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Proceed with caution: an economic perspective on the UK's value based pricing proposals

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Summary

The shift from the Pharmaceutical Pricing Regulation Scheme to Value Based Pricing (VBP) is an important change in the way that medicines will be priced, and consequently, reimbursed in the United Kingdom. Whilst the opportunity to purchase new medicines based on value to society is one that should be welcomed, we should proceed with caution. We highlight ten issues that should be considered relating to innovation, the role and meaning of funding threshold and the adjustments to reflect burden of illness, therapeutic innovation and improvement and wider societal factors.

Most importantly, the assessment of value should continue to be based on the characteristics of the displaced activities (e.g. the health produced). To a large extent, all that is changing under VBP are the characteristics being considered; weighted health rather than unweighted health. In addition, we should not totally abandon a cost-utility framework for appraisal just because its current formulation does not match the wider perspective now desired by government.

1. Introduction

The current Pharmaceutical Pricing Regulation Scheme (PPS) was reviewed by the Office of Fair Trading in 2007 which recommended the introduction of Value Based Pricing (VBP) and this is scheduled to start on 1st January 2014 (OFT 2007). The objectives of the proposed VBP scheme as set out on page 11 of the Department of Health's consultation document (Department of Health 2010) are to:

a) improve outcomes for patients;

b) stimulate innovation;

c) improve the transparency and predictability of decision-making;

d) include a wide assessment of the range of factors through which medicines deliver benefits for patients and society;

e) ensure value for money and best use of NHS resources

The purpose of the consultation document is to gather opinion on the principles and practicalities of the scheme as set out in 20 questions. The purpose of this paper is not to give a point-by-point response to all 20 questions as others are much better placed to answer some of the more process orientated questions. Instead, we aim to highlight issues that we feel have been sidelined in the flurry of opinion about VBP, but which are apparent to us from our perspective as academic health economists with experience of economic evaluation, health technology assessment, benefit valuation and other related topics.

In particular, we focus on objectives (b) and (d), as these represent the greatest departure from the current NICE Technology Appraisal (TA) process. Indeed, one could argue that (a), (c) and (e) are already addressed by the current process; the NICE TA process is already the most transparent reimbursement process in the world and is widely regarded the world over as examining effectiveness and cost-effectiveness in a robust manner. The current process, however, does not cover all patented medicines and so its coverage is incomplete. It should also be noted that innovation and other factors are included within

the current TA process (NICE TA Guidelines 2008) although the influence they have on decisions is not as pronounced as some may wish it to be (Kennedy 2009).

2. Innovation

Issue 1: Innovation in itself should not be rewarded

This issue was considered in the OFT report on pharmaceutical pricing and categorically rejected. Their reasoning was:

> "Some have suggested that a pricing system should also reward stages in the innovative process –'innovation in itself' – over and above clinically beneficial outcomes. In practice, this would mean that a pricing scheme would recognise, in prices, any drug making a major step forward in treating a serious disease (for example by pioneering the pharmacological mechanism) even if it were ultimately ineffective (or at least no more effective than alternatives) and subsequent technological leaps were required before a clinically useful product could be achievable.
>
> However, it is unlikely to be possible to define any meaningful pricing system that could address this problem. Such a system would call for a great number of discretionary awards based on suppositions about companies' chances of success against many – potentially esoteric – scientific challenges with no clinical outcomes. **It would therefore not only be inefficient for the NHS to spend money on ineffective drugs that could be allocated to fund proven medicines for patients with other conditions, it would also fail to provide transparent, clear investment incentives to companies.**" (OFT 2007, Bold in the original report)

Issue 2: Additional incentives for innovation are highly questionable

Even if the OFT argument is rejected, it is not clear why VBP should be considered an appropriate mechanism for stimulating innovation in the development of pharmaceutical products. The reasons for this are 4-fold:

a) Innovation is currently stimulated/rewarded through patents (i.e. monopoly status) and research and development (R&D) tax credits.

b) There are plans for a massive stimulus through a 'patent box' whereby the rate of corporation tax on profits relating to UK-based patents will be set at a rate of 10%, as opposed to the general rate of corporation tax of 27% (Her Majesty's Revue and Customs 2010). In steady state, the cost of the patent box to Her Majesty's Revenue and Customs (HMRC) and, conversely, the size of the stimulus to innovation is estimated to be £1.1 billion per annum (HM Treasury 2010). Putting aside the debate as to whether this is over- or under-stimulus, it is felt that such approaches are more appropriate as they are not taken from the budget of a single service such as the NHS. If it is argued that innovation has spillover effects into the general economy through its creation of knowledge, exports and wealth, then policies aimed at stimulating innovation are best shared across all sectors of the economy.

