The Board is asked to consider a proposal.

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The response to public consultation on changes to aspects of NICE’s methods for appraising new health technologies

Introduction

1. The methods that NICE uses in its technology appraisal programme to make recommendations on the use of new drugs and other health technologies have evolved almost continuously since they were first used in 1999 and are regarded by many as the global standard. They inform some of the most difficult decisions taken in British public life and influence the care that millions of people receive when they use the NHS.

2. The debate about the detail of our methods right reignites frequently and particularly when we recommend against the routine funding of a new treatment. Most people directly involved in or affected by our work have an opinion it. Many regard our methods as a fair approach to reconciling the aspirations of patients, health professionals and life sciences companies with the resources available to the NHS. When pressed, just about everyone agrees that the NHS needs to have some system for deciding how to best use its fixed resources.

3. About every three years, we ask anyone who is interested what they think of our approach to technology appraisals. At other times, as with this consultation, we ask for views on changes to specific aspects of our methods for technology appraisal. We think that our arrangements have improved each time we have done this. However, whenever we have asked for views on the details of our approach, more fundamental questions are often asked about, for example, what the NHS should be paying for, what values should underpin our decisions, how the value of new treatments should be defined and weighted, whether innovation, as an investment for the future should be taken into account (and paid for by the NHS), and in what circumstances, if any, the NHS should be prepared to pay a higher cost for a new treatment.
4. This most recent set of proposals has caused these questions to be asked again. This may be because the title of the consultation, *value based assessment*, implied a fundamentally new approach, an expectation that might also have been raised as a result of its origins in an earlier consideration, by the Department of Health, of what was then described as *value based pricing*. However, though important, neither of the proposals at the core of this consultation represents a comprehensive overhaul of our approach to our work. Some respondents expressed their disappointment that this was the case and in various, sometimes inconsistent ways, many respondents indicated that the proposals did not address their real concerns about our work and its broader context.

5. This is not surprising since the context in which NICE frames its recommendations for new technologies is beginning to change dramatically. Upstream from a NICE appraisal, national and international initiatives to accelerate the development and regulatory approval of new drugs, medical devices and diagnostics are being put in place. The UK wants to be at the forefront of this movement, so it can deliver better access to clinically and cost effective treatments. NICE is deeply involved in these initiatives, increasing our influence on the nature of the value proposition put forward for new products. The kind of technologies that NICE will be asked to appraise is also beginning to change, with targeted therapies offering more confident outcomes for fewer patients but at a higher cost per patient.

6. In addition, downstream from the technology appraisal process and through the work of NHS England, new opportunities are beginning to emerge to better manage the entry of new technologies into the NHS. Though not limited to cancer drugs, these possibilities will be explored initially through the initiative recently announced by NHS England and the Department of Health in relation to the Cancer Drugs Fund.

7. NICE operates at the interface between the world in which new treatments are developed and the NHS in which they are used. We, more than any other national
agency, experience and have to deal with the frequently inconsistent ambitions for what the NHS should do. Although this presents enormous challenges, it also provides us with a unique opportunity to help reconcile these ambitions. We can do this by acting not simply as the appraiser but by informing and stimulating better value propositions, providing a space for innovation in both the utility of new treatments and their adoptability in the NHS, by working with NHS England and others, such the academic health science centres and networks to manage down uncertainty through carefully controlled real world studies, and by encouraging companies to develop innovative pricing schemes.

8. There is an opportunity for NICE to enhance its contribution to a more productive relationship between the NHS and the life sciences industries, to achieve a better alignment of the ambitions of those who work in both, with the expectations that the public has of its NHS. This consultation was not about this opportunity, but the response to it has highlighted the need for NICE to grasp it. Critically, it is not simply about what NICE does. Just changing our methods will not overcome the concerns that are expressed about how the NHS accesses new treatments. In particular, without simultaneous evolution of other processes and assumptions, including the model of pharmaceutical research and development, the expectations that companies and patient groups have about how risk and reward is shared between the industry and a publically funded NHS, and in the arrangements for commissioning expensive new treatments, changes to the way NICE operates will have a limited effect.

9. The issues raised in this consultation and the contribution that NICE can make to resolving them need to be considered in the context of a wider review of the way new treatments are developed, evaluated and supported for adoption in the NHS. This needs to involve all of NICE’s partners, in the patient advocacy movement, the NHS, the life sciences industries, the research communities and in academia.
The consultation proposals

10. In July 2013, the Department of Health asked NICE to take into account additional terms of reference (see Appendix A) in the appraisal of new health technologies. They were intended to supplement but not replace the approach that we currently take to assessing the clinical and cost effectiveness of new treatments. The terms of reference asked us to include a simple system of weighting for burden of illness that appropriately reflects the differential value of treatments for the most serious conditions, encompass the differential valuation of treatments designed to extend life at the end of life used in the current approach within a new system of burden of illness weights and include a proportionate system for taking account of wider societal benefits.

