Demonstrating cost-effectiveness. Can we use risk-sharing rather than one-off payer decisions at launch?

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Abstract

This paper will explore how payer demands for cost-effectiveness evidence on product launch can be reconciled with pharmaceutical industry concerns that cost-effectiveness can only be assessed when there is experience of routine use of a product in clinical practice. In particular, it will consider the theory and potential for practical application of: (i) risk-sharing, whereby the price that the company receives depends ex post on the performance of the product; and (ii) value of information approaches in which the costs associated with ex post incorrect decisions (to list or not list) are weighed alongside the time and out-of-pocket costs of additional data collection pre- or post-launch.

1. Introduction

A number of payers are now seeking information on the cost-effectiveness of pharmaceutical products at launch. NICE has attracted great interest, following Australia and several Provinces in Canada, most notably Ontario. Elsewhere in Europe, official guidelines for economic evaluation have been produced in support of recently established or forthcoming requirements that economic data be provided when applying for public reimbursement of a new product. All price applications to the Finnish authorities have been rejected since 1998 if they do not contain an economic element while, in Norway, economic evaluations will be required from 2002, the date at which a similar reimbursement requirement is expected to come into force in the Netherlands. France and Denmark have included economics in their new criteria for making reimbursement decisions, the Portuguese authorities are able to request economic studies from companies to support reimbursement claims and the new price negotiation model published in Italy in 1997 includes a cost-effectiveness ratio. In the USA, some HMO's are seeking this information, and one, Regent, has published guidance as to how it wishes manufacturer submissions to be made.

The payer perspective is that it is inefficient for health care technologies to be used if they do not represent good value for money as represented by their cost-effectiveness. The money would be better spent elsewhere – either in the health care system or elsewhere in public or private consumption. Such an approach presupposes that:

(i) at best there is some agreement as to what is an appropriate threshold for the cost-effectiveness of treatments, or as a minimum there is agreement as to who is empowered to make such judgements. This paper does not explore the extent to which this is the case but assumes that one of these situations does hold, and that we have a cost-effectiveness threshold established by one of these routes;

(ii) evidence of cost-effectiveness is available when a product is launched, hence it is possible and appropriate to assess the cost-effectiveness of a product at this point;

(iii) Type I errors (where the null hypothesis is incorrectly rejected) in which resources are expended on treatments that are subsequently found not to be cost-effective are of greater concern than Type II errors (where the null hypothesis is incorrectly accepted) and resources that could be used to deliver cost-effective care are spent less efficiently. This leads to a propensity to refuse to pay for products until there is strong evidence of cost-effectiveness.

The pharmaceutical industry has argued against the validity of each of these assumptions. In particular that the rationing involved does not have public support, (implicitly assuming that people would rather pay more for health care), that the evidence of cost-effectiveness available when a product is first launched is limited and does not give a good guide to actual cost-effectiveness in routine clinical use, and that denying patients access to treatment that is cost-effective (a Type II error) is more serious than a Type I error where patients receive treatment that is effective but not cost-effective.

This paper considers issues (ii) and (iii). In particular, it considers:

(i) whether the choice between assessment at launch and assessment some period after launch can be assisted by risk-sharing arrangements which align incentives and lead to the payer and the manufacturer bearing efficient shares of the full cost of an incorrect decision (and the benefits of a correct decision);

(ii) whether approaches in the literature which consider the incremental value of information relative to the incremental cost of acquiring can, in principle, be used to identify how much information should be collected pre-launch and how much post-launch.

These two approaches should be complementary. One examines the social cost and benefits of information collection, the other how appropriate contractual arrangements can be put in place to provide the correct incentives to achieve the socially optimal solution.

This paper is structured as follows:

- section 2 briefly discusses the issues that arise in using cost-effectiveness data for pricing and reimbursement decisions at launch;

- section 3 outlines types of risk sharing arrangements that one might expect to see in pharmaceuticals;

- section 4 sets out an algebraic representation of the problem from societal, payer and manufacturer perspectives, and explores value of information approaches, and how they can be linked to risk sharing arrangements;

- section 5 sets out some initial thoughts on the implications of the analysis of risk sharing for the timing of the collection of information.

