Review of methods, processes and topic selection for health technology evaluation programmes: conclusions and final update

Introduction

Summary

We regularly review how we evaluate medicines and other health technologies, to make sure our evaluations are high quality, timely and robust, and support prompt and evidence-based access to valuable innovations for patients and the NHS. We have conducted a comprehensive and in-depth review of all aspects of our evaluations, covering how we identify and choose topics to evaluate (topic selection), the steps and stages in each evaluation (processes), and how evidence is collected and considered (methods). We present a broad package of improvements that will be included in new, combined manuals for health technology evaluations, to benefit stakeholders across the health and care system. Through this review, we are evolving our approach alongside advances in medicines, medical technologies and evidence, to continue to deliver excellence. The changes make sure we continue to support patients in accessing valuable new innovations, while providing companies with greater predictability, flexibility when it counts and transparency in our recommendations. In this way, we support innovation and deliver value for money for the NHS, now and into the future.

This final stage of the review aimed to:

* consider comments from the consultation on our proposals and draft manuals, and finalise the manuals ready for use
* determine how the new methods and processes will be used
* explore how we can make sure our methods and processes stay up to date in the future.

This report summarises the comments we had in the consultation, our responses to them, and our final conclusions and changes. The final manuals for health technology evaluations will be published after this report. An appendix with more details on key aspects of the methods, and accompanying documents on the consultation response, implementation of the changes, impact assessment and future plans, will be also be published after this report.

Overview of the review

NICE’s methods and processes of health technology evaluation are a crucial tool for delivering our high-quality guidance to the NHS. They underpin the robust, consistent and transparent decision making on which our guidance is based and are pivotal in supporting NICE’s objective to secure rapid and fair access to clinically effective health technologies that provide value for money in the NHS. Our guidance both informs shared decision making and shapes the value companies put forward for their technologies. We navigate a complex environment of ensuring the NHS gets the best value out of the products it uses, while at the same time promoting innovation and supporting the life sciences industry in its journey through regulation, health technology evaluation and patient access. The methods and processes we use provide an important bridge between the two.

We regularly review the processes and methods for health technology evaluation at NICE, to optimise them in supporting the ambition of the NHS to provide high quality care that offers good value to patients and to the NHS. Ensuring rapid access to clinically effective health technologies that provide value for money is critically important to patients, the NHS and the life sciences industry. To continue to support the needs and aspirations of all parts of the system, we must ensure that the methods and processes of health technology evaluation maintain and improve upon key objectives about quality, dependability, speed, flexibility and value for money.

The current review was started in 2019. It was divided into 3 key aspects: 1 focussing on topic selection, 1 on processes in general and 1 on methods. This review did not start with a blank sheet of paper, but rather is an incremental development of our existing world-class approach to evaluating new health technologies.

As well as meeting our ambition to optimise and maintain our methods at the cutting edge of health technology evaluation, this review also responds to a commitment in the 2019 voluntary scheme for branded medicines pricing and access (2019 Voluntary Scheme), agreed by the government and the Association of the British Pharmaceutical Industry (ABPI) in December 2018, for NICE to review its processes and methods for the Technology Appraisal Programme and the Highly Specialised Technologies Programme. We took the opportunity to extend the review to include the methods and processes of the Medical Technologies Evaluation Programme and the Diagnostics Assessment Programme and align them when appropriate to ensure that health technology evaluation is pragmatic, agile and robust, while also being able to adapt to environmental changes and system partners’ requirements.

In that context, a core objective of this review was to produce a single guidance development programme manual covering 4 health technology evaluation guidance programmes (the Diagnostic Assessment Programme, the Highly Specialised Technologies Programme, the Medical Technologies Evaluation Programme and the Technology Appraisals Programme). This replaces multiple existing individual process and methods guides and reduces unnecessary duplication of content. This approach to communicating our methods and processes is anticipated to be easier for stakeholders to engage with. A new, separate topic selection manual has been developed that will be published as a stand-alone document to accompany the guidance development manual. The topic selection manual also incorporates the topic selection process for all aforementioned guidance programmes and includes the Interventional Procedures Programme.

To date, this review has involved 4 distinct consultations to shape and develop the final manuals, culminating in approximately 30 weeks of public consultation:

* **September 2020**: consultation on the principles of change for topic selection
* **November 2020**: consultation on the principles of change for methods
* **February 2021**: consultation on the principles of change for processes
* **August 2021**: consultation on proposed changes and draft unified manuals for health technology evaluation guidance development and topic selection.

Building on these consultations, the objectives of this final phase of the review were to:

* review stakeholders’ comments on the proposals and the draft manuals and make changes accordingly when needed
* more broadly, review the draft manuals (that were presented for illustration) and develop them into refined, aligned final manuals ready for implementation
* develop an implementation plan
* start planning for future methods and process reviews – ensuring the methods and processes remain responsive, adaptable and future proof.

Improvements to methods, processes and topic selection

Overall, the final changes provide:

* a broad package of support for innovation
* earlier access to valuable new innovative treatments
* more equitable access for people with severe diseases
* decision-making flexibility when appropriate
* improved ability to embrace the full evidence base and new data sources
* increased clarity, predictability and transparency into how we develop guidance and decision-making approaches
* an approach for continuous improvements in methods and process developments to support innovation.

The review accounted for the remit of the individual programmes, arrangements for topic identification and selection, and the ability to receive evidence from sponsors of the technology of interest, among other things. It also included removing the interim nature of the current Highly Specialised Technologies Programme methods and processes.

We believe the changes we have made to topic selection, methods and processes will provide a clear foundation for delivery of the government’s Life Sciences Vision. They represent the ambition expressed in the vision for our methods, our role in the system, the processes of engagement we use, and the synergistic collaborations with health system partners across the landscape and countries of the UK, for a wide-ranging set of technologies from drugs and devices to diagnostics and digital.

Consultation on the proposals for change and draft unified manual

The public consultation on the draft aligned manual was open for a total of 8 weeks and closed on 13 October 2021. We received responses from over 170 stakeholders.

Not all stakeholders commented on all aspects of the consultation; 157 respondents commented on the methods proposals, 132 commented on the process proposals and 127 commented on the topic selection proposals.

The majority of comments (~75%) received from the consultation were from the life sciences industry and patient and carer organisations (figure 1). We also received comments from other NHS organisations, the clinical community, academic partners, members of the public and NICE evaluation committee members (figure 1).

Figure 1. Consultation responses by stakeholder type. Respondents could choose more than 1 option.



In addition, over the course of the consultation we held [5 different webinars for stakeholders on the topic selection, methods and process review](https://www.youtube.com/playlist?list=PLRbwbc3dfXUMV8wyt59VOgIQxjxtyAqss) with a significant attendance rate across all webinars. A number of additional meetings with key stakeholder groups were also held during the consultation.

This report summarises the key themes raised by stakeholders during the final consultation, our response, and the final changes for topic selection, processes and methods.

Topic selection

Summary

We received a range of views across our stakeholder community and from members of the public in the consultation. Many responses agreed with the changes that we had proposed. Some responses disagreed or offered alternative proposals for change. In this section of the report, we highlight the responses received and have outlined when changes and compromises have been accepted, along with our intentions for future engagement on significantly cost-incurring devices.

In response to these comments, the revised manual now includes more explanation on how briefings for devices, diagnostics and digital technologies are developed and confirms that the medical technologies innovation briefing (MIB) is an integral part of the topic selection process (see section 5 of the manual).

We have also clarified which types of guidance may be developed for different technologies and their different value propositions (see section 6 of the manual).

