

At University College London Hospitals NHS Foundation Trust, the use of medicines committee has endorsed a policy of switching from atorvastatin 10 mg and 20 mg (no longer stocked) under new statin guidelines.⁷ The first line statin is simvastatin 40 mg, which is substituted when a newly admitted patient has been taking atorvastatin 10 mg or 20 mg. If simvastatin is not tolerated or considered inappropriate, the alternative is pravastatin 40 mg, another cheap generic statin. This simple change will save the hospital trust £80 000 a year.

However, most statins are prescribed in primary care. In at least three London primary care trusts partnerships with local general practitioners and systematic switching programmes are in place to realise large scale savings. These important local initiatives need to be replicated nationally to realise the full economic benefits of generic simvastatin, as has happened in some European countries, most notably Germany.

It is time for the United Kingdom to implement therapeutic substitution of simvastatin 40 mg nationally by switching patients currently taking atorvastatin 10 mg and 20 mg, and prescribing generic simvastatin for new patients needing primary prevention of coronary heart disease. This policy would save £2bn, increase value for money, and release much needed resources to other areas of the NHS.

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The great medicines scandal

New initiatives offer hope that global inequity in access to medicines will be reduced

Sick people in poor countries are deeply disadvantaged. The millions who have “neglected” tropical diseases lack safe and effective drugs.¹ Those afflicted with “Western” diseases (and 80% of the 35 million annual deaths from chronic diseases occur in low and middle income countries²) can ill afford treatment, a new report states.³

The failure of pharmaceutical companies to invest in research and development of medicines for neglected diseases is long standing. A recent analysis shows that only 21 of the 1556 new chemical entities marketed between 1975 and 2004 were targeted at African trypanosomiasis, leishmaniasis, helminthic infections, schistosomiasis, onchocerciasis, Chagas’ disease, malaria, and tuberculosis.¹ Ten of the 21 drugs—including four of only five developed since 1999—were marketed for malaria and tuberculosis.

A different but no less bleak situation is exposed in a new report on medicines for chronic diseases.³ This presents data collected between 2001 and 2005 on the price, availability, and affordability (in both public and private sectors) of a core list of drugs used to treat diabetes, hypertension, asthma, epilepsy, and psychiatric disease in 30 low and medium income countries drawn from all six WHO regions.

Although the picture varies from country to country, common threads emerge. Governments are usually able to purchase drugs at prices close to their international reference price, but in many countries the availability of medicines in the public sector is extremely limited. In addition, the taxes and duties levied on medicines, and the mark-ups made by dispensing doctors and pharmacies, result in high—often prohibitively high—prices for patients. Availability is better in the private sector but prices range from three times to 100 times the international reference price.

The standardised methodology used in the surveys includes comparisons of the cost of a standard course of treatment in each country with the daily pay of the lowest paid unskilled government workers (see figure on bmj.com).⁴ The report’s findings make explicit what has long been recognised: that the cost of medical care impoverishes or is simply beyond the reach of many people in developing countries.⁵ Its recommendations thus are unsurprising. All countries, the report states, should measure and monitor the price, availability, and affordability of essential medicines and develop, implement, and enforce policies that lower costs and increase availability.

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Amid the gloom, however, there is some light. Simply collecting data and presenting it to governments can stimulate action. (Many governments are unaware of what its citizens pay for drugs, two of the report's authors told the *BMJ*.) In the Lebanon, the survey included in the report was done by the Ministry of Health, and in response it reduced a number of fixed drug prices. In Kuwait, access to free essential medicines was extended to non-Kuwaitis after its survey was published. Current efforts to develop new drugs for neglected diseases offer further encouragement. Research undertaken by the public-private partnerships set up over the past five years has a good chance of delivering eight or nine new chemical entities within the next five years.⁵

Furthermore, thanks to persistent and passionate lobbying by Kenya and Brazil, augmented by the input and signatures of 5000 eminent scientists, physicians, policy makers, Nobel prize winners, MEPs (members of the European Parliament), and industry representatives, a landmark resolution was adopted at last week's World Health Assembly. This commits the World Health Organization to producing a blueprint for a new system of prioritising and financing pharmaceutical research aimed at stimulating the development of drugs, vaccines, and diagnostics for diseases that member states identify as health priorities: a marked contrast to the status quo, where priorities and prices depend primarily on Western based industries. One of the most important suggestions

of the resolution is that incentives for research and development should be linked to health outcomes.

Shock and sadness at Dr Lee Jong-wook's untimely death permeated this year's World Health Assembly. If WHO's commitment to redress the research imbalance delivers on its promise to provide more effective and affordable medicines for the most disadvantaged sick people in the global village, there can be no more fitting legacy.

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Are older antipsychotic drugs obsolete?

No

Antipsychotic drugs have been essential in treating schizophrenia since chlorpromazine was introduced in the mid 1950s. By 1980 over 20 other antipsychotic medications were available, and all of them are now sold as generics. Ever since clozapine was shown in the late 1980s to be more effective for treatment resistant patients with schizophrenia than the older antipsychotic agents,¹ numerous new antipsychotic drugs have been synthesised and released, with claims of greater efficacy and better tolerability than the older generic agents. Are these claims true, and how should clinicians go about choosing the appropriate drug for their patients with schizophrenia?

Several authoritative and widely adopted treatment guidelines for the use of antipsychotics, such as the TIMA algorithm (Texas Implementation of Medication Algorithms), recommend only the newer antipsychotic drugs as first and second line treatments, reinforcing the perception that the older drugs are therapeutically inferior. These new antipsychotics are often referred to as "atypical" or "novel" agents, suggesting that their mechanism of antipsychotic action is different from that of the older drugs. Yet both old and new medications appear to exert antipsychotic effects via blockade of dopamine D2 receptors in the brain.²

With regard to efficacy, an early meta-analysis conducted by Leucht et al found no significant advantage of risperidone, olanzapine, or quetiapine over the older drug haloperidol, despite the data being from studies funded by the manufacturers of the new agents.³ Leucht et al did, however, find a lower incidence of

extrapyramidal side effects associated with the newer drugs. Davis et al, on the other hand, in a separate meta-analysis of all available studies purporting to examine the differences between novel and conventional agents concluded that the newer agents had both efficacy and tolerability benefits over the older ones.⁴

A more wide ranging meta-analysis comparing low potency, older antipsychotics with newer agents found little or no difference in either efficacy or tolerability, including extrapyramidal side effects.⁵ Similarly, the few independently sponsored head to head studies found no differences in therapeutic benefits between olanzapine and chlorpromazine⁶ or between olanzapine and haloperidol (with prophylactic benztropine).⁷

Starting in December 2000 the National Institutes of Mental Health sponsored a large randomised controlled trial of over 1400 patients with schizophrenia, comparing the effectiveness of olanzapine, risperidone, quetiapine, and ziprasidone with that of a conventional antipsychotic, perphenazine (Clinical Antipsychotic Trials of Intervention Effectiveness, CATIE).⁸ Surprisingly, perphenazine was not only as effective as three of the four newer agents but also did not cause more extrapyramidal side effects. Olanzapine alone showed marginally higher effectiveness, but it was associated with a significantly greater risk of weight gain and other adverse metabolic changes.

The results of the CATIE study permit a range of interpretations, depending on one's priorities or biases. Thus, one might argue that ziprasidone is the "best" drug because its effectiveness is in the middle of the

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