



EDITORIALS

New uses for old drugs

Low cost generics are an untapped source of therapeutic innovation

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Cost constraint is a major concern for health systems globally. High unmet needs, increased demand because of demographic change, and the rising prices of new drugs conspire to exacerbate financial strains.¹ Of these three factors, only drug pricing is amenable to influence in the short to medium term. Drug repurposing—the use of existing licensed drugs for new medical indications—has the potential to help reduce costs.²

Many candidates for repurposing are widely used low cost generics. For example, the Repurposing Drugs in Oncology project (<http://www.redo-project.org>) has identified more than 230 licensed non-cancer drugs with data supporting anti-cancer activity, of which over 75% are off-patent.³ As the drugs are already in routine clinical use for other purposes early phase clinical trials can be bypassed, saving time and money.

The potential for repurposing extends to all areas of medicine, with much activity in oncology, neurology, psychiatry, and infectious diseases. Several drugs are already being used for new indications, including the repurposing of propranolol for infantile haemangioma, thalidomide for multiple myeloma, and topiramate for migraine prophylaxis.

There are many more disease areas in which repurposed drugs can potentially fulfil unmet needs. For example, propranolol, a widely used non-selective β blocker, shows evidence of activity against a wide range of malignancies,⁴ including angiosarcoma, a rare soft tissue sarcoma for which current treatments produce response rates of 25–40%. Several case reports and case series suggest propranolol could achieve high response rates in patients with advanced disease as well as long lasting remissions.⁵ The drug has recently been given orphan drug designation in angiosarcoma, but additional clinical trials are needed to confirm efficacy.

Another example is epilepsy, which affects 65 million people worldwide.⁶ Current antiepileptic drugs fail to suppress seizures in a third of patients. Recent research suggests that genomics could be used to identify repurposed drugs that are more efficacious.⁷ The Prescribable Drugs with Efficacy in Experimental Epilepsies (PDE3) project has identified 173 drugs licensed for other conditions that have antiepileptic efficacy in

animal models.⁸ Research investment is now needed to develop the most promising candidates further.

However, there are specific financial disincentives to repurposing generic drugs. Investment is required to prove efficacy and to extend the licence of the drug for the new indication. While a commercial sponsor with a patent on a product might invest in the hope of realising a return on investment, there is less to gain from repurposing a generic drug. A generics manufacturer who invests in repurposing risks seeing competitors benefit from any increase in sales. Indeed, when a commonly prescribed drug is newly licensed for a rare disease the increase in sales may not even register above background variation.

Other barriers to repurposing include restrictions on who is able to apply for label extensions—for example, applicants must hold a marketing authorisation for the drug in question.

Given these obstacles, drugs that are promising candidates for repurposing risk being bypassed in favour of more expensive new drugs or ignored altogether, to the detriment of patient health and the public purse. This is a global problem, but the effects—and potential benefits—are greatest in low and middle income countries, where the costs of newer medications are especially onerous.⁹

Attempts at a legislative solution stalled in the UK when the off-patent drugs bill failed to win government backing in 2014 and 2015 despite widespread parliamentary and public support. In response, a drug repurposing group was convened, moderated by the Association of Medical Research Charities with the support of the Department of Health and Social Care, to look at non-legislative solutions. Bringing together research charities, clinicians, industry representatives, the National Institute for Health and Care Excellence, the Medicines and Healthcare Products Regulatory Agency, and other stakeholders, this group recently published recommendations to tackle the problem of incentives.¹⁰

Specifically, it proposes amending the tax credit rules for research and development so that generics manufacturers have more incentive to license generics for new indications. Crucially,

this scheme was designed to ensure that newly licensed repurposed drugs would not be subject to price hikes, which would undo the benefits of public investment. The report also recommended the creation of a UK “catalyst fund” to supply the necessary investments.

These recommendations are welcome. Additionally, European research funders should be more willing to support repurposing trials for drugs that do not have patent protection. Many valuable repurposing leads have come from serendipitous discovery thanks to careful observation and reporting by treating clinicians—this is to be encouraged. Clinicians may further facilitate repurposing by supporting clinical trials and trial applications when they occur. Finally, we ask scientists, citizens, doctors, and patients to join forces, and voices, in support of repurposing old drugs for new indications.

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