2. Issues at launch

A number of familiar issues arise with regard to the availability of information on the cost-effectiveness of a new product at the time of launch and, in particular, the reliance of cost-effectiveness estimates on evidence from phase III clinical trials designed to establish efficacy for licensing purposes. Of course, these trials can be expanded to collect relevant information on resource use and on patient quality of life, but concerns often remain about the relevance of the clinical setting, patient selection, and the choice of comparator, of outcome measure and of trial end point. There are three central issues – internal versus external validity; how to extrapolate from trial end points to longer term health outcomes; and whether cost-effectiveness is likely to change over time.

Of course using estimates of cost-effectiveness at launch is more likely to lead to efficiency in resource use than relying only on efficacy evidence. The issue that is addressed in this paper is whether multi-stage review linked to risk sharing may produce a better profile of information collection. Such an approach would recognise the importance to companies of generating funds from the diffusion of new products in order to justify and finance post-launch studies in order to derive improved estimates of value for money.

3. Types of risk sharing arrangements

The most common form of risk sharing between payers and manufacturers is a volume-price or revenue sharing regulatory contract which does not involve assessing health outcomes or cost-effectiveness. In France, for example, companies agree expected volumes at the same time as they negotiate prices with the economic regulator. After two years, planned and actual sales are compared and, if necessary, an adjustment is made to the price. In the UK the PPRS is a form of banded profit control (albeit with a subsidiary price control) in which companies have a range of profitability above which they must reduce prices and below which they can apply to increase prices. In Ontario in 1998 the provincial government proposed that if companies exceeded their sales forecasts for new products on the provincial formulary then they should refund any excess revenues in full. The industry proposed that risk be shared so that companies would be compensated if expenditures were lower than expected. In the event a plan for closer utilisation monitoring with no sanctions was agreed. These examples are of a form of risk sharing that is about usage of the product, or of a portfolio of a company's products. An extreme version of this, which is often discussed (as opposed to used) in the USA is capitation, in which a company receives either a fixed amount per patient regardless of how much of the product is needed by that patient, or a lump sum irrespective of the number of prescriptions issued for the product. Volume-price or revenue risk sharing may be particularly appropriate for the pharmaceutical industry because it is characterised by high fixed, sunk, costs and low marginal costs. However, it is not relevant to our discussion of cost-effectiveness.

The second type of risk-sharing is where the price received by the company depends directly on the effectiveness or cost-effectiveness of the product. The standard form that this seems to take is for a rebate of the cost of the product, either in cash, or in kind (i.e. replacement stock) for patients that fail to respond to the therapy. Examples are included in Appendix 1. These are taken from a search of four publications which cover the pharmaceutical and medical devices sector – the Pink Sheet, the Gray Sheet, Clinica and Scrip. Strictly such discounts could be interpreted as either a rebate for poor performance or as a disguised discount if, in effect, a drug is known to have responders and non-responders and non-responders are being identified ex post and the payer is being refunded. For the purposes of this paper, however, we treat money back guarantees as a form of outcome related performance contract.

Money back contracts are (probably) the simplest form (in terms of information requirements and monitoring costs) of performance contracts to enter into. However, they can be seen as a variant of a two stage review process, whereby an initial assessment of expected performance is made by the payer and the company to be followed by a later ex post appraisal. This second stage review can lead to a revenue or price adjustment being made. In the next section we seek to develop a generalised model for multi-stage review.

4. Multi-stage review

4.1 Formal presentation of the problem

We assume that the payer has a cost-effectiveness threshold k, such that a new therapy (x) is considered cost-effective by payers for their patients relative to an existing treatment (y) if:

$$\Delta C_{x,y} / \Delta E_{x,y} < k_p \qquad (1)$$

where $\Delta C_{x,y}$ and $\Delta E_{x,y}$ represent the incremental change in costs and in health effects and k_p is the threshold cost per QALY at which an intervention is considered cost-effective for the treatment of patient group p. For ease of analysis, we assume that k_p is the same for all groups of patients and that all health outcomes are measured in QALYs. We assume that $\Delta C_{x,y}$ includes changes in societal costs and not just costs borne by payers, and also includes the price of the new therapy P_x.