A clear vision has been set out for the Highly Specialised Technologies Programme to explain the aims of the programme. The programme’s routing criteria have been refined to give more clarity on the types of technologies that may be selected for the programme. For a technology to be considered through this programme it will only need to fulfil 4 criteria, rather than 7 previously. The vision and routing criteria have been refined to reflect feedback received from stakeholders. These will make the routing decision clearer, consistent, more transparent and precise to provide greater clarity, precision and predictability for the routing of topics through the Highly Specialised Technologies Programme (see section 7 of the manual). It is not the intention of the refined criteria to increase or decrease the number of topics routed to the Highly Specialised Technologies Programme. The changes will assist stakeholders to better understand which topics would most likely be routed to this programme.

The company (or person who suggested the topic to NICE) can challenge routing decisions made by the topic selection oversight panel, but this may impact the timing of the evaluation (see section 10 of the manual).

Overview

The consultation focussed on 3 main areas, including:

* the Highly Specialised Technologies Programme vision, principles, and routing criteria
* eligibility criteria for devices, diagnostics, and digital technologies
* the draft topic selection manual.

Stakeholders were asked to comment on the clarity of the consultation document and draft topic selection manual and were given the opportunity to provide detailed comments and responses.

Findings from the consultation, updates to the final manual and next steps

Highly specialised technologies – the vision, principles and routing criteria

The consultation on the refined Highly Specialised Technologies Programme topic routing criteria asked stakeholders 3 questions:

* How clear or unclear is the aim of the Highly Specialised Technologies Programme?
* How clear or unclear is the refined routing criteria for this programme?
* How clear or unclear is the eligibility criteria for devices, diagnostics and digital technologies?

Summary of comments received

A large majority of stakeholders were dissatisfied with the proposed vision, expressing that the vision and the proposed criteria were misaligned, and that there was a divergence with the aims set out in the wider policy landscape.

Stakeholders were also dissatisfied with the proposed population numbers in the refined criteria and indicated the evidence base used to develop the refined population numbers was imperfect.

Stakeholders were also disappointed that there were 3 types of population mentioned in the refined criteria; 1 for long-term treatments, another for one-off treatments and a third for multiple indication therapies. Stakeholders believed using a different approach for long-term and one-off treatments was not a valid approach to take. This was combined with the dissatisfaction of setting a total population of 500 on multiple indication therapies. Some challenged that we had not adequately explained how the decision was made to add a limit of 300 eligible patients in the licensed indication or of 500 across all indications.

The ABPI did its own analysis on the impact of the proposed criteria, which it submitted as part of its consultation response.

The medical technologies and diagnostics industry fed back that the criteria proposed were too medicine focussed and did not take account of the types of products that its industry would put forward.

Our response and changes to the topic selection manual

In response we have updated the vision, making the aims of the Highly Specialised Technologies Programme clearer, acknowledging that the programme is for very rare diseases, not for all rare diseases, and explaining our role in the healthcare ecosystem. We have also added narrative that explains the wider impact on the NHS and the displacement that occurs when NICE recommends a topic through this programme. The text that explains the vision of this has been added to the topic selection manual and has also been included below (sections 33 to 35).

Highly specialised technologies vision and routing criteria

The Highly Specialised Technologies Programme is designed to be used in exceptional circumstances. Its purpose is to evaluate technologies for very rare diseases (with very small patient numbers) with no other satisfactory treatment options, or the technology is likely to be of significant additional benefit to existing treatment options, when the uniqueness of the very rare condition creates challenges for research and difficulties with evidence generation.

The Highly Specialised Technologies Programme aims to:

* encourage research and innovation in very rare conditions when there are challenges in generating an evidence base that is robust enough to bring the product to market
* secure fairer and more equitable treatment access for very small populations with very rare diseases
* recognise that an approach that maximises health gain for the NHS may not always be acceptable: it could deliver results that are not equitable.

The Highly Specialised Technologies Programme acknowledges that:

* It is important for NICE to apply appropriate limits on the very rare populations that can potentially be routed to the programme. This is because the Highly Specialised Technologies Programme is a deliberate departure from the standard technology appraisal process (valuing the benefits from these technologies more highly by having a much higher incremental cost-effectiveness ratio [ICER] threshold) for the reasons outlined above.
* Each time NICE routes a topic to the Highly Specialised Technologies Programme it is deciding that, if the technology is recommended, the NHS must commit to allocate resources that would otherwise have been used on activities that would be expected to generate greater health benefits.
* NICE has sought to strike a balance between the desirability of supporting access to treatments for very rare diseases against the inevitable reduction in overall health gain across the NHS that this will cause. Both considerations are valid and important, and neither can be given absolute priority over the other. Therefore, the Highly Specialised Technologies Programme criteria and their anticipated application intentionally do not seek to capture every case when there are challenges in generating an evidence base or when there is a small population with a rare disease.
* This approach ensures that technologies routed to the Highly Specialised Technologies Programme fulfil the vision of this programme and manages the displacement in the wider NHS.

We reviewed the ABPI impact assessment and concluded the assessment was done without the insights, evidence and deliberation done by the topic selection oversight panel. Therefore, the assessment submitted was likely to have come to inaccurate conclusions. Having triangulated the assessment with ours we are confident that our analysis supports the approach we are taking; in particular, noting that it was not the intention of the refined criteria to increase or decrease the number of topics routed to the Highly Specialised Technologies Programme.

In response to the comments, the refined Highly Specialised Technologies Programme routing criteria have been amended to remove reference to the population for one-off treatments. The criteria and how they are applied will also be communicated through a range of vignettes that will be available on the NICE website.

We have chosen to retain the multiple indication population number as it supports us to achieve the aims and vision of the Highly Specialised Technologies Programme.

In response to feedback from the medical technologies industry we commit to exploring the applicability of the Highly Specialised Technologies Programme criteria to accommodate these types of technologies in the wider activities being done in the medical technologies work programme.

The final routing criteria for the Highly Specialised Technologies Programme are:

* The disease is very rare – defined as 1:50,000 population in England.
* Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications.
* The very rare disease for which the technology is indicated significantly shortens life or severely impairs quality of life.
* There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options.

Eligibility criteria for devices, diagnostics and digital technologies

Summary of comments received

The majority of respondents said that the eligibility criteria for devices, diagnostics and digital technologies were unclear.

Stakeholders said that the role of the MIB to support the topic selection oversight panel’s decision making should be clarified, and it was not clear how cost-incurring medical technologies are selected for technology appraisal guidance. Stakeholders asked for clarification on the selection and routing considerations for devices, diagnostics and digital technologies that are cost incurring rather than cost saving.

Our response and any changes to topic selection manual

In response we have updated the manual to explain how briefings are developed for devices, diagnostics and digital technologies and clarified that the MIB (if available) is an integral part of the briefing that is presented to the topic selection oversight panel to aid its decision making.

We have added text that explains further the selection process for devices, diagnostics and digital technologies, making it clear that a technology may be selected if is expected to be significantly cost incurring (with a clear value proposition), cost neutral (with greater clinical effectiveness) or cost saving. We acknowledge that further engagement with industry, stakeholders, and system partners to identify and discover those significantly cost incurring devices, diagnostics and digital technologies is needed before further details can be provided. Engagement on this will begin in 2022.

The Health Technology Evaluation Topic Selection function will work closely with the NICE [Office for Digital Health](https://www.nice.org.uk/about/what-we-do/digital-health/office-for-digital-health) to identify digital technologies that offer the greatest potential to improve health and wellbeing. We are continuing to develop and foster relationships and networks with key external NHS system partners to increase our horizon scanning and intelligence of emerging digital products. We demonstrate this through actively engaging with and supporting the Accelerated Access Collaborative’s AI award selection process.

