The development of innovative drugs in areas of need is risky and expensive for drug companies compared with modifying existing compounds to create “me too” drugs. Most new drugs fall into the second category, and the NHS spends billions of pounds each year on them, even though they often have little or no incremental value over alternative agents. Effectively, the NHS is rewarding the drug industry for poor investment and creating a disincentive for risk taking and genuine innovation. When resources are limited, giving one patient an expensive drug with no added value when cheaper alternatives exist stops other patients getting treatments they need.

In the top 10 prescribed drug classes by cost, over £3bn was spent in England alone on branded drugs where in most cases equally cost effective low cost generic alternatives are available. By contrast, new innovative drugs approved by NICE between 1999 and 2004 added £800m a year to the UK drugs bill. This is money well spent especially if they are first in class drugs acting on newly discovered biological pathways in areas of unmet need. However, only a fifth of all new drugs brought to market offer any advantage over existing therapies. Furthermore, drug companies spend three times more on marketing (much on “me too” drugs) than on research. Society should explicitly and preferentially redirect funding towards important but riskier research and development.

**Missed opportunities**

The total annual saving of a concerted NHS campaign to use the most cost effective medicines could be more than £1bn a year (table). A more pragmatic switching rate of 50% would save £500m a year and would preserve doctor-patient prescribing choice and autonomy. Even when generic switching does take place, it is often started too late to realise maximum savings, as the following two examples show.

### Simvastatin

After the patent on simvastatin expired in England and evidence that it is therapeutically indistinguishable from atorvastatin was highlighted, national programmes were started to switch patients from atorvastatin 10 mg or 20 mg to simvastatin 40 mg. The use of atorvastatin 10 mg halved in three years (from 5.6 million prescriptions in 2006 to 2.9 million in 2009), with an expected saving of £1bn (£1.2bn; €1.6bn) by the time atorvastatin’s patent expires in November 2011. However, because the initiative did not start until after the patent had expired, and less than half of patients were switched, only half of the possible maximum saving has been realised, and £175m a year is still spent on low dose atorvastatin where simvastatin 40 mg would cost £11m. However, when the atorvastatin patent expires, high dose atorvastatin (40 mg and 80 mg) will become a “best buy,” and much of the annual expenditure of £124m on rosuvastatin and ezetimibe will be wasteful by comparison.

### Losartan

In March 2010, losartan came off patent, the first of the angiotensin II type 1 receptor blockers to lose market exclusivity. With £277m spent on angiotensin receptor blockers in 2009 in England, this group is the fourth highest drug cost in the NHS (table). The price of...

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**Getting better value from the NHS drugs budget**

The NHS wastes billions on “me too” drugs that confer little or no added therapeutic benefit. James Moon and colleagues propose a way to restructure healthcare prescribing to get better value for money and persuade drug companies to invest in developing innovative drugs.
Losartan fell fourfold in the first four months after generics became available, saving £53 m a year. However, only 0.3 million of the 1.6 million patients taking angiotensin receptor blockers in England are taking losartan. In other words, on 1.3 million occasions, prescribing decisions were made that cumulatively cost £200 m a year more than if losartan had been prescribed. Resources would have been saved if patent expiry had been systematically anticipated. These potential savings are conservative estimates because the price of losartan may drop further, as it has with other drugs.

At University College London Hospital, the Use of Medicines Committee considers losartan to be all but clinically indistinguishable from other angiotensin receptor blockers (box 1). All other angiotensin receptor blockers have been removed from the formulary, and a pharmacist led drug substitution policy is being implemented. All admitted patients who are taking an angiotensin receptor blocker for hypertension are automatically switched to losartan unless they have known intolerance, which is rare. Anyone who is taking an angiotensin receptor blocker for heart failure at less than the maximum dose is switched to losartan and the dose increased incrementally, aiming for 150 mg/day. Similar switching programmes are already being proposed or enacted in other trusts, primary care trusts, and internationally, but every month that passes before any national implementation equates to an unrecoverable £20 m lost opportunity.

Box 1: Angiotensin II receptor blockers

Angiotensin receptor blockers are a group of seven once daily oral drugs for heart failure and hypertension.

Blood pressure

- A Cochrane review concluded all drugs in the group have a statistically equivalent effect on blood pressure.
- Small differences in blood pressure lowering effect are likely to be unimportant in clinical practice, where blood pressure is treated to target with diet and exercise as well as drugs.
- Losartan costs 43 p per month per mm Hg systolic blood pressure reduction (figure).
- Valsartan, telmisartan, eprosartan, and irbesartan lower blood pressure less and are up to four times more expensive per mm Hg reduction.
- Olmesartan and candesartan are slightly more effective than losartan but each incremental mm Hg reduction beyond that of losartan costs 11-40 times more.

Heart failure

A large, robust body of evidence supports use of angiotensin receptor blockers in heart failure but there are no head to head trials of different drugs. Losartan is the only one for which an optimal dose is known (150 mg/day).

**Bigger picture**

The two cases above are just selected examples of prescribing that have been subject to retrospective fixes—that is, once funds have already been wasted. But these scenarios are ubiquitous in modern medicine. Generic drugs have often been shown to be therapeutically equivalent yet many times more cost effective than some newer, branded therapies. Once a drug’s patent protection expires the price can tumble overnight but the clinical effectiveness remains the same. Having a choice of two, three, or four drugs in a class is useful for the varied and rich scenarios in medicine but to have seven angiotensin receptor blockers and 14 angiotensin converting enzyme inhibitors developed and brought to market (let alone the others that nearly made it) represents bad investment and enormous hidden waste at several hundred million pounds per drug.