However, we assume that the price of the new therapy is a function of the social surplus that is achieved by the therapy. If we ignore the marginal cost of producing the product, then the social surplus is given by the maximum price (P_x^{max}) at which the new therapy is cost effective:

$$P_x^{max} = k\,\Delta E_{x,y} - \Delta C^*_{x,y} \qquad (2)$$

Where:

$$\Delta C_{x,y} = \Delta C^*_{x,y} + P_x \qquad (3)$$

At the price P_x^{max}, the payer is accepting a total incremental price for the treatment of k. Assume that payers typically set the actual price at some fraction α of the maximum price, where α reflects the share of the social gain that accrues to the innovator and $(1 - \alpha)$ is the share captured by the payer, so:

$$P_x = \alpha\, P_x^{max} \qquad (4)$$

By substituting for $\Delta C^*_{x,y}$ using equation (3) we can show that:

$$P_x = \alpha / (1 - \alpha)\,[k\,\Delta E_{x,y} - \Delta C_{x,y}]\ ^{1} \qquad (5)$$

Now we examine the likely cost-effectiveness of the new product. Let:

- $H_{e,t}$ be the expected cost effectiveness of the new treatment[2] based on the information available at time t;

- $H_{a,t}$ be the actual cost effectiveness of the new treatment in routine clinical use at time t.

We assume two important attributes of $H_{a,t}$. Firstly, it may vary over time as treatments are better targetted (or used more widely) or as clinicians learn how to use the product more cost-effectively. Secondly, we assume that the value of $H_{a,t}$ is never known. Instead we collect a stock of information It which improves the estimate of $H_{a,t}$, such that:

$$H_{a,t} = f(H_{e,t}) + \phi \qquad (6)$$
$$H_{e,t} = g(I_t) + \gamma \qquad (7)$$

Where ϕ, γ are random error terms.

[1] Thus the payer benefit is $(k\,\Delta E_{x,y} - \Delta C_{x,y})$ which is $(1 - \alpha)\,[k\,\Delta E_{x,y} - \Delta C^*_{x,y}]$ and the manufacturer benefit is $\alpha / (1 - \alpha)\,[k\,\Delta E_{x,y} - \Delta C_{x,y}]$, which is $\alpha\,[k\,\Delta E_{x,y} - \Delta C^*_{x,y}]$.

[2] We are taking $H_{e,t}$ as $\Delta C_{x,y} / \Delta E_{x,y}$. It could be argued that $\Delta C^*_{x,y} / \Delta E_{x,y}$ is more relevant as it reflects the potential societal gain. However, $\Delta C_{x,y}$ tends to $\Delta C^*_{x,y}$ as $\Delta C_{x,y} / \Delta E_{x,y}$ tends towards k, because P_x tends towards zero. Thus $\Delta C_{x,y} / \Delta E_{x,y}$ and $\Delta C^*_{x,y} / \Delta E_{x,y}$ are always on the same side of k.

The amount of information on cost-effectiveness that is collected is a function of elapsed time (t) and the effort that has been expended (e). Information can be collected during product development or after the launch of the product. Thus t=0 at the point at which the product enters clinical development. Thus, the amount of information available at a time t1 is a function of the amount of effort that has been expended in each time period since the product entered development. Thus:

$$I_{t1} = \Sigma^{t1}_{t=0} (e) \qquad (8)$$

However, there are limits to the amount of information that can be collected in any particular time period, irrespective of the effort that is put in. The maximum amount of information that can be collected by time t is given by I^*_t and this produces the best possible value of $H_{e,t}$ which we call $H^*_{e,t}$. However, it may not make sense to collect I^*_t because there is a cost attached to collecting information. We assume that each unit of effort incurs a cost (c). The total cost of information collection incurred at a point in time t_1 (ignoring discounting) is thus:

$$TCI = \Sigma^{t1}_{t=0} (e\ c) \qquad (9)$$

Let us assume these costs are shared by the manufacturer and the payer in the proportions β and $(1 - \beta)$.

To look at the potential benefits to be gained from collecting information on cost-effectiveness we now consider the value of information.

4.2 The value of information

Information will be of value in enabling decision makers to avoid two different types of error that can occur:

a) The most important is when an incorrect assessment is made as to whether the new treatment lies above or below the cost-effectiveness threshold k,
i.e. $H_{e,t} > k > H_{a,t}$ or $H_{e,t} < k < H_{a,t}$.
The latter occurs de facto during any period of time in which a cost-effective product is available (i.e. has a product licence and has been launched) but is not used pending the conduct of an appraisal.

b) A secondary, but still important error is when the assumption about how cost-effective the product is turns out to be incorrect, but not so wrong as to mean that it moves across the threshold k.