The topic selection manual

Summary of comments received

Most comments from respondents about the topic selection manual were positive. Stakeholders said that the presentation of the manual would be improved with the addition of process and flow charts to aid and improve user understanding. Stakeholders welcomed the inclusion of a challenge process for routing decisions but commented that challenges should be subject to an independent panel rather than an internal process.

Our response and changes to the topic selection manual

The manual will be supported by additional and complementary information, such as flowcharts, on the NICE website that will be developed, updated and published when needed.

We recognise the benefits and importance of an independent appeal panel for guidance development and the reference to the appeal process for technology appraisals and highly specialised technologies in the NICE regulations. However, it is not an appropriate function for topic selection because the topic selection oversight panel’s remit is to select and route topics for guidance evaluation, not to make recommendations for use of a technology in the NHS. To add an independent appeal panel for topic selection would cause significant delays to the process, thus meaning topics will have to be considered earlier with less available data. When needed, challenges will be considered by the topic selection oversight panel and if necessary, the re-consideration step will be ratified by a member of the NICE executive team. It has been made clear that if a challenge is received, it may impact or delay the timing of the evaluation.

Other

Stakeholders again challenged the proposal to route technologies to the NICE Clinical Guidelines Programme instead of a formal health technology evaluation, citing that the commitment to rapid, robust and responsive evaluation of new technologies cannot be delivered by the Clinical Guidelines Programme. It was also noted that commitments in chapter 3 of the 2019 Voluntary Scheme must take precedence. We acknowledge our ongoing commitments to the statements from the 2019 Voluntary Scheme, which notes that NICE will appraise all new active substances in their first indication, and extensions to their marketing authorisations to add a significant new therapeutic indication, except when there is a clear rationale not to do so. The latter part of the statement adds an important clarification that there is not a guarantee that NICE will appraise all new medicines or extensions to their existing licences and that other NICE (or wider system) products or guidance are more suitable to the particular decision problem posed.

Process

Summary

In this stage of the process review, we considered the responses from the consultation, updated the draft manual and developed plans to implement new processes and opportunities to align our work. In this section of the report, we highlight the responses that we received from consultation and the final conclusions that we have reached. This review represents the latest iteration of NICE’s processes of health technology evaluation.

We received a range of views across our stakeholder community and from members of the public in the consultation. Many responses agreed with the changes that we had proposed. Some responses disagreed or offered alternative proposals for change. We have considered all responses in detail and have outlined when changes and compromises have been accepted.

By considering all our health technology evaluation programmes together, it presented an opportunity to align our processes, consider areas for additional improvements and ensure those stakeholders who work with us have a consistent and predictable experience. We have also been clearer on processes that we use in our commercial and managed access functions to help streamline and simplify patient access to new innovative health technologies.

Through this review, we present a package of process improvements and clarifications including flexibility in the application of different steps and stages to provide a faster process. At the same time, we will remain robust and efficient in our approach. We have removed some older processes that were not working efficiently and have established new processes that will better benefit what patients and colleagues in the NHS need to be able to meet the challenges and changing needs for technology evaluation.

We have also increased the opportunity for stakeholder involvement at different stages in the work programmes. We hope that this will provide more transparency and increase input, understanding and satisfaction of the external organisations and people that we work with.

Overview

The consultation paper issued in summer 2021 proposed a broad range of updates to our processes of guidance development, building various cases for change into consolidated and aligned process changes. It was presented alongside a draft process manual for illustration. In summary, the proposed changes were categorised into 3 themes:

* alignment of the current guidance development processes
* opportunities for new process improvements and ways of working
* commercial and managed access processes.

The consultation focussed on 8 main areas, including:

* technical engagement
* treatment eligibility criteria
* draft scope consultation timescales
* rapid review of guidance for biosimilars
* managing company submissions with a high base ICER
* clarity of commercial processes
* clarity of managed access processes
* fast track appraisal process
* other process topics and proposals.

Stakeholders were asked to comment on the clarity of the consultation document and process sections of the draft manual and the extent to which they agreed with proposals, and were given an opportunity to provide detailed comments and responses.

Findings from the consultation, updates to the final manual and next steps

We received feedback on the themes and areas that we had highlighted with specific questions. These are discussed in more detail in the sections below. Stakeholders also took the opportunity to respond to other areas. Particular areas that received positive feedback were:

* pragmatism to the requirement for standard committee meetings for decision making
* the introduction of a summary of information for patients to assist our patient and carer stakeholders in their participation in the process
* additional levels of detail as to the involvement of experts during the evaluation processes
* opportunities for early engagement with companies, particularly for complex technologies.

Processes – new ways of working

Summary of comments received

We received differing views on the proposals to change draft scope consultation timings. Stakeholders were pleased to see that the draft guidance consultation timings had not been shortened (a change that we had reversed between the first and second consultation). However, the draft manual stated that draft scope consultations could be between 7 and 28 calendar days. Stakeholders, particularly patient groups, were concerned as to the ability of external organisations and individuals to be able to respond to consultations within 7 calendar days, even when using such a short consultation period when NICE has a significant amount of corporate knowledge in the disease area under assessment. Some identified and offered a compromise in this regard and suggested that a 14 calendar day consultation period would be acceptable. Some stakeholders requested that NICE consult with stakeholders on individual topics to agree where and when shorter consultation periods could apply.

Stakeholders were encouraged to see that NICE had retained the use of a technical engagement step in the NICE process, particularly the technology appraisal process, and believed that this should be viewed as a core stage of the process. It was acknowledged that the step will no longer be a mandatory part of the process but stakeholders expressed caution about making the decision on whether to hold technical engagement on a case-by-case basis. Industry called for technical engagement to be removed from the process only on the basis of a joint decision between NICE and the company.

Industry also called for other changes to the technical engagement meeting, by re-instating the involvement of the clinical and patient experts in the meeting between NICE and the company. They also suggested that when technical engagement is not held, NICE should seek to bring forwards the committee meeting to shorten the time spent in appraisal, when possible.

Industry also highlighted the new process proposed for a rapid review of guidance for a technology with loss of exclusivity (biosimilars and generics). Industry respondents cited that although they were supportive of the principle, they would like to see more information before they can fully support the proposals. Industry respondents are keen to ‘balance the need for patient access with efficiency’ but are cautious to ensure equity in terms of company competition and cost recovery is appropriately managed alongside access to company proprietary economic models.

Stakeholders also reacted strongly to the processes we had clarified in the draft manual about the management and transparency of treatment eligibility criteria. Although there was acknowledgement of the ambition of NICE to ensure that the processes were standardised and documented – adding clarity and transparency – there was fundamental disagreement with the application of additional treatment eligibility criteria because of the effect they have on restricting access to treatment. Industry signalled the opinion that the proposals outlined in the consultation and draft manual could undermine the role of NICE.

We also saw some disagreement with the proposals for managing high company base case ICERs. We received positive feedback recognising the additional clarification in the draft manual that the Associate Director will engage with the submitting company. However, there remains concern that NICE will take a unilateral decision to terminate evaluation topics, which may not be the most appropriate course of action in some cases.

Our response and changes to the manual

When we have seen a high level of positive support for the proposals of new processes and ways of working, we have reflected these changes in the final unified manual, adding more content and information as necessary.

