**Title page**

**A framework for using cost-effectiveness analysis to support pricing and reimbursement decisions for new pharmaceuticals in a context of evolving treatments, prices and evidence**

**Running head:** Pricing and reimbursement of new pharmaceuticals in an evolving landscape

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# **Abstract (150 to 250 words)**

Current approaches to the pricing and funding of new pharmaceuticals often focus on a one-time decision about a product for each clinical indication. This can result in multiple options being available to health systems without a clear signal about how to prioritise between them. This runs the risk that, as available treatments, evidence, and drug prices evolve, clinical and patient choices may not be aligned with the objective of allocating resources to promote population health. In this paper, we propose a framework for using cost-effectiveness analysis (CEA) to support pricing and funding policies for new pharmaceuticals in multi-comparator indications, some of the key aspects of which evolve over time. The framework comprises three core considerations: (1) designing proportionate processes; (2) assessing the costs and benefits of recommending multiple treatment options; and (3) appropriate application of CEA “decision rules” to support recommendations and price negotiations. We highlight that proportionate processes require prioritisation of topics for re-assessment to be aligned with clear objectives, the need for full flexibility of decision making at the point of reassessment and identification of contexts where contractual re-specification rather than typical deliberative HTA processes may be more appropriate. We discuss reasons why the recommendation of multiple treatment options rather than a single cost-effective treatment may be appropriate and urge HTA bodies to address explicitly the trade-offs that may be associated with recommending multiple treatments. Finally, we discuss how value-based pricing could be achieved when multiple competitor manufacturers offer confidential discounts.

**Key points:**

* HTA appraisals are typically undertaken shortly after launch of a new product or new therapeutic indication, but after this timepoint competitor technologies may enter the market, and there may be other important changes to evidence and pricing especially as generic and biosimilar versions of comparators become available.
* This article proposes a framework for using cost-effectiveness analysis to support pricing and funding decisions for new pharmaceuticals in a context of evolving treatments, prices and evidence.
* We highlight the need for decision makers to design proportionate processes, to explicitly consider the costs and benefits of recommending multiple treatment options, and to specify how value-based pricing can be achieved when multiple products have confidential prices.

# **Statements and Declarations**

**Competing interests**: Beth Woods sits on the Board of Directors for the York Health Economics Consortium, a health economics consultancy company wholly owned by the University of York. This is an unpaid role. Alfredo Palacios has no competing interests to declare. Mark Sculpher has no competing interests to declare.

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# **Introduction**

Decisions about the pricing and funding of new pharmaceuticals are pivotal to health systems worldwide. Health technology assessment (HTA) processes and pricing and funding decisions typically focus on evaluating new pharmaceuticals at the time of their launch or when they are approved for new therapeutic uses.[2, 3] For example, in the UK, the National Institute for Health and Care Excellence (NICE), through its Single Technology Appraisal (STA) and Highly Specialised Technologies programmes, aims to appraise all new medicines or new therapeutic indications[[1]](#footnote-1) within 3 months of licensing. When positive guidance about a medicine is issued, this requires the NHS to pay for the product when prescribed within NICE guidance.[4] HTA processes for revisiting these decisions are, however, less well developed. For example, NICE and the National Authority of Medicines and Health Products in Portugal (INFARMED) allow for reassessments within their HTA processes,[5, 6] but these are rarely implemented in practice. The Pharmaceutical Benefits Scheme in Australia and the Swedish Dental and Pharmaceutical Benefits Agency (TLV) have post-marketing review processes that can be initiated in response to health system needs for specific drug classes or therapeutic areas and there are some examples of these processes being used.[7, 8]

In the many contexts where reassessments are not conducted, multiple treatment options are often available without a clear signal to the health system of how to prioritise between them. This runs the risk that, as available treatments, evidence, and drug prices evolve, clinical and patient choices may not be aligned with the objective of allocating resources to promote population health.[9] This often leads to the introduction of mitigation strategies at the local level (for example, multiple regional updates of cost-effectiveness analyses). However, this runs the risk of unwarranted geographical variation and may not be feasible depending on local analytic capacity. NICE has recently undertaken consultations on a pilot approach to address these issues via a process embedded within its clinical guideline workstream.[10] Similarly, in Canada, the Canadian Agency for Drugs and Technologies in Health (CADTH) is piloting a new committee to support decision making across the lifecycle of new pharmaceuticals.[11] These initiatives reflect a growing recognition of the need for dynamic, evidence-based policy approaches to guide pricing and funding decisions.

