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Twenty Years of Using Economic Evaluations for Reimbursement Decisions What Have We Achieved?

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What Have We Achieved?

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Abstract

The objective of this paper is to examine the impact of economic evaluation on the reimbursement process for pharmaceuticals. Before the introduction of economic evaluation, a range of arrangements existed across different jurisdictions, varying from reimbursement based on clinical criteria alone and price controls, to a total absence of controls over price or reimbursement. The changes in the structure of reimbursement policies necessary to incorporate economic evaluation have been accomplished without major difficulty in most jurisdictions. However, several methodological differences in international guidelines for economic evaluation exist, only some of which can easily be justified. A number of beneficial changes in reimbursement processes have also been observed, such as a trend towards requiring the measurement of more meaningful clinical endpoints and increased engagement between manufacturers, drug regulators and payers. A consistent finding in studies of reimbursement decisions is that economic considerations have been influential, second only to the strength of the clinical evidence for the drug of interest. The impact of economic evaluation on the allocation of healthcare resources is hard to ascertain because of the difficulties in specifying the counterfactual and the fact that little is known about the extent to which reimbursement decisions actually lead to changes in healthcare practice. However, there is evidence that economic evaluation has assisted price negotiations and enabled reimbursement agencies to target drugs to those patients who will benefit the most. In publicly financed healthcare systems, an evidence-based system of pricing and reimbursement for drugs, considering societal willingness-to-pay, is a reasonable policy objective to pursue.

1. Introduction

In 1991 the Commonwealth of Australia announced that, from January 1993, economic analyses would be required in submissions to the Pharmaceutical Benefits Advisory Committee (PBAC), the body that advises the minister on the listing of drugs on the Pharmaceutical Benefits Schedule (the national formulary of publicly-subsidized drugs). A new set of submission guidelines, including economic analyses, was produced (Department of Health, Commonwealth of Australia, 1992) and submissions were invited initially on a voluntary basis.

Since that time this policy has become fairly widespread, with approximately half the countries in the European Union requesting economic analyses to varying degrees, plus New Zealand and various Canadian provinces. In the last five years several payers in the US and countries in Latin America and Asia have also expressed an interest in receiving economic data.

Although economists have advised governments for many years, particularly in the area of healthcare financing, the requirement for economic analyses as part of the reimbursement process was regarded by many as a big step forward in the recognition of the importance of economic considerations in healthcare decision-making. However, it has not been without its detractors. Birch and Gafni (2007) have consistently argued against the policy, at least in the way it has been implemented, and have described it as 'the economists' nightmare'. In addition, Morgan *et al* (2000) have argued that economists may have been 'captured' by the pharmaceutical industry and that, rather than representing an additional barrier to the industry, economic analysis has been used to the industry's advantage. However, most importantly, the rationing decisions that have resulted from the use of economic analysis, and the analytic techniques behind them, have been widely criticised by economists and others.

Therefore, this paper reviews the development of 'economics-based reimbursement' over the past 20 years and assesses what, if anything has been achieved. It begins with a brief discussion of the state of the world before the widespread use of economic evaluation and then discusses the changes that have been brought about, in the decision-making structure for reimbursement, the processes involved and the outcomes, in terms of reimbursement decisions and the resulting allocation of healthcare resources in the jurisdictions concerned.

2. Pricing and reimbursement of drugs before economic evaluation

Some countries that subsequently adopted economic evaluation had pre-existing pricing and reimbursement controls. For example, the PBAC already existed in Australia and was making comparative clinical assessments of products prior to the introduction of economic considerations. The same situation existed in New Zealand and several Canadian provinces.

Some countries, such as France had, and still have, price controls based on the added clinical value that the product brings, as compared with existing drugs for the clinical indication concerned. If the product brings no added value the best the company can expect is an equivalent price.

Some countries, such as The Netherlands, had a therapeutic reference price system, where similar drugs are 'clustered' and reimbursed at the same level. When economic evaluation was introduced in The Netherlands, it was used to help set a price for drugs that could not be placed in an existing cluster.

Finally, there were some countries, such as the United Kingdom, where the vast majority of new drugs were automatically reimbursed by the health care system, with prices being regulated indirectly by the Pharmaceutical Price Regulation Scheme, which controlled the overall level of company profits. However, in the UK and many other healthcare systems, the use of drugs was also regulated at the local level, through the existence of local formularies and budgetary controls on health authorities. This led to the spread of 'postcode prescribing', whereby some expensive medications were available in one locality, but not others. Indeed, this was one of the problems that the National Institute for Health and Clinical Excellence (NICE) was created to rectify.

Therefore, in only a minority of jurisdictions was there a completely unrestricted use of new medications before the introduction of reimbursement systems including economic evaluation. We will return to this point later, when we consider the impact that this new policy has had on the allocation of healthcare resources.

3. Changes in the decision-making structure of reimbursement

Committee structure

With the advent of economic evaluation, there were two main changes in the decision-making structure. First, the composition of existing expert committees was changed or new committees created, in order to add economic expertise. In some jurisdictions, such as Australia, an economics sub-committee was formed to advise the PBAC. In the UK the NICE Appraisal Committee was formed. However, the majority membership of committees has remained clinical, including practising physicians and epidemiologists.