In response to the consultation comments about the draft scope consultation timelines, we acknowledge that the information provided in the draft manual was misleading. The manual referred to a 7 day ‘short’ consultation and a 28 day ‘long’ consultation. A 7 day ‘short’ consultation period has been used in the Medical Technologies Evaluation Programme for some time now. This will be retained for this programme. We recognise that stakeholders are concerned that using such a short timescale for consultation in other guidance-producing programmes may not provide enough time to adequately engage with an important part of the process. However, we do still believe that there are circumstances in which it may not be necessary to hold a full 28 day consultation period for some draft scopes when NICE has a significant amount of corporate knowledge in the disease area under assessment (for new topics or updates of published topics). We believe that a 14 day consultation period would be acceptable in these circumstances. This change would reduce the total time spent ‘in evaluation’, and potentially accelerate access to new technologies.

We have also changed the approach to the company submission stage of the medical technologies guidance development process to align with the other guidance development programmes. Previously, the company was asked to split its submission into 2 parts; the first being the clinical evidence which was submitted 14 days after the invitation to submit, and the second being the cost evidence 42 days after the invitation to submit. This has now been updated to allow the company longer to work on the full evidence submission. The new manual removes the request for the submission to be split into 2 and now indicates that the company should submit the full evidence package 42 days after the invitation to submit.

We have formally discontinued what was the fast track appraisal process:

* There has been a new ‘cost comparison’ process established to replace and refresh the previous fast track appraisal process. This is a shorter process than the standard appraisal process, does not formally use the technical engagement step, and allows the opportunity for the committee decision to be taken outside of a formal meeting. This process maintains the 30 day implementation period following publication of final guidance.
* The low ICER fast track appraisal process has been formally discontinued. If a company wishes to submit a value proposition with a highly cost-effective technology (that is, with an ICER of less than £10,000 per quality-adjusted life year [QALY] gained and a high degree of certainty) NICE can flexibly adapt the standard appraisal process (including the use of the technical engagement step) to expedite progression through guidance development. The 30 day implementation period for technologies with such a low ICER will be maintained and explicitly referenced in the guidance documentation.

The new manual contains information and additional clarity on the process that would be used for a rapid review of guidance for a technology with loss of exclusivity (biosimilars and generics).

As proposed in the draft manual, the technical engagement stage is now regarded as an optional stage of the technical evaluation process. During consultation, industry requested that other changes could be made to the technical engagement step (when held) such as including the company, NICE, clinical experts, patient experts, and the academic group in a single meeting. Although we recognise the argument that industry makes about the efficiency of holding 1 meeting, we have received feedback from other stakeholders to indicate that the separation of the discussion is helpful, increases their understanding and involvement and ensures that the conversation during the meeting does not become overly ‘technical’. The requirement for meetings with industry representatives and selected experts during the technical engagement stage are documented in the process manual although the exact logistics of how the meetings are conducted are not provided in detail. This allows flexibility to continue to improve the approach to the meetings. At this point in time, we will continue to hold the company and expert meetings separately but will continue to review the effectiveness of this approach.

We have also updated the manual to describe the circumstances in which evaluation committees may not need to formally meet to make a decision. This bears significant relevance to the cost comparison process and managing commercial proposals that are introduced following the first committee meeting.

Considering the concerns raised about the treatment eligibility criteria, these points do not account for the important function that treatment eligibility criteria perform in providing an indication about which patients are most likely to benefit from treatment based on the evidence presented, and by providing a mechanism to mitigate uncertainty about value for money. On balance, NICE will retain this important clarification to enhance the transparency of this process and to provide an opportunity for all stakeholders to now be able to comment on proposals about treatment eligibility criteria.

We acknowledge that stakeholders are concerned that NICE would take unilateral decisions about the progression of individual evaluations, particularly the use of a technical engagement stage and managing company submissions that include significantly high base case ICERs. However, it cannot be assumed that receipt of a submission from a company automatically guarantees progression to an evaluation committee meeting. In the draft process manual we sought to reassure stakeholders that before any decisions would be taken, we would engage appropriately with relevant stakeholders. Ultimately, there will be occasions when a final and accountable decision must be made. This will be the responsibility of NICE as the owners and officers for delivery of the process of guidance development.

Commercial and managed access

Summary of comments received

Industry welcomed the inclusion of text from the June 2021 interim statement ‘Procedures for the review of commercial and managed access requests’ adding recognition for increased transparency in this important area of the NICE processes.

Industry called for NICE to pay attention to particular areas of concern about timings of commercial and managed access activity. In particular, the requirement for prompt review of commercial and managed access requests from companies, but also noting that some of the requirements for companies to respond to requests for clarification on commercial and managed access proposals are challenging and may not be met consistently by companies. Industry also requested further clarity on the role of NHS England and NHS Improvement, and transparency of NHS England and NHS Improvement input. Industry also suggested that the submitting company should have sight of the final NICE commercial and managed access request commentary that informs the committee deliberations.

Some stakeholders also reflected that the proposals for managed access will now only be considered eligible for funding through the Cancer Drugs Fund (CDF) or the forthcoming Innovative Medicines Fund (IMF). Stakeholders were concerned that this was a deliberate departure from previous approaches to managed access in the Highly Specialised Technologies Programme whereby clinical uncertainty has been addressed by further data collection while being funded through routine commissioning.

We also received feedback that the following should be added to the guide to improve clarity:

* description of the participants in the commercial and managed access processes alongside roles and responsibilities
* clear definitions of different commercial arrangements available
* separation of patient access scheme (PAS), commercial access agreements and managed access agreements to clarify when alignment and differential approaches apply
* ensuring that the statement noting that a simple PAS is the default commercial option is made front and centre and repeated.

It was also highlighted that the draft manual referred to the identification of topic experts to support commercial and managed access activity. The clarity and apparent lack of consistency with the approach taken to nomination and selection of experts through the standard evaluation process was questioned.

Stakeholders also reflected that text used in the draft manual for the commercial and managed access section implied that these sections related to medicines only. Stakeholders asked that, when this is the case, this should be made much clearer.

It was noted that the reference made to the 2014 Pharmaceutical Price Regulation Scheme (PPRS) was inappropriate as this policy no longer exists. The principles in the 2014 PPRS should be clearly stated in the draft manual.

Although stakeholders welcomed the expansion of managed access initiatives beyond treatments for cancer, it was also stated by industry that it is not possible to submit a cost–utility analysis at such an early stage and in line with the regulatory process, because relevant data are likely to be too immature. There was suggestion that NICE could instead use a process like the Scottish Medicines Consortium (SMC) has for ultra-orphan drugs or pricing arrangements such as those used in Germany and Italy.

Industry also supported the continued inclusion of the opportunity for rapid review of guidance. It did ask that this updated process be available up to 16 weeks after NICE guidance has published rather than the 12 weeks referred to in the draft manual.

Our response and changes to the manual

In response to the requests made by stakeholders during the consultation, we have made changes to the draft manual to provide additional clarity. More information has been added about timelines, roles and responsibilities, and we have confirmed the documentation that companies will have access to. The requirement for a simple PAS to be the default commercial option has been given more prominence in the manual, alongside more references to commercial and managed access proposals during the early stages of guidance development. We have also confirmed that the existing commercial and managed access processes are designed and intended for the evaluation of medicines and have sought to make this clearer in the wording. We have amended the timeframe for which a rapid review can be considered after NICE guidance publication and set this to be 16 weeks (instead of 12). The process for selection of experts involved in commercial and managed access activity mirrors that used in the main guidance development process. To reduce unnecessary content duplication, this information has been removed from the commercial and managed access section, and the reader pointed to the appropriate section in the manual for further information.

The final unified manual outlines an aligned single process for guidance reviews for technologies to be re-assessed at the end of a period of managed access. The existing separate CDF review process will be discontinued. The full review process for managed access will include an update to the scope for the original appraisal (and associated consultation). Depending on the level of changes to the scope, NICE may choose to hold a short 14 day consultation on the new scope.