In principle, cost-effectiveness analysis (CEA) is well placed to generate coherent estimates of the costs and effects of all relevant options, based on the best available current evidence.[12-15] However, its application to inform pricing and reimbursement decisions for new pharmaceuticals, in a context of evolving information and multi-comparator indications, raises several policy challenges. Firstly, CEA is typically used to identify *a single* cost-effective intervention in the population of interest.[9] However, this may not be the most appropriate policy response for a range of reasons including heterogeneity in costs and effects, patient preferences, price competition, risk diversification across suppliers, differences across geographies/settings in costs or constraints, and incentives for innovation. Secondly, a range of “events” (e.g. new products becoming available, changing evidence, evolving drug prices) may modify cost-effectiveness and, although it would be impractical to respond to every such event with a reassessment, there is a question of the appropriate policy responses to these events.

In response to these challenges, this paper proposes a framework for using CEA to support pricing and funding policies for new pharmaceuticals in multi-comparator indications with evolving evidence. Though many of the considerations apply to other health technologies, we focus on pharmaceuticals as they represent a significant part of HTA efforts and present unique challenges due to price changes expected over the product life cycle (e.g. due to entry of generic and biosimilar versions of products). In addition, pharmaceutical pricing can be considered as “endogenous” to the HTA process. Prices for new pharmaceuticals are not determined by the cost of production but, instead, set by the manufacturer to maximise revenue within the period of patent protection.[1, 16] In health systems using CEA to inform pricing and funding decisions, this typically leads to manufacturers setting a price such that the incremental cost-effectiveness ratio (ICER) is just below the cost-effectiveness “threshold” used by decision makers. This is often operationalised via confidential discounts. Whilst the framework is developed with a focus on the UK context, it has international relevance given the shared policy challenges.

# **Methods**

The development of the framework was conducted in three stages. In the initial stage, discussions and a workshop with UK decision-makers at the national and sub-national level were organised to identify and clarify current policy challenges related to pricing and reimbursement decisions for new pharmaceuticals post-launch. The workshop was attended by individuals with experiences of UK HTA, price negotiations at the national level, and those with responsibility for local decision making relating to the use of new pharmaceuticals.

These consultations identified two primary challenges: (1) how to assess and incorporate the costs and benefits of reimbursing multiple treatment options, as opposed to a single cost-effective treatment, within the pricing and funding decision-making process, and (2) how to account for the evolving landscape of treatments, pricing, and evidence in these decisions.

In the second stage, a scoping review of the health economics literature was undertaken to explore existing methodological approaches that could address the identified challenges. The review aimed to gather relevant literature that could inform the development of the framework. This was complemented by consultations with experts in the field of health economics to enhance coverage of pertinent topics. In addition, we drew on general literature focussing on the principles of using CEA to inform pricing and funding decisions. Further details on both the scoping workshops and literature review are provided within the supplementary materials.