This begs the question of what impact the addition of a minority of economists has made. The most detailed analysis of the work of such a committee is the study by Bryan *et al* (2007) of the NICE Appraisal Committee. They found that economic considerations (eg. the Incremental Cost-Effectiveness Ratio (ICER) quickly became prominent in the Committee's deliberations, although some economist committee members did express frustrations that issues of opportunity cost were not being adequately addressed. There were also some limits on the level of influence of the economic considerations, owing to the perceived methodological weaknesses in the economic analyses presented to the Committee.

Submission guidelines

The other major change in structure was the amendment of existing submission guidelines, or the creation of new guidelines, to accommodate the need for economic analyses. It is worth noting that, even now, the bulk of the submission of data in all jurisdictions relates to the clinical data, with the economic analysis comprising only one section of the submission.

There have been several studies comparing the methodological content of the various jurisdiction-specific 'pharmacoeconomic' guidelines. (See Hjelmgren *et al*, 1991; Sculpher and Drummond, 2006; Barbieri *et al*, 2010). In addition, the most extensive review and classification of the content of the guidelines can be found on the website of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR, 2011).

The general conclusion of these reviews is that most of the guidelines embody the main methodological principles of economic evaluation, but that they differ in detail. Sculpher and Drummond (2006) note that some of these differences are understandable, since they relate to local preferences (eg. over whether the perspective for analysis should be confined to the healthcare sector, or should be broader, including costs and benefits from a societal perspective).

However, some of the inter-jurisdiction differences are less easy to explain and may reflect a lack of understanding of the methodological principles. For example, Barbieri *et al* (2010) noted that, in discussing issues of the cross-jurisdictional transferability of clinical data, 50 per cent of the guidelines they reviewed did not make the key distinction between data on baseline risk of disease and data on relative clinical effect. In general, the more detailed the scrutiny of the methods guidelines, the greater the differences that emerge. In a recent study, Mauskopf *et al* (2011) argue that these differences are substantial enough as to cause difficulties for a manufacturer wishing to make submissions to satisfy the requirements in several jurisdictions.

4. Changes in reimbursement processes

Evaluation of economic submissions

The main change following the incorporation of economic evaluation was that industry submissions had to include an economic analysis, conducted in a manner consistent with the methodological guidelines in each jurisdiction. This has not been without its difficulties. For example, in a review of 326 pharmacoeconomic analyses submitted to the PBAC, Hill *et al* (2000) identified 249 methodological problems. On the other hand, Lim *et al* (2010) found, in a review of 153 economic evaluations published between 2001 and 2006, a base set of nine methodological standards, as outlined in the Canadian guidelines (CADTH, 2006), were followed in more than 50 per cent of the cases.

The other main challenge has been in the evaluation of the industry submissions received. In some jurisdictions this evaluation is conducted by staff within the government, or the relevant health technology assessment (HTA) agency. In others the evaluation is conducted by an independent individual or group, normally (but not always) based in an academic institution. This raises the question as to how thorough, and time consuming, that review should be. Initially, NICE in the UK provided substantial funding for independent academic groups to conduct their own study and to compare it with the industry submission(s). A comparison conducted by NICE (Miners *et al,* 2005) showed that on the majority of occasions the estimate of cost-effectiveness of the product was more favourable in the industry submission than in the equivalent independent study, suggesting some important differences in the interpretation of the data.

More recently, NICE has fallen into line with the majority of jurisdictions, which require only a critique of the industry submission, as opposed to an independent study. Some analysts have taken advantage of the natural experiment that took place in the UK, whereby in Scotland the Scottish Medicines Consortium (SMC) has only requested critiques, whereas in England NICE initially required independent studies. Cairns (2006) found very little difference between the resulting decisions of NICE and the SMC, whereas Barbieri *et al* (2009) found important differences between the two bodies, with NICE placing more restrictions in use on the drugs that were approved.

Developments in processes

There have been several developments in reimbursement processes over the last 20 years and it is interesting to discuss which of these are likely to be closely associated with the incorporation of economic evaluation. Three developments in particular are quite likely to have occurred as a result of the use of economic analyses.

First, there has been a trend towards the consideration of price (of the new drug) as a variable in the economic evaluation and a discussion of what would constitute a 'value-based price' (Department of Health, 2010). Previously, in any assessments of the clinical data alone, price was considered as an exogenous variable determined by the manufacturer, or something to be negotiated separately by the ministry or other payer.

Secondly, there has been a growth in 'risk-sharing' arrangements, whereby the new drug is given reimbursement, but only on the understanding that further research will be conducted to determine whether it constitutes good value for money. (The presumption is that the price might be lowered unless adequate value for money is established in the long run.) These arrangements are not without their difficulties (Raftery, 2010; Towse, 2010), but it is hard to understand how they could even be applied without having a policy of economic evaluation to identify the situations whether risk-sharing might be appropriate and to undertake the required research.

Thirdly, the perceived success of incorporating economic evaluation into the reimbursement of drugs has led to its extension to other technologies. For example, in the United Kingdom, NICE now evaluates medical devices, diagnostic services and public health interventions (NICE, 2011).

In addition, there have been other developments in reimbursement approaches in which the incorporation of economic evaluation has most likely had a major influence, although it may not have been the sole, primary, cause.

First, there has been a growing recognition of the need for more relevant endpoints to be measured in clinical trials of new drugs. Many of the clinical trials undertaken for drug licensing purposes measure disease progression or surrogate endpoints. The need, in economic evaluation, for data on the impact of therapies on length and quality of life has led to a reconsideration of clinical trial design. More recently, this trend has manifested itself in a movement towards early engagement (of manufacturers) with payers on the issue of data requirements and the development of parallel advice (to manufacturers) from drug regulators and payers on the most appropriate clinical trial design (Backhouse *et al*, 2011).

