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Editors' view

Money makes the world go round: the pervasiveness of pharmacoeconomics

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Introduction

Some years ago, before the era of electronic access to the academic literature, requests for reprints were common. Remember those postcard-like requests with collectable stamps from far-away exotic places! A biochemical pharmacologist colleague was pleasantly surprised but initially mildly baffled to be inundated with requests for a paper he had authored on P450. The explanation lay in the keywords, which included both 'sex' and 'drugs' – evidently a near-irresistible combination even without the rock and roll; addition of 'money' might have brought the East Acton postal services to a permanent halt. We have commented previously on pharmacoeconomics [1] in the context of a study from Edinburgh [2]. The subject has little to do with classical pharmacology but a great deal to do with drug utilisation, and pharmacoeconomics has come to pervade many aspects of clinical pharmacology and therapeutics. Selection of drug targets (and hence drug discovery), choice of drug delivery systems, formulations and dosage regimens (and hence drug development), prescriber choice (and hence national pricing and subsidisation policies, local prescribing advice and writing of scripts) are all influenced by economic issues such as potential profitability, affordability (benefit /harm ratio related to cost) and so on. Indeed the inter-individual variation in P450 activity, initially perceived as a rather arcane academic issue, will probably be crucial in personalised medicine, which is both a commercial threat and an opportunity to the pharmaceutical industry. Implausible as it seemed in the 1970s, my biochemist colleague might well include 'pharmacoeconomics' among the keywords in 2009.

The global nature of the pharmaceutical industry and of randomized controlled trials (see for example the analysis by Heerspink et al in the present issue of the *Journal*, [3]) weakens the bargaining positions of individual nations as regards drug pricing, but strengthens the evidence base on which rational therapeutics ultimately rests. This leads to difficult balancing acts. A successful pharmaceutical industry delivers great benefits to citizens in terms of prolonging life and improving health, employs a substantial skilled workforce (including many of our graduate pharmacologists) and contributes to the national purse via taxation. Conversely, money spent on drugs by a health provider such as the UK's NHS means that less is available for salaries to employ doctors and nurses, and for hospitals, ambulances and all the other health-related services that the NHS is committed to provide. Inevitably, this results in fierce argument as to how to split the cake, and intense politicization. The setting up in 1999 of the National Institute for Health and Clinical Excellence (NICE) was a response to this. NICE underwent a health select committee (HSC) inquiry in 2007 to examine why its decisions have been increasingly challenged (gaming the appeals process is one candidate) and whether public confidence in it has waned. The report [4] was generally positive, as was the government's response and the recent Darzi proposal [5, 6], and the status and stature of NICE are evolving impressively [7].

NICE and several analogous bodies outside the UK have approached the problem of finite resource via a pharmacoeconomic tool – the 'quality-adjusted life year' (QALY) – that has its (extremely vocal) critics but which, despite its limitations, offers a rational basis for discussing what the NHS can or can not afford. This is surely an advance on the emotive special pleading of patient organizations and their medical advocates, however well-intentioned. Such advocates seldom call for reduction in price of new drugs as a means to increase availability, and industry funding of such organizations and individuals is becoming a moral issue. The industry justifies high drug prices by pointing to the high risks inherent in drug discovery and development, the long time frame involved in getting a new drug to market (around 12 years) and high costs [8] (now claimed to be over US$1 billion). Others argue that such costs are deliberately disguised, subjected to spin, and grossly inflated [9].

Profitability is strongly influenced by patent life, extension of which is used in the USA as an inducement to encourage innovation by the industry however the decline in new drugs being registered does not support its effectiveness. In the UK an agreed prescription pricing scheme has been used in an analogous manner. It has been argued that these 'carrots' have not been doing their job properly: faced with an investment choice between a novel drug for a poorly-served disease versus developing the pharmacologically active isomer of a tried-and-true racemate (where is the risk in that?) the commercially savvy will surely go only one way. However, although the risk of harm to patients may be all but eliminated by taking the easy road residual commercial risks remain. Is the 'new' molecular entity truly novel? Is the inventive step 'non-obvious'? If there is ambiguity then increasingly self-confident manufacturers of generic drugs may challenge the patent.

These naive musings have rather modest intentions: first, to stimulate those of you with expertise in these important areas to submit your work to the *Journal* for peer review; second, to whet your appetite for reviews on different aspects of pharmacoeconomics that we plan to solicit; and third to raise awareness of the pervasive influence of economic issues in drug development and the rational use of medicines. As regards this last goal, two examples from the present issue will serve to illustrate the point: first, the use of drugs in children and, second, the influence of funding source on reporting of trials.

Use of drugs in infants and children

Paediatric clinical pharmacology is a Cinderella, particularly because it has been perceived to be commercially unattractive (hence the link with pharmacoeconomics), the widespread unlicensed use of drugs in paediatric prescribing and partly because of ethical problems surrounding trials in children. In 2005 the Journal published an issue focussed on clinical pharmacology in that group of important individuals on the occasion of the report of a tripartite meeting towards optimising drug dosage for children convened by Nigel Baber and Ros Smyth [10]. We hoped that this would stimulate work in this important area and it is a pleasure to see an acceleration in submission rate of first rate papers across the spectrum of paediatric clinical pharmacology that has followed [see for example 11–15]. The current issue is particularly rich in papers addressing a wide range of topics of paediatric relevance spanning the influence of labour on the pharmacokinetics (PK) of amoxicillin [16], population PK of diclofenac for acute pain in children [17], a PK and pharmacogenetic analysis of 6-mercaptopurine in children with acute lymphoblastic leukemia [18], the efficacy and safety of dexibuprofen compared with the racemate in children with respiratory infections [19], and the public awareness and opinions on the use of unlicensed medicines in children [20].

Influence of funding source on the reporting of interventional drug therapy studies

Possible consequences of pharmaceutical industry funding on reporting of clinical trials has been studied and systematically reviewed [21, 22]. The reviews have identified a potential link between funding source and publication of results that favour the effectiveness of the sponsor's product. What of adverse effects of drugs? This has not previously been systematically addressed and Golder and Loke [23] have sought to rectify this. Using a comprehensive search strategy they identified only six methodological studies that met their eligibility criteria, highlighting a need for future methodological evaluations of a wider range of drugs with rigorous ascertainment of funding source. In the studies they identified they found no evidence that industry funding biased reporting of raw adverse event data, but they highlight the subjective nature of the description of such data and raise a concern that biased interpretation could sway the discussion and conclusions drawn. Caveat emptor! – good advice also for those of us choosing gifts to mark Divali, Eid, Hannuka, Christmas or New Year. With which we wish all our readers a very happy and peaceful holiday season, and (of course) a prosperous New Year.

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