We look at the value of information in each of these cases.

a) **Avoiding an incorrect use or non-use of a product.**

The social cost of a wrong decision in a particular time period is

$$|H_{a,t} - k|\ \Delta EN \qquad (10)$$

where N is the number of patients treated in period t. (We ignore any discounting issues around ΔE[3]). This is because we assume that society's willingness to pay is k and thus if a product is not used when it offers a net benefit, then the cost is the difference in cost per effect multiplied by the number of effects i.e. the incremental net benefit per treatment multiplied by the number of patients treated. Thus if the threshold k were £20,000 per QALY and a treatment was used on 100 patients in time t with an expected incremental cost of £30,000 per QALY giving each patient an incremental benefit of 5 QALYs (so the treatment costs £150,000) then the inefficiency would be £5m. A similar inefficiency arises if a treatment with a cost per QALY of £10,000 was not used on 100 patients who could have benefited from the incremental health benefits of 5 QALYs that it would have bought.

We assume that there is a probability θ_t of making a wrong decision at time t and $(1- \theta)_t$ of making the right decision. However, $\theta_t = f(I_t)$ i.e. by expending more effort and cost on information collection we can reduce θ_t. We want to collect information up until the point at which the marginal benefit from additional information collection is equal to the marginal cost of collecting it:

$$\Delta\theta_t \left| H_{a,t} - k \right| \Delta EN = \Delta e_t \, c \qquad (11)$$

Problems arise because we cannot observe $H_{a,t}$. We are looking at whether $H_{e,t} > k$. Information about the treatment both improves the central estimate of $H_{e,t}$ and reduces the variability of the estimate so reducing the probability of making an error.

b) **Changing the estimate of cost effectiveness within the threshold**

As we collect more data our estimate of cost-effectiveness may change, but without crossing the threshold k. As we are assuming a distribution of social benefit in the ratio α and $(1 - \alpha)$ this should lead to a price revision using equation (5) above, but also to a retrospective adjustment, again in the ratio α and $(1 - \alpha)$, of the difference in estimated cost-effectiveness:

$$\left| H_{e,t2} - H_{e,t1} \right| \Delta EN \qquad (12)$$

However, we have also to take account of the payments that have been made to manufacturers. In other words it is the social benefit including these payment which has to be taken into account. We return to this in our discussion in section 4.4.

Such an adjustment will also be applicable when a product has been used but is subsequently shown not to be cost-effective. As well as the social loss identified in a) above, there will be a need for a retrospective adjustment from the incorrect estimate to the k value.

$$\left| H_{e,t1} - k \right| \Delta EN \qquad (13)$$

Again, account will need to be taken of the payments already made to manufacturers.

The next section explores the issue of attaching a value to additional data collection.

[3] We are also implicitly assuming that ΔE does not change. If ΔE_{t1} is not equal to ΔE_{t2} (i.e. the estimate of effectiveness changes) then the formulas are slightly more complicated.

4.3 Approaches reported in the literature

A limited number of studies in the literature have attempted to apply an economic approach to the evaluation of undertaking a study of an intervention, as opposed to the intervention itself. Townsend and Buxton (1997) estimated the cost-effectiveness of a hypothetical trial of hormone replacement therapy, making various assumptions about the likely outcomes of the trial, the costs and QALY gains from resulting policy changes and the cost of undertaking the trial. Their calculations of the potential overall costs and QALYs with or without the trial allowed them to derive an estimate of the cost per QALY gained of undertaking the trial. Decision makers could compare this kind of information with cost-effectiveness data on other uses of health care resources when deciding upon investments in research.

Rather than using a cost-effectiveness ratio to summarise the benefits of conducting a study, Hornberger and Eghtesady (1998) attached a monetary value to undertaking a randomized trial of an experimental treatment versus placebo. By valuing a QALY in monetary terms, these authors estimated a 'loss function', taking account of lost QALYs for treatment successes and failures under both active treatment and placebo, treatment costs and the costs of undertaking the trial. Using these estimates, they derived the increase in success rate compared with placebo that would justify a switch to the experimental treatment and showed that using information from the trial would reduce the overall 'expected losses' for the treatment population compared with not undertaking the trial.