Secondly, there has been much more discussion of the range of relevant treatment alternatives (to the new drug of interest) and the need for evidence on relative treatment effect. In turn, this has led to discussion of the needs for adequate methods of evidence synthesis, particularly in situations where head-to-head clinical trials do not exist for the alternative therapies under consideration.

This review (of randomised trials) has gone well beyond the methods initially pioneered by the Cochrane Collaboration, to include Bayesian methods of indirect and mixed treatment comparisons (now being called network meta-analysis) (Jansen *et al*, 2011). In the main this research has not been led by economists, but largely arises from the need, in economic evaluation, to consider relevant treatment comparisons, as opposed to those made in the existing clinical trials.

Thirdly, there has been a growing recognition that clinical and cost-effectiveness can vary by patient sub-groups. Prior to the incorporation of economic evaluation, in all but a few jurisdictions a drug would be approved for reimbursement within its licensed indications, which could often be quite broad. The consideration of cost-effectiveness has thrown into sharper relief the fact that a given drug could deliver high value for money in one patient sub-group, but offer almost no added value (compared to the alternatives) in another patient sub-group. This is evidenced by much of the guidance issued by agencies considering economic evaluations, where in many cases the use of the drug is restricted *within* its licensed indication (see later).

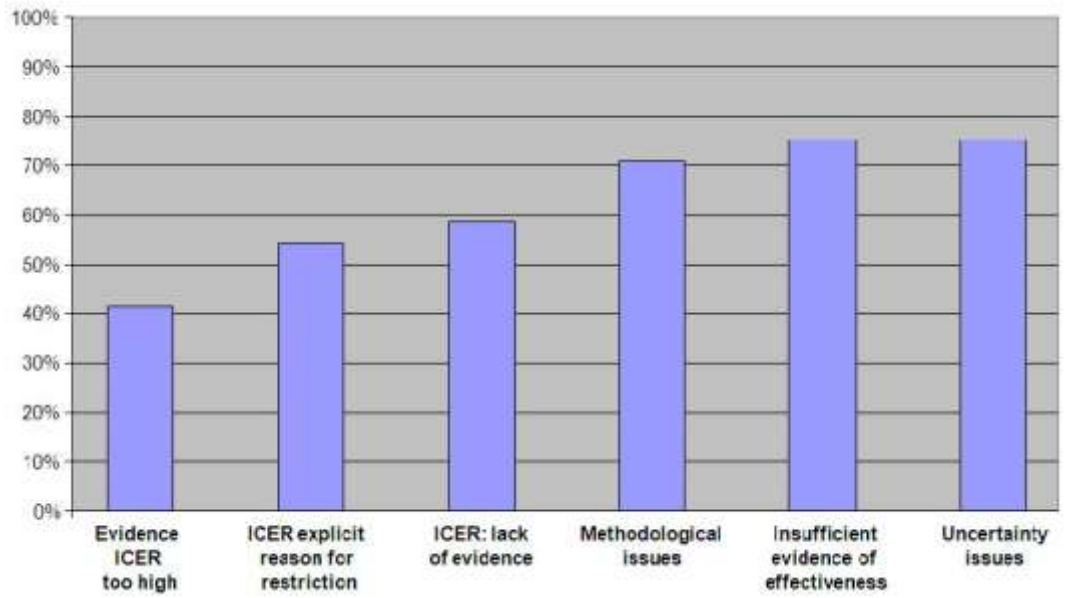
Finally, over time there has been a trend toward more transparency and stakeholder involvement in reimbursement processes (Drummond *et al*, 2008). It would be wrong to attribute this mainly to economics, but it is clear that the addition of the economic dimension to decision-making has meant that decisions have become more complex to explain. It is easy for the public to accept that a drug does not generate clinical benefit, or does more harm than good. However, it is harder for them to accept that, while the drug is clinically superior to the alternative, the added value does not justify the additional cost.

5. Changes in reimbursement decisions

There is a growing literature on the impact that the inclusion of economic evaluation has had on the decisions of reimbursement agencies. This can be divided into: descriptive studies (either within one jurisdiction or comparing jurisdictions); multivariate analyses; and qualitative analyses (including stated preference studies).

Descriptive analyses

These studies seek to describe, or explain, the reimbursement decisions in different jurisdictions and to assess the importance of economic considerations. For example, Mason and Drummond (2009) analysed NICE's guidance on new cancer drugs from May 2000 to March 2008. They found that 55 per cent of the drugs were allowed for unrestricted use within their licensed indications, 15 per cent were totally restricted, and 29 per cent allowed with some restrictions (eg. for only sub-sets of the patient population). The reasons for restrictions, where these could be determined, are given in Figure 1. It can be seen that issues related to the ICER were prominent, but that methodological concerns and insufficient evidence of effectiveness were also very important. This reinforces the point, made earlier, that reimbursement committees view the adequacy of the *clinical* data somewhat differently than licensing agencies.



Source: Mason & Drummond (2009)

Figure 1. Reasons for NICE restrictions: % drug evaluations (N=24)

Anell and Persson (2005) studied the decisions of the Swedish drug reimbursement agency (the LFN) from October 2002 to March 2005. Of 107 drugs considered, 13 were rejected, 12 given limited listing and 82 were approved with no restrictions on use within the licence. Cost-effectiveness considerations were important in the decisions, but other considerations included 'clinical need' and 'degree of priority'.