The manual also now includes clarity as to the approach that may be taken following the first evaluation committee meeting with regard to commercial proposals and the opportunity to efficiently consider how a draft negative recommendation could be changed into a positive recommendation avoiding the requirement for public consultation. This additional information aims to manage expectations, increase transparency and find ways to expedite decision making, accelerating patient access to new technologies.

NHS England and NHS Improvement and NICE are currently jointly consulting on the impending [Innovative Medicines Fund (IMF)](https://www.engage.england.nhs.uk/consultation/imf-engagement-on-proposals/consult_view/). This provides the policy perspective in which managed access will be considered in England. The IMF has been designed to enable patients to benefit from early access to promising new medicines building upon the significant success of the CDF, by supporting patients with any condition, including those with rare and genetic diseases, to get early access to the most clinically promising treatments when further data is needed to address uncertainties. The introduction of new assessment pathways or changes to medicines pricing policy (as proposed by stakeholders in their suggestions to use a process like the SMC ultra-orphan drug pathway or pricing arrangements used in other European countries) are outside the scope of the methods and process review.

In response to the challenge about the commissioning arrangements for managed access in current highly specialised technology topics, we have clarified that this has been misinterpreted and it must be made clear that managed access cannot be regarded as routine commissioning. Access is granted on an interim basis for the duration of the managed access period. We have not changed the existing text of the manual but have added this as a point of clarification.

Other

Some stakeholders noted that they had understood that changes to the Highly Specialised Technologies Programme processes were out of scope for this consultation, which is not the case. The process alignment and new ways of working proposals also covered this process (when applicable) and were included in the consultation. When published, the new process and methods manual will update and replace the interim Highly Specialised Technologies Programme process and methods statements.

Stakeholders also noted the lack of diagrams, process charts and timelines in the draft manual. They urged us to include more visual information and timelines wherever possible. As with the updates made to the topic selection manual, the final guidance development manual will be supported by additional and complementary information, such as flowcharts, on the NICE website that will be developed, updated and published when needed.

Some pharmaceutical industry respondents highlighted a lack of consistent referral to the multiple technology evaluation process. So much so, that they questioned whether this process remains an option for the appraisal of medicines. That said, these stakeholders reflected that multiple technology evaluations are complex and burdensome and challenged whether they indeed generate efficiencies during the guidance development process. NICE maintains that multiple technology evaluations are indeed resource efficient but that we recognise the use of this process is not appropriate for all technologies that need guidance. They are particularly beneficial for products coming to market in the same indication in a relatively short time period, and also for review updates of multiple individual single technology appraisals.

Industry also reflected on the support that clinical experts are given to effectively engage in the guidance development process. Industry respondents suggested that support for clinical experts should mirror that provided for patient experts, emulating the wide success and recognition of the NICE Public Involvement Programme.

Methods

Summary

In this stage of the methods review, we considered the responses from the consultation, updated the draft manual, and developed plans to implement the new methods. In this section, we describe the final conclusions reached and why. More information will be presented in an appendix and in accompanying documents on the consultation response, implementation of the changes, impact assessment and future plans, which will be published after this report.

In the consultation, we received a wide range of views from across those interested in our work. Many, but not all, responses agreed with our proposals and recognised important benefits from the changes. We considered in detail the questions and concerns that were raised, which included:

* The overall size and effects of the changes – for example, the additional weight given to health benefits in the most severe conditions (the ‘severity modifier’) and the proposal not to change how we think about costs and benefits that arise in the future (the discount rate). We emphasise that NICE’s methods must strike a balance within our broad responsibilities in supporting innovation, ensuring value for money, and protecting patients and the NHS from the potential knock-on effects of additional costs.
* Specific issues on topics including how we are aligning our methods for different types of evaluation (such as medicines, medical devices and diagnostics), the proposed changes to how we value the benefits of medicines and other health technologies, and the proposed changes to how we look at different types of evidence (such as real-world evidence, health-related quality of life [HR-QoL] and costs).
* How we will implement the new methods. We have developed a document to accompany the manual describing a range of activities to support people in using the new methods, which will be published after this report.
* How we will keep the methods up to date in the future. We have developed another document to accompany the manual describing how we will design our future updates and involve people and organisations in that process, which will be published after this report.

Our final conclusions are:

* We will give additional weight to health benefits in the most severe conditions (a ‘severity modifier’), using the approach proposed in the consultation and using weights of 1.2 and 1.7 as the lower and higher weights (‘option 1’ in the consultation). The additional considerations for life-extending treatments at the end of life (the ‘end of life criteria’) have been removed.
* No changes have been made to how we consider health inequalities – this is an important and complicated area to include in our methods, and more work is needed.
* We have clarified how we will handle ‘uncertainty’, particularly in circumstances when evidence from research trials or elsewhere is especially difficult to generate.
* No change to the discount rate has been made. We will collect evidence on the effect of discounting in future health technology evaluations, to help us contribute to further discussions on this issue.
* The draft manual has been updated, to make sure it is clear, robust and appropriate for different types of evaluation. This includes:
	+ better information about how we will use real-world evidence
	+ clearer descriptions of how to measure HR-QoL when our preferred tool (the EQ-5D) is unsuitable, and on the correct prices to use for medicines

other updates that are particularly relevant for medical devices and diagnostics.

Overview

This review represents the latest iteration of NICE’s methods of health technology evaluation. It combines our existing, well-established methods and more than 20 years of health technology evaluation experience with a detailed review of the latest methods research and policy developments, to ensure our methods remain robust, up to date and fit for the future. At the same time, it presents an opportunity to align our methods across our health technology evaluation programmes, and ensure they are flexible and adaptable for all health technologies and circumstances. Through this review, we present a broad package of methods improvements with benefits across the health and care ecosystem – including prompt access to health innovations for patients, responsive, flexible and predictable evaluations for the life sciences industry, and robust, fair and evidence-based access for the NHS. Key developments in how we value the benefits of health technologies and further support for a comprehensive evidence base combine to ensure NICE evaluations continue to support prompt, equitable and evidence-based access to valuable innovations, now and into the future.

Building on the first 2 stages of the review (the case for change and the proposals for change), this stage of the methods review aimed to:

* review stakeholders’ comments on the proposed changes and draft manual and make changes when needed
* review the draft manual in full and develop it into a refined, aligned final manual ready for implementation
* develop an implementation plan
* start planning for future methods updates – ensuring the methods and processes remain responsive, adaptable and future proof.

The [methods review consultation paper](https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/chte-methods-and-processes-consultation) proposed a broad range of updates to our methods, building from 56 cases for change across 5 topics into consolidated and aligned methods changes. It was presented alongside a [draft programme manual](https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/nice-guidance/chte-methods-and-processes-consultation/health-technology-evaluations-manual.docx) for illustration. The consultation focused in particular on:

* valuing the benefits of health technologies: the severity modifier, uncertainty, health inequalities, aligning modifiers across programmes and discounting
* understanding and improving the evidence base: implementing the proposed changes on evidence and HR-QoL, real-world evidence, and costs
* other methods topics and proposals.

Stakeholders were asked to comment on the extent to which they agreed or disagreed with the proposals, and were given the opportunity to provide detailed comments and responses.

