NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CHTE methods review

Costs used in Health Technology Assessment

Task and finish group report

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Executive summary

Background

The methods manuals for each of the Centre for Health Technology Evaluation's guidance producing programmes include advice on the costs that should be included in appraisals. However, there are some areas where additional clarity could be provided on which costs should be used. These include the preferred cost-data sources, incorporating costs of medical devices and in-vitro diagnostics, and the preferred costs to be used for biosimilar and generic products. Additionally, the task and finish group was asked to explore the potential implications of including future unrelated healthcare costs in appraisals. The recommendations made by the group are summarised in Appendix 1.

Sources of costs

A variety of sources can be used in appraisals for medicine prices. In particular, prices for biosimilars and generics are not always transparent and may vary across the NHS. To ensure the most appropriate source is used, a priority list of price sources has been developed based on their availability across the NHS, their transparency, and the period for which they are guaranteed. Guidance for committees on any limitations of these sources will also be included in the methods guide.

The current methods guide was judged to provide sufficient direction on: using microcosting; methods of expert elicitation; the cost sources for NHS and personal social services carers; and addressing uncertainties on using outdated or non-UK

costs. Additions to the methods guide were recommended to provide clarity on the preferred approaches to currency conversion and adjusting for inflation.

The potential effect on appraisals of changes to the way Healthcare Resource Group costings are calculated was also examined. No case for change to the methods guide was identified based on the way these costs are calculated.

Incorporating the costs of medical devices and diagnostics

The approach to incorporating the costs of medical devices and diagnostics was discussed at a workshop attended by representatives from industry, NICE and the external membership of the costs task and finish group. There was consensus that new submission templates would highlight the costs to be included. These templates are currently being developed by NICE, and will be circulated to industry representatives for comment before being introduced.

Two areas where there are several potential approaches to incorporating costs are high-cost technologies that may have additional indications in the future, and technologies with multiple uses. The Diagnostics Assessment Programme methods manual contains guidance on these areas. It is proposed that, because this guidance may apply to other technology types, it should be included in the unified methods manual. However, there was no clear consensus at the workshop about how volume-dependent pricing structures and high-cost devices with multiple indications should be factored into assessments. So, this may need to be explored further once the new submission templates have been developed.

Future unrelated healthcare costs

NICE commissioned the Decision Support Unit to produce a report examining the issue of future unrelated healthcare costs. The report considered:

- the arguments for and against including future unrelated costs
- how other health technology assessment bodies handle unrelated costs
- the methods available to NICE to estimate unrelated costs
- the implications of including or excluding unrelated costs in NICE appraisals.

Based on these considerations, several research questions were identified that would need to be explored in detail before deciding whether NICE should change its methods to include future unrelated healthcare costs. Broadly, these challenges include: addressing ethical and equity concerns; determining the feasibility of creating a toolkit to estimate future unrelated costs; and addressing various methodological challenges about including future unrelated costs in appraisals.

Incorporating the biosimilars and generics position statement

NICE has previously produced a position statement outlining its approach on biosimilars. There is parallel work being done to consider how NICE should approach scenarios in which the reference product was not submitted to or not recommended by NICE in a particular indication that a biosimilar becomes available. The position statement will be reviewed as part of this parallel work.

Introduction

The costs used in health technology assessment (HTA) task and finish group was tasked with answering 3 key questions. These were broken down into sub-questions by the group:

1. What sources of costs should be used in an assessment?
    a. When is it appropriate to use each potential source of cost data, for example, using microcosting or non-UK studies in the absence of nationally published costs?
    b. What bias is likely to be introduced by correcting for non-UK or out-of-date cost information?
    c. What effect will NHS Improvement's changes to the Healthcare Resource Group (HRG) costing methodology have on assessments?
    d. What sources should be used to estimate NHS and personal social services (PSS) carer costs?
    e. What sources should be used for the costs of biosimilar and generic medicines?
2. How should the costs of medical devices and in-vitro diagnostics be incorporated into assessments?
    a. How should costs be apportioned for technologies that have high acquisition costs but multiple uses?
    b. How should volume-dependent and similar pricing structures be incorporated into an assessment?
    c. What costs related to the use of a technology should be included (for example, training and quality assurance costs), and what sources can be used for estimating these?
3. Do other HTA agencies include future unrelated costs in their analyses, and which methods of calculating these costs are available?

This report outlines how each of the questions was addressed by the group, and makes recommendations either for further work, or suggested revisions to the methods guide.

Key questions

Key question 1: what sources of costs should be used in an assessment?

When is it appropriate to use each potential source of cost data, for example, using microcosting or non-UK studies in the absence of nationally published costs?

On cost sources, the methods guide states:

- include costs related to resources under control of the NHS or personal social services (PSS):
  - value using prices relevant to the NHS or PSS
  - identify cost data systematically
- use public list prices or nationally agreed discounts
- use Healthcare Resource Groups (HRGs) to estimate resource use
- if HRG data is not appropriate, microcosting may be used but:
  - define methods used to identify literature sources of costs
  - when alternative sources are available, justify the chosen costs justified and do sensitivity analyses using other sources when appropriate.