11. We were not asked to make any other changes to our current methods and we were specifically asked not to include a further weighting for therapeutic Innovation and Improvement (our existing terms of reference already require us to take account the potential for long term benefits to the NHS of innovation) or to change our current cost effectiveness threshold, subject to the application, in individual cases, of a number of modifying factors.

12. We made a set of proposals to incorporate these new terms of reference into our technology appraisal methods. We then asked six questions about them:

- Does proportional QALY shortfall appropriately reflect burden of illness?
- Does absolute QALY shortfall provide a reasonable proxy for wider societal impact of a condition?
- Does a maximum weight of 2.5 in circumstances when all modifiers apply function as a reasonable maximum?
- Should we allocate specific ‘weights’ to each of the ‘modifiers’ so that they add up to a maximum of 2.5? If so, do you have a view on what weight should be added in each case?
• Will the approach outlined in this document achieve the proposed objectives of improving consistency, predictability and transparency in the judgements made by our independent Appraisal Committees when they consider the clinical and cost effectiveness of health technologies?

• Are there any risks which might arise as a result of adopting the value-based assessment approach as outlined above? If so, how might we try to reduce them?

13. We proposed that proportional and absolute QALY loss values would be calculated as part of a technology appraisal and that they are used as the basis for assessing burden of illness and wider societal impact respectively. The Appraisal Committees would be asked to adopt a more favourable approach when considering treatments for people whose conditions have a progressively higher burden of illness and wider societal impact. These factors would be considered, alongside other modifiers referred to in paragraph 8, meaning that ICERs above £20,000 per QALY gained would be acceptable in circumstances where these factors are considered relevant and where absolute and proportional QALY shortfall is high.

14. We expressed the need to place an upper limit on acceptability of an ICER, because valuable care elsewhere in the NHS might be displaced without at least an equally valuable gain being achieved. This holds true even when taking into account burden of illness and wider societal impact.

15. The maximum weighting applied by the Appraisal Committees using their current flexibilities is 2.5 and this is normally only applied to end of life treatments. We expressed the belief that this represents the maximum weighting that the Appraisal Committees should consider when taking into account the cumulative impact of all the modifiers, including burden of illness and wider societal impact. While this would not extend the upper limit of an acceptable ICER, it will broaden the circumstances in which an ICER above the £20,000 baseline might be acceptable.
16. During consultation we held three stakeholder engagement sessions with patients, industry and NHS professionals. We also met with Patients Involved in NICE, and presented the proposals at a number of conferences (such as NICE annual conference, Health Technology Assessment International, and PharmaTimes).

The response we received

17. We received more than 900 comments from 121 organisations and individuals; their response totaling over 300 pages. The life science industry and patient groups each made up approximately a third of the responding organisations. The majority of the rest were from academics and clinical/professional organisations, with the remaining response from a small number of health technology assessment agencies, NHS organisations (including NHS England) and the English Department of Health.

18. We scored the response to each of the questions as a ‘yes’, ‘no’, or ‘partial’. There was a mixed response to the questions. The responses to question 1 (does proportional QALY shortfall appropriately reflect burden of illness?) showed a relatively consistent split across the categories (33% commenting 'yes', 28% 'no' and 39% 'partial'). The majority of responses (59%) to question 2 noted that absolute QALY shortfall did not provide a reasonable proxy for wider societal impact of a condition (with 10% 'yes' and 31% 'partial'). For question 3, 73% of responses noted that a maximum weight of 2.5 in circumstances when all modifiers apply did not function as a reasonable maximum, with 12% responding that it was a reasonable maximum, and 13% were 'partial'. The majority of responses (79%) to question 4 noted that we should not allocate specific weights to each of the modifiers, to a maximum of 2.5, with 5% responding that we should allocate specific weights and 16% of responses were 'partial'. Similarly, 72% of responses for question 5 were that the approach would not achieve the objectives of improving consistency, predictability and transparency in the judgements made the Appraisal Committees, although some agreed it would (2%) and some responses were 'partial' (26%). All responses to question 6 agreed that there were
risks which might arise as a result of adopting the outlined approach for value-based assessment.