This paper gives an overview of the findings from the consultation, our response, and the associated activities and outcomes from the review. In addition, as part of this final phase of work, we will also publish:

* An appendix, which provides additional details and discussions for key topics raised in this stage of the methods review, underpinning the conclusions and the final methods presented in the programme manual.
* The programme manual, which represents our finalised methods for implementation. It builds on all the work that contributed to the review, including the valuable contributions from stakeholders and the public through the working group, steering group, task and finish groups and consultations.
* An implementation paper, which explores challenges and presents activities and resources to support implementation of the updated methods.
* An impact and equality impact paper, which describes key issues on the effects of the final methods on patients, the life sciences and the NHS, and discusses issues of equality and fairness within our legal and ethical duties.
* A future perspectives paper, which outlines key considerations for the next iterations of methods and process reviews and continuous improvement of health technology evaluations at NICE in the future.

Findings from the consultation and our response

A full analysis of the consultation responses received is presented in the second consultation response task and finish group report that will be published after this report. The analysis focussed primarily on the detail of the written responses; quantitative analysis of the extent of agreement with the proposals primarily informed initial signals for areas of concern and operational aspects (such as resources and prioritisation) of the full review.

Responses to the consultation were reviewed in detail, taking into account the range of overall support by stakeholder type, evidence and reasoning presented. From this, we explored potential actions and changes to the methods when appropriate. In this document we focus specifically on the key topics and areas of concern; additional issues that were raised but that are not shown in this document were considered but no further discussion was needed. This section gives a summary of the findings from the consultation and our response.

Overall findings and common themes

We received a wide range of views from across the stakeholder community. In most areas there were divergent views. Although there were common arguments and some degree of consensus particularly within stakeholder groups (for example, industry respondents), there were few clear areas of complete consensus across all stakeholders.

In general, many stakeholders agreed with the proposals and recognised important benefits from the proposed methods changes. In particular, there was broad agreement with the principles underlying the proposed changes, perhaps reflecting the value of the first consultation on the cases for change. Stakeholders did not agree with all of the proposals, and challenges were raised across several key topics. Important questions and concerns were raised, often focusing on the detail of the proposals, and these are explored in this document.

Several comments related to the overall scale and impact of the changes, and their effects on patients, access to health technologies, the life sciences and the NHS. This includes, for example, comments on the scale of the proposed severity modifier and the discussion of the reference case discount rate. It is important to note that these methods must strike a balance within NICE’s broad responsibilities across the healthcare and life sciences ecosystem, valuing the benefits of health technologies and supporting valuable innovations while also ensuring value for money for the NHS and protecting patients from risks and inappropriate displacement of care and services. In particular, when stakeholders present options that would increase costs to the NHS (such as a larger modifier or lower discount rate), we must consider the impact of such options on the NHS and the potential for care and services to be displaced elsewhere. This challenge is perhaps never more acute than as the NHS responds to the COVID-19 pandemic, and faces significant pressures and resource challenges.

Many other comments related to the implementation of the methods. We recognise this is a key challenge at this phase of the review. As a result, we present with the final methods a range of activities and resources to support implementation, ranging from training and engagement activities to resources and advice.

Stakeholders also explored future considerations, thinking ahead to how NICE will continue to keep its methods up to date and cutting edge as the health and care landscape continues to evolve. We share this view, and therefore will present a further document that explores how we will develop and shape future activities; this document will be published after this report. This includes the more dynamic, modular methods update pattern we have previously espoused, as well as ongoing monitoring, evidence collection and research to inform such updates. Stakeholders queried how they could participate in such future activities, and we will make sure that broad and active participation from across the stakeholder community is built into our plans.

Aligning the methods across health technology evaluation programmes

An important objective of this stage of the methods review was to update and refine the draft manual, to ensure it is appropriate, relevant and aligned across NICE’s health technology evaluation programmes. Stakeholders raised queries about the alignment of the methods and the implications for medical technologies and diagnostics evaluations in particular.

* The draft manual has been refined and rebalanced throughout, to ensure the methods are clear, robust and appropriate for different types of evaluation.
* Particular updates relevant to medical technologies and diagnostics have been incorporated. These include clarifications and refinements to terminology and additional details on the types and uses of evidence in medical technologies and diagnostics contexts.

Severity of disease

Stakeholders expressed a broad range of views on the proposed modifier for the severity of disease. Many supported the introduction of a severity modifier and recognised its value. Issues raised included the overall size of the modifier (including the principle of ‘opportunity cost neutrality’), its design (including the cut-offs for absolute and proportional shortfall, the QALY weights applied, the dataset used to generate the modifier, and issues of fairness and equality), and how it will be implemented in practice.

Size of the modifier

Several stakeholders commented on the overall size of the proposed modifier, and its effect on access to health technologies and health technology pricing. In particular, some stakeholders proposed that we should adopt a larger modifier, and argued that the 2019 Voluntary Scheme meant that this would be possible without additional spending or cost impacts on the NHS.

As described in section 104, the methods must strike a balance within NICE’s responsibilities, including in supporting innovative health technologies and in ensuring effective use of NHS resources. This means that we must consider both the advantages of the severity modifier in valuing health benefits and innovation in severe diseases and the effects of healthcare displacement and opportunity cost in the NHS. Importantly, while the 2019 Voluntary Scheme is a valuable agreement with important benefits for the health system, it does not remove the need for robust, evidence-based health technology evaluations, and it does not eliminate the potential displacement effects and opportunity costs of introducing new health technologies. Having considered the consultation responses in detail, we conclude that the proposed size of the severity modifier, based on opportunity cost neutrality compared with the end of life modifier, provides an appropriate balance between the importance of valuing severity and the displacement impact on the NHS.

Design of the modifier

The consultation revealed broad support for the overall design of the modifier based on proportional and absolute QALY shortfall and corresponding cut-offs and QALY weights. Key concerns included the following:

* The number of steps to reflect the spectrum of severity. Although there may be theoretical appeal to a sliding scale or greater degree of granularity in the definition of severity, we consider that it would not be practical. There will inevitably be uncertainties in the shortfall calculations, but we still need to support rapid, predictable and consistent decision making, efficient commercial negotiations and timely patient access. We conclude that the 2-step modifier strikes an appropriate balance between reflecting the range of severe conditions and the practicalities for implementation in practice.
* The cut-offs and weights applied within the modifier. Because of the principle of opportunity cost neutrality (confirmed in section 110), any change in cut-offs or weights would mean compensatory changes elsewhere, and so would be difficult to justify.
* The dataset used to calculate the average QALY weights. We acknowledge the data has some uncertainties, particularly because it uses retrospective data to inform a future modifier. For completeness, we expanded the dataset to cover a wider date range (January 2009 to March 2021; 99 additional decisions). This did not change the conclusions from the data. The additional analysis is reassuring, and provides no signal that a change in QALY weights or cut-offs is needed.
* Concerns about fairness and equalities. Stakeholders raised concerns particularly about age, and we also explored wider questions including the effects of disability. Analysis of past appraisals showed no clear age profile in the modifier, and this was not changed by alternative cut-off options. We conclude that the proposals do not create inappropriate unfairness on the basis of age, and that there is no signal that a change in modifier design or shortfall cut-offs is needed. We also conclude that there are no additional equality concerns for disability associated with the proposed modifier.

Having established that there is no case to depart from the principle of opportunity cost neutrality and no case to reconsider the weights and cut-offs proposed in the consultation, we need to establish a preferred weighting profile from the 2 options presented for consultation. The consultation comments provided no clear mandate to choose between the options. On balance, option 1 has the benefits of retaining the maximum QALY weighting used for end of life, and ensures some degree of consistency between end of life and the most severe conditions.

Implementing the modifier

Stakeholders raised a range of questions about how the proposed modifier would work in practice. Detailed discussion of how the methods will be implemented, and the support and activities in progress, will be published after this report. We have explored several details for how the modifier will be calculated and used.