Some of the features of this study appear in the more formalised Bayesian approach to the value of information by Claxton and Posnett (1996) and Claxton (1999). In this analysis, a decision maker is faced with the choice between two mutually exclusive alternatives, an experimental treatment and current treatment, for a given patient population. From the decision maker's point of view, the choice of treatment is determined by the incremental net benefit of experimental treatment, where net benefit is defined in either health effects or in monetary terms. Expressed in monetary terms, using the notation in equation (1) above, net benefit is given by:

$$\text{Net benefit} = k\,\Delta E_{x,y} - \Delta C_{x,y}$$

When net benefit is positive, the experimental treatment (x) should be selected and, conversely, when net benefit is negative, current treatment (y) should be selected.

In the Bayesian framework employed, the decision maker decides between the two treatment options based on prior net benefit. However, there is the possibility, due to its variance, that a decision using an estimate of net benefit based on prior information will be wrong and an 'opportunity loss' will be incurred. When an incorrect treatment decision is made, then the potential net benefit from making the correct decision is forgone. The 'opportunity loss' is therefore the difference in net benefit between the best choice and the actual treatment chosen. This is equivalent[4] to the expression given above:

$$\left| H_{a,t} - k \right| \Delta EN \qquad (10)$$

[4] Strictly the Claxton approach looks at the difference between the two treatments. We are implicitly assuming that the net benefit of the alternative treatment (y) is k.

The benefits of acquiring additional data are then assessed in terms of the potential to reduce these opportunity losses.

Expected value of information

The first stage in deciding whether or not to collect further sample information is to calculate the expected value of perfect information (EVPI). Perfect information in this context is assumed to be obtained from an infinite sample and by definition completely removes the possibility of making a wrong treatment decision. Since perfect information eliminates opportunity losses entirely, its value is equivalent to the expected opportunity loss estimated using only prior information. By expressing net benefit in effectiveness terms and thus presenting the threshold cost-effectiveness ratio as a separate term, and assuming that health outcomes and their probabilities are normally distributed, the EVPI can be calculated using the normal loss integral as follows:

$$EVPI = k\,\sigma_x\,L(|NB_x - NB_y| / \sigma_x)$$

Where $|NB_x - NB_y|$ is the absolute difference between the mean net benefit (in effectiveness terms) for experimental treatment (x) and the point of indifference between experimental and usual treatment (y), while L( ) indicates the normal loss integral.

EVPI is therefore a function of:

i) the threshold cost-effectiveness ratio.
ii) the difference in net benefit between the best choice and the alternative actually chosen.
iii) the standard deviation, σ_x, of the prior distribution of net benefit for the experimental treatment, expressed in effectiveness terms.

The opportunity loss at any given value of net benefit will depend upon the first two of these, while the probability of incurring opportunity losses will be influenced by the spread of the prior net benefit distribution (as reflected in its variance). In order to derive an expected value, the sum of the products of opportunity losses and their respective probabilities must be calculated.

The EVPI for a patient population gives the maximum value of collecting additional data and is therefore only an initial test of whether additional data collection is worthwhile, given its cost.

In order to decide whether it is worthwhile collecting more information, the expected value of sample information (EVSI) is required. (An assumption is being made that a trial is the only available source of information.) EVSI is dependent upon those factors which enter the expression for EVPI plus the sample variance of net benefit, which is determined by the sample size. The expected net benefit of sample information (ENBS) can then be calculated as the EVSI less the variable costs associated with collecting the information (which are the treatment and reporting costs and are assumed to be a linear function of sample size). With constant marginal costs of enrolling additional patients into the study, the costs of increasing the size of the sample will increase at a constant rate. EVSI, on the other hand, will continue to increase as the sample size increases but at a decreasing rate. There will therefore be some point at which the ENBS (the difference between EVSI and the marginal costs of collecting data) will be at a maximum, i.e. the marginal net benefit of increasing sample size at this point is zero.

The ENBS therefore represents the maximum cost that it is worthwhile to incur to undertake the research and, at the optimal sample size, is equivalent to the expected net present value of research. It can therefore be used to obtain maximum benefit from a research and development budget.

Our approach is thus similar to the Claxton one. The information collected (I_t) will be less than the maximum information that could be collected (I^*_t). It differs in the treatment of information collection. We assume that information may come from clinical trials or other sources, and there are limits to how much information can be collected in any time period irrespective of the effort put in.