To supplement what is already stated by the methods guide, and to add clarity on certain issues, the task and finish group explored whether the methods guide should explicitly:

- provide a hierarchy of preferred sources of costs
- state methods for adjusting out-of-date or non-UK costs
- state which sources should be used to estimate NHS and PSS carer costs.

The group searched for guidance from other health technology assessment (HTA) bodies. It found EUNetHTA guidance that covered the issue of variation in costing data between countries, and also out-of-date cost data. It concluded:

Conclusions for sources for data on costs: “As unit costs generally vary between countries, it is difficult to transfer cost from one country to another. In order to facilitate adaptations to local settings, it is therefore recommended that resource use is clearly presented in natural units.”

Conclusions for updating costs to the relevant year and currency: “Based on the results of the current review of guidelines use by EUnetHTA partners and previous guidelines, it is recommended to convert costs to the most recent price year by using relevant indices. The index used and the original price year should be clearly indicated.”

The group also noted technical support document 13 from the NICE Decision Support Unit, which suggests a hierarchy of evidence for cost data.

No explicit reference is currently made in the methods guide about adjustments for inflation. The group explored the options available. It noted that the commonly used Hospital and Community Health Services price index has been stopped, with the PSS Research Unit (RU) unit costs guide recommending the use of the NHS cost Inflation Index.

The group explored the issue of when microcosting studies should be used. Microcosting is a cost-estimation method. It involves the direct enumeration and costing of every input consumed in a defined process, such as treatment in a particular patient or running a certain laboratory test. They are considered to be more precise than average or resource group estimates, and can be useful for determining costs when no cost is established or accessible. There currently appear to be no published guidance or methods on doing microcosting studies. Also, 1 of their draw backs is that they are data heavy and time consuming. Because of this, they are likely to be of limited use in NICE evaluations unless a recently published microcosting study is available. The methods guide currently supports these findings, and states that micro costings can be used when data based on HRGs are not available.

Table 1: summary of key question 1a

Item	Current approach	Case for change	Recommendations and rationale
Use of non-UK studies	UK studies are preferred. The guidelines methods guide explicitly states the approach to currency conversion.	Methods for using non-UK studies should be aligned across programmes	Approach to currency conversion should be stated explicitly: base wording on the guidelines methods guide
Adjustment for inflation	The guidelines methods guide explicitly states the approach to currency conversion. It refers to the index no longer in use.	Methods for using adjusting for inflation should be aligned across programmes	Approach to adjustment to inflation should be stated explicitly: base wording on the guidelines methods guide. Replace reference to the Health Service Cost Index with the NHS cost Inflation Index.

Use of microcosting and cost and resource use data from literature	Can use microcosting when data based on Healthcare Resource Groups are not appropriate. Methods used to identify sources of costs and resource use should be defined (systematic review preferred). When alternative sources are available, the choice should be justified and sensitivity analyses done when appropriate.	No change needed: the current approach is sufficient	It may be appropriate to clarify preferred sources of costs by presenting a hierarchy of evidence (this would depend on whether it was felt including hierarchies of evidence in the methods guide is appropriate)
Expert elicitation	There is limited explicit guidance on how this should be done. The guidelines methods guide suggests consensus approaches for model inputs.	No change needed directly as a result of considering costs	Using experts for cost data varies across programmes. Formal elicitation techniques may not always be pragmatic, particularly for the Medical Technologies Evaluation Programme: explicit elicitation recommendations for costs are not needed.

What bias is likely to be introduced by correcting for non-UK or out-of-date cost information?

The task and finish group's view was that this question was related to uncertainty and did not need additional consideration. This was because doing scenario or sensitivity analyses around uncertain inputs is already recommended. Any bias introduced by these uncertainties should already be captured and explored to enable a committee to a reach a judgement on whether the bias is influential in its decision. No changes to the methods guide are therefore needed.

What effect will NHS Improvement's changes to the HRG costing methodology have on assessments?

The way costs are collected is changing nationally. It means that, instead of aggregated costs, patient-level datasets are now requested from providers for admitted patient care, outpatients, and accident and emergency. This will expand over time to include acute, mental health and ambulance providers, and a voluntary pilot planned for community. Using patient-level datasets will change the way reference costs are calculated. This may lead to differences in reference costs that are attributed to a change in methodology, rather than solely to inflation.

A subgroup of the working group discussed whether this new way of calculating reference costs would mean that changes needed to be made to the methods guide. Two options were discussed: starting to use the patient-level data reported in the patient-level information costings system; or continuing to use the reference costs for healthcare resource groups calculated by NHS England and Improvement. The methods guide currently states:

"Healthcare resource groups (HRGs) are a valuable source of information for estimating resource use. HRGs are standard groupings of clinically similar treatments that use common levels of healthcare resources. The national average unit cost of an HRG is reported as part of the annual mandatory collection of reference costs from all NHS organisations in England. The use of these costs can reduce the need for local microcosting (costing of each individual component of care related to the use of a technology). Care must be taken to ensure that all relevant HRGs have been taken into account. For example, the cost of hospital admission for a serious condition may not account for time spent in critical care, which is captured and costed as a separate HRG.

