How Do We Evaluate Technologies That Are Not Cost Effective at Zero Price?

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KEY POINTS . . .

Clinically effective technologies may be found not to be cost-effective – even if the acquisition price is zero – when the costs incurred during periods of additional survival do not outweigh the QALYs gained during those periods.

There remains an ongoing methodological debate over the inclusion of unrelated costs incurred during periods of additional survival, but in practice the exclusion of unrelated costs is unlikely to provide a solution in many cases.

HTA agencies may wish to consider whether there are any ethical reasons for recommending a treatment that cannot demonstrate cost effectiveness at zero price, and may also need to consider how to distribute health resources in the fairest way in society as a whole.

This is the first of two articles in this issue on the topic of evaluation and innovation. Ms. Davis and Dr. Akehurst describe why some technologies may fail to demonstrate cost effectiveness even when the acquisition price is set to zero, and why the evaluation of these technologies raises both methodological and ethical questions for health technology assessment (HTA) agencies.

The acquisition cost for new health technologies is usually a key determinant of whether the technology is considered to be cost effective by health technology assessment (HTA) agencies, such as the UK's National Institute for Health and Care Excellence (NICE). However, there are several scenarios under which clinically effective technologies may be found not to be cost effective even if the acquisition price is zero. Rejecting these technologies on the grounds that they lack cost effectiveness is extraordinarily difficult to justify to the general public, raises serious ethical issues, and is likely to have undesirable implications for future investments in innovative technologies.

In this article, we describe why some technologies may fail to demonstrate cost effectiveness even when the acquisition price is set to zero, and why this raises both methodological and ethical questions for HTA agencies. Our discussion of these issues is informed by a NICE Decision Support Unit (DSU) report on this topic [1], and by the discussion at the Issue Panel on this topic at the ISPOR 18th Annual European Congress in 2015 [2].

When Does This Situation Arise?

This situation occurs when the technology being evaluated increases the costs incurred during the patient's lifetime by increasing some form of health care resource use other than the acquisition cost of the technology. If the quality-adjusted life years (QALYs) gained are not sufficient to offset these costs, then the technology may not be cost effective, even if it can be acquired at zero cost.

In the simplest case, the costs of delivering the technology, such as regular infusions for a complex chemotherapy, may outweigh the health benefits achieved even when the acquisition price of the technology is zero. But there are scenarios in which a technology may fail to demonstrate cost effectiveness even when it can be acquired and delivered at zero cost. The NICE DSU report describes four similar but distinct scenarios that may result in a technology failing to demonstrate cost effectiveness at zero price [1]. These were identified by examining case studies from NICE's Technology Appraisal (TA) Programme.

In the first scenario, the technology increases survival in a patient population already receiving a high cost maintenance treatment, resulting in additional costs for the maintenance treatment which may not be offset by the QALYs gained during the period of additional survival. In the appraisal of cinacalcet for the treatment of secondary hyperparathyroidism (SHPT) in patients with end-stage renal disease (ESRD) on maintenance dialysis therapy, the ratio of costs and benefits for additional time spent on dialysis was found to be in excess of £20,000 per QALY [1], the lower limit of NICE's threshold [3]. The cost of dialysis makes it difficult for technologies to demonstrate cost effectiveness in this population if they extend life but do not reduce the need for dialysis.

In the second scenario, the technology is administered alongside other high-cost treatments and it prolongs the length of time the patient continues to receive those other high-cost treatments. In the TA of pertuzumab, the addition of pertuzumab to the treatment regimen of trastuzumab and docetaxel was found to improve progression-free survival in patients with breast cancer [4]. All three drugs are continued until progression. The annualised cost of remaining in the progression-free health state, including treatment with trastuzumab and docetaxel, was £27,253 even when assuming a zero price for pertuzumab [1].

This made it difficult for pertuzumab to demonstrate cost effectiveness even at zero price in this population [1].

In the third scenario, the technology prolongs the duration of survival in a later disease state. In the appraisal of vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract, vinflunine resulted in additional survival post-progression even though treatment ended at the time of progression [5]. The post-progression state was associated with substantial costs, largely driven by the provision of supportive interventions such as hospice care and home visits by community nurse specialists [5]. The combination of a high cost and low utility for the post-progression health state meant that additional time spent in the post-progression state adversely affected the cost effectiveness of vinflunine [1].

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In the fourth scenario, the technology results in a period of additional survival and a high-cost adverse health event occurs at some time in the future during that period of additional survival. This scenario is slightly different as it assumes no relationship between the disease being affected by the technology and the future adverse health event. For example, a smoking cessation programme may successfully extend a patient's life, but during the period of additional survival, that patient may go on to develop a condition such as arthritis which is more common in older people.

The common theme across these four scenarios is that costs are being incurred during periods of additional survival and these costs outweigh the QALYs gained during those periods of additional survival.

Could We Exclude Costs Incurred during Periods of Additional Survival?

NICE's current method guide recommends excluding costs that are unrelated to the condition or technology of interest [6]. So, could one solution be to define costs incurred during periods of additional survival as being unrelated?