c) Most aspects of innovation that are identified in the literature are already captured by cost-effectiveness analysis (CEA) through their impact on costs and quality adjusted life years (QALYs). Take two examples; improved side-effects profiles and improved compliance due to more convenient administration. Improved side-effects profiles are included within current CEAs through increased QALYs (due to reduced utility reductions) and reduced costs (due to reduced medical intervention). Improved compliance is included through increased QALYs due to increased effectiveness. Whilst there may be room for improvement in the way in which some of these aspects are incorporated within the QALY model, there is little doubt that they can be incorporated.

d) It is difficult to envisage how an adjustment to a price in the UK to encourage the development of products with specific characteristics that the Department of Health deem are innovative, will change the R&D portfolio of multi-national pharmaceutical companies; the UK represents around 3.5% of global pharmaceutical revenues (Department of Health 2010). The DH's Impact Assessment (2010) that accompanies the consultation recognises that "…a single

small country cannot, by its actions, have a significant effect on the global incentives to invest in R&D". Its own analyses show how VBP incentivisation can lead to net losses to the UK (p38, IA 2010) due to benefits being shared globally, but with the cost being borne in the UK only.

3. The role and meaning of lambda

The basic approach being proposed is to adjust the funding threshold (typically referred to as lambda, λ) in line with weightings associated with selected benefits provided by new medicines. This will produce multiple thresholds intended to reflect a broader range of relevant benefits. For a given set of 'broader factors' a threshold is identified and the price is set accordingly.

The consultation document states that "the price threshold structure is determined as follows:

- there would be a basic threshold, reflecting the benefits displaced elsewhere in the NHS when funds are allocated to new medicines;
- there would be higher thresholds for medicines that tackle diseases where there is greater "burden of illness": the more the medicine is focused on diseases with unmet need or which are particularly severe, the higher the threshold;
- there would be higher thresholds for medicines that can demonstrate greater therapeutic innovation and improvements (I&I) compared with other products;
- there would be higher thresholds for medicines that can demonstrate wider societal benefits."

Consultation Document, p13

Issue 3: Multiple thresholds are nonsensical and ignore the added benefits displaced

The development of multiple thresholds obscures the meaning of the threshold. As recognised in the above quotation, λ represents the value of displaced activity. These

activities do not necessarily change according to the characteristics of the new medicine (although it is recognised that lambda can vary systematically by therapeutic area (Martin et al 2008)).

Additionally, if other costs and benefits are to be factored into the funding decision, then they need to be incorporated into the evaluation of the new medicine and the displaced activities. So, if the benefit weighting for 'severe illness' is twice that of 'mild illness', the threshold should not necessarily be doubled. This would only be true if all the displaced activity were for mild illness. It is likely that the displaced activity will represent a mix of disease severities, innovation and wider effects. Consequently, lambda needs to change to recognise the socially weighted value of the displaced activity. This re-weighing would also need to be applied to the 'basic threshold' (using the terminology of the consultation document).

The consultation document alludes to the correct meaning of lambda and highlights that using multiple thresholds is equivalent to adding in the benefits to appraisal of the new medicine. This is misleading; it is only equivalent if a lambda is set that appropriately includes the social value of the displaced activity and the weightings used to generate the additional thresholds are relative to the characteristics of the displaced activity.

A more preferable approach would be to estimate a socially weighted lambda and keep this fixed (thus retaining the true meaning of the threshold), but to apply weights to the outcome measure in the CEA. If the benefit weighting for 'severe illness' is twice that of 'mild illness', then 1 QALY gained by treating a severe illness can be expressed as 2 severity-weighted-QALYs gained.

4. Adjusting the threshold to reflect burden of illness

The first thing to note regarding this factor is that 'burden of illness' is not being used in its conventional epidemiological sense, that is, the total amount of ill health for a population; it is the burden of illness for an individual. In its epidemiological sense, burden increases with the prevalence of the condition. As such, it is unclear how burden of illness is defined for the purposes of the VBP.

The document states that the most important factors relating to burden of illness are severity of the condition and level of unmet need. As an example of how this could be operationalised, the consultation document suggests that severity *could* reflect health status, *could* be assessed by QALY loss and unmet need *could* reflect existing treatments. Whilst this is fine in principle, if there is to be an empirical basis for the adjustment, there are two important problems that need resolving that are discussed below (Issues 4 and 5).

Issue 4: Focusing on an individual patient characteristic without reference to others, risks unexpected policy implications

Let's assume burden of illness is operationalised using the example in the consultation document (and given in the preceding paragraph). However, is QALY loss (a) the inability to have 'normal' health status for their disease-specific life expectancy, or (b) their inability to have a 'normal' health status and 'normal' age-specific life expectancy? If it is (a), unmet need (and hence, price) is small for patients with short disease-specific life expectancies. If it is (b), unmet need (and hence, price) will be greatest for diseases that reduce life expectancy in younger people, and in essence, it would operationalise a notion of 'fair innings' equity (Williams 1997).