Data based on HRGs may not be appropriate in all circumstances (for example, when the new technology and the comparator both fall under the same HRG, or when the mean cost does not reflect resource use in relation to the new technology under appraisal). In such cases, other sources of evidence, such as microcosting studies, may be more appropriate. When cost data are taken from literature, the methods used to identify the sources should be defined. When several alternative sources are available, a justification for the costs chosen should be provided and discrepancies between the sources explained. When appropriate, sensitivity analysis should be used to assess the implications for results of using alternative data sources."

The subgroup noted that the potential for inconsistencies may be greater if the Patient Level Information and Costing System is used directly, and that the default should be to use HRG's when possible. There is therefore no case for change identified as a direct result of the changes to the way costs are collected. Additional work is being done by NICE's Resource Impact Assessment team to ensure that

differences between provider and commissioner perspectives can be considered in costings tools that are produced by the team.

What sources should be used to estimate NHS and PSS carer costs?

The group noted that the methods guide does not explicitly state the source of NHS and PSS carer costs, and that this leads to inconsistencies when they are included in assessments. Where costs are estimated, there are often insufficient details provided on the methods used to get the estimates. The main published source of NHS and PSS carers costs identified by the group is the PSS RU costs. This is already recommended as the main source of NHS and PSS costs for use in assessments. The group was not asked to examine the costs of informal care, for example, care provided by family members.

Table 2 summary of key question 1d

Item	Current approach	Case for change	Recommendations and rationale
NHS and personal social services (PSS) carer costs	Source of NHS and PSS carer costs are not explicitly stated. PSS Research Unit (RU) costs are generally used.	No change needed the current approach is sufficient	Similar to other costs, the cost of NHS and PSS carers can be got from the PSS Research Unit: there is no compelling reason to make explicit reference to the cost of NHS and PSS carers in the methods guide

What sources should be used for the costs of biosimilar and generic medicines?

The HTA task and finish group was asked to determine the best way to incorporate drug prices, including list prices, patient access schemes (PAS), commercial access agreements (CAAs), Commercial Medicines Unit (CMU) prices, prices from the Drugs and Pharmaceutical electronic Market Information Tool (eMIT) and prices from the drugs tariff, into health technology evaluations. It is integral to the principle of HTAs that an accurate price is used, and that these prices are transparent as possible.

Accurate prices are needed for a technology when it is the intervention being evaluated, or if it is a comparator, a prior or subsequent treatment, or a combination

treatment. The most appropriate prices to be used for diagnostic testing and medical devices are being considered in a separate paper.

The current methods guide, in section 5.5.2, states that: “The public list prices for technologies (for example, pharmaceuticals or medical devices) should be used in the reference-case analysis. When there are nationally available price reductions, for example for medicines procured for use in secondary care through contracts negotiated by the NHS Commercial Medicines Unit, then the reduced price should be used in the reference-case analysis to best reflect the price relevant to the NHS. The Commercial Medicines Unit publishes information on the prices paid for some generic drugs by NHS trusts through eMIT; focusing on medicines in the National Generics Programme Framework for England. **Analyses based on price reductions for the NHS will only be considered when the reduced prices are transparent and consistently available across the NHS, and if the period for which the specified price is available is guaranteed.** When a reduced price is available through a patient access scheme that has been agreed with the Department of Health, the base-case analysis should include the costs associated with the scheme. The review date for the appraisal will be informed by the period of time over which the manufacturer or sponsor can guarantee any such pricing agreements.”

In this section of the report, we have highlighted 3 considerations on the use of different pricing sources and the points that must be deliberated. We have also recommended 5 different updates to the methods guide, and these feed into the overall output and recommendation for consideration by the group.

Consideration 1 – transparency of the prices

List, Drug Tariff and eMIT prices are transparent to all and available in the public domain. Most of the discounted prices (CMU, simple PAS, CAAs) are transparent to the NHS in England, but are not available in the public domain because of their confidential status. However, complex PAS are not confidential. A balance must be found to ensure appraisals take account of the actual confidential prices being paid by the NHS while ensuring that how NICE guidance has been developed is as transparent as possible. All drugs have a list price, and these are available in the public domain via the BNF or Monthly Index of Medical Specialities. Prices paid to primary care are also detailed in the drugs tariff, which is publicly available. The CMU and eMIT contain lists of alternative drug prices, but the lists differ for the following reasons:

a) NHS CMU as the pricing source – not available in public domain

All licensed medicines (branded, biosimilar and generic medicines) go out to tender via the NHS CMU in England, and via the national procurement organisations in the devolved administrations. The CMU prices negotiated in England are not available to

the devolved nations (Wales, Scotland and Ireland). So any analyses containing these prices may not reflected prices paid in these countries.

