Drug utilization and clinical pharmacology

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The insatiable appetite for safer more effective, but increasingly more expensive, therapy in the face of increasing government reluctance to feed this demand has put the study of drug utilization and pharmacoeconomics centre stage. Clinical pharmacologists are uniquely positioned to determine the cost benefit and utility of modern therapy and give impartial advice on safe, effective and economic patient care. To mark the Quatercentenary Celebrations of Trinity College Dublin, eight speakers addressed this theme in a symposium held in conjunction with the British Pharmacological Society Meeting in July 1992.

Drug utilization—Potential and assessing the prescriber

Professor D. G. McDevitt (Dundee) defined drug utilization as the 'marketing, distribution, prescription and use of drugs in a society with special emphasis on the resulting medical, social and economic consequences'. Information comes from a variety of sources—both PACT (Prescribing Analysis and Cost) and SPA (Scottish Prescription Authority) data provide individual prescribing information against a background of general performance. This information can be used to monitor overall prescribing trends, comparing regional or even national differences in the use of drugs. It can quantify the economics of prescribing and in certain circumstances reflect the incidence of disease or the prevalence of adverse reactions to drugs. It may also allow audit of drug policy adherence or the usefulness of educational strategies. However, in all of these measures the quality of the information provided is determined by the limitations of the data collection. In general detailed information—who is being treated, by whom, for what condition, why, with what benefit, and adverse effect—is unavailable. While the Defined Daily Dose provides a measure of the number of patients receiving a particular compound, in general drug utilisation data are reduced to the role of a crude indicator of prescribing trends, the reasons for which become a matter of speculation or interpretation. By way of example, Professor McDevitt reported on a marked decline in the use of benzodiazepines in Tayside but closer scrutiny reveals the change has occurred with anxiolytics and only a very small decline in hypnotics. Paradoxically there was an increased use in an important at risk group, the elderly female.

General Practitioners (GPs) make decisions on prescribing for a number of reasons including advice from hospital colleagues. Direct treatment recommendations will follow clinical referrals and are likely to influence prescribing patterns. Dr D. N. Bateman (Newcastle

upon Tyne) reviewed the sources of data including discharge and outpatient prescriptions, records of drug purchases by hospital and community pharmacists, and PACT. For some drugs prescribing trends show some parallel between hospital and general practice, but with a lag period of 1–2 years. For example—the swing back from ranitidine to cimetidine in the Northern Region has not yet been seen in practice while the heavily promoted switch from isosorbide dinitrate to isosorbate mononitrate was obvious in hospital practice for 2 years before the change occurred in general practice. It is easier to follow change with new drugs (e.g. the impact of the manufacturer's letter and the Drugs and Therapeutic Bulletin on xamoterol prescribing) than with older drugs. Dr Bateman concluded that it was difficult to quantify the impact of hospital prescribing on general practice, but its effect cannot be neglected.

For some 16 years drug utilization data have been used by Dr H. McGavock (Belfast) to influence the 955 GPs in Northern Ireland. The basis for discussion in biennial visits is the doctor's own prescribing records, and the prescribing visitor indicates subtly those areas where the GP partners might become more efficacious, safe and cost-effective prescribers. Four forms of intervention are used.

(1) The 'Best Buy' list—shows doctors where they may achieve near optimal cost-effectiveness by following the best advice currently available instead of their present choices. This list gives comparative prices of generics *versus* branded products, advises against out-dated drugs, or those for which undue claims are made, or which are more potent than is usually required in general practice.

(2) The 'range' of drugs used—research has shown that in any therapeutic group the range of drugs a practice

uses correlates significantly with the number of partners. Illustrating the risks of serious illness in using more than a few selected drugs in each group is a powerful argument for using an agreed practice formulary.

(3) Specificity of prescribing—shows GPs what proportion of their prescribing is for specific treatment of confirmed disease, what proportion is for relief of symptoms only, and what proportion is mainly on the basis of a presumptive diagnosis (e.g. antibiotics are 'presumptive' if prescribed for children with upper respiratory infections, before any bacteriology results are available). Dr McGavock suggests that presumptive prescribing is unscientific, carries risk and is economically wasteful. Less than average specific prescribing may suggest missed diagnoses or a healthier practice population.

(4) Drug information is given at the prescribing visit and on a regular basis by seminars and mail-shots. At his request the Northern Ireland government ran a television advertisement emphasising that not every symptom requires a prescription. This was popular with doctors and had a strong impact on the public.

On average, a saving of £18,000 per annum per practice was forthcoming with a total saving for Northern Ireland of £6.4 million (population *circa* 1.6 million) between 1983 and 1986. The Northern Irish GP academic detailing techniques are now being implemented throughout the United Kingdom, and the Scottish authorities are using the 'specific, symptomatic and presumptive' classification in its GP prescribing feedback software.

Influencing the prescriber

While there was general agreement that medical representatives have a significant influence on GP prescribing, Dr J. Greenwood (Aberdeen) was able to quantify this impact through a random survey of 332 General Practitioners in the UK Trent region and of 195 medical representatives UK wide, on prescribing source awareness and influence. Around 90% of GPs were found to maintain some degree of contact with medical representatives.