We now introduce risk sharing into the model.

4.4 Incorporating risk sharing

We assume that there is an initial assessment of cost-effectiveness $H_{e,t1}$, and then a subsequent assessment $H_{e,t2}$. There are four scenarios:

(i) the product is used and is confirmed at time t2 to be cost-effective, $H_{e,t1}$, $H_{e,t2} < k$. If $H_{e,t1}$ is not equal to $H_{e,t2}$ then some readjustment of price (prospectively and retrospectively) may be needed.

(ii) the product is used but is then found not to be cost-effective, $H_{e,t1} < k < H_{e,t2}$

Adapting equation (10) above, there is a social loss of $|H_{e,t2} - k|\Delta EN$. In addition there is a need for an adjustment to take account of the distributive effects of the error $|H_{e,t1} – k|\ \Delta EN$ identified in equation (13).

(iii) the product is not used and it is then confirmed not to be cost-effective, $H_{e,t1}$, $H_{e,t2} > k$. No further action is required.

(iv) the product is not used (or its use is delayed), but it is cost-effective. $H_{e,t2}, < k < H_{e,t1}$

As in (ii), there is a social loss of $|H_{e,t2} - k|\Delta EN$.

How should the costs and benefits be distributed in cases (ii) and (iv)? Let us initially assume that they are split in the same proportions α and $(1 - \alpha)$ as the original social surplus was divided in order to set a price for the new treatment (x).

Case (ii) Use of a non cost-effective product

There are two components of the payer's losses $|H_{e,t2} - k|\Delta EN$ (which is a social loss) and $|H_{e,t1} – k|\ \Delta EN$ (which is a distributive issue). The payer has paid the company a price

$$P_x = \alpha / (1 - \alpha) [k\ \Delta E_{x,y} - \Delta C_{x,y}] \qquad (5)$$

A critical issue is whether we treat the loss requiring redistribution as including the monies paid to the company for the product, i.e. whether we take as our base $\Delta C_{x,y}$ or $\Delta C^*_{x,y}$. If we take $\Delta C^*_{x,y}$ as our base then the company needs to rebate the cost of the product to the payer. The

balance of $|H_{e,t1} - k|\ \Delta EN$ is thus the payers share of the redistributive loss. In addition a contribution is required of $\alpha\ |H_{e,t2} - k|\Delta EN$ from the company towards recovery of the social loss. Thus money back guarantees do not in theory meet the requirements for compensation as they only meet the redistributive element of the loss and do not include a share of compensation for the social loss. However, if incremental non-pharmaceutical costs associated with using treatment (x) are small or negative then it will provide full compensation. We might expect such deals to be more attractive to payers therefore when this is the case. The examples in the Appendix are arguably ones where incremental non-pharmaceutical costs are low or potentially negative.

Case (iv) Non-use of a cost-effective product

There is a social loss of $|H_{e,t2} - k|\Delta EN$. However, there is also a redistributive effect. As in our discussion of (ii) above, the choice of $\Delta C_{x,y}$ or $\Delta C^*_{x,y}$ as base is crucial. Had $H_{e,t2}$ been the estimate at time t1 then the manufacturer would have received a price of $\alpha\ [k\ \Delta E_{x,y} - \Delta C^*_{x,y}]$, which is $\alpha / (1 - \alpha)\ [k\ \Delta E_{x,y} - \Delta C_{x,y}]$. The payer benefit would have been $(1 - \alpha)\ [k\ \Delta E_{x,y} - \Delta C^*_{x,y}]$ which is $(k\ \Delta E_{x,y} - \Delta C_{x,y})$ or $|H_{e,t2} - k|\Delta E$. Arguably therefore the appropriate risk-sharing arrangement is for the payer to bear the cost $|H_{e,t2} - k|\Delta EN$ and the manufacturer to bear the cost $N\ P_x$ i.e. the loss in revenue.

We can note that in both cases the manufacturer ends up losing its revenue from the product for the period for which an error was made. The payer incurs its share of loss in the form of lost efficiency in health care purchasing. It may be that the incentives facing the company are sharper than those facing the payer.