The prices for branded, biosimilar and newer generics on the CMU framework are highly confidential and are not in the public domain. The NICE Commercial Liaison Team liaises between the CMU and committee teams for requesting and sharing these prices.

b) eMIT as the pricing source – available in the public domain

eMIT provides information about prices of generic drugs and their usage in hospitals in England. It focuses on medicines in the National Generics Programme Framework for England, and publishes the average price paid for these medicines by hospitals in England.

Recommendation 1 for inclusion in the methods guide

Update wording to add the clarification: "Analyses based on price reductions for the NHS will be considered when the reduced prices are transparent **to the NHS. This is to ensure the current prices being paid by the NHS for a technology in the relevant indication are incorporated in any analyses**".

Consideration 2 – prices consistently available across the NHS

List prices, Drug Tariff prices, PAS and CAAs are not region specific. This makes the associated prices consistently available across the NHS. The average price paid for older generic medicines by hospitals in England is published on eMIT and is again consistently available across the NHS. However, where contracts are awarded by the CMU, the prices for a medicine can differ between regions meaning there is no single price consistently available across the NHS.

Recommendation 2 for inclusion in the methods guide

Add the clarification: "CMU prices may not be consistently available across the NHS, and this must be considered when selecting the most appropriate price to include in any analyses. For generics, eMIT should be used when possible, to provide an average price paid for use in the NHS in analyses."

There is no overall consistently available pricing source or source of an average price paid for branded, biosimilar and newer generic medicines. This could lead to a combination of historic averages prices and current prices being incorporated in analyses.

Options investigating how regional CMU prices could be incorporated into appraisals are presented in table 3. It is important to note that, when considering these options, the CMU price is only taken into account for comparator products (unless the intervention is a biosimilar). It is also important to note that the reverse pros and cons may be true when the CMU price is for a prior or subsequent treatment on the intervention side.

Table 3 Possible options to ensure consistency throughout appraisals needing comparator CMU prices generally for biosimilars and generics (including the originator product)

Option	Pros	Cons
1. Using cheapest Commercial Medicines Unit (CMU) discounted price for comparator (including the originator product)	• Lowest risk for NHS, 'best case scenario' (although not for NICE?) • Maximises cost effectiveness for NHS.	• May not be available nationally • May force incremental cost-effectiveness ratio (ICER) to appear higher than it really is 'worst-case scenario for intervention' • Favours comparator or older drug • Risks a negative recommendation and decision error?
2. Using most expensive CMU discounted price for comparator (including the originator product)	• ICER could be artificially lowered • Favours intervention under appraisal 'best case scenario'	• May not be available nationally (although NHS will be paying this price or less) • May force ICER to appear lower than it really is, so disadvantage NHS • Risks a positive recommendation and decision error?
3. Using mean CMU price for comparators (including the originator product)	• Mean is less work for the evidence review group then using a	• Increase risk of errors because average price • Does not represent a 'true' price paid by the NHS

	range of prices (highest and lowest) • Considers all possibilities (not done in option 1 or 2) • Ideal for probabilistic sensitivity analyses • Economically neutral (in terms of risk or surplus) • Uncertainty can be incorporated into modelling • Consistent with approach for other uncertain or variable parameters	
4. Using a weighted CMU price for comparators (including the originator product)	• Tries to take account of actual usage	• Increase risk of errors because of weighted prices • No reliable up-to-date market share or usage data
5. Using both the cheapest and most expensive CMU price for comparators (including the originator product)	• Considers both upper and lower possibilities • Could show that the price does not have an effect, for example, if both ICERs are below the threshold	• Does not give any direction to the committee, especially if the range crosses the threshold • Could increase the length of time of appraisals and discussions • Could be complicated with multiple CMU prices
6. Using no CMU prices and instead use the list price for comparators (including the originator product)	• Transparent prices available in the public domain • Nationally available • All prices from same source providing consistency	• NHS rarely pays this price • Does not provide true cost effectiveness

A combination of option 3 (average CMU price) and option 5 (cheapest and most expensive CMU prices) is preferred. This is because it would allow committees to consider the average, best- and worst-case scenarios from different stakeholder perspectives.

Recommendation 3 for inclusion in the methods guide

Add wording: “When confidential CMU prices are used by committees, they will use the average, cheapest and most expensive CMU price (including the originator) for comparators.”

Consideration 3 – period for which the specified price is guaranteed

CMU prices are renegotiated twice a year, so may change during and between appraisals, particularly in the first 1 to 2 years of a medicine having a framework price. However, PAS and CAA prices are guaranteed for the duration of the guidance, and will generally only ever decrease over time meaning these should take precedence.

Recommendation 4 for inclusion in the methods guide

Add wording: “When eMIT or confidential CMU prices are used by committees, they will be aware that those prices are not guaranteed for the duration of the guidance.”