Several studies have compared the decisions made in different jurisdictions. Lexchin and Mintzes (2008) compared the recommendations of the PBAC in Australia, the SMC in Scotland the Common Drug Review (CDR) in Canada. Overall there were no statistically significant differences between the agencies in the percentage of drugs assigned to the three categories (no restriction, restricted listing and no listing). However, the comparisons are complicated by the fact that different drugs were

considered in each jurisdiction over the time period studied. The recommendations for the drugs that were assessed by all three agencies did show some discordance (see Figure 2).

Recommendation as of September 2006

Drug	CDR	PBAC	SMC
CDR, PBAC, SMC Concordant			
Adalimumab	Restricted	Restricted	Restricted
Atazanavir	Restricted	Restricted	Restricted
Brimonidine/timolol	Restricted	Restricted	Restricted
Cinacalet	No	No	No
Laronidase	No	No	No
Memantine	No	No	No
Pegfilgrastim	Restricted	Restricted	Restricted
Tenofovir	Restricted	Restricted	Restricted
Voriconazole	Restricted	Restricted	Restricted
CDR and PBAC Concordant, SMC Discordant			
Abacavir/lamivudine	Restricted	Restricted	Yes
Atomoxetine	No	No	Restricted
Efalizumab	Restricted	Restricted	No
Fosamprenavir	Restricted	Restricted	Yes
Mycophenolate sodium	Restricted	Restricted	Yes
Teriparatide (rDNA origin)	No	No	Restricted
Travoprost and timolol	Restricted	Restricted	Yes
CDR and SMC Concordant, PBAC Discordant			
Erlotinib	Restricted	No	Restricted
Pregabalin	No	Restricted	No
Tipranavir	Restricted	No	Restricted
PBAC and SMC Concordant, CDR Discordant			
Insulin aspart/insulin aspart protamine	No	Yes	Yes
Insulin detemir	No	Restricted	Restricted
CDR, PBAC, SMC – All Discordant			
Insulin glargine	No	Yes	Restricted

Legend: CDR = Common Drug Review; PBAC = Pharmaceutical Benefits Advisory Committee; SMC = Scottish Medicines Consortium; Yes = 'Unrestricted listing' or 'recommended for use'; Restricted = 'List with criteria', 'restricted benefit' or 'recommended for restricted use'; No = 'do not list' or 'not recommended for use'.

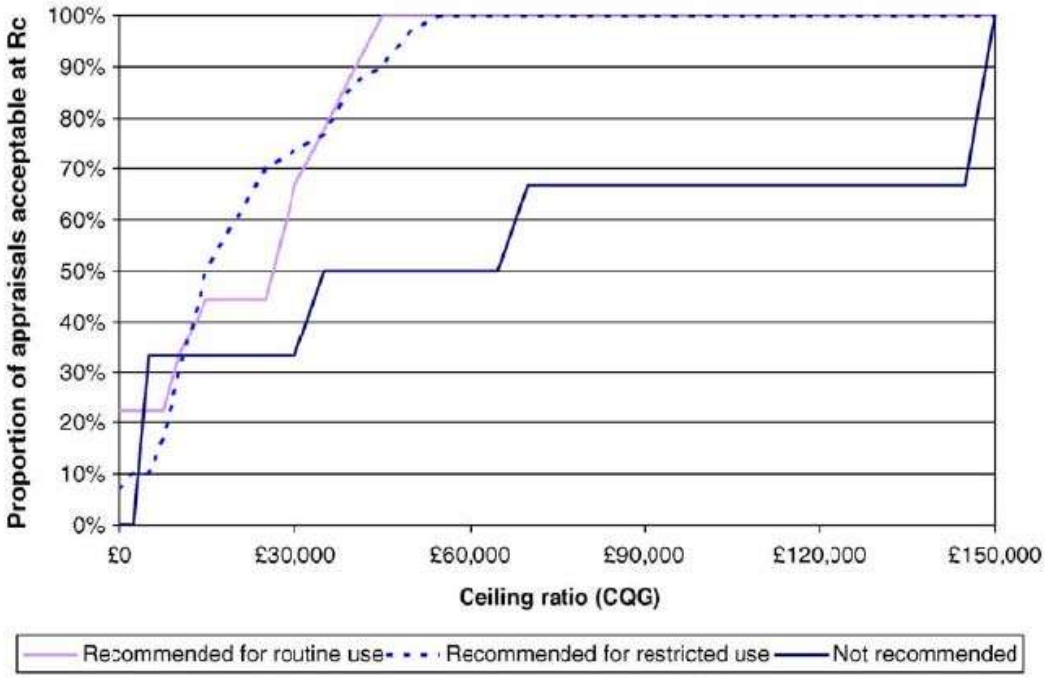
Figure 2. Recommendations for drugs assessed by all three agencies

Clement *et al* (2009) compared the decisions by NICE, the PBAC and CDR up until the end of 2008. Overall, the percentage of drugs listed (unrestricted or with restrictions) was 87.4 per cent for NICE, 54.3 per cent for the PBAC and 49.6 per cent for the CDR. (The corresponding figures for the sub-set of drugs considered by all three agencies were 84 per cent, 73.6 per cent and 52.6 per cent.) The authors discuss the potential reasons for these differences and argue that the high rate of listing by NICE resulted from the agency being more willing to explore patient sub-groups for which the drug was cost-effective. On the other hand, in contrast to the two other agencies, the PBAC was more willing to negotiate on price, allowing resubmissions at a lower price, or more willing to recommend risk-sharing arrangements. Since the time period studied by Clement *et al*, NICE appears to have followed the PBAC's lead on price negotiation, through its greater use of 'patient access schemes'. In these schemes a drug that is facing possible rejection can be given positive guidance if a financially attractive deal is offered. This can be to offer some courses of therapy free, to cap dosing, or to give refunds in situations where the patient does not respond to therapy. Implicitly, many of these schemes represent price reductions.