5. Implications of risk sharing for information collection

We set out in equation (11) above a relationship between the costs and benefits of acquiring information.

$$\Delta\theta_t\ |H_{a,t} - k|\ \Delta EN = \Delta e_t\ c \qquad (11)$$

Information acquisition costs money but improves $H_{e,t}$ the estimate of $H_{a,t}$ and so reduces the probability of making a Type I or Type II error. To the extent that the costs of making an error are shared between the parties at the margin then logically the costs of information collection at the margin should fall in the same ratio, thus the shares α and $(1 - \alpha)$ of error costs borne by the manufacturer and the payer respectively should equal the shares of the costs of information collection β and $(1 - \beta)$ respectively.

In the absence of any payer (or prescriber) requirement for cost-effectiveness information then expenditure on information collection by either party will be low. There will be few occasions on which cost-effective products are not listed by the payer (unless arbitrary cost controls are used) but many more when products that would not be regarded as cost-effective by central agents of the payer are prescribed. In the absence of risk sharing, the costs of inefficiency will fall on the payer.

In the case of a payer (or prescriber) requirement for cost-effectiveness information of the type we are seeing emerging around the world then most information costs fall on the manufacturer. Only the costs of review fall on the payer. The payer's objective is to avoid the diffusion of new treatments that are not cost-effective. In this situation there are likely to be more

occasions on which cost-effective products are not listed by the payer and fewer in which products not regarded as cost-effective are used, because the payer is more concerned to avoid using products where $H_{a,t} > k$ than to ensure it is using products where $H_{a,t} < k$. This tendency will be reinforced as in the absence of risk sharing the payer faces the prospect of not only incurring the loss $\left| H_{a,t} - k \right| \Delta EN$ if it uses a product that is not cost-effective, but also not being able to recoup expenditure on the product NP_x. It is not surprising that, in the absence of any risk sharing arrangements, the pharmaceutical industry complains about cost-effectiveness requirements, whilst payers argue that they are eminently reasonable.

What would risk sharing arrangements mean for the timing of the collection of information? If we made the assumption that the quality of information available per unit of effort (e) is higher post-launch than pre-launch, and note that there is an opportunity cost associated with collecting data earlier rather than later, then we might expect more emphasis on post-launch data collection. It would depend in part on the willingness to take risks. If the payer was more risk averse than the company, then the payer would seek more pre-launch data collection than the company. It may be, however, that given freedom under risk-sharing arrangements to collect information later rather than earlier companies prefer to invest in pre-launch data collection in order to reduce the likelihood of having to make significant payments to payers following a post-launch reassessment of a product's cost-effectiveness.

Many issues remain to be clarified in exploring risk sharing approaches to costs and benefits and to information collection. These include:

- who determines the initial view of θ, and of $H_{e,t}$ upon which decisions to collect subsequent information are based;
- how is the value of additional information determined i.e. what is the link between $\Delta\theta$ and Δe?

Overall this analysis suggests that **some** of the controversy about demands for cost-effectiveness information could in theory be mitigated by the introduction of new approaches to risk-sharing of the sort that are being used – albeit infrequently – in North America.

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Appendix I Examples of Risk Sharing

Proscar Canadian money-back guarantee

Merck Frosst in Canada has given a money-back guarantee on its benign prostate hyperplasia therapy, Proscar (finasteride), in the province of Saskatchewan.

If a patient covered by the provincial health plan requires surgery after using Proscar for 12 months, the company will reimburse the cost of the drug under an "innovative drug effectiveness guaranty programme" signed this month. Proscar costs Can$750 for one year's treatment compared with Can$3,000-6,000 for the surgical procedure, TURP (transurethral resection of the prostate), according to Merck Frosst.

The agreement comes several months after Duane Adams, the Deputy Minister at Saskatchewan Health, called on companies to enter into risk-sharing arrangements with the government. If a pharmacoeconomic analysis for a specific drug promises fewer side-effects, fewer or shorter hospital stays, of fewer trips to the doctor, the drug company must be willing to compensate individuals, the public at large and/or the health system if the promises are not fulfilled, Mr Adams said (Scrip No 1980, p20).

Merck & Co offers a money-back guarantee on Proscar in the US, and its Canadian subsidiary is discussing similar arrangements with other provincial health ministries. The programme will also apply in the three provinces – Quebec, Manitoba and British Columbia – where the product was already reimbursed. The onus will be on the provinces to monitor patient compliance.