Conclusion

There would appear to be a list of priority order for the sources of prices based on their availability across the NHS, their transparency and the period for which they are guaranteed. Discounted prices should generally be used over the list price because the discounted prices are more reflective of the prices being paid by the NHS. The priority list is**:**

1. PAS or CAAs – nationally available, confidential (except complex PAS) and guaranteed for the duration of guidance.

2. Drugs and pharmaceutical eMIT or Drug Tariff – nationally available, average prices (eMIT), are transparent but not guaranteed for the duration of guidance.

3. Commercial Medicines Unit Framework Prices – not nationally available, confidential outside of the NHS and not guaranteed for the duration of guidance. Where CMU prices are incorporated in an appraisal the mean selling price should be used in the base case and tested in sensitivity analysis using both the cheapest and most expensive CMU price for comparators (and intervention if applicable).

4. List prices if none of the above sources are available.

Recommendation 5 for inclusion in the methods guide

Add a priority list of sources for prices based on their availability across the NHS, their transparency and the period for which they are guaranteed (taking setting into account):

1. Patient access scheme or commercial access agreement
2. Drugs and Pharmaceutical electronic Market Information Tool or Drug Tariff
3. Commercial Medicines Unit Framework Prices
4. List prices

Key question 2: how should the costs of medical devices and in-vitro diagnostics be incorporated into assessments?

The question of how the costs of medical devices and in-vitro diagnostics should be incorporated into assessments included:

a. How should costs be apportioned for technologies that have high acquisition costs but multiple uses?
b. How should volume-dependent and similar pricing structures be incorporated into an assessment?
c. What costs related to the use of a technology should be included (for example, training and quality assurance costs), and what sources can be used for estimating these?

A workshop was held in London in February 2020 to explore this question. It was attended by 11 representatives from industry, NICE staff and representatives of the external group for this task and finish group. The industry representatives were nominated by the Association of British HealthTech Industries (ABHI), AXREM and the British In Vitro Diagnostics Association (BIVDA). The workshop explored the types of costs that should be requested for assessments of medical devices and diagnostics, looked at how these are used and explored where inconsistencies may arise, both within and between assessments.

There was consensus among the attendees that new submission templates for costs should be developed; stakeholders highlighted the key items for inclusion. An example of a template is provided in Appendix 2 to this report. This will not directly affect the methods guide. However, consistent submission of costs will help the issue of inconsistencies to be explored further. Also, it will provide external assessment groups with more definitive advice on ensuring a consistent approach to estimating an average price using the information provided by companies. The submission templates will be developed by NICE and circulated to industry representatives for comment before they are introduced for routine use.

No consensus on how volume-dependent pricing structures and high-cost devices with multiple indications should be factored into assessments could be reached This may need further exploration with a subgroup of Inter-TASC (Technology Appraisal Support Collaboration) representatives once submission templates have been developed. The are several key scenarios that will need to be explored:

High-cost technologies with potential additional future indications

For the first appraisal of a high-cost device, including the capital costs of a new technology when calculating its cost per use would appear to be a reasonable approach. However, if this technology may free up capacity of existing devices (or allow these to be decommissioned without being replaced) there may be cost savings for the NHS, and it is not clear how these should be accounted for in modelling.

It is also unclear what consideration should be given to potential (but currently unapproved) future indications. This may have implications for innovation and fairness. For example, including the full capital cost in an appraisal may mean it is very difficult for the technology to be cost effective. This may have the unintended effect of discouraging innovation. While considering potential use in other indications when calculating cost per use may encourage innovation, it could be unfair to technologies that are only used for 1 indication.

In subsequent appraisals for new indications for an established high-cost technology, it is not clear how costs should be calculated. Several approaches could be taken, for example, calculating cost per use for the new indication only (for example, by determining the proportion of time the technology will be used for this indication or including the full capital cost of the technology). The ideal approach may be context dependent, for example, including the full capital cost may be appropriate for technologies that are not well established in current clinical practice. Therefore, it may be appropriate to present multiple approaches as scenario analyses to address any uncertainties in the cost estimates. The Diagnostics Assessment Programme manual currently advises:

“Diagnostic tests should generally be priced at average cost. The average cost should be based on the expected total use of the technology in the settings in which it would be installed. In some cases, if a device is already recommended for use for another purpose and sufficient spare capacity exists to allow the use for the condition envisioned in the current assessment, an analysis using marginal costs may be supplied in addition to the analysis based on average costs.”

This should be incorporated into the unified methods guide because this may be seen for many technology types. Additional guidance may be needed on the contexts where this is appropriate to ensure consistency.

Apportioning costs for technologies with multiple uses at present

Assessments may also include technologies that have multiple uses in practice; for example, a CT scanner is used across a very broad population and is part of several diagnostic pathways. However, an assessment may only be looking at once specific use. Attributing the entire purchase cost of the technology to just 1 of the indications may not accurately reflect the cost of the technology in practice. The Diagnostics Assessment Programme manual currently states:

“For devices with multiple uses, where only some uses are being evaluated, the average cost should initially be identified based on the expected usage or throughput of the device for only the uses being evaluated. Additional sensitivity analyses may be carried out using average costs computed through assigning some of the fixed costs to other uses of the device, if there is evidence that the other uses also provide good value for money.”