Generic substitution has been used with partial success in other European countries including Austria, the Netherlands, Norway, and Sweden. Although substitution is well accepted by patients, the process requires time and effort. Doctors naturally want to care for the individual rather than deliberating apparently esoteric economic concepts such as cost effectiveness and opportunity costs. Within the NHS the current initiatives and schemes to encourage efficient prescribing, based on the above analysis, seem to be a long way from providing the most cost effective care. This suggests that NHS drug prescribing practice could be greatly improved.

**More efficient prescribing**

Fundamental prescribing reform based on the following strands could help improve cost effectiveness.

**Prescribing reform**

Scrutiny of high spend drug classes (>£100m/year)—When generic (or pending generic) alternatives exist, NICE should assess their cost effectiveness in collaboration with professional societies. This extended NICE remit should have equal priority to the existing remit of assessing new therapies.

**Types of generic switching**

- Therapeutic substitution—eg, losartan instead of branded angiotensin receptor blockers
- Reduced prescribing of combined formulations—eg, simvastatin–ezetimibe or angiotensin–diuretic combination switched to individual products
- Active enantiomer to racemic mixture substitution—eg, esomeprazole to omeprazole; escitalopram to citalopram
- Rationalisation of unnecessary modified release preparations—eg, standard release metformin rather than sustained release formulations
- Generic substitution—eg, non-proprietary clopidogrel instead of Plavix

**Financial and regulatory reform**

Zero cost generics—Key generic drugs (eg, simvastatin, losartan) that have branded equivalents with no added value should be centrally funded, making them zero cost for prescribers (hospitals, general practitioners, primary care trusts), or with no prescription charge, or both. These drugs would be free from the day of patent expiry, which would encourage generic anticipation and make the development of “me too” drugs less attractive.

Central funding of NICE decisions—Savings from the prescribing reform would be used to centrally fund NICE decisions, making local budgets more predictable and explicitly linking prescribing reform with resources for new drugs in areas of need.

Reassessment of NICE threshold for approval—To incentivise genuine innovation, the NICE quality adjusted life year (QALY) threshold (currently £20 000-£30 000/QALY and higher for end of life treatments) could be increased to the higher end of life threshold for all innovative treatments.

We believe that implementing these reforms could redirect roughly £1 bn a year (about 10% of the total drug budget) to innovative drugs. The
Reducing spending on medicines with no added value would free up money to spend in other areas

The success of these proposals requires the recognition of a problem, deep commitment within the NHS, political support, and extensive overhaul of NHS prescribing and financial systems. All the expertise exists for implementation: NICE (with a broadened remit) and professional societies to assess switching and exceptions to the “generic first” rule; the National Prescribing Centre to implement and manage the changes, are the ones that need to be asked case by case with the patient actively involved in the process (“no decisions about me without me”). Nevertheless, Moon and colleagues are right to highlight this issue. The current economic challenge facing the NHS does call for radical action to make savings and improve quality. However, the very organisations that are needed to implement such changes are the ones that are undergoing major structural reform (primary care trusts and general practice commissioning consortia) or are having their remit reviewed (NICE). Until there is greater stability in these key parts of the NHS, the ability to realise the savings will be limited.

Medicines represent one of the largest non-salary areas of NHS expenditure and have been under close scrutiny for many years. In 1994 “inappropriate spending” on medicines prescribed by general practitioners was estimated to cost around £300m (£360m; $470m) a year, and 13 years later a National Audit Office report found “over £200 million of potential efficiency savings” by looking at just 19% of the primary care drugs bill. Financial efficiency of prescribing in secondary care has been questioned in a national review. As a result the past 20 years has seen the evolution of management systems and support processes across primary and secondary care to improve efficiency; these include formulary committees, local prescribing guidelines, “therapeutic switch” programmes, decision support software (such as ScriptSwitch), local education initiatives, academic detailing, benchmarking prescribing performance data, outreach visits, prescribing support staff, and prescribing incentive schemes.

Moon and colleagues raise the stakes yet further by suggesting that more than £1bn could be saved by using “the most cost effective medicines.” They propose a series of reforms that would involve assessments carried out by the National Institute for Health and Clinical Excellence (NICE), alongside national programmes of generic and therapeutic substitution to produce wholesale prescribing of “cheaper” products. The evidence for their recommendations comes from existing systems within secondary care (restricted formularies and pharmacist led substitution policies) and generic substitution policies in operation elsewhere in Europe. They propose that the resulting savings could be reinvested in “innovative drugs.”

A detailed analysis of the figures aside (and no costs are included for introducing and managing the changes), are the recommendations achievable? The challenge of getting national agreement among clinicians and professional societies on drugs that can be substituted should not be underestimated. Furthermore, initiatives that work in hospital do not necessarily translate to primary care, where the management structures are different and the implementation processes more complex. But most importantly, these proposals need to be tested against the principle of patient centred care. Alterations to complex treatment regimens (such as for asthma, heart failure, or schizophrenia) need to be assessed case by case with the patient actively involved in the process (“no decisions about me without me”).

References are available on bmj.com.

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