* **Data sources for calculating QALY shortfall:** A recent and robust source of population HR-QoL and survival should be used in the calculation; we do not specify a preferred source at this stage. It is reassuring to note that QALY shortfall is not sensitive to the choice of population EQ-5D or survival data source.
* **Aligning modifiers across programmes:** We note stakeholders concerns about the severity modifier not being applied outside the Technology Appraisals Programme, but no case to reconsider our approach was identified.
* **Challenging circumstances:** Questions were raised about how the severity modifier would operate in various complex and challenging circumstances, including for subgroups, multiple comparators, when there is uncertainty and when EQ-5D is not appropriate. The methods manual sets the fundamental principles on which the severity modifier operates, but does not aim to specifically describe all possible circumstances and scenarios. Rather, it is appropriate that the committee considers each evaluation individually, taking into account the specific circumstances, evidence and context for each topic.

Conclusion

Based on our detailed exploration of these issues, we conclude that the proposed severity modifier will be introduced as a quantitative modifier that gives additional weight to health benefits in the most severe conditions (table 1). It is based on the principle of opportunity cost neutrality as an appropriate and relevant consideration, and uses the QALY weights proposed in ‘option 1’ in the consultation (that is, 1.2 and 1.7 for the lower and higher weights). The additional considerations for life-extending treatments at the end of life (the ‘end of life criteria’) have been removed.

Detailed discussion of how the severity modifier will be implemented and the support and activities in progress will be published after this report.

Table 1. Final severity modifier cut-offs and QALY weights

|  |  |  |
| --- | --- | --- |
| QALY weight | Proportional QALY shortfall | Absolute QALY shortfall |
| 1 | <0.85 | <12 |
| x1.2  | 0.85 to 0.95 | 12 to 18 |
| x1.7 | ≥0.95 | ≥18 |

Health inequalities

Stakeholders supported the view that health inequalities are an important consideration but that more work is needed before a formalised modifier could be introduced. No changes have been made. It may be appropriate to prioritise health inequalities in future modular updates.

Stakeholders also raised rare diseases in the context of health inequalities. They argued that there was a case to reconsider adding a modifier for rare diseases. However, our evidence review previously found that there was no evidence that society values more highly health benefits in rare diseases, and the information presented during consultation does not provide evidence to support adding a modifier for rare diseases. Other elements of the methods review (including the severity modifier, flexibility in uncertainty considerations and the emphasis on a comprehensive evidence base) will mitigate the challenges faced by rare disease technologies. No changes have been made.

Uncertainty

Stakeholders generally supported the proposals to clarify the additional flexibility in considering uncertainty when evidence generation is difficult. They raised questions about the implementation of the considerations in practice, which will be addressed through implementation activities. These may include worked examples, training and resources. We acknowledge the importance of ensuring the methods for uncertainty are robustly and consistently used by committees and are transparently reported.

Some stakeholders requested additional clarity or precise definitions for the circumstances in which the additional flexibility can apply. This is not possible in the confines of the methods guide, and these concerns highlight that the draft manual was not fully clear. The acceptance of greater uncertainty is a deliberative decision for committees. They will decide whether to accept uncertainties based on an understanding of how those uncertainties have arisen and how they relate to challenges in generating evidence and the circumstances in which such challenges occur, rather than simply applying flexibility in an all-or-nothing fashion if a particular criterion is met. As a result, we have refined the description of the circumstances in which additional flexibility can be applied. Additional text has been added to clarify when and how additional consideration of uncertainty when evidence generation is difficult should be applied, focusing on how and why the uncertainty has arisen and the association with the nature of the condition and/or technology.

Stakeholders also commented on issue of visualisation tools for uncertainty to support decision making. We agree this could be a valuable resource, which may be appropriate to prioritise as an implementation and ongoing development activity. We have developed further ideas and scheduled additional engagement events to develop and refine this approach.

Discounting

The consultation highlighted substantial disagreement with the proposal to retain the current reference case rate of 3.5%, particularly from the pharmaceutical industry and patient groups. Concerns included the alignment with the evidence case and the HM Treasury Green Book, links to policy developments, and the effects of maintaining the current discount rate. Conversely, academic stakeholders, NHS organisations and NICE committee members were more supportive of retaining the current discount rate, and acknowledged the need for further work and coordination with other health bodies.

Some stakeholders queried the policy and financial implications and interdependencies highlighted in the consultation.

* One of the most visible system implications of a change in discount rate for NICE health technology evaluations is the financial impact. Reducing the discount rate will make most technologies appear to be more cost effective. In the absence of a change in the level at which technologies are considered cost effective, this would likely lead to higher prices for those health technologies, with knock-on effects on care and services elsewhere in the NHS. Some stakeholders argued that the 2019 Voluntary Scheme would allow a lower discount rate to be used without affecting NHS budgets. However, the 2019 Voluntary Scheme does not remove the need for robust evaluations nor eliminate displacement effects from additional spending on health technologies. Given NICE’s responsibilities to the NHS and patients (to consider the broad balance between the benefits and costs of providing health services or social care in England) and the tight funding and resource constraints facing the NHS (particularly as we respond to the COVID-19 pandemic), the financial impact of the discount rate must be taken into account.
* Another important consideration is that of consistency between different parts of the health technology evaluation system, and in how different health technologies and health interventions are evaluated. Such interactions and interdependencies go beyond the reach of this methods review alone.
* Stakeholders noted the importance of the discount rate for innovative technologies such as ATMPs and, by extension, rare diseases. This effect has already been considered in the methods review, and no new information was identified in the consultation.
* It was suggested that we could apply a 1.5% discount rate to selected technologies or circumstances, perhaps as a ‘pilot’. Such an approach would carry the same policy and system implications and interdependencies as a change in the reference-case rate. Therefore, a selected or pilot application of a 1.5% discount rate is not appropriate.

Overall, we believe that no new information has been identified that was not previously considered, and therefore there is no case to depart from the previously established position. We therefore maintain our view that there is an evidence-based case for changing the reference-case discount rate to 1.5% for costs and health effects, but because of the wider policy and fiscal implications and interdependencies that are beyond the reach of this review, no change to the reference-case discount rate can be made.

NICE will contribute to system-wide and policy discussions regarding discounting through established channels and ongoing collaborations with stakeholders and health system partners. To support our contribution to such discussions, we will prospectively collect evidence on the effects of discounting (for example, on ICERs and prices) in evaluations.

Understanding and improving the evidence base

Stakeholders raised queries about the methods relating to real-world evidence, HR-QoL, surrogate outcomes and costs.

* The draft manual has been updated to refine the recommendations on real-world evidence, to create a better balance between different types of technology, contexts and use cases for real-world evidence. We have also updated the manual to improve the balance between prospective data collection and evaluation of existing data. Real-world evidence remains an active area of interest for NICE, with significant work ongoing across the institute, and the manual directs readers to ongoing work supporting real-world evidence across NICE, such as the real-world evidence framework.
* Stakeholders accepted the proposed hierarchy for measuring HR-QoL when the EQ-5D is unsuitable, but queried the evidence requirements particularly for rare diseases. The methods correctly set clear evidence requirements for showing the EQ-5D is not appropriate, and the hierarchy is retained. However, clarification of flexibilities in the evidence requirements has been added to avoid inappropriate barriers when evidence generation is challenging.
* Stakeholders commented on the evidence requirements for surrogate outcomes. We consider that the manual provides appropriate detail on the evidence requirements, and includes appropriate flexibility. No further changes are needed.
* Stakeholders commented that, when sourcing evidence on prices for medicines with price discounts other than PASs (non-PAS prices), the prices used should be nationally available, stable and agreed for the duration of the appraisal. We reemphasise the critical principle that the prices used in a health technology evaluation should reflect as closely as possible the prices that are paid in the NHS, but acknowledge the proposed wording was not fully clear. Changes have been made to the manual improve clarity and reduce ambiguity.
* Clarifications have been incorporated for how evaluations should use reference-case and non-reference-case analyses for technologies that extend survival in populations for which the NHS is providing high-cost care, and for technologies for which costs may be apportioned or adjusted. Stakeholders raised conflicting concerns about these scenarios, with some expressing concern that the methods would not be used whereas others considered that the permitted circumstances were too broad. The changes highlight that both reference-case and non-reference-case scenarios should be presented together, and both should considered in decision making. The wording has also been strengthened to support implementation of the non-reference-case analyses, including details of what factors may go into the consideration of reference-case and non-reference-case scenarios.