This should be incorporated into the unified methods guide because this may be seen for many technology types. Additional guidance in the submission templates, and for assessment groups, may be needed to ensure that a consistent approach is taken. Exploring how this is accounted for in budget impact assessments may be needed.

Key question 3: do other HTA agencies include future unrelated healthcare costs in their analyses and which methods of calculating these costs are available?

To explore this question, the group commissioned a report from the NICE Decision Support Unit (DSU). The following provides an overview of the report and the DSU’s findings.

Currently, future unrelated healthcare costs are excluded from economic evaluations done during guidance production in the Centre for Health Technology Evaluation. The group considered the implications of this. Four key considerations were identified:

1. Identify the current arguments in the literature for and against including future unrelated healthcare costs.

2. Review how other health technology assessments (HTAs) handle unrelated costs in appraisals

3. Review the methods available for estimating unrelated costs in NICE appraisals

4. Discuss the potential implications of including or excluding unrelated costs within NICE appraisals.

Consideration 1: Identify the current arguments in the literature for and against including unrelated healthcare costs

The existing literature to support including unrelated healthcare costs in economic evaluations falls into 2 key points: internal and external consistency. The argument for internal consistency is that unrelated healthcare costs should be included if unrelated health effects are included (it is often maintained that the latter should be in economic evaluations). Otherwise, this can have the effect of making life-extending treatments appear more cost effective than they are.

The more prominent and important argument is about external consistency, which concerns allocative efficiency. This is that including unrelated outcomes (both health effects and costs) will result in more accurate estimates of the true costs of a treatment (and so more accurate decisions) than if they are excluded. The logic of this argument is clear. Budgets are fixed and health resources finite, and once consumed those resources cannot then be allocated elsewhere. Therefore, if the purpose of HTA is to help make decisions about how best to allocate a fixed budget to maximise patient outcomes, all unrelated outcomes should be included.

The arguments for excluding unrelated costs focus on the practical and ethical implications of including them. The main practical issue concerns how to consistently estimate unrelated costs and health effects. The level of data collection and accuracy needed to accurately measure future unrelated healthcare costs is difficult to achieve. The data would need to be sufficiently detailed to separate out unrelated costs for end-of-life care (decedent costs) from other costs (survivor costs), to avoid double counting costs from related diseases, and enable adjustments for patient characteristics and co-morbidities. A similar level of granularity would be needed for calculating unrelated healthcare benefits for consistency. Not including unrelated healthcare costs could introduce its own biased estimates, leading to inefficiencies.

The ethical objection is principally that, if we include unrelated healthcare costs, life-extending treatments would no longer be judged on their own merits. This could lead to situations in which novel and cost-effective treatments are not approved. For example, it could be no longer cost effective when the additional healthcare resources in treating an unrelated condition resulting from the extension of life are considered. If we considered a lifetime horizon, as used in the NICE reference case, this could create controversies over what should appropriately be included over a lifetime. For example, in the case of females, this might appropriately include any costs from giving birth, and any costs incurred by children born, because these unrelated costs would not have occurred had their life not been extended.

Consideration 2: Review how other HTAs handle unrelated costs in appraisals

Searches were done to discover how other national HTA bodies deal with future unrelated healthcare costs.

A total of 40 relevant guidelines were identified. These ranged from official recommendations to support country specific HTA submissions to position statements published by experts. There were inconsistencies in terminology; unrelated costs were often referred to as 'indirect' costs. Most guidelines did not distinguish between unrelated healthcare costs and unrelated non-healthcare costs. When a guideline gave a recommendation on unrelated healthcare costs, but only discussed non-healthcare indirect costs, it was assumed that the guideline did not make any specific recommendation on unrelated healthcare costs.

Five (12.5%) of the 40 guidelines identified explicitly recommended the inclusion of unrelated medical costs, while 15 (37.5%) recommended their exclusion. A further 2 guidelines were not prescriptive but stressed the importance of a consistent approach when dealing with unrelated costs and benefits. Of the 5, 3 were from national bodies supporting HTA submissions, in the Netherlands (Dutch National Health Care Institute [ZIN]), Israel, and Thailand. The remainder were from the US. ZIN provides a supplementary costing manual, along with a tool for calculating unrelated medical costs. Thailand and Second Panel, US provided an explicit recommendation to model utilities by age and sex.

Fifteen recommended the exclusion of unrelated healthcare costs. Most of these did not provide an explicit rationale for their recommendation to exclude these. Where a justification was provided, unresolved ethical and practical issues were cited.

While not an HTA, the HM Treasury Green Book was consulted. This does not explicitly discuss unrelated costs, but states that, when possible "All relevant costs and benefits which may arise from an intervention should be valued and included". The definition of what is relevant is left open to interpretation.