Surveys reliant upon subjective measures of influence suggest that commercial sources are used by GPs relatively more at product awareness stages, while professional sources are used more in evaluative prescribing contexts, where the decision is taken whether to use the drug [1]. Similar results were obtained in this GP survey in response to questions posed out of a prescription context; practitioners acknowledge the importance of representatives in product awareness, but not their influence on use. However a different pattern is evident in relation to questions asked about a prescription event, despite the underlying reliance upon subjective identification of sources. The closer a surveyor gets to actual prescribing events the higher the degree of influence of medical representatives appears to be.

A more objective test of influence is to explore prescriber beliefs about products in a therapeutic context where messages of efficacy sharply differ between commercial and professional sources. In the case of four therapeutic areas the commercial view was favoured by

77%, 55%, 28% and 13% of GPs respectively. Those GPs who held the commercial view for at least three of these products were significantly more likely to rate representatives highly in a variety of prescribing contexts (current products, product awareness and evaluation). A similar relationship was not found to exist in the case of other sources of prescribing information. The greater the number of medical representatives seen by a GP the more likely he or she was to hold the commercial view.

Representative influence is greatest amongst older GPs, those trained overseas and, less certainly, those with largest list sizes. These groups are particularly targeted, with companies directing some 40–50% of representative calling activity at only 10–15% of GPs using data which enable location of high volume and cost prescribers in specific therapeutic categories. Influence appears to be exerted through the face to face contact with the medical representative, through the timesaving element of conversational updating, and as a result of the absence of mechanisms for postgraduate therapeutic updating. Of all the information and selling methods available to firms, only the representative is able to fulfil all six parts of the selling process—establishing customer contact; arousing interest; creating product preference; making a specific proposal; closing the sale; and ensuring post purchase satisfaction to generate future sales.

Few GPs see representatives as neutral information sources, and a large majority were found to be highly critical of the quality and partiality of the information given in response to a range of questions. Paradoxically, a relatively high degree of use of the medical representative was indicated in the surveys of medical representatives and GPs for the transmission of adverse reaction reports—approximately ten times the number of reports made to the Committee on Safety of Medicines in the 12 months preceding survey work, although it is not known what proportion of these were trivial or well established.

Training provided by industry for medical representatives was found to be limited, with a 5–6 week training course typical. Few had formal backgrounds in medicine (29%) or therapeutics (23%). The presence of two broad groups of representatives emerged, distinguished by their approaches to the nature of the work they undertake. Those who had entered employment for 'ethical reasons' viewed the purpose of a visit to a GP as informational rather than promotional, had a more professional attitude to their own updating and training, and were more aware of their professional codes of practice. For the sample as a whole, only a minority of the 108 representatives who had recently been involved in the schedules of a post marketing surveillance study appeared to be aware of the joint BMA/ABPI code of practice which govern their operation.

Professor John Feely (Dublin) reported a number of instructive examples of how economic and other factors significantly influence prescribing. After a change from a fixed salary payment to doctors to a system of fee per item of service in Ireland there was within 5 years a 330% rise in prescriptions and drugs costs. During the same period costs in the United Kingdom, which has very similar morbidity, drug use rose by only 160%. A recent change to a capitation system has not altered the steady rise in costs of medicines.

Experience suggests that prescribers circumvent

attempts by the State to reduce therapy for patients often to the extent of choosing potent expensive therapy which is without cost to patients instead of inexpensive symptomatic remedies for which patients would pay. On the other hand a small fee 'encouraged' a fifty fold increase in the rate of reporting adverse drug reactions through the yellow card system, suggesting that when doctors agree with the objective they may be more easily motivated. Recent data also suggests that patient expectations and precedents commonly influence the prescriber who is subsequently often uncomfortable with such prescribing.

Drug prices in Ireland are linked to those of the United Kingdom, and analysis [2] suggests that prescribing rates in the European Community (except for less affluent states that have recently joined, viz. Spain, Portugal and Greece) are inversely and strongly related to drug costs. Thus, high drug costs are balanced by low prescribing rates in Ireland. Where drug use is relatively low the industry charges more. The political decision to allow high drug costs may be linked to the major beneficial contribution of the pharmaceutical industry to the national economy. It is not reasonable, however, to ask the prescriber to bear the brunt of effecting economy in drug use if the major and undisclosed decisions with regard to drug price are made at a higher level and with different and possibly contrary objectives.

Experience with hospital formularies had also confirmed their potential to reduce costs significantly and to improve the quality of prescribing and medical practice for as long as there is active intervention through feedback, education and 'policing' of the formulary. Removal of these interventions led within a year to loss of previous gains.