SCRIP No 2004 March 3rd 1995 p14

Taxotere launched in Canada

RPR has also developed a risk-sharing programme in Canada to ensure a benefit from using Taxotere. The programme links to the product's efficacy to a reimbursement guarantee to hospitals, and ensures its correct use. The programme is said to be the first of its kind in Canada.

Because the disease continues to progress in some patients despite treatment, RPR will replace the drug used to treat patients who fail to respond, or who discontinue treatment because of side-effects. Hospitals need only submit a claim form acknowledging that Taxotere was administered in accordance with its labelling, and that a patient's treatment was discontinued upon completion of the first three cycles of therapy because of disease progression or an adverse side-effect.

SCRIP No2062 September 22nd 1995 p 19

Siemens/Cleveland Clinic ultrasound risk-sharing deal based on per-use equipment fees.
Siemens Ultrasound Risk-sharing Deal with Cleveland Clinic involves payment for the equipment on a per-scan, "sliding fee" schedule whereby increased use of the machines lowers the per-scan charge. The per-scan fees, paid by Cleveland Clinic on a monthly basis, will be re-evaluated periodically.

The Gray Sheet. 1997 February 17. 23(7). Page I&W-11.

Baxter distribution unit gaining ability to expand shared-risk deals as separate firm; revenue growth of 5-8%, operating margin of 5-6% projected
Baxter currently has 17 risk-sharing agreements with hospitals throughout the US. In July 1994, the company entered one of its first such deals with Duke University Medical Center in Durham, North Carolina.

Under that supply arrangement, Duke pays Baxter 50% of savings if the hospital's costs fall short of the budgeted costs per procedure. If supply costs exceed the budget, Baxter must pay Duke half the difference. In addition to giving the cost management company greater flexibility in seeking new agreements, the split would provide it with more or a financial cushion to absorb potential losses if supply costs in risk-sharing accounts run higher than budgeted.

The Gray Sheet. 1995 December 4. 21(49). Page 3.

Bard antimicrobial Foley catheter marketing strategy includes risk-sharing offer.
In sales presentations, Bard reps are asking hospitals to weigh the additional cost of Bard's catheter ($10.85 versus $5.85 for a conventional catheter) against the potential cost of a UTI, which is about $600. The company is offering to sell the antimicrobial catheter for the price of a traditional catheter as long as the hospital will split with Bard any savings from the prevention of UTIs. After evaluating the economics of risk-sharing option, no hospitals have opted for the plan and those who are using the antimicrobial catheter are buying them at full price, Bard says.

The Gray Sheet. 1995 May 29. 21(22). Page I&W-2.

MedXL, Hoechst-Roussel's managed care client services; operation, will support DUR and risk sharing.
MedXL's concept of risk sharing "can take many forms," the company noted. Calling capitation a "typical example," the company explained this risk-sharing scheme as "working with a managed care organization to set parameters for use of a drug or group of drugs and fixing reimbursement based on those parameters. Use above or below the agreed reimbursement triggers savings or loss, shared by both partners."

The Pink Sheet. 1995 April 10. 57(15). T&G-14.

Ortho Procrit replacement program in place for certain customers; Flozin capitated agreements being signed.

Ortho Biotech Procrit product replacement programme "replaces product free if it is used appropriately but the patient does not respond to treatment," Ortho Biotech President Dennis Longstreet told the Biotechnology Industry Organization annual meeting in Toronto May 25. Ortho has the programme in place "in certain contractual arrangements," he said.

Longstreet described the programme as based on treatment guidelines developed by managed care customers to use Procrit (epoetin) for anemia. "By delineating appropriate candidates for treatment and establishing dosing regimens, managed care organisations can develop clear guidelines for usage and avoid wasting valuable health care resources which are really critical to these customers." Longstreet said. "Once the guidelines are in place, then the companies

The Procrit programme appears to be similar to Merck's risk-sharing programme for the benign prostatic hyperplasia treatment Proscar. Under that programme, Merck refunds the value of Proscar therapy if compliant patients do not respond after six months ("The Pink

Ortho has also capped the cost of Procrit therapy to patients at $8,000 per year, Longstreet noted, although some AIDS patients "really require up to $12,000-$14,000

Ortho is among the early group of companies to enter into capitated agreements with hospitals. The firm is understood to have signed contracts to supply its quinolone antiobiotic Floxin for a fixed rate regardless of quantity used.

The Pink Sheet. 1994 May 30. 56(22). T&G-3.