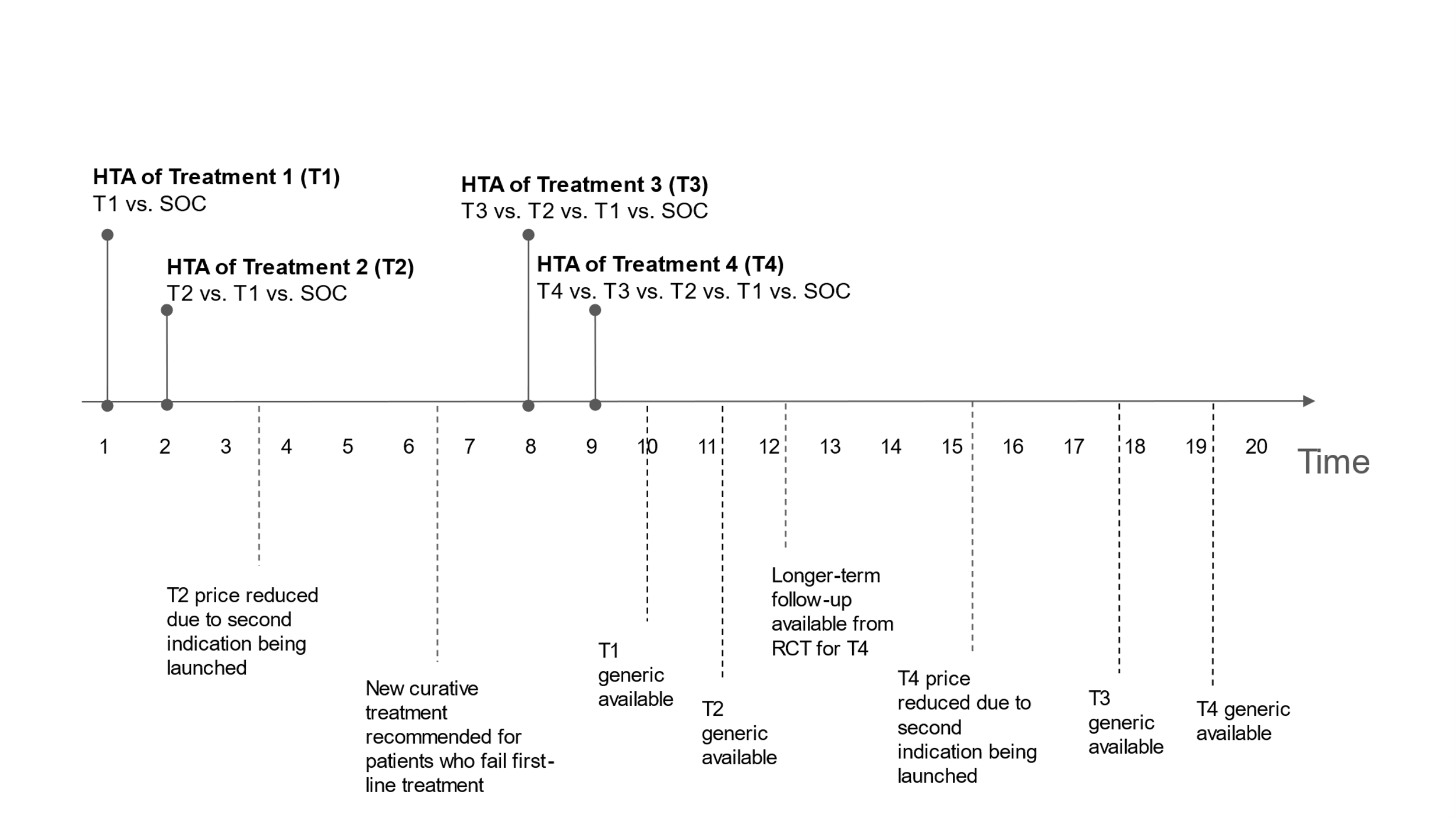
In the final stage, the research team synthesised the findings from the literature review and workshop, identifying three key considerations for structuring the framework: (1) designing proportionate processes, (2) evaluating the additional costs and benefits of recommending multiple treatment options, and (3) the appropriate application of “decision rules” to support both recommendations and price negotiations. The structure and order of these considerations reflects the sequential approach an HTA body would likely follow when incorporating these considerations within their decision-making processes.

# **Proposed framework**

## 2.1 Designing proportionate processes

Many events may change the assessment of the cost-effectiveness of the available treatments. Figure 1 provides a plausible though hypothetical example of an indication where four new drugs become available over a ten-year period. There are two instances of changes to the evidence and treatment pathway, two changes to prices for the new drugs relating to additional indication launches, and four instances of entry of generic versions of the products. It is therefore important to consider whether, when and how re-appraisals should be conducted, considering that there are significant transaction costs associated with re-appraising medicines, renegotiating the terms of contracts with pharmaceutical manufacturers, and disseminating any changes in guidance to clinical communities.[12]

**Figure 1: Illustrative example of evolving landscape for a hypothetical first-line treatment**



Abbreviations: HTA: Health Technology Appraisal; SOC: Standard of care; T1, T2, T3 and T4 denote treatments 1, 2, 3, and 4 respectively.

