 diabetes

It is known that mutations that reduce the function of the melatonin receptor are associated with insulin resistance and type 2 diabetes. A previous cross-sectional study of people without diabetes has shown that lower nocturnal melatonin secretion is associated with increased insulin resistance.

In a study published recently in the *Journal of the American Medical Association* McMullan and colleagues looked at the association between melatonin secretion and the risk of developing type 2 diabetes. They used a case-control study nested within the Nurses Health Study cohort. Among trial participants who did not have diabetes and who provided urine and blood samples in 2000 (at baseline) they identified 370 women who then developed type 2 diabetes from 2000 to 2012 and matched 370 controls.

Their main outcome measures were associations between melatonin secretion at baseline and the incidence of type 2 diabetes. They controlled for demographic characteristics, lifestyle habits, measures of sleep quality and biomarkers of inflammation and endothelial dysfunction.

They found that the onset of diabetes was linked with higher body mass, low exercise levels, poor diet, poor sleep patterns, a history of hypertension and a family history of diabetes, as well as high markers of inflammation and endothelial dysfunction.

Even after accounting for these factors, melatonin concentrations were predictive of developing type 2 diabetes. When women were divided into thirds according to their morning urine levels of melatonin, those in the upper third (4 times higher than levels in the bottom third) had half the risk of developing diabetes. It remains to be seen whether or not this risk factor can be modified.

McMullan CJ, et al. JAMA 2013;309(13):1388-1396. [http://dx.doi.org/10.1001/jama.2013.2710]