Consideration 3: Review the methods available for estimating unrelated healthcare costs in NICE appraisals

A review of existing methods used by HTA bodies and of UK specific approaches for dealing with unrelated healthcare costs was considered.

The approach done by ZIN, discussed in the previous section, was considered in detail. To support its recommendation, ZIN provides a toolkit referred to as the 'Practical Application to Include future Disease costs' (PAID). This estimates unrelated disease costs and provides results by age and gender, and separately for the last year and other years of life. It is possible to define the related diseases of

interest, to ensure that they are not included in the estimates of unrelated disease cost, so avoiding double counting. PAID uses bottom-up costings and the present version contains per capita costs for 99 diseases, stratified by age, gender and proximity to death.

ZIN shows that, even though there will be gaps and imperfections, creating a robust system to estimate unrelated healthcare costs is feasible. Possible routes specific to the UK to emulate and improve on such a system were considered, along with the literature in this area.

Hospital Episode Statistics (HES) collects data on secondary care admissions and includes information on the patient's age, gender, co-morbidities and deprivation to enable granular costing. Linked datasets can also be used to incorporate the effect of time to death on hospital costs. HES is only concerned with secondary care so neglects primary care, which represents around half of healthcare costs in the UK. As such, it would need to be supplemented by primary care datasets. In this area, there several possibilities with published evidence of practical application. These include QResearch and the Clinical Practice Research Datalink (CPRD). The CPRD can be further augmented with the Mental Health Services Data Set to cover mental health services. While these approaches provide a lot of granularity, there are still gaps, most notably in social services, and there would need to be a level of data cleaning to make it workable.

The 'Briggs approach' based on work done by Briggs, Scarborough and Wolstenholme in 2018 was discussed. This uses top-down (gross) costing, as opposed to the bottom-up approach used in the previously discussed datasets. The principal source for the Briggs approach is NHS England cost curves. These provide estimates of relative healthcare expenditure by age and gender, broken down by 4 categories of care: general and acute; mental health; prescribing; and primary care. These do not include maternity services and specialised services. However, overall expenditure for both areas is available. To generate age and gender breakdowns, Briggs applied those from national data, other disease areas and historic data. In summary, the approach used by Briggs to calculate unrelated costs involved:

- subtracting related disease costs from the overall NHS healthcare budget, thus providing an estimate of overall expenditure on unrelated diseases.
- allocating this overall unrelated expenditure to the 5 categories of care.
- applying estimates of relative healthcare expenditure by age, gender and category of care to the overall expenditure (by category) to obtain estimates of spending on unrelated diseases by these characteristics.

Outside of national datasets, the possibility and use of regional datasets in the UK and EU was considered. However, an adapted form of the Briggs approach was

considered to be the most practical for using the top-down costing approach with aggregate data, but supplementing this with more granular data from HES, CPRD and regional datasets.

Consideration 4: Discuss the potential implications of including or excluding unrelated costs within NICE appraisals

The current approach of including future unrelated benefits (although not stated or quantified), but excluding unrelated costs, creates an internal inconsistency. It also underestimates the true cost on the healthcare budget of life-extending treatments.

The inclusion of unrelated costs would have consequences which, in themselves, would need adaptions to our processes to address the resultant ethical and equity issues. Most notably including unrelated healthcare costs penalises treatments that are life extending but do not improve quality of life. These potentially would no longer be funded, which could deny individuals access to costly maintenance treatments such as dialysis. Without an explicit approach to deal with such examples, there could be inconsistencies in decision making across NICE committees, contrary to our stated aim to reduce health inequalities.

There is currently no standardised source for future unrelated costs. Possible sources have been discussed. However, even if a suitable evidence source was identified, there are unresolved methodological issues about which covariates to include (for example, should the number of morbidities be a factor), and the approach to statistical modelling of cost data. If NICE does consider including future unrelated costs, they would need to be accompanied with the consistent inclusion of indirect health benefits. The inclusion of unrelated healthcare costs would broaden the set of costs that are included in NICE appraisals, and may raise questions as to why it is not broadened further to include unrelated non-medical costs. This may address some of the effect of including unrelated medical costs because individuals who live for longer have greater opportunity to contribute to society.

Recommendations

This section has considered the arguments for and against the inclusion of future unrelated healthcare costs. The approaches of other HTA bodies has been examined and possible methods for their replication and refinement in an English HTA setting have been considered. If NICE is going to change its methods to include future unrelated healthcare cost further research will be needed to determine:

- whether it is possible to create a toolkit for estimating unrelated costs, like PAID and, if so, which methods and data sources would be the most appropriate to use
- if a toolkit is used, whether it is sufficient to use the PAID approach, or should any other factors (such as the number of morbidities) be accounted for

- whether the distributional effects of incorporating unrelated costs can be anticipated in advance to avoid increasing inequalities in health outcomes
- whether the process of NICE decision making needs adjustment to place greater emphasis on equity concerns
- how the inclusion of unrelated costs will affect the NICE cost-effectiveness threshold
- whether the NICE methods guide should be more prescriptive about the inclusion of unrelated health effects, in particular, whether it should age-adjusted utilities
- when extrapolating survival gains, the methods that should be used to provide assurances that the effect of unrelated diseases and unrelated treatments is accounted for
- whether unrelated costs should be included in situations when there is no life extension (if treatment allows for additional future unrelated treatment).