Whether or not an indication represents a priority for re-appraisal will depend on the expected impact of the re-appraisal on patients and the health system. This can, in principle, be quantified in terms of population-level net health effects (NHEs) associated with reassessment, which will depend on whether it is likely either to change guidance or change pricing, and the importance of those changes. Net health effects of an intervention, or policy change, are the health effects minus the health opportunity costs associated with funding the intervention or policy. Net health effects have been used to represent the effects of individual interventions on population health, as well as to address broader policy questions.[17-19]

Changes to guidance can improve patient health directly by increasing uptake of more effective options or better targeting treatments according to patients’ characteristics. Changes to guidance and pricing can improve patient health indirectly by reducing expenditure on medicines within the indication under consideration and freeing up funds for other forms of care within the health system. The overall benefit of any change at the population level will depend on the expected per patient NHE benefit, the size of the population affected by the change, and whether any change to guidance is expected to be long-lasting or rapidly superseded due to further changes to the landscape.[20] Quantifying all of these aspects robustly would be similar to conducting a full reassessment. Further research could usefully establish the evidence, metrics or heuristics to focus on for the purposes of prioritisation.

There are different approaches to revisiting pricing and funding decisions.[21] To promote population health, it is essential that not only guidance wording is updated but that price re-negotiation is permitted and the possibility of withdrawing funding or reimbursement is available for cases where a price level consistent with health system value cannot be agreed.

The most appropriate policy response is likely to depend on what factors have triggered the decision to re-appraise products in a certain indication.[21] For example, where there is additional evidence, a change to the clinical pathway or the introduction of a new comparator, a process that is deliberative and allows input from multiple stakeholders is likely to be important. Where the primary trigger for re-appraisal is a price change for an originator drug or the availability of a generic/biosimilar version of a comparator, then the value of stakeholder engagement and deliberative decision making is less clear, and an abbreviated process focused on price renegotiation and contract re-specification may be more proportionate. Indeed, inclusion of provisions for comparator price changes within contracts or other funding arrangements from the outset may be efficient. For instance, in its recommendations on ravulizumab for atypical haemolytic uraemic syndrome, the Irish HTA body, the National Centre for PharmacoEconomics, advised that the price for raviluzumab should not exceed that of a comparable biologic, including when biosimilar versions of the comparator become available.

The nature of any amendments to guidance wording is also likely to have significant implications for how prescribing decisions are made. A common response to a situation in which a treatment is not considered cost-effective in the context of all treatment options, is to recommend the treatment in those contexts where the cost-effective option is contraindicated. However, terms like ‘contraindication’ are open to interpretation and run the risk that treatments will be prescribed when alternative options could be used and would represent a better value for money For example, NICE technology appraisal 228 recommends bortezomib only for those patients with multiple myeloma who are unable to tolerate, or have contraindications to, thalidomide (amongst those patients who can take thalidomide that is the cost-effective treatment).[22] However, in practice, the use of bortezomib is much more widespread than permitted by the guidance due to the difficulty of defining and monitoring clinical use.[23] Use of bortezomib where thalidomide is a feasible option is expected to lead to large health opportunity costs for NHS patients (Rogers. Decision-making in multi-comparator decision-spaces [Unpublished report]).

## 2.2 Assessing additional costs and benefits of recommending multiple treatment options

There may be benefits to recommending multiple treatment options even where one comparator offers the highest NHEs. This may be considered relevant where there is heterogeneity across patients in the expected health effects or costs of treatment, where there is a desire to allow patients’ preferences about health outcomes, healthcare processes or non-health attributes to inform decisions, to allow price competition, to reduce the risk of drug shortages, or to accommodate local cost differences or constraints to delivery. The decision to offer a single or multiple options within an indication may also influence incentives for drug research and development. We consider each of these areas in turn.

***2.2.1 Heterogeneity in costs and outcomes, and patient preference***

There are established methods for reflecting heterogeneity in costs and outcomes in CEA.[24] Where characteristics of patients are expected to be associated with important differences in cost-effectiveness, these methods will ideally be applied to inform funding decisions for specific subgroups defined by these characteristics. However, this is not typically undertaken for all relevant subgroups due to factors like the time constraints associated with HTA processes and frequent uncertainties associated with the available modelling. There may be options to adapt HTA processes to incorporate more analysis of heterogeneity for high priority appraisals.

