2 Chen H, Aiello F. Trimethylaminuria in a girl with Prader-Willi syndrome and del(15)(qllq13). *Am J Med Gen* 1993;45:335-9.
3 Ayesh R, Mitchell SC, Zhang A, Smith RL. The fish odour syndrome: biochemical, familial, and clinical aspects. *BMJ* 1993;307:655-7.
4 Lee CWG, Yu JS, Turner BB, Murray KE. Trimethylaminuria: fishy odors in children. *N Engl J Med* 1976;295:937-8.
5 Shelley ED, Shelley WB. The fish odor syndrome. *JAMA* 1984;251:253-5.
6 Patel M. Phew what's that stink? *The Independent* 1990 June 19;15.
7 Al-Waiz M, Ayesh R, Mitchell SC, Idle JR, Smith RL. A genetic polymorphism of the *N*-oxidation of trimethylamine in humans. *Clin Pharmacol Ther* 1987;42:588-94.
8 Pike MG, King GS, Pettit BR, Leonard JV, Atherton DJ. Lactulose in trimethylaminuria, the fish-odour syndrome. *Helv Paediat Acta* 1988;43:345-8.
9 Ziegler DM. Flavin-containing monooxygenases: enzymes adapted for multisubstrate specificity. *Trends in Pharmacological Sciences* 1990;11:321-4.
10 Higgins T, Chaykin S, Hammond KB, Humbert JR. Trimethylamine *N*-oxide synthesis: a human variant. *Biochem Med* 1972;6:392-6.
11 Dolphin C, Shephard EA, Povey S, Palmer CNA, Ziegler DM, Ayesh R *et al.* Cloning, primary sequence, and chromosomal mapping of a human flavin-containing monooxygenase (FMO1). *J Biol Chem* 1991;266:12379-85.
12 Dolphin CT, Shephard EA, Povey S, Smith RL, Phillips IR. Cloning, primary sequence and chromosomal localization of human FM02, a new member of the flavin-containing monooxygenase family. *Biochem J* 1992;287:261-7.
13 Lomri N, Gu Q, Cashman JR. Molecular cloning of the flavin-containing monooxygenase (form II) cDNA from adult human liver. *Proc Natl Acad Sci* 1992;89:1685-9.

Drugs: from prescription only to pharmacy only

The benefits are clearer than the risks

The range of medicines available over the pharmacy counter is set to increase.[1] The Medicines Control Agency has revised its procedures to speed up the reclassification from prescription only medicine (POM) status to pharmacy only (P) status. In addition, the Medicines Act has recently been revised to ensure, by five yearly review, that the prescription only status of a medicine continues to be justified.

Economic and philosophical considerations underlie these moves. Economic considerations include an escalating growth in spending on health care, which includes a drug bill, growing at around 12% every year. One solution is to shift more of the financial burden to individuals by encouraging them to treat themselves with non-prescription drugs. What is more, the current controls on drug spending have constrained profits in the drug industry, so more companies are moving into the over the counter market.[2] The government's philosophy on health care is that individuals should take greater responsibility for their health[3]; trends towards less medical paternalism and more consumerism favour greater freedom to choose self treatment for palliation and cure.

All drugs have some potential to cause harm, and reclassifying some from prescription only to pharmacy only increases the community's exposure to hazard: although the secretary of state for health claimed that patients' safety would be a prime consideration,[1] how good are the data on safety? Clinical trials are usually done on a restricted range of patients under controlled conditions and may not predict what happens in general use. Postmarketing surveillance studies are often poorly planned and executed,[4] and the Committee on Safety of Medicines collects only a small proportion of adverse effects.

It can be difficult to extrapolate from similar changes in other countries. For example, in Denmark cimetidine was made available without prescription in 1989 and the pattern of adverse reaction reports did not change.[5] Changes in reimbursement and advertising controls complicate interpretations of the change in status, and the amount of the drug sold over the counter was small, with much of it probably bought by patients who had previously been prescribed it. The true effect on the community will not be seen until the drug is widely purchased by people who are taking drugs with which cimetidine may have clinically serious interactions—such as phenytoin, warfarin, and theophylline.

In Britain the Medicines Control Agency has the task of assessing these data. Are the mechanisms to prevent inappropriate use and detect adverse effects sufficiently robust to support a substantial shift in policy? The main checks to stop patients misusing a drug are restricting its sale to a pharmacy (where the pharmacist need not speak to the customer) and the inclusion of a readable patient information leaflet. The effectiveness of a leaflet will depend not only on the purchasers' ability to read and understand it but also on whether they heed any warnings. Having spent their money, customers may well choose to take the drug despite the leaflet. How sensitive the yellow card system is for detecting serious adverse effects of self medication is unclear. The risk of an adverse effect depends on the drug, the population exposed to it, and how it is used. Both the population and method of use may change with a change of status.

New approaches to managing risk should accompany the increase in drugs available without prescription. A strategy based on gatekeeping, informing, and monitoring is needed. In Australia pharmacists can fulfil these roles because of their legal obligation to give advice and elicit information before some drugs can be sold over the counter; while not perfect, this approach has some merits. Perhaps all drugs that change from prescription only to pharmacy status should be sold in person by the pharmacist for the first three years. Information would be given and elicited at each sale, depending on whether the sale was for a first or repeat supply. Patients with excessive use or suspected adverse effects would be referred to their general practitioner. Gatekeeping could include the pharmacist recommending only self medication from a list of nationally agreed "preferred medicines."[6]

Overall, the shift from prescription only to pharmacy only medicines should be welcomed as it gives greater freedom of choice to patients and allows them to treat symptoms quickly. But there are risks that patients may delay consulting about serious conditions and that an unacceptably high incidence of adverse effects may result from the way that the general population uses the drug. In this risk-benefit equation only the benefits are clear; the risks, and the burden of harm that may accrue, are hard to predict. The push from prescription only medicine to pharmacy only medicine needs to be supported by further research, including anthropological studies, and the new approaches to managing risk.

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1 Mrs Bottomley set on curbing drugs bill. *Pharm J* 1992;249:748.
2 Connon H. Drug firms find a new elixir. *Independent* 1993 Feb 1:21.
3 Department of Health. *The health of the nation.* London: HMSO, 1992.
4 Waller PC, Wood SM, Langman MJS, Breckenridge AM, Rawlins MD. Review of company postmarketing surveillance studies. *BMJ* 1992;304:1470-2.
5 Andersen M, Schou JS. Adverse reactions to H2 receptor antagonists in Denmark before and after transfer to cimetidine and rantidine to over-the-counter status. *Pharmacol Toxicol* 1991;69:253-8.
6 Herxheimer A, Upton D, Spivey P, Sharpe D, Tugwell C, Barrett C, *et al.* Wanted: a formulary for self-care. *The Pharmaceutical Journal* 1993;251:179.