Multivariate analysis

In these analyses the listing decision (expressed as a binomial reject/accept, or a multinomial variable relating to the extent of listing) is the dependent variable, with the range of explanatory variables typically comprising the quantity and quality of clinical evidence, the disease area, the ICER, the number of alternative therapies, the size of the patient population, etc. The aim is to assess the relative importance of the various factors in explaining the decision and, in the case of the ICER, to estimate the threshold, or threshold range of 'acceptable' cost-effectiveness.

In an early study, Devlin and Parkin (2004) estimated that NICE's cost-effectiveness threshold was somewhat higher than the £20,000-£30,000 per QALY gained that was often stated. A later study, Dakin *et al* (2006) showed that interventions supported by more RCTs were more likely to be recommended for routine use. Higher ICERs increased the likelihood of rejection, but did not affect the decision between routine and restricted use (see Figure 3).



Proportion of interventions in each outcome category with a cost per QALY gained (CQG) below a range of ceiling ratios (*Rc*). The vertical axis shows the proportion of appraisals in each category that had a CQG below the ceiling ratio shown on the horizontal axis. This is equal to the proportion that would be acceptable at each ceiling ratio ignoring all other factors. Source: Dakin et al (2006)

Figure 3. Relationship between ceiling ratio and type of NICE recommendation

A third study focussed on NICE's 'mixed' decisions: namely those where the drug was recommended for use on only a sub-set of the patient population. It was found that, overall, NICE recommended use for less than half of the licensed population; in one third of cases the recommendation for use covered less than 10 per cent of the licensed population (O'Neill and Devlin, 2010). Overall, in all the multivariate studies reviewed, the ICER was shown to be a prominent factor in decision-making.

Qualitative studies

These studies involve interviews with decision-makers, asking them about the reasons for their decisions. As mentioned previously, the study by Bryan *et al* (2007) involving participant observation and semi-structured interviews, showed that the ICER was prominent in discussions of the NICE Appraisal Committee.

A stated preference binary choice experiment with members of the same committee suggested that increases in the ICER, economic uncertainty and the availability of other therapies were associated with a statistically significant reduction on the odds of a positive recommendation (Tappenden *et al*, 2007). Similarly, a discrete choice experiment among Dutch healthcare professionals showed that severity of disease, cost per QALY gained, individual health gain and budget impact were the most important decision criteria (Koopmanscap *et al*, 2010).

Evidence of deliberative decision making

Finally, although all the studies discussed in this section seek, in various ways, to assess the importance of economic and other considerations in reaching the decision, feedback from those involved in the process points to the deliberative nature of decision-making. Namely, in the discussion, various factors, quantified or non-quantified, play a role. Some of the qualitative studies begin to throw some light on this, but evidence is sparse. Rawlins and Culyer (2004) give some examples of how value judgements (eg. on equity of access to care) influenced decisions of the NICE Appraisal Committee.

In addition, a study by George *et al* (2001) of decisions made by the PBAC showed that, whilst there was a clear relationship between the ICER and the likelihood of a drug being rejected, or being recommended only if the manufacturer was willing to lower the price, there were several outliers (ie. drugs that appeared not to be very cost-effective, yet receiving a positive recommendation, and *vice versa*). They argue that, in its deliberative decision-making process, the committee was giving consideration to issues such as the seriousness of the health condition the drug was indicated for, the existence (or not) of alternative therapies to the drug under study, the affordability of care to patients if the drug was not reimbursed and the overall budgetary impact of the decision to list the drug.

6. Changes in the allocation of healthcare resources

Of course, the ultimate test of incorporating economic evaluation into the reimbursement process is whether it has improved healthcare provision (eg. has it made the provision of healthcare more efficient, more equitable, or both?).

The first problem in addressing this question is that there are often difficulties in implementing the decisions made by reimbursement agencies, particularly in the case of 'mixed' decisions (ie. where the drug is recommended for use, but only for a subset of the patient population). In different jurisdictions various mechanisms have been used to enforce adherence to the decisions or recommendation of the agencies. These include making guidance mandatory on the healthcare system, designating treatments to be 'on authority' (ie. allowed only when the physician verifies that the patient meets the eligibility criteria), the use of prescribing incentive schemes, audit of local practices/decisions and the use of 'risk sharing schemes'. Study of the implementation of decisions is sparse, but one study in the UK showed that the implementation of NICE guidance was patchy (Sheldon *et al*, 2004).