19. There was no consistent response to any of the questions.

20. All the comments received during consultation will be available on the NICE website (X).

The responses in more detail

Burden of illness

21. The large majority of respondents in both the industry and patient categories argued for retaining ‘end of life’ as a stand-alone modifier. Many commented that only when it is shown that a different approach leads to the same, or similar, outcomes should NICE consider replacing it. Moreover, once a comparative analysis is performed, and if an alternative approach is still preferred, most stressed the need for further consultation.

22. A number of respondents raised the concern that an approach to burden of illness based on QALY shortfall re-enforces existing problems with measuring quality of life using QALYs and EQ-5D, and that such an approach continues NICE’s reliance on QALYs. Others commented on the potential for counting existing value elements twice. Others query how the impact of the condition on carers’ and families’ health related quality of life are captured in the QALYs lost.

23. A mixed view was expressed about whether proportional or absolute QALY shortfall should be used to define ‘burden of illness’. While a significant number of respondents supported the use of proportional shortfall, some argued that it would disadvantage conditions with a delayed diagnosis, that an approach to burden based solely on it would ‘imply a large and unjustified discrimination against younger people’ and that it would result in a system that would be heavily biased in favour of terminal illnesses. Others considered absolute shortfall to intuitively better reflect the severity of the condition, and appropriately reflect the notion that
‘a year of life in good health for an older person is worth just as much as for a younger person, and vice versa’, and proposed for it to be used for all but ‘end of life’. A small number of respondents suggested using both proportional and absolute QALY shortfall in the deliberations by Committee.

**Wider societal impact**

24. Some respondents agree that using absolute shortfall allows for a pragmatic approach to reflect on the societal impact of a condition, but that it would also necessitate a greater flexibility in the other types of evidence to be submitted, including qualitative evidence from family and carers. Others argue that ‘participation’ is already captured in the measure of quality of life - ie ‘usual activities’ in the EQ5D. Some raise the concern that the same absolute shortfall of, say 10 QALYs, can come from either just a loss of length of life, or just a loss of quality of life, or from a combination of the two, with quite different implications for potential participation in society, but that the proposals don’t appear to have accounted for this.

25. Despite the reassurances in the consultation document, most respondents were anxious, that by using absolute QALY shortfall as a proxy for wider societal impact, the potential for age discrimination remains. Others note that absolute QALY shortfall as defined doesn’t capture the impact of a condition on those supporting the patient - family and carers - and that it isn’t clear how co-morbidities will be dealt with. One respondent suggests that appropriate calibration of this measure would be required in order to ensure that the weight given to it in an appraisal reflects the benefits that the medicine can provide.

26. A number of respondents caution that the non-linear relationship between changes in an individual’s health and the wider impact this has on their ability to contribute to society is invisible in wider societal impact as defined in the proposals; that is, a particular amount of QALY shortfall doesn’t have an equal impact on societal contribution.
27. Although most respondents agree that the approach explored for ‘wider societal benefit’ (the approach not favoured in the consultation document) would be incompatible with the work of NICE, many are nevertheless concerned that that the wider societal impact approach doesn’t recognise the wider benefits a new medicine might bring, and argue that where such evidence exists, including ‘productivity effects’, submission should be allowed and considered. The fact that impacts of treatment on wider society would not be explicitly measured or captured, leads to one respondent to argue that the proposals in this area are not fully compatible with the Terms of Reference for Value Based Assessment. As an alternative this respondent suggested to consider using improvements in health related quality of life as a proxy for wider societal impacts.

28. A number of respondents note that when both proportional and absolute QALY shortfall are used, but for different modifiers, this could lead to potential double counting.

**Weights to be applied**

29. Respondents from industry generally argue for any one of the modifiers to be able to command the maximum weight, rather than the combination of all modifiers. Furthermore, they do not support the use of a fixed weight of 2.5 which cannot be exceeded in appropriate circumstances, at the discretion of Appraisal Committees, noting that the cap is arbitrary and that there is no theoretical or empirical evidence supporting it. Other respondents also comment that setting the maximum weight at 2.5 would effectively cap the maximum acceptable cost per QALY at £50,000, which in their mind conflicts with evidence from the Office of Health Economics\(^1\) that suggests that NICE has issued positive recommendation for technologies with incremental cost effectiveness ratios in excess of £50,000/QALY. Moreover, they express concern that this cap would mean an

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effective reduction in the threshold for end of life treatments (which tend to occur later in life when the absolute QALY shortfall may be smaller).

