Chronic diseases: the case for urgent global action

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When *The Lancet* published its first series and call to action on chronic diseases in October, 2005, we labelled global efforts to control non-communicable conditions as "the neglected development goal". 2 years on, although chronic diseases are yet to be included formally in the existing eight Millennium Development Goals, no serious conversation about global health can now take place without at least citing chronic disease as a critical part of international health strategies. This progress is largely thanks to WHO's consistent advocacy for the non-communicable disease agenda, which was given a huge injection of energy with the agency's 2005 report, *Preventing chronic diseases: a vital investment*.[1]

Thanks to a continued collaboration between *The Lancet* and a remarkable team of scientists from WHO, together with public health experts from the USA, India, Mexico, New Zealand, Australia, UK, and Switzerland (all working together under the independent umbrella of the Chronic Disease Action Group), we now launch a second, deeper, and we believe more nuanced report that aims to extend our understanding, not only of the impact of chronic diseases on human development but also of what can be achieved through interventions at the population and individual levels to prevent and treat some of these conditions.

The authors of this latest *Lancet* report selected 23 countries that account for 80% of the total burden of chronic disease in developing nations. These nations include the most populous (India and China) as well as some of the most resource-poor (Democratic Republic of Congo, Ethiopia, and Nigeria). Addressing chronic disease is not a marginal matter. If the global goal set by WHO was met—a further 2% reduction in mortality annually between 2006 and 2015—24 million deaths would be averted in these 23 countries alone. An additional 2% mortality reduction would also save US$8 billion by limiting labour and treatment costs.

As one might expect, the cost-effectiveness evidence for tobacco control, salt restriction, and drug treatment for high-risk cardiovascular disease is compelling in low-income and middle-income countries. Gaps remain, however, in the evidence to support policies to reduce dietary saturated and trans fat. And although arguments about causality and probable benefit would favour broader behavioural and health-system reforms to avert chronic diseases such as diabetes, specific data on cost-effectiveness remain to be gathered. Policymakers face a difficult judgment call. What level of evidence should they require before intervening? The authors of *The Lancet* report argue that evidence is not dichotomous—it is not merely present or absent. Instead, our reasoning is a continuum that should, under certain conditions, trigger action combined with careful evaluation.

Our report also describes estimates of the likely benefits and costs of these interventions. Salt reduction and tobacco control, for example, could avert almost 14 million deaths in these 23 priority countries, at a cost of less than $0·40 per person per year in low-income settings. Scaling up treatment with aspirin and drugs to lower blood pressure and cholesterol would avert almost 18 million deaths over the next 10 years. The average cost would be about $1·10 per person per year. The sum total annual cost of individual and population interventions combined is nearly $6 billion.

WHO/Chris De Bode

Woman in Pakistan with diabetes complications

WHO has been particularly successful at creating the global leadership in science and public health to build a convincing case for intervening to control non-communicable diseases. By striking contrast, many donors have been tone-deaf to these increasingly robust scientific arguments. The World Bank, foundations, the private sector, and governments need to play catch-up. A few enlightened nations, such as the UK and Canada, are enthusiastically responding to invitations to act.

Together with the recent *Lancet* series on Global Mental Health—and the parallel launch of a new Global Movement for Mental Health—this latest report on chronic disease lays down the scientific foundations to build civil society and professional advocacy, and so change national and global policy. The value of independent science generated through innovative collaborations across countries and between institutions, mediated through established scientific reporting channels, has the potential to transform our approach to some of the most intractable health challenges facing humankind.

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1 World Health Organization. Preventing chronic diseases: a vital investment. 2005. http://www.who.int/chp/chronic_disease_report/full_report.pdf (accessed Nov 13, 2007).
2 *Lancet* Global Mental Health Group. Scale up services for mental disorders: a call for action. *Lancet* 2007; **370:** 1241–52.

CETP inhibition

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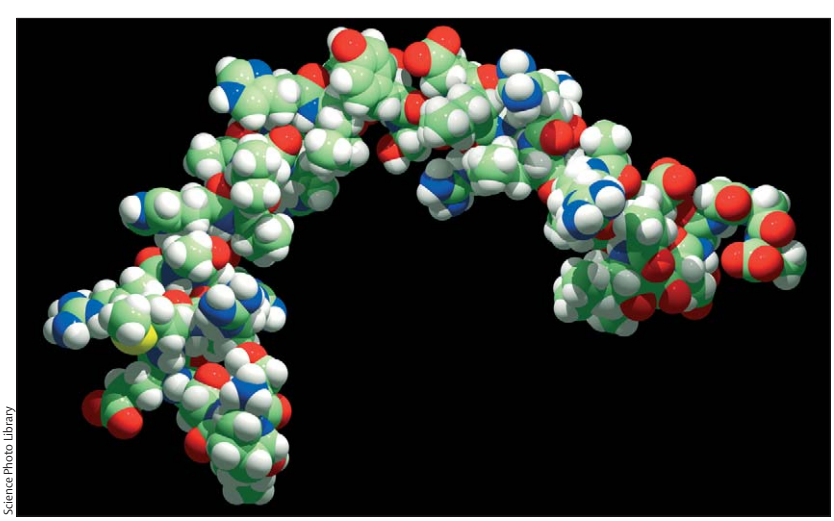
In today's *Lancet*, Rajesh Krishna and colleagues report two doubled-blind, placebo-controlled, randomised phase I studies with the cholesteryl ester transfer protein (CETP) inhibitor, anacetrapib, in healthy individuals and in patients with dyslipidaemia.[1] The drug increased HDL cholesterol and decreased LDL cholesterol. Importantly, there was no effect on blood pressure.

LDL and HDL are independent factors that modulate the risk of cardiovascular disease, and increases in HDL cholesterol might decrease cardiovascular risk.[2] CETP inhibitors raise HDL and decrease LDL. Torcetrapib was the first tested in large long-term trials (ILLUMINATE,[3] RADIANCE I,[4] RADIANCE II,[5] and ILLUSTRATE[6]). On Dec 2, 2006, all torcetrapib clinical trials were stopped in the interests of patients' safety. The data and safety monitoring board on ILLUMINATE recommended termination of the study because there were significantly more major cardiovascular events in the group receiving torcetrapib in combination with atorvastatin than in the group receiving atorvastatin monotherapy.[3] In the other trials, torcetrapib failed to reduce the development of atherosclerosis in the common carotid[4,5] and coronary arteries,[6] but increased blood pressure in every study.



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Apolipoprotein A-I, a fragment of HDL

Torcetrapib induced significant increases in systolic blood pressure (5·4 mm Hg) and in serum concentrations of sodium, bicarbonate, and aldosterone, and a significant decrease in serum potassium.[3] Increased risk of death was higher when the increase in bicarbonate or decrease in potassium was greater than the median change.[8] This off-target effect might have been associated with the increased mortality and morbidity in ILLUMINATE, although further analyses are needed to interpret this relation.

Further long-term studies in larger populations will be necessary to confirm the absence of an off-target effect on blood pressure with anacetrapib. This prudence is necessary because torcetrapib and anacetrapib are in the same structural class, and because the effect of torcetrapib on systolic blood pressure was found in large long-term studies;[3-6] the effect was lower[7] and even not statistically significant[8] in phase 2 studies. Furthermore, in ILLUMINATE,[3] the standard deviations of log-rank tests for the effects of torcetrapib on systolic blood pressure