The second problem is that, in most healthcare settings, very little is known about the range of options facing the physician, or other decision-maker, when considering the implementation of the reimbursement agency's decision. For example, if a decision-maker in the UK operating under a fixed budget, decides to make a given treatment available in accordance with NICE guidance, what is actually displaced? It could be a highly cost-effective service, but one which had not been assessed by NICE, or it could be another treatment option for which there was no reliable evidence. One function of adopting a cost-effectiveness threshold would be to reflect this opportunity cost, but for most jurisdictions either no explicit threshold exists, or the basis for establishing the threshold is inadequately researched.

Finally, in common with the evaluation of most policy changes, it is difficult to specify the counterfactual. Namely, how would decision-making processes in the various jurisdictions have developed if economic evaluation had not been incorporated into the reimbursement process. Of course, bearing in mind the variations in the state of the world prior to the incorporation of economic analyses, the counterfactual may be different for different jurisdictions.

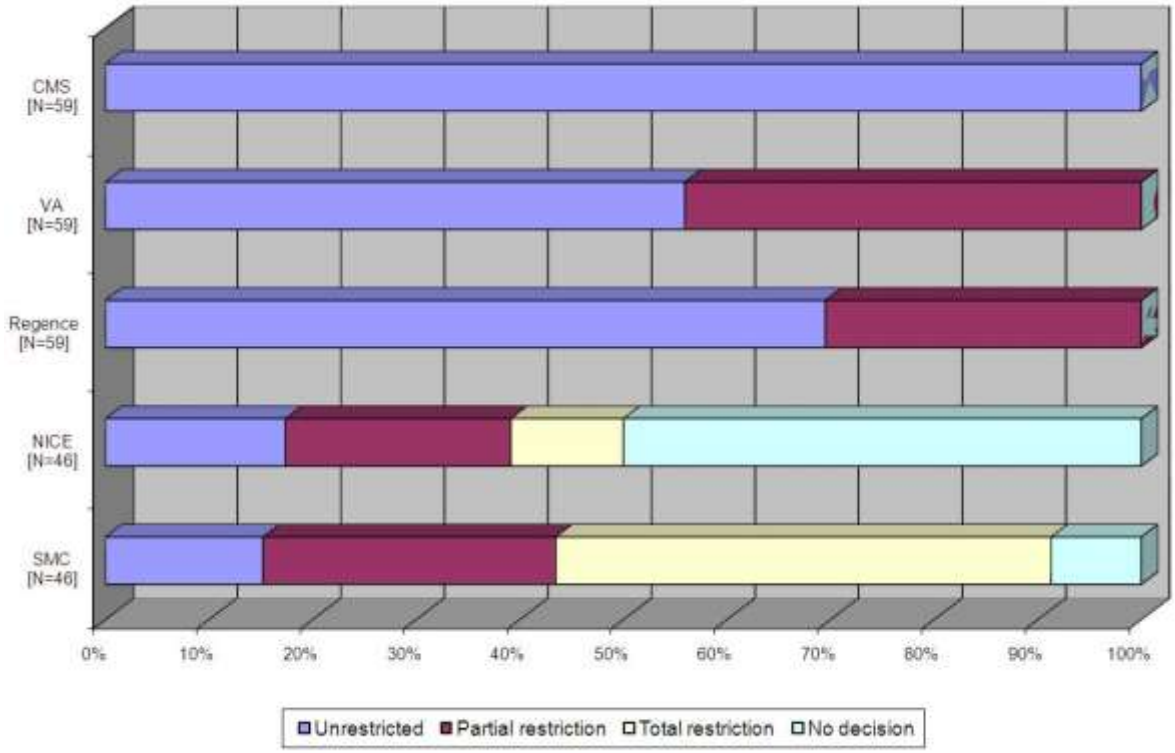
These uncertainties have led some analysts, most notably Birch and Gafni (2007) to argue that the 'nightmare counterfactual' cannot be ruled out. Namely:

- The explicit or implicit decision-making threshold, of acceptable cost-effectiveness, has been set higher than that which would have been used by decision-makers operating under a budget constraint;
- As a result of using economic evaluation, manufacturers just priced up to the threshold, whereas otherwise prices would have been lower;
- The process, of considering incremental cost-effectiveness of new products, gave attention to technologies of marginal value that would otherwise have been ignored by healthcare decision-makers with limited budgets.

There is no straight-forward rebuttal to these arguments. Certainly there is no comprehensive analysis that demonstrates that jurisdictions applying economic analysis deliver healthcare in a more efficient, or equitable, manner than those who do not. However, evidence can be cited that suggests this policy is likely to lead to lower prices for drugs and their more efficient use.

The evidence from jurisdictions where economic evaluation has been applied shows that, in order to meet the acceptable level, of cost-effectiveness, manufacturers often have to accept a lower price than that being applied on an international level. This happens in Australia, where in some instances the PBAC will only recommend listing if the manufacturer lowers the price. It is also beginning to happen in the UK, through the patient access schemes. Also, as a result of using economic evaluation, therapy is being delivered in a more targeted way. Depending on the jurisdiction, between 15 and 20 per cent of drugs are rejected for reimbursement altogether. Around another 20 to 30 per cent are reimbursed only for a sub-set of the patient population. Targeting medicines to those patients that will benefit most is probably the main way in which a more cost-effective use of healthcare resources has been obtained.

The comparison of experience in the US and the UK with the reimbursement of anti-cancer drugs illustrates the consequences of applying stringent cost-effectiveness criteria. In a study of all anti-cancer drugs licensed by the FDA since 2004, all were reimbursed in the USA, often with no restrictions, whereas in the UK much greater restrictions on use were applied (Mason *et al*, 2010) (see Figure 4). It is possible that such restrictions could have been applied without the existence of a body like NICE, but, given the emotion surrounding end-of-life care, the most likely alternative scenario would be postcode rationing, as existed in the past.