30. Some point to experiences in other countries, in which the World Health Organisation’s view that the basic cost effectiveness threshold should be within the region of 1 to 3 times the Gross Domestic Product per capita', has been applied. Some respondents, referenced the approach used in the Netherlands where a maximum incremental cost effectiveness ratio of up to around £65,000 is used, taking into account burden of illness. Others note that recent evidence suggests that the 'true' opportunity costs of investing in a new treatment is £13,000/QALY, referring to the work by the Centre for Health Economics in York².

31. Some respondents note that the consultation document shows the lower end of the threshold at £20,000/QALY, when in their mind NICE has in practice been operating at the upper end of £30,000/QALY, citing again the study by the Office of Health Economics referred to above. A number of these respondents further suggest that a 'rigid, fixed, upper limit' should not now be required because of the provisions of the current PPRS agreement to 2018.

32. A number of respondents are concerned that the proposals don’t allow for weights that could be 'negative' or below a weight of 1 for conditions where the burden of illness or wider societal impact are lower than for the average displaced treatment. They argue that this will lead to NICE approving more treatments than the NHS can afford. Others go as far as suggesting that the proposals fail to address a key aspect of the Terms of Reference; 'displacement', the notion that with fixed resources, any new technologies adopted in the NHS displace something already being done.

33. The Department of Health's advice to NICE in consultation is that: *Better access to effective medicines is a priority for the Government and, in the context of the*  

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agreement of the Pharmaceutical Price Regulation Scheme 2014 (PPRS), the Department has agreed that the baseline cost-effectiveness threshold will be kept at a level consistent with the current range (c.£20,000-£30,000 per QALY subject to the application, in individual cases, of a number of modifying factors) for the duration of the agreement. This is possible [largely] because of the financial protection offered by the limit in the growth in most NHS spending on branded medicines agreed as part of the scheme. Moreover, while it is generally accepted that society places greater value on treatments for the patients with the greatest need, and recognition of this view is reflected in the current threshold range, the Department is not aware of any basis in evidence for extending the range beyond the current limit – which could impose significantly greater costs on the rest of the NHS, particularly in the long term. We want to make sure we get the best possible results for all NHS patients with the resources we have — which means using taxpayers’ money responsibly and getting good value for money. In keeping with this, the Department considers that, for the majority of appraisals, the maximum weight to guide the work of Appraisal Committees should remain, as now, no higher than around 1.5 times the lower boundary of the current cost-effectiveness threshold range. [As noted above,] the Terms of Reference set out that the current End of Life flexibilities should be retained within a wider framework of burden of illness weights, and the Department would support retaining a maximum weighting no higher than 2.5 times the lower boundary of the current cost-effectiveness threshold range only for technologies that meet the End of Life criteria, consistent with the current position ... The best available evidence indicates that the current cost-effectiveness threshold range includes a substantial premium above the cost-effectiveness of alternative uses of NHS funds. In the context of the 2014 PPRS, the current threshold can be seen as a strong incentive for innovation.’

34. Other comments received in this respect suggest for more extensive use of 'multi criterion decision analysis', and for a net benefit approach to presenting cost effectiveness evidence. One respondent notes that the Department of Health’s Economic Evaluation Policy research Unit (EEPRU) work that underpinned the
preference for 'burden of illness' revealed that this was a relatively weak preference and that a much stronger public preference favouring those who would experience a large QALY gain was expressed, by the respondents to the EEPRU survey and hence, this respondent argued, the additional modifiers should receive a low weighting compared with the base case results.

35. A large number of respondents call for further research to help with establishing the individual weights to be applied to each of the modifiers, including an evaluation of the implications of using weights (for HTA outcomes, innovation and patient care). Many also call for involvement of patients and the public in these further explorations, and for further consultation if weights are to be applied to individual modifiers. Some argue that certain modifiers should not be given a weight (i.e. ‘(un)certainty’), while others should receive a relatively low weight to acknowledge the uncertainty in social preferences for the modifiers.

Other matters

26. A number of respondents warn that EQ5D doesn’t capture all relevant health related quality of life impacts of a condition, and hence this should be accounted for in proposals too. Others are concerned that supplementing the QALY analysis with any modifiers risks double counting, or cancelling out of effects.

27. A number of respondents call for the addition of 'rarity' as an additional modifier.

28. Industry respondents call for further exploration of the 'innovation' modifier, with at least one suggesting that this should include consideration of the 'promising innovative medicine (PIM)' designation that will be issued as part the new Early Access to Medicine Scheme in England.

Risks and benefits

30. A large number of respondents value the potential for a more transparent system because NICE currently operates four Appraisal Committees. Some note that whilst the proposed approach is theoretically simple, it is not necessarily
transparent or equitable, and is poorly equipped to deal with complexities. Others propose that the scoping stage should be enhanced to discuss each of the modifiers and their potential to contribute to the resulting decision, and for clear communication tools to be developed for stakeholders and Committees.