Another policy response to this is to recommend a range of medicines and allow treatment to be individualised based on patient and clinician decision making. This would unambiguously improve overall population health (i.e., NHEs) if patient and clinician treatment decisions aligned perfectly with the NHE-maximising treatment choice.[25-29] However, this is not expected to be the case as patients’ and clinicians’ decisions will depend on their access to relevant information, and will include and weight attributes of benefit differently from the way this is conducted when NHEs are estimated within the NICE process. The NICE methods guidance requires that, when quantifying health outcomes for CEA, these should reflect the average HRQoL and mortality in the target population, and that HRQoL should be valued using public preferences.[30] Importantly, in many health systems, patients’ and clinicians’ assessment of benefit will not typically internalise differences in the total costs between alternative medicines as individuals and clinicians typically focus on the maximisation of patient health or other outcomes without taking into account the consequences of their decisions for costs and, therefore, the health opportunity costs borne by others.[27, 28, 31]

There is very limited evidence quantifying the effects of offering choice between medicines on NHEs and this is an area for potential further research.[25-28, 32] If offering patient choice is expected to reduce overall population health (i.e. NHEs), normative questions need to be addressed regarding trade-offs between population health and individual preferences and choice. These considerations are likely to have broader implications, for example if non-health outcomes or health care processes are considered important aspects of benefit then it may be appropriate to reflect these additional objectives more formally when conducting evaluations at the population level.

***2.2.2 Aspects of medicines market efficiency: competition and supply***

The availability of multiple treatment options within an indication has the potential to increase price competition and drive down prices. In the UK there are limited routes for this to occur except for therapeutic tenders in specific circumstances. The extent of on-patent price competition is likely to vary across countries and is challenging to quantify given the widespread use of confidential discounts on list prices for new medicines. Nonetheless, the available evidence suggests very limited on-patent price competition in high income countries.[33]

The availability of multiple products may also reduce the risk of medicines not being available when needed. Though most drug shortages affect off-patent medicines with low prices, this may be a relevant consideration for some on-patent biologic and blood products.

***2.2.3 Local cost differences or constraints to delivery***

Due to regional differences in models of care delivery, total costs associated with different drugs may vary. There may also be constraints on delivery due to capacity (e.g. some centres not being able to meet the needs for more frequent drug infusions) or due to specific forms of care not being available in all areas (e.g. specific specialist clinics). These may make some treatments more challenging and expensive to deliver in some settings than others and imply that recommending several products nationally would have advantages locally. Further research could explore how to identify indications where local variation in costs or constraints is likely to materially influence decisions and identify the most efficient approach to supporting appropriate local resource allocation in these contexts. Allowing for such local differences does, however, raise the potential for trade-offs between enhancing population health (by allocating resources efficiently according to local constraints and costs) and ensuring geographical equality in medicines access.

***2.2.4 Innovation effects***

There is a long-standing debate about whether existing international approaches to pricing and funding of medicines encourages the development of “me-too” innovations (i.e. medicines that are similar to existing products). The concern is that encouraging the development of “me-too” products diverts R&D resources away from “breakthrough” products both directly, and indirectly as the true innovator receives reduced revenue.[34] However, there are also arguments in support of allowing me-too innovations including that products in a crowded market place are more incentivised to differentiate their products via improved safety, reduced drug interactions, improved modes of delivery or, by demonstrating safety and efficacy in underserved subpopulations.[34] Further research could usefully address the innovation incentives associated with alternative pricing and funding policies in multi-comparator indications.

## 2.3 Appropriate application of decision rules

Within NICE processes, cost-effectiveness is most frequently assessed by calculating ICERs and comparing these to approval norms (i.e. the cost-effectiveness threshold used to guide decision making). Computing and interpreting ICERs for multi-comparator settings can become complex. An equivalent approach to decision making is to consider an intervention as cost-effective if it delivers the highest expected NHEs of the available interventions. Use of NHEs can be simpler in multi-comparator settings.[35-37] In multi-comparator contexts, NHEs may also be more informative than ICERs as they allow comparators to be ranked and the magnitude of difference in cost-effectiveness between comparators to be assessed.[35-37] This is particularly useful when decision makers need to assess the trade-offs associated with recommending multiple treatment options (Box 1).