For both such definitions, treatments for kidney cancer may receive a low priority; disease-specific life expectancy is short and due to the age profile of the patient group (which has a median age of around 65), the normal age-specific life expectancy is not large. Yet, treatments for kidney cancer are currently supported through both the supplementary end-of-life guidance within the NICE TA process and from the additional funds within the Cancer Fund.

These unexpected results are caused by focussing on a single marker of 'deservedness' (e.g. unmet need) without reference to other related markers of 'deservedness' (e.g. life expectancy) that people may have preferences over. This highlights that for any given definition of unmet need, the derivation of weights must be considered in relation to related concepts (i.e. unmet need as measured by QALYs are necessarily related to quality of life and age-specific life expectancy). Whilst this interdependency is

recognised within the Impact Assessment (IA 2010, p18), it appears to be ignored within the consultation document.

Issue 5: Best methods are not known

Whilst several studies have attempted to identify the relative value of additional factors related to treatments, there is no consensus on what the best approach is to estimating the relative values despite a long history of attempts, including two NICE funded studies (Baker et al 2008, Dolan et al 2008).

These studies appear to demonstrate large framing effects that impact on the results and even when the results appear intuitive in terms of their ordering, the absolute estimates appear extreme (Baker et al 2008, Dolan et al 2008). In a review of social preferences Nord identified 200-fold differences in some weightings (Nord 2001). The policy implications of such weightings would be dramatic.

Consequently, any attempt to produce weightings will require a large scoping study to pilot empirical studies. It is also possible that the results may need to be moderated if they are considered to be invalid or implausible. Obtaining consensus on these methods will be vitally important if VBP is to be successful.

5. Adjusting the threshold to reflect therapeutic innovation and improvement

There appears to be little justification for rewarding innovation in its own right (Issue 1) and we have also highlighted that innovation is already rewarded four times through patent, R&D tax credits, patent box and inclusion within current methods of cost-effectiveness (Issue 2). The NICE Decision Support Unit (DSU) has also undertaken further analysis to demonstrate why further reward for innovation is not justified (Claxton et al 2009).

So, is there anything new relating to the proposals that has not been considered previously? One issue that has not received a great deal of interest is the notion that additional value should be given to medicines that demonstrate a ‘step change’ in the treatment of a particular illness. The reasoning behind rewarding step-change appears to

be three-fold. Firstly, to disincentivise the production of 'me-too' formulations and as such focus attention on novel compounds. Secondly, it could be argued that society values large changes in utility/QALYs greater than small changes. Thirdly, 'step changes' indicate innovation. We will not address the third point here as this has been previously discussed.

Issue 6: VBP will disincentivise 'me-toos' without this adjustment

When the first formulation within a new class of drugs is produced, it is rewarded with a patent. Subsequent drugs will also benefit from patents, but as value is assessed relative to all other drugs, including the first formulation, their potential profitability will be reduced as the first formulation will go generic before their patent period has been completed. As such, the need for further adjustments to disincentivise 'me-toos' as part of VBP is questionable.

Take golimumab for instance. It is currently being appraised by NICE for use in rheumatoid arthritis. It is the most recent in a long line of 'biologics'. The first drug in this class – etanercept – comes off patent in 2012 and as such, any generic formation of this will reduce the value based price of the entire class regardless of their patent details, thereby limiting their profitability. The manufacturers of etanercept were well rewarded for its therapeutic innovation and improvement. However, golimumab, could in essence only receive 2 years of premium pricing.[1]

Issue 7: Valuing large gains more than small gains limits access to new medicines

The notion of society valuing big health gains more than small health gains is plausible. So, if faced with a choice of treating 1,000 patients with drug 'x' that produces (on average) a 1 QALY gain per patient, and treating 100 patients with drug 'y' that produces 10 additional QALYs per patient, it could be argued that society would prefer funding drug 'x' due to its larger gains (even though the same number of QALYs are produced).

[1] We recognise that generic formulation of biologic therapies have particular issues with respect to manufacturing and regulation which may complicate this specific example.

A consequence of this, of course, is that fewer patients will have access to a new and effective treatment.

Furthermore, there is evidence to suggest that, provided the size of the benefit per patient is over a (as yet unidentified) threshold, people prefer to disperse the overall benefit of a drug to a larger number of patients than to concentrate it to a smaller number of people (Rodríguez-Míguez, Pinto-Prades, 2002; Dolan et al, 2008).

6. Adjusting the threshold for wider societal factors

Issue 8: Very few of these factors are mentioned in the consultation document, and as such, it is difficult to comment on the proposals.

We attempt to examine the issues relating to the incorporation of wider societal factors by listing those wider effects that have been prominent in the literature (for example, Kanavos and colleagues 2010):

- Informal carer costs and quality of life. Carer health-related quality of life is already included within the NICE reference case.
- Societal perspective on costs. By definition, this includes informal carer costs. It also includes production losses, for which there is no agreed method of valuation (although this in itself should not prevent it being included).