There have been various attempts to define unrelated costs within the literature. Grima et al. defined costs for background therapies, such as dialysis, as being unrelated if the need for or intensity of that background therapy is not affected, but any additional costs are driven purely by increased survival [6]. Nyman stated that anything that influences the incremental QALYs should be considered related and included in the incremental cost in order to maintain the internal consistency of the ICER [7]. In the definition put forward by van Baal et al., a future health event and any associated costs can be considered to be unrelated if it occurs as a result of a condition whose prognosis or incidence is in no way affected by the technology of interest [8]. Others argue that both related and unrelated medical costs should be included in order to ensure that the ICER is externally consistent with the decision maker's remit of allocating health care budgets to maximise population health gain [9].

There are several difficulties with excluding unrelated costs incurred during periods of additional survival from economic evaluations. Firstly, it is not clear which definition should be adopted and where the line should be drawn between related and unrelated costs. Under NICE's current guidance, the distinction between whether a cost is related or unrelated comes down to whether the cost is 'related to the condition of interest' [3]. In the appraisal of cinacalcet described above, the rationale for exclusion then comes down to a fairly arbitrary decision as to whether SHPT or ESRD is the 'condition of interest' for that appraisal. Making these fairly arbitrary judgements on a case-by-case basis may lead to inconsistencies between different appraisals undertaken within the same HTA agency. Secondly, ...excluding costs because they are defined as being unrelated does not remove the opportunity cost associated with those unrelated costs and the QALY gains forgone elsewhere in the health care system [10]. Finally, in most of the case studies identified within the DSU report, the costs were clearly related to the technology being appraised or the condition being treated by the technology, so this solution may have limited application in practice.

Have We Undervalued the Benefits of Treatments Given Alongside or After the Technology being Appraised?

Perhaps this situation arises because the benefits of high-cost treatments that are provided alongside or after the technology being appraised have been undervalued. This may be particularly relevant for treatments such as palliative care where there may be benefits falling on families and caregivers in addition to patients, or where benefits may not be properly captured by generic quality-of-life measures. It is also worth considering whether there may be some treatments, such as dialysis and palliative care, that society may consider worthwhile despite their poor cost-effectiveness and whether the value placed on these treatments by society is not fully captured by the health benefits accrued. If those additional benefits cannot be quantified, then calculating the ICER including the health benefits of the background intervention, but not its costs, would provide a lower bound on the true ICER.

Could Pharmaceutical Companies Offer More Innovative Pricing Arrangements?

At the Issue Panel there seemed to be support from some for companies to find more creative solutions when marketing a drug that is given alongside other high-cost treatments (e.g., whether discounts could be offered on both the technology being appraised and the drugs given alongside, or whether they could have been marketed as a single combination therapy with a single price).

What are the Implications for the Development of Future Technologies?

Not recommending treatments that are given as add-ons to existing high-cost treatment regimens would provide an incentive for companies to develop treatments that replace existing treatments and reduce treatment burden for patients.

However, there is a downside to not recommending clinically effective interventions that cannot be shown to be cost >

effective even at a zero price, particularly in populations with high background costs, as this may act as a disincentive for companies to invest in developing technologies that improve survival in those populations. HTA agencies should be mindful to avoid recommending technologies with poor or marginal cost effectiveness, since if these are incorporated into standard care any future technology that prolongs the duration of standard care may fail to demonstrate cost effectiveness. In some situations there may be a case for disinvesting from existing treatments that form part of standard care, provided the benefits have not been underestimated.

Are There Other Reasons to Recommend These Technologies?

Decisions made by NICE are not solely driven by considerations of cost effectiveness, although the ethical underpinnings of the need to consider opportunity costs figure prominently. NICE's Social Value Judgement policy describes the need for NICE to consider factors other than cost effectiveness, including 'the need to distribute health resources in the fairest way within society as a whole' [11].

Consider the situation where a particular treatment is found to be cost effective within the general population, where average health care costs are low, but not cost effective in a specific population who already receives a high-cost maintenance treatment. In this situation, it is clear that it would not be fair or equitable for treatment to be recommended in the general population but denied to the group of patients who have high background care costs. Indeed, any such recommendation is likely to be deemed to contradict the Institute's existing Social Value Judgements policy [1]. This raises the question of whether it is also inequitable to deny patients a treatment when the failure to demonstrate cost effectiveness is driven by the high background care costs in the indicated population, even if the treatment is not indicated in populations with lower background care costs.

It was pointed out at the Issue Panel that it would be inequitable to fund technologies that are not in themselves cost effective, but to refuse to fund life-extending treatments in that population, as this effectively denies a patient from receiving more of a fund treatment already prolonging their life when a new patient would be able to receive it. The costs and benefits for the latter two groups would be identical, but the decision would be different.

HTA agencies may therefore wish to consider whether there are any ethical reasons for recommending a treatment that cannot demonstrate cost effectiveness at zero price, including the need to distribute health resources in the fairest way in society as a whole.

Conclusions

At the Issue Panel, it was clear that evaluating technologies that are not cost effective at zero price raises several important issues. Whilst there remains an ongoing methodological debate over the inclusion of unrelated costs incurred during periods of additional survival, in practice the exclusion of unrelated costs is unlikely to provide a solution in many cases. There is inevitably tension between a utilitarian approach, which seeks to maximise net population health from a limited budget, and the egalitarian approach, which seeks to ensure that each individual has fair access to health care resources.

References

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Additional information:

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