Regardless of whether ICERs or NHEs are used to assess cost-effectiveness, the appropriate value for the threshold is the subject of much debate.[1, 16, 38, 39] For decisions based on CEA to align with the objective of maximising population health from available health care budgets, the threshold needs to reflect a measure of health opportunity cost. Health opportunity cost is a measurable property of the health system and the best available evidence suggests that the marginal cost of producing a QALY in the UK is £15,000/QALY or below,[40] with the Department of Health and Social Care using £15,000/QALY as an operational value to inform health impact assessments.[41]. When making decisions about the funding of new pharmaceuticals within the NHS, NICE uses an approval norm of £20,000-£30,000 per additional QALY, with some higher values for specific contexts.[30] When the approval norm exceeds the measure of health opportunity cost, then new medicines approval will result in reductions in population health overall, at least within the period of patent protection.[1] Within this section we illustrate principles using £15,000/QALY as a measure of health opportunity cost and £30,000/QALY to reflect the NICE approval norm.

**Box 1: Using NHEs to compare the relative cost-effectiveness of multiple treatment options**

Table 1 shows the cost-effectiveness results for a hypothetical comparison of five interventions. In this case, using a cost-effectiveness threshold of £15,000/QALY, Treatment A is cost-effective, Treatment B is dominated, Treatment C is extendedly dominated, and Treatment D is associated with an ICER of £25,400 and is not therefore considered cost-effective. This provides no information about the *relative* cost-effectiveness of the options.

The NHEs are more informative and can be summarised within tables or NHE indifference curves as shown in Figure 1. NHE indifference curves allow information about NHEs to be visualised alongside information about costs and health effects on a cost-effectiveness plane. The points where each indifference curve meets the horizontal and vertical axes represent the NHE and net monetary benefit (NMB) for all strategies on that curve. Interventions on lower indifference curves are more cost-effective than those on higher curves, with the most cost-effective intervention being on the lowest curve. The NHE estimates and NHE indifference curves show the trade-offs associated with recommending options other than the cost-effective option. For example, recommending Treatment B would result in a loss in NHEs of 0.18 QALYs for every patient treated with this option rather than Treatment A, recommending Treatment C a loss in NHE of 0.33 QALYs, and recommending Treatment D a loss of 0.69 QALYs.

**Box 1, Table 1. Cost-effectiveness results for hypothetical example**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Strategy** | **△Cost** | **△Benefit (QALYs)** | **ICER (per QALY)** | **△NHE (QALYs)** |
| Non-pharmacological management | £0 | 0.00 | - | 0.00 |
| Treatment A | £9,600 | 1.50 | £6,400 | 0.86 |
| Treatment B | £12,100 | 1.49 | Dominated | 0.68 |
| Treatment C | £17,000 | 1.66 | Extendedly dominated | 0.53 |
| Treatment D | £35,000 | 2.50 | £25,400 | 0.17 |

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**Box 1, Figure 1. Cost-effectiveness plane including NHE indifference curves**

Consideration of the appropriate decision rule in multi-comparator indications also raises normative questions about the role of HTA bodies when making treatment recommendations. Dixon[42] proposes that a broader range of treatments should be offered to patients, with the “most cost-effective” (i.e., highest NHE) intervention recommended alongside all options associated with lower total costs but less effectiveness than the cost-effective intervention. Figure 1 illustrates the implications of the Dixon rule for a set of treatments A-D, with treatment A being the cost-effective treatment and offering the highest NHEs. In the figure, the options that would be considered for funding under the Dixon rule are enclosed within the dashed black triangle. Thus, in addition to treatment A, treatment B would be considered as an option for funding, but C and D would not.

**Figure 2: Illustration of the “Dixon rule”**

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Abbreviations: NHB=net health benefit; NMB=net monetary benefit.