  Such an approach is also consistent with including the health care costs in added years of life. Currently, the status of costs not directly attributable to the treatment under consideration is unclear. In some appraisals, the cost of treatments incurred in the additional years of life produced by the new drug have been excluded, for example, in the appraisal of cinacalcet (NICE 2007). There is little sense including costs to all other sectors and the broader economy, but then excluding some of the costs falling on the health service.
- Externalities. It can be argued that some benefits of health care production have benefits that fall beyond this process. Knowledge/spillover is frequently cited; however, it is unclear how much of this is not captured by the manufacturer (and

as such helps generate future medicines at lower cost, thereby increasing profit). A caring externality can be envisaged, such that the treatment of certain diseases is seen as a moral imperative, or generates 'warm glow' in non-patients. Three issues are noted with this. Firstly, such externalities may well exist in the displaced activities, too. Secondly, some essence of this may well be incorporated within the proposed burden of illness weightings. Thirdly, it is not clear to what extent such values should be valued and included within public policy analysis (Milgrom 1993).

- Process utility. This can be included within the current CEA framework. For example, work has been published that has examined the utility decrement associated with medication frequency/flexibility (Boye 2010) and surgery (Cook 1994).

Whilst it is difficult to make precise comment on factors that have not been identified, it should be recognised that a cost-utility framework can accommodate many of the wider benefits mentioned in the literature. A wider valuation and costing perspective is not the death knell of cost-utility analysis (CUA); it is merely a change to the decision problem to which CUA can be applied.

7. Other issues not raised in the consultation document

Issue 9: Uncertainty is not recognised within the approach outlined

The evidence on which a price is to be determined is inherently uncertain and this needs to be considered within the pricing decision. The issue of uncertainty relating to the ICER has been examined in detail by Claxton and colleagues (2011). They highlight the fact that the value of collecting further evidence should be considered by decision makers as this may exceed the incremental benefits of a new technology. Additionally, they argue that the typical framework for economic evaluation masks the profile of costs, such that if access is limited in the future, prior to the full benefits of an intervention being realised, the drug would not be considered cost-effective as all the up-front costs will

already have been borne by the NHS. Incorporation of these two effects may have the effect of reducing the price at which a drug is considered to be good value.

However, it should also be recognised that the evidence on which the categorisation of the medicine/population into different levels of burden of illness, innovation and wider effects will also be uncertain. It is not clear how this will be factored into the proposed framework; presumably, a medicine/population can either be ascribed a particular threshold, or not, which will then be open to appeal. If, instead, burden of illness, innovation and wider effects were included within the ICER, a clear framework exists by which the uncertainty can be described and incorporated within the analysis (NICE 2008).

Issue 10: It is unclear how combination drug regimens will be evaluated

When a drug is licensed in combination with another (or several others), its price will partly be determined by the incremental gain in QALYs associated with it. However, disentangling the marginal effect of one drug from that of several others may not be straight forward; A vs A+B is the simplest example, with the manufacturers of B claiming the full additive incremental effect, but the manufacturers of A may claim a synergistic effect.

8. Conclusion

The shift from the PPRS to VBP is an important huge change in the way that medicines will be priced, and consequently, reimbursed in the United Kingdom. The current system of pricing is not based on the value of the benefits produced; the NICE TA process makes this assessment using a health maximisation framework based around health-related budgets and QALYs. The NICE framework enables an assessment of whether the benefits of a new treatment are greater than the health losses associated with the displaced activities.

The need to assess the value of new interventions based on the characteristics of the displaced activities (e.g. the health produced) must remain. To a large extent, all that is changing under VBP is the characteristics being considered. The current system balances health gains (from the new medicine) with health losses (from the displaced activities). The new system should balance socially-valued health gain and wider benefits (from the new medicine) with socially-valued health losses and wider negative impact (from the displaced activities).

As well as emphasising this need to recognise the value of displaced activities we have also drawn attention to problems with yet further reward for innovation, difficulties in estimating preference weights, the need to recognise uncertainty and problems of double counting when not clearly defining the various benefits to be valued. We have also highlighted areas where a cost-utility framework, contrary to some claims, is capable of addressing wider benefits, for example, innovative features of drugs, disincentivisation of 'me-toos' and incorporation of wider impacts.

So, whilst the opportunity to purchase new medicines based on value to society is one that should be welcomed, we should proceed with caution. The underlying decision rule on which value should be based should not change, nor should a cost-utility framework be totally abandoned just because its current formulation does not match the wider perspective now craved by government. However, the immediate challenge will involve identifying methods to assess social values in a robust manner; twenty years of research has not produced a preferred method, yet we have less than three to derive a suitable set of weights.

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