The operation of a Drug and Therapeutic Committee was reviewed by Dr M. J. Brodie (Glasgow) where the Health Board established an Area Committee in 1989 under the chairmanship of a clinical pharmacologist with some 20 members representing hospital doctors, pharmacists and administrators. Initially it was wholly concerned with hospital prescribing and subgroups were constituted to consider specific aspects of prescribing, for instance, cardioactive, oncological and antimicrobial drugs. From these and other sources a series of advisory bulletins (around one per month) on therapeutic topics were circulated widely and a Glasgow hospital formulary is being produced. Local hospital committees linked to the Area committee are producing and monitoring notional drug budgets for the clinical units within their influence.

Since April 1991 a New Drugs Subgroup, also chaired by a clinical pharmacologist, advises the main committee on all new agents, formulations and indications and whether these drugs should or should not be available for routine use by hospital prescribers. Of the first 24 drugs considered three were supported unreservedly, 14 were not approved for hospital stocking and restricted prescribing of the remaining 7 (29%) was allowed. Audit of outcome of use of newly-introduced drugs has been encouraged. An appeals mechanism has been implemented to allow reconsideration of these decisions when more data have become available.

The Area Committee has extended its remit to advising on prescribing in general practice. Three family doctors

were appointed together with a pharmacy facilitator to the medical practise adviser. The hospital/practice interface and the prescribing of specialist drugs, such as growth hormone, are currently being considered and the bulletins are now sent to all family doctors. Free flow of information is encouraged between local and area committees. Systems have been put in place to monitor and control drug prescribing and expenditure throughout Glasgow. This is being undertaken by clinicians themselves and led by clinical pharmacologists. No drug need be denied to a patient for whom it is the best treatment. Neither, however, should every doctor be allowed to prescribe any drug to any patient regardless of efficacy and expense.

The natural development of this view is the production of a limited list either by exclusion (black list) or inclusion (white list) by consent or by imposition. Despite its widespread appeal and extensive use. Dr M. Henman (Dublin) concluded from the literature that the costs and benefits of such a policy have yet to be carefully delineated. The first major study of the effect of prescribing restrictions [3], using government data on per capita medical care expenditures and recipient drug expenditures from nineteen U.S. States, found no clear-cut relationship between these values and the use of an open or a closed formulary. More recently in Scotland, the overall impact of the restrictions was considered to be an increase in the prescribing of H₂-receptor antagonists and in the U.K. prescribing (as measured by prescription items) has continued to rise. In Ireland the de-listing of 'simple' analgesics (i.e. aspirin, paracetamol and combinations), antacids, cough and cold preparations was associated with a rise in prescriptions for mefenamic acid, H₂-receptor antagonists and carbocysteine [4]. Nevertheless, while the limited list produced a short lived reduction in the rate of increase in medical expenditure the policy objective was not attained and total costs have continued to rise. More recently, Soumerai *et al.* [5] examined the effect of non-reimbursement of drugs of questionable efficacy by following cohorts of patients and showed that prescribers substituted both desirable and undesirable drugs, as assessed by an expert group, for those that were no longer reimbursable and costs were increased.

Drug utilization and the future of Clinical Pharmacology

Professor A. Breckenridge (Liverpool) developed a number of these topics in the application of economic theory to pharmacotherapy—pharmacoeconomics. In UK for many years prescribing costs accounted for some 8–10% of the overall health care budget, but is now approaching 15%. In primary care prescribing accounts for 36% of costs but there is also a regional variation. These considerations involve not only health care economists and administrators, but also clinical pharmacologists, pharmacists and patients. Whereas prescribing until recently has been dominated by discussion of risk-benefit, in the future aspects such as cost-benefit, cost-effectiveness and cost-utility will also be taken very much into account.

At government level, there are four stratagems to keep down the cost of drugs. First, it can restrict the

profits which drug companies make. In UK this is done through the Pharmaceutical Price Regulation Scheme (PPRS) which puts a ceiling on profits which companies make, leaving them to decide how much to charge for individual drugs. Second, government can force companies to charge less; many countries have tried this with varying success. Third, an overall limit for drug spending by doctors can be set; the UK is currently involved with this approach. Fourthly, national formularies can be adopted; Germany, Netherlands and Australia have published lists of drugs for which governments will not pay.

At hospital level, pharmacoeconomics is practised largely through setting up of hospital formularies, insistence on generic prescribing, and transferring drug costs to the primary care sector. It is at the hospital-primary care interface that most advances can be made, but most problems exist.

In general practice, prescribing is not cost limited

(although for fund holding general practices overall costs are finite). Indicative prescribing amounts are set for each practice; in theory these could be enforced but up to now they have not been. At regular intervals practitioners are informed in considerable detail of their prescribing costs; some of these are outwith their control (e.g. transfer of hospital prescribing). While accepting the concept of appropriate drug usage where benefit exceeds the negative consequences by a sufficiently wide margin that therapy is worth administering, the use of public and expert panels to rank benefits as in the Oregon Health Care has had limited use. There is a need for better measures employing information strategy systems.

The future of prescribing is finance-based as well as pharmacology-based. Everyone must know the rules. The meeting concurred that the challenge for clinical pharmacologists to act as therapeutic referees must be addressed.

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