The “Dixon rule” is consistent with the view that patients and clinicians should be given the opportunity to exercise choice between options which may offer different profiles of health and non-health outcomes, but not when this would impose opportunity costs on others. Whether this is a more appropriate approach to decision making is a normative choice and depends in part on whether the role of HTA bodies is to provide guidance to clinicians on effective care, or whether HTA bodies aim to identify those treatments that are worthwhile at the system level. Concerns have also been raised that this approach may not reduce opportunity cost if, in the absence of cheaper alternatives, patients choose a “do nothing” option, and that it could lead to inconsistent decision making where a cost-ineffective treatment is initially not recommended but then subsequently considered for funding due to the availability of a more costly and effective but cost-effective alternative[[2]](#footnote-2).(Rogers. Decision-making in multi-comparator decision-spaces [Unpublished report])

A further consideration is how decision rules should be applied for new pharmaceuticals where prices are set by manufacturers in expectation of the HTA body approval norm, and pricing of competitor products. Many current appraisal processes, by focusing on a single technology, allow manufacturers to set prices taking other manufacturers prices as fixed. This is not the case when multiple technologies are appraised simultaneously and there is the opportunity for each manufacturer to adjust their price.

An approach to pricing that would be consistent with NICE’s current processes and levels of manufacturer reward would be to allow each manufacturer to price up to the approval norm. To implement this in a multi-product setting would require manufacturers to be offered the opportunity to propose prices (e.g. via PAS applications) only after NICE Committees had carefully considered the evidence. At this point the most plausible assessments of the level of non-product costs (e.g. costs to the NHS associated with product delivery, monitoring, or disease management) and QALYs associated with each comparator are available and could be supplied to the manufacturers to inform their pricing decisions. Due to the interdependency of prices, this policy requires that at least one comparator is not a “new” product. This could be a non-pharmaceutical comparator or a comparator consisting of one or more generic drugs or biosimilars. The application of this approach is illustrated in Box 2. Whether the manufacturer will choose to offer this price will depend on the overall expected impact on revenue which will, in turn, depend on a range of factors including whether the product is used in other indications, the cost of producing the medicine and expectations about other manufacturers’ pricing.

Although this would be consistent with the current levels of reward offered to manufacturers, there may be better approaches to pricing in multi-comparator indications. Further research could usefully explore the appropriateness of alternative approaches such as the application of competitive tenders or formulary management.[33, 43]

**Box 2: Application of decision rules and pricing implications in multi-comparator indications**

Box 2, Table 1 provides an example where the approval norm is set equal to the measure of health opportunity cost (£15,000/QALY). Excluding prices of the new products, the NHEs associated with non-pharmacological management, New Product 1 and New Product 2 are 9.5, 11.0 and 11.5 QALYs, respectively. This means that new product 1 could charge up to £22,500 and new product 2 could charge up to £30,000 per patient to be considered cost-effective at an approval norm of £15,000/QALY.

**Box 2, Table 1: Application of decision rules assuming an approval norm and measure of health opportunity cost of £15,000/QALY**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Product | Non-product costs | QALYs | Net health effect excluding brand price (in QALYs) | Price for branded product | Net health effect including brand price (in QALYs) |
| Non-pharmacological management | £7,500 | 10.0 | 9.5 | NA | 9.5 |
| New Product 1 | £15,000 | 12.0 | 11.0 | £22,500 | 9.5 |
| New Product 2 | £15,000 | 12.5 | 11.5 | £30,000 | 9.5 |

Where approval norms above the measure of health opportunity cost are used, this is equivalent to assuming a higher weight (i.e. societal value) being placed on QALYs generated by new medicines than on health gains generated via other healthcare spending. The implications of this are shown in Box 2, Table 2. For example, if an approval norm of £30,000/QALY is used, this is equivalent to assuming that QALYs generated via the use of new medicines are worth twice as much as QALYs generated via other healthcare spending. Excluding prices relating to the new products, the re-weighted NHEs associated with non-pharmacological management, New Product 1 and New Product 2 are 9.5, 13.0 and 14.0 QALYs, respectively. This means that New Product 1 could charge up to £52,500 and New Product 2 could charge up to £67,500 per patient to be considered cost-effective at an approval norm of £30,000/QALY. This would result in unweighted NHEs of 9.5, 7.5, 7.0 reflecting that, when approval norms exceed the measure of health opportunity cost, use of new products will reduce overall population health during the patent period.[1]