Source: Mason et al (2010)

Figure 4. Coverage restrictions for eligible anticancer drugs, FDA approved 2004 2008

The restrictions on access in countries like the UK raise the question of what, if any, impact the incorporation of economic evaluation into reimbursement decisions has had on the equity of healthcare provision. In the UK, NICE was founded, in part, to deal with geographical inequity. As a result, the provision of costly high-profile drugs is more even across the country than it was before. However, as was mentioned earlier, NICE has only sought to standardise which new drugs are adopted, not what is displaced as a result.

In addition, in commenting on the differences between the US and UK, Malin (2010) observed that two quite different rationing processes were being applied, the one in the US being driven by co-pay as opposed to central direction. She remarked, “We have a choice. Do we use science to help us reach consensus on what we are willing to pay for new therapies and innovation, or do we leave individual patients to wrestle with the skyrocketing costs of cancer care and treatment determined by their ability to pay?”

The impact of economics-driven reimbursement processes on vertical equity within healthcare is difficult to assess. Much of the debate has centred on value judgements behind the construction and use of the quality-adjusted life-year (QALY) measure. This debate is currently unresolved, but the indications are that the simple application of equally-weighted QALYs may not adequately reflect societal preferences for the allocation of healthcare resources.

7. Conclusions

Before the introduction of economic evaluation as a formal part of the reimbursement process for drugs, a range of arrangements existed across different jurisdictions. These included reimbursement based on clinical criteria alone and price controls. Some jurisdictions had no controls on the price or reimbursement of drugs and any restrictions on access were merely a result of general budgetary restrictions or local formulary decisions.

The changes in the structure of reimbursement policies necessary to incorporate economic evaluation have been accomplished without major difficulty in most jurisdictions. However, several methodological differences in international guidelines for economic evaluation exist, only some of which can easily be justified.

Several changes in reimbursement processes have taken place in those jurisdictions incorporating economic evaluation. Some difficulties in making and evaluating economic submissions have occurred, although in the main this has been a smooth transition. A number of beneficial changes have been observed, such as a trend towards requiring the measurement of more meaningful clinical endpoints and increased engagement between manufacturers, drug regulators and payers. The extent to which these changes can be attributed to the introduction of economic evaluation is variable.

Various studies of changes in reimbursement decisions have been conducted. A consistent finding is that economic considerations (eg. the size of the ICER) have been influential, second only to the strength of the clinical evidence for the drug of interest. Where decisions in different jurisdictions have been compared, differences in the decision outcomes have been observed. However, in many cases these differences can be explained. However, the same evidence package does not guarantee the same decision in all jurisdictions, because of differences in local circumstances.

The most important question is whether the incorporation of economic considerations into the drug reimbursement process has led to a more efficient and/or equitable allocation of healthcare resources. This is difficult to ascertain because of the difficulties in specifying the counterfactual and the fact that little is known about the extent to which reimbursement decisions actually lead to changes in healthcare practice.

Nevertheless, given the increasingly high prices of many new drugs (eg. in areas such as cancer) and the difficulties in obtaining substantial improvements in health gain, it is likely that the explicit consideration of costs and benefits has moved us closer to an efficient and equitable allocation of resources than the policies that existed in the past. In social insurance systems, the systems in most of the jurisdictions adopting this policy, an evidence-based system of pricing and reimbursement for drugs, considering societal willingness-to-pay, is a reasonable policy objective to pursue.

References

Anell A, Persson U. Reimbursement and clinical guidance for pharmaceuticals in Sweden: do health-economic evaluations support decision making? *The European Journal of Health Economics* 2005;6: 274-279.

Backhouse M, Wonder M, Hornby E, Kilburg A, Drummond MF, Mayer FK. Early dialogue between the developers of new technologies and pricing and reimbursement agencies: a pilot study. *Value in Health* 2011;14:608-615.

Barbieri M, Drummond MF, Rutten F, Cook J, Glick HA, Lis J, Reed SD, Sculpher MJ, Severens JL, on behalf of the ISPOR Good Research Practices Economic Data Transferability Task Force. What do international pharmacoeconomic guidelines say about economic data transferability? *Value in Health* 2010;13:1028-1037.

Barbieri M, Hawkins N, Sculpher M. Who does the numbers? the role of third-party technology assessment to Inform health systems' decision-making about the funding of health technologies. *Value in Health* 2009;12:193-201.

Birch S, Gafni A. Economists' dream or nightmare? maximizing health gains from available resources using the NICE guidelines. *Health Economics Policy and Law* 2007*,* 2: 193-202.

Bryan S, Williams I, McIver S. Seeing the NICE side of cost-effectiveness analysis: a qualitative investigation of the use of CEA in NICE technology appraisals. *Health Economics* 2007;16:179-193.

Cairns J. Providing guidance to the NHS: the Scottish Medicines Consortium and the National Institute for Clinical Excellence compared. *Health Policy* 2006;76:134-143.

Canadian Agency for Drugs and Technologies in Health (CADTH). *Guidelines for the economic evaluation of health technologies: Canada,* 2006, CADTH, Ottawa.