31. Finally many respondents consider that without having been presented with an impact assessment of the proposals, it is difficult to comment on the potential risks and benefits. Some point to the need for a system to cover the gap that will be left when the Cancer Drugs Fund expires in 2016. Others warn of the opportunity cost of an increase in positive appraisals, which would reduce the remaining discretionary spend of the NHS. Some caution that industry should not be incentivised to price at the maximum or be rewarded for not properly collecting the relevant evidence.

37. Following the Working Party meeting the Department of Health clarified that their response should be interpreted as indicating that the ‘end of life’ modifier is to be considered after all others have been taken into account, as it is now, rather than considering the ‘end of life modifier’ as an alternative to all others. Furthermore, it clarified that it would have expected for most modifiers to allow for scores that are lower than zero. This would reflect the fact that a score of ‘zero’ indicates the margin beyond which an investment would result in health lost - the ‘opportunity cost’ - and hence lower scores should result in acceptance of ICERs lower than the chosen lower end of the threshold range for cost effectiveness.

Conclusions

38. Broad support was expressed for the incorporation of burden of illness as one of the criteria to be considered, but respondents were not agreed on the way this criterion should be measured, and valued.

39. The Department of Health has advised in its response to the consultation that it now wishes us to retain the current approach in which a QALY weighting is
applied to drugs designed to extend life at the end of life (the ‘end of life treatments protocol’).

40. Although most respondents welcomed consideration of the wider impact of technologies, few felt that the proposal to use wider societal impact of the condition, using absolute QALY loss as a proxy, was the right approach. No support was expressed either for the alternative wider societal benefit approach.

41. Although their reasons varied, few respondents supported the proposal to extend the application a maximum QALY weight of 2.5 for the combined effect of all proposed criteria, for all treatments. Some regarding it as too restrictive and others too generous.

Next steps

42. The Board is recommended that:

43. No changes to the technology appraisal methodology should be made in the short term. This will meant that the current End of Life treatments protocol will be retained in its current form.

44. Using the response to consultation, further consideration should be given to the use of QALY shortfall as a means of quantifying burden of illness.

45. Taking into account the response to consultation, the desirability and practicality of incorporating wider societal benefits into the appraisal methodology should be reviewed, in conjunction with the Department of Health.

46. The further consideration of burden of illness and wider societal benefits should be taken forward in the context of the broader consideration of the way in which new treatments are developed, evaluated and supported for adoption in the NHS described in the introduction to this paper. NICE should explore ways of stimulating this review in conjunction with its partners and with the Department of Health.
Appendix 1

Terms of Reference to NICE from the Department of Health

The methods for value assessment of branded medicines under VBP should:

- Be applied to medicines within the scope of the VBP system, and incorporated into the methods for other categories of guidance at NICE’s discretion
- Adopt the same benefit perspective for all technologies falling within the scope of VBP, and for displaced treatments (1)
- Be as transparent and predictable as possible
- Be informed by the best available evidence
- Include a simple system of weighting for burden of illness that appropriately reflects the differential value of treatments for the most serious conditions (2)
- Encompass the differential valuation of ‘End of Life’ treatments in the current approach within the system of Burden of Illness weights
- Include a proportionate system for taking account of Wider Societal Benefits
- Not include a further weighting for Therapeutic Innovation and Improvement
- Produce guidance for patients and the NHS which describes the clinical and cost effectiveness of the technology and its position in clinical practice

(1) That is, the value of a new treatment is considered net of the value of what is displaced, and the valuation methodology is applied consistently across treatments, including where the net value impact in respect of an element of VBP may be negative
(2) For example, using a simple percentage weighting that is proportionate to the QALY loss suffered by patients with the condition
(3) The perspective adopted for measuring Wider Societal Benefits should, in principle, be as set out in the HMT Green Book for Appraisal and Evaluation in Central Government - which specifies the cross-Government approach for evaluating costs and benefits of spending decisions. However in practice it will be important to reflect uncertainties in the evidence for the magnitude of Wider Societal Benefits, the novelty of the approach, and the degree of consensus among stakeholders. Options may in practice include constraining the weight given to different elements of Wider Societal Benefits in the valuation of treatments, or initially taking a selective approach to the types of benefit included in the assessment framework, in order to support incremental broadening of the value perspective. It will be important to ensure that the approach to incorporating Wider Societal Benefits applied systematically and consistently.
(4) To ensure that innovation is rewarded only when the technology’s use brings extra value.