Implementation and future considerations

Summary

As we reach the end of this review, we are considering next steps, including:

* how we use the updated methods and processes
* what effects they will have
* how we make sure our methods and processes stay up to date in the future.

An assessment of the effects of this review, and issues of equality and fairness, will be available in a separate report that will be published after this report.

The new methods and processes will be used for all new evaluations (including reviews) starting after the new programme manual is published. We will present a range of activities and resources to help people use the new methods, including worked examples and case studies, training sessions and webinars, templates, and other resources and advice.

In the future, we will continuously improve how we do health technology evaluations, using smaller ‘modular’ updates. We will design procedures for these future updates, making sure we involve people from across the stakeholder community. We will also monitor the use of the new methods, and support further research as needed.

Introduction

The final programme manual and topic selection manual mark the culmination of one of NICE’s largest reviews of its processes and methods of health technology evaluation. The manuals build on more than 20 years of successful evaluations and more than 2 years of detailed scrutiny and review spanning all aspects of methods and processes, providing a robust foundation for our evaluations now and in the future.

Nevertheless, this is not the end of the story. In the short term, we are exploring the impacts and benefits of the updated methods and processes, as part of a comprehensive programme to ensure the new methods and processes are used consistently and effectively to realise those benefits for NICE, the NHS and the stakeholder community. In the longer term, there will remain a need for NICE to continue to monitor, review and improve its methods and process into the future, making sure our methods, processes and guidance remain cutting edge as the healthcare landscape continues to evolve.

Impact and equalities

Throughout this review we have considered the impacts of proposed changes on all parts of the health and health technology ecosystem. As we finalise the programme manual, we have considered again those impacts both individually and as a whole package. Further discussion of the impacts of the methods and process changes will be provided in the impact report, which will be published after this report.

Of particular importance is the impact of the proposals on equalities and fairness, and on our moral and legal duties to eliminate discrimination and promote equality. Again, this has been a critical consideration throughout the review, to ensure our proposals are fair, ethical and lawful. Discussions of equality issues in the earlier stages of the review can be found in, for example, the task and finish group reports that accompanied the case for change, the case for change consultation paper and the proposals for change consultation paper. Further details will be provided in the impact report, which will be published after this report.

Implementation

 The new methods and processes will apply to all new health technology evaluations that start (that is, have their invitation to participate issued) after the final programme manual is published. This includes new reviews (including post-managed access reviews). Evaluations that are ongoing when the new manual is published will continue to use the methods and processes that were current at the time of their invitation to participate.

The topic selection manual will be implemented from 01 February 2022. All selection and routing decisions will be applied prospectively to topics from this date forwards. The updated Highly Specialised Technologies Programme routing criteria will also be applicable from this date.

To ensure the benefits of this review are realised, it is critical to ensure the updated methods and processes are swiftly and comprehensively implemented. We also note stakeholder comments during response to the consultation, particularly from industry respondents, which asked that NICE sets out how it intends to ensure that the policies, processes and methods changes are consistently adopted as intended by the individual committees; similar considerations apply to all other participants and stakeholders in evaluations.

To this end, we will present a broad package of activities and resources to support effective implementation of the updated methods and processes. This is already underway and will continue through 2022, in parallel with the new methods and processes operating for new topics starting after the final manual is published. This will include:

* worked examples and case studies – for example, exploring key challenges for using the severity modifier in practice
* training sessions – aimed at different parts of the stakeholder community
* templates – to ensure efficient and consistent use of the new methods and processes and clarity for all stakeholders
* additional resources and advice – to help stakeholders and committees use the methods and the methods guide; these will be helpful for stakeholders and committees to consider, but will not be fixed or binding – that is, they may take it into account or take a different approach, if they consider it appropriate.

The implementation programme will span all relevant aspects of the methods and process changes. Full details will be provided in the implementation report, which will be published after this report.

Future view: continuous improvement, monitoring and modular updates

While the updated programme manual provides a comprehensive and robust basis for NICE health technology evaluations, we will inevitably need to continue to review, refine and improve how we do evaluations in the future. Detailed discussion of future considerations, including continuous improvement in how we do our evaluations, our modular update approach, and plans for evidence collection will be provided in the future considerations report, which will be published after this report.

We described at the start of this review that this would be the last full manual update, and instead we will move to a modular format, allowing us to predict and respond to changes in the methods, policy and healthcare landscape rapidly and efficiently, as they arise. Such a modular approach is a substantial departure from our previous practice, and so will need careful consideration to establish. Considerations will include:

* how we will consider methods, process and operational issues, and the overlaps between them
* how different types of technology and evaluation (including medicines, medical technologies, diagnostics and future innovations) will be affected, and how the topic interlinks with other parts of NICE and the healthcare system
* governance, oversight and engagement, and participation with the stakeholder community
* resourcing, and ensuring proportionality of modules (that is, simple, light-touch updates for simple issues and more sophisticated and detailed updates for more complex issues)
* how we identify, prioritise and schedule potential methods and process topics, including horizon scanning for upcoming methodologically challenging technologies, and how we obtain the background information needed to inform this process.

An urgent priority is to begin to identify topics that may need modular updates. Several topics have been identified already, both through the current review and through other sources; we will review all topics in detail as we establish processes and procedures for modular updates. Potential topics might include, for example:

* processes to facilitate rapid entry to managed access, and to manage technologies with multiple indications
* methods issues for digital, genomic and antimicrobial technologies; these were identified for future modules at the outset of this review and remain relevant topics
* further methods issues, such as the societal value of health benefits in severe diseases, health inequalities, HR-QoL in children and carers, and further support for a comprehensive evidence base
* operational issues, such as presenting and visualising uncertainty, efficiency and resource use in NICE evaluations, and continuing improvement in patient involvement.

Hand in hand with our modular update approach, we will need to maintain our processes to monitor the use and impacts of our methods and support further research when needed. For example, for the methods, we will need to monitor the use of the new severity modifier in practice, and will prospectively collect evidence on the effects of discounting in evaluations. We have also explored in detail the need for further research into the societal value of health benefits in severe conditions. It will be important that the modular update approach both informs such monitoring and research, and allows us to rapidly respond to the findings when they arise.

NICE has already acknowledged the need to develop new processes to:

* facilitate rapid entry to managed access
* manage technologies with multiple indications.

The challenges we face in these areas were highlighted in previous consultation rounds and received significant support for the potential efficiencies and speed of decision making that such processes could create. This needs further engagement with stakeholders to engineer streamlined and robust processes that account for the appropriate level of risk involved in this alternative approach. As such, more time will be needed to develop this proposal. The outcome will be one of the first modular updates to be published following launch of the new unified manual.

We also place significant importance on the activity and continued success of horizon scanning and topic selection. To continue the efforts in this space, and collectively improve our approach across NICE, we will be placing a renewed focus on working to harmonise intelligence, prioritisation and topic selection techniques with the wider guidelines programme.