Clement F, Harris MA, Li JJ, Yong K, Lee KM, Manns BJ. Using effectiveness and cost-effectiveness to make drug coverage decisions: a comparison of Britain, Australia, and Canada. *Journal of the American Medical Association* 2009;302: 1437-1443.

Dakin H, Devlin ANJ, Odeyemi IAO. "Yes "No" or "Yes, but"? multinomial modelling of NICE decision-making. *Health Policy* 2006;77:352-367.

Department of Health. A new value-based approach to the pricing of branded medicines: a consultation, 2010. London: Department of Health.

Department of Health, Commonwealth of Australia. *Guidelines for the pharmaceutical industry on preparation of submissions to the pharmaceutical benefits advisory committee, including submissions involving economic analyses*, 1992. Canberra: Australian Government Publishing Service.

Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis'. *Health Economics* 2004;13:437-452.

Drummond MF, Schwartz JS, Jönsson B, Luce BR, Neumann PJ. Key principles for the improved conduct of health technology assessments for resource allocation decisions. *International Journal of Technology Assessment in Health Care* 2008;24:244-258.

George B, Harris A, Mitchell A. Cost effectiveness analysis and the consistency of decision making - evidence from pharmaceutical reimbursement in Australia (1991 to 1996). *Pharmacoeconomics* 2001;19:1103-1109.

Hill S, Mitchell RAS, Henry DA. Problems with the interpretation of pharmacoeconomic analyses - A review of submissions to the Australian pharmaceutical benefits scheme. *Journal of the American Medical Association* 2000;283:2116-2121.

Hjelmgren J, Berggren F, Andersson F. Health economic guidelines - similarities, differences and some implications. *Value in health* 2001;4:225-250.

International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Pharmacoeconomic guidelines around the world, Lawrenceville, NJ. ISPOR 2011. Retrieved 13 September 2011, from http://www.ispor.org/peguidelines/index.asp

Jansen J, Fleurence R, Devine B, Itzler R, Barrett A, Hawkins N, Lee K, Boersma C, Annemans L, Cappelleri J, on behalf of the ISPOR Good Research Practices Task Force. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR task force on indirect treatment comparisons good research practices: part 1. *Value in Health* 2011;14:417-428.

Koopmanschap MA, Stolk EA, Koolman X. Dear policy maker: have you made up your mind? a discrete choice experiment among policy makers and other health professionals. *International Journal of Technology Assessment in Health Care* 2010;26:198-204.

Lexchin J, Mintzes B. Medicine reimbursement recommendations in Canada, Australia, and Scotland. *American Journal of Managed Care* 2008;14:581-588.

Lim ME, Bowen JM, O'Reilly D, McCarron CE, Blackhouse G, Hopkins R, Goeree R, Tarride J-E. Impact of the 1997 Canadian guidelines on the conduct of Canadian-based economic evaluations in the published literature. *Value in Health* 2010;13:328-334.

Malin JL. Wrestling with the high price of cancer care: should we control costs by individuals' ability to pay or society's willingness to pay? *Journal of Clinical Oncology* 2010;28:3212-3214.

Mason A, Drummond M, Ramsey S, Campbell J, Raisch D. Comparison of anticancer drug coverage decisions in the United States and United Kingdom: does the evidence support the rhetoric? *Journal of Clinical Oncology* 2010;28:3234-3238.

Mason A, Drummond MF. Public funding of new cancer drugs: is NICE getting nastier? *European Journal of Cancer* 2009;45:1188-1192.

Mauskopf J, Walter J, Birt J, Bowman L, Copley-Merriman C, Drummond M. Differences among formulary submission guidelines: implications for health technology assessment. *International Journal of Technology Assessment in Health Care* 2011;27:261-270.

Miners AH, Garau M, Fidan D, Fischer AJ. Comparing estimates of cost effectiveness submitted to the National Institute for Clinical Excellence (NICE) by different organisations: retrospective study. *British Medical Journal* 2005;330:65-68.

Morgan S, Barer M, Evans R. Health economists meet the fourth tempter: drug dependency and scientific discourse. *Health Economics* 2000;9:659-667.

National Institute for Health and Clinical Excellence (NICE). Our Guidance, 2011, retrieved 13 September from http://www.nice.org.uk/

O'Neill P, Devlin NJ. An analysis of NICE's 'restricted' (or 'optimized') decisions. *Pharmacoeconomics* 2010;28:987-993.

Raftery J. Multiple sclerosis risk sharing scheme: a costly failure. *British Medical Journal* 2010;340: 1282-1284.

Rawlins MD, Culyer AJ. National Institute of Clinical Excellence and its value judgments. *British Medical Journal* 2004;329:224-227.

Sculpher MJ, Drummond MF. Analysis sans frontiers: can we ever make economic evaluations generalisable across jurisdictions? *PharmacoEconomics* 2006;24:1087-1099.

Sheldon T, Cullum AN, Dawson D, Lankshear A, Lowson K, Watt I, West P, Wright D, Wright J. What's the evidence that NICE guidance has been implemented? results from a national evaluation using time series analysis, audit of patients' notes and interviews. *British Medical Journal* 2004;329:999.

Tappenden P, Brazier J, Ratcliffe J, Chilcott J. A stated preference binary choice experiment to explore NICE decision making. *PharmacoEconomics* 2007;25:685-693.

Towse A. Value based pricing, research and development, and patient access schemes: will the United Kingdom get it right or wrong? *British Journal of Clinical Pharmacology* 2010;70:360-366.