**Box 2, Table 2: Application of decision rules assuming an approval norm of £30,000/QALY and measure of health opportunity cost of £15,000/QALY**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Product | Non-product costs | QALYs | Net health effect excluding brand price (in re-weighted QALYs) | Price for branded product | Net health effect including brand price (in re-weighted QALYs) | Net health effects (in QALYs) |
| Non-pharmacological management | £7,500 | 10.0 | 9.5 | NA | 9.5 | 9.5 |
| New product 1 | £15,000 | 12.0 | 13.0 | £52,500 | 9.5 | 7.5 |
| New product 2 | £15,000 | 12.5 | 14.0 | £67,500 | 9.5 | 7.0 |

# **Discussion and conclusion**

Despite widespread acknowledgment of the importance of reassessing the cost-effectiveness of new pharmaceuticals as new evidence emerges, and market conditions change, there is a lack of guidance about how HTA bodies can appropriately translate such evolving information into guidance. Given the large number of events that could, in principle, trigger a reassessment, there is a need to consider when reassessment is justified. Furthermore, there is a need to consider whether only the cost-effective treatment should be reimbursed, or whether there are advantages to recommending multiple treatments.

This paper provides a framework for using CEA to support pricing and funding policies for new pharmaceuticals in multi-comparator indications with evolving treatments, prices and evidence. This was developed based on engaging with UK decision-makers to identify challenges in pharmaceutical pricing and reimbursement post-launch, conducting a scoping review of health economics literature to explore potential solutions, and synthesising findings within a framework comprising three key considerations. This framework highlights the importance of evidence-based topic prioritisation as the first consideration. This is important given the significant transaction costs associated with updating guidance and pricing.[44] Secondly, HTA bodies and others involved in pricing and funding decisions need to provide clarity on when multiple treatment options should be recommended. Where reflection of these considerations would lead to decisions that conflict with the objective of maximising population health or would lead to geographical variation in access to medicines, there is need for clear specification of the situations where such trade-offs are considered appropriate, and the evidence required to support this type of decision. Thirdly, HTA bodies should provide clarity on the “decision rules” of CEA that will be applied in multi-comparator settings, and how this will be integrated with price (re)negotiation.

This paper builds on the “living HTA” literature [12-14] which seeks to develop methods for efficiently integrating new information within systematic reviews and cost-effectiveness analyses. We do so by discussing how the principles of economic evaluation can be leveraged to make decisions about when to re-visit decisions about the pricing and funding of new pharmaceuticals, and what should be considered when interpreting the findings of these reassessments where there may be complex decisions relating to multiple incumbent products with confidential prices. A related topic, is the reflection of the value of future genericisation of new pharmaceuticals within launch prices.[45-47] This is an important debate but relates to the question of how new medicines should be valued and how this should be reflected in pricing. In this article we focus instead on how a selected approach to value-based pricing can be extended to contexts where there are multiple comparators and an evolving evidence base.

This study has several limitations. Firstly, our workshops focused on UK policy makers, the policy challenges and their importance may differ in other countries. Secondly, our scoping review is unlikely to have been exhaustive and we may have missed relevant literature. Relatively little is known about the population health implications of allowing discretion at the level of individual clinical decisions (e.g. via a shared decision-making process), making it difficult to evaluate the benefits or costs of recommending multiple treatments rather than a single cost-effective option. We found limited information about how pricing policies could appropriately promote price competition in markets where prices for new pharmaceuticals are regulated through the HTA process. Both areas represent important areas for further research.

In conclusion, timely post-launch reassessments are critical if health care systems are to achieve value from their expenditure on new pharmaceuticals. This research identifies a series of considerations for HTA bodies in developing appropriate processes and decision-making approaches when reassessing new pharmaceuticals. Translating these principles into practice will require HTA analytic and administrative capacity to be devoted to reassessments. It will also require the political will to pursue changes to pricing and reimbursement that may reduce pharmaceutical company revenue and result in withdrawal of access to previously approved medicines. In the UK, these considerations seem to have stalled proposals at NICE.[48] Further research could usefully assess the potential overall population health benefits of robust reassessment processes and serve as a call to action to HTA bodies internationally.

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1. Except where there is a “clear rationale” not to do so. [↑](#footnote-ref-1)
2. It is possible that further refinement of Dixon’s rule could address the inconsistency issue, though not the more fundamental normative question.(Rogers. Decision-making in multi-comparator decision-spaces [Unpublished report]) [↑](#footnote-ref-2)