Biosimilars and generics position statement

NICE has previously produced a position statement outlining its approach on biosimilars. There is parallel work being done to consider how NICE should approach scenarios in which the reference product was not submitted to or not recommended by NICE in a particular indication that a biosimilar becomes available. The position statement will be reviewed as part of this parallel work.

Appendix 1 – summary of recommendations

Sources of costs

- Approach to currency conversion should be stated explicitly in company submission – updated methods guide wording to be based on guidelines methods manual.

- Approach to adjustment for inflation should be stated explicitly in company submission – updated methods guide wording to be based on guidelines methods manual. Reference to Hospital and Community Health Services index to be replaced with the new NHSII.

- The preferred sources of medicine costs will be clarified, with additional guidance around the choice of source for the costs of biosimilars and generics. This will include:

    - Clarifying that prices transparent to the NHS will be considered

    - Clarifying that analyses should consider the fact that prices may not be available consistently across the NHS:

        - When available, prices from the electronic Market Information Tool (eMIT) should be used for generics.

        - When confidential Commercial Medicines Unit (CMU) prices are used, the committee will consider the average, cheapest and most expensive CMU price.

    - Instructing committees to note that eMIT and confidential CMU prices may not be guaranteed for the duration of the guidance

    - Providing a priority list of sources for prices

- No updates to the methods guide are proposed in the following areas, because these are adequately covered in the current methods guide(s):

    - use of micro-costing

    - use of expert elicitation

    - use of costs from Healthcare Resource Groups

    - sources of costs for informal care

Incorporating the costs of medical devices and diagnostics

- A new submission template will be developed to aid the submission of costs for medical devices and in-vitro diagnostics. This will not directly affect the methods guide. Industry will be consulted on the contents of the template before routine use.

- The following advice from the Diagnostics Assessment Programme manual will be incorporated into the unified methods manual:

    - advice on technologies with multiple indications

    - advice on technologies with multiple uses

Future unrelated healthcare costs

- Further research is needed to determine whether NICE should incorporate future unrelated healthcare costs in a subsequent methods update.

Incorporating the biosimilar and generics position statement

- The biosimilar position statement will be reviewed as part of parallel work that is underway.

Appendix 2 – example of costs to be submitted for medical devices and in-vitro diagnostics

Large medical device

For example, a CT scanner or surgical robot

What is the capital cost of device?
What is the estimated lifespan of the device?
Are any enabling or building works needed to install the device? If so, please state the estimated cost of these.
Are there any decommissioning works needed once the device has reached the end of its lifespan? If so, please state the estimated cost of these.
Does the device need to be connected to existing information technology infrastructure? If so, please state the estimated cost of this.
Are there any software costs associated with the use of the device? If so, please state the costs of any licences or upgrades that are likely to be needed.
What is the cost of the consumables per use?
Are the consumables single use? If not, please state the costs associated with sterilising multiple use consumables.
What is the estimated lifespan of the multiple use consumables?

Are there any maintenance costs associated with the device? If so, please state the cost and frequency of maintenance.
Are there any quality assurance or calibration costs associated with the device? If so, please state the cost and frequency of quality assurance, calibration or both.
Which staff are needed to operate the device?
Is any training needed to operate the device safely? If so, please provide details of how long training takes to complete.

In-vitro diagnostic

Does the test need an analyser?
How is the analyser purchased? Please provide details of either the capital cost or the lease arrangements?
What is the throughput of the analyser?
What is the estimated lifespan of the analyser?
Is the analyser intended to be used in a laboratory or in a near patient setting?
Does the test rely on existing transport infrastructure where a test is sent to the lab? Are there any additional sample transport costs (please state)?
Are any enabling or building works needed to install the analyser? If so, please state the estimated cost of these.
Are there any decommissioning works needed once the analyser has reached the end of its lifespan? If so, please state the estimated cost of these.
Does the analyser need to be connected to existing information technology infrastructure? If so, please state the estimated cost of this.
Are there any software costs associated with the use of the test? If so, please state the costs of any licences or upgrades that are likely to be needed.

Please state the cost of the consumables. Please describe how throughput may affect the cost per use? Consumables may include but is not limited to the reagents, sample collection devices, sample transport media, controls.
Are there any maintenance costs associated with the analyser? If so, please state the cost and frequency of maintenance.
Are there any quality assurance or calibration costs associated with the analyser? If so, please state the cost and frequency of quality assurance, calibration or both.
Which staff are needed to process, run and report test results?
Is any training needed to use the test safely? If so, please provide details of how long training takes to complete.