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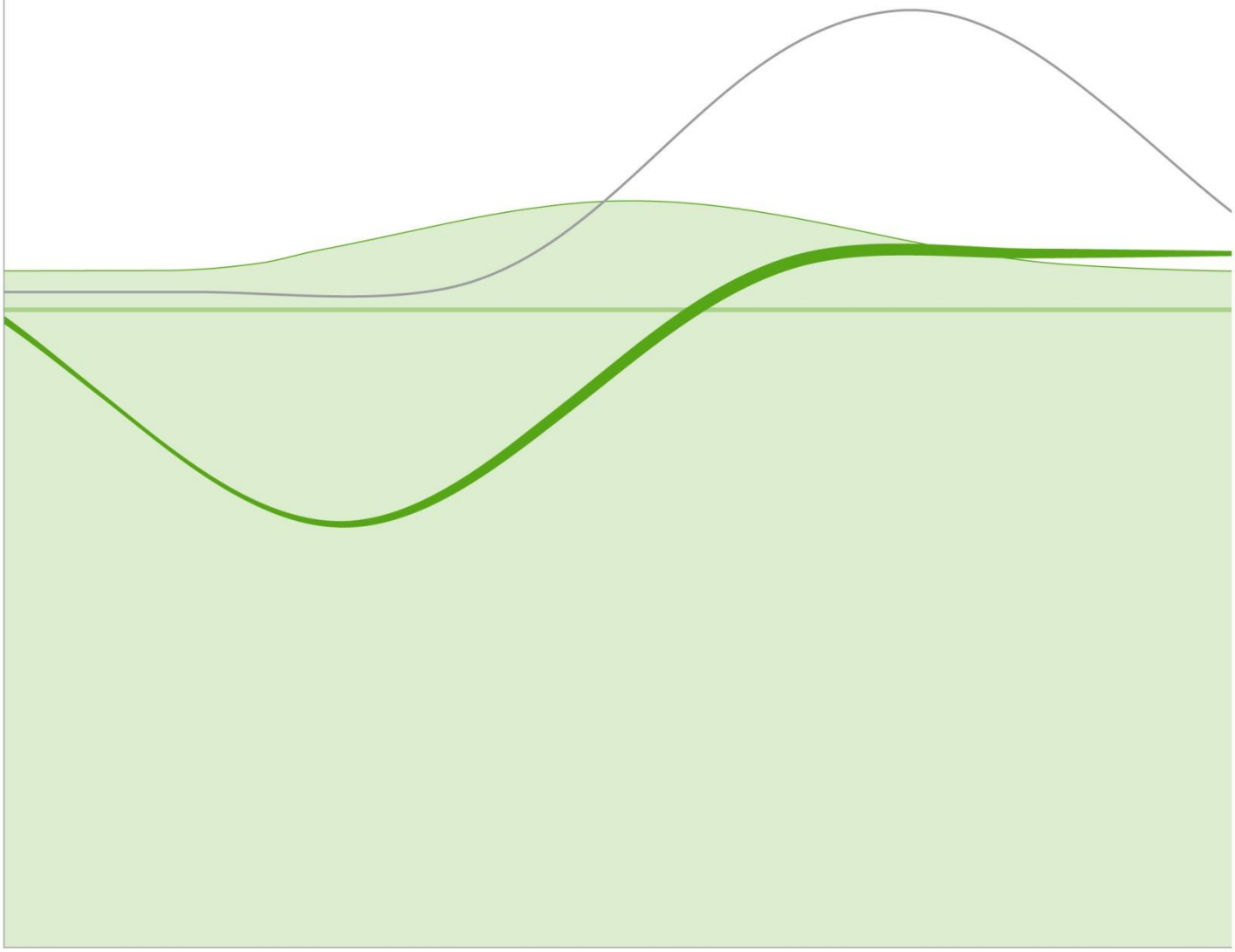

A Review of NICE Methods Across Health Technology Assessment Programmes: Differences, Justifications and Implications

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Abstract

Background: All NICE decisions exert an influence on the allocation of fixed NHS budgets, but decisions for different types of health interventions (for example drugs and devices) are handled via different 'programmes' within NICE. These different programmes use different methods and decision processes. To date there has been no systematic comparison of methods across these programmes.

Objectives: To carry out a systematic comparison of five of NICE's health technology assessment programmes (Technology Appraisal Programme, Medical Technologies Guidance, Diagnostic Assessment Programme, Highly Specialised Technologies Programme, and Clinical Guidelines) with the aim of establishing how differences in methods and processes between the programmes may impact on allocative efficiency within the NHS. Such a comparison has not been undertaken previously.

Methods: Data were extracted from the NICE programme manuals to allow for a systematic comparison between the programmes. Eight qualitative interviews were carried out with NICE members of staff and committee members to explore the reasons for the differences found.

Results: The processes overall were broadly similar. However, there were differences in the required review period (the amount of time after which the evidence must be reviewed to see if the guidance needs updating), and methods of evaluation, specifically the provision of a reference case, the requirement for and type of economic analysis, and the decision making criteria used for appraisal.

Conclusion: All NICE programmes affect the allocation of resources from the same fixed NHS budget. Differences in approaches between the programmes could therefore lead to the misallocation of resources. Many of the differences found can be justified on grounds of practicality and relevance to the health technologies under assessment. However, from a strict utilitarian view there are several potential areas of inefficiency, although many of these are eliminated or reduced if an egalitarian view is taken. The challenge is finding the optimal balance within the equity-efficiency trade-off, and determining where society is willing trade health gains between different people.

1. Introduction

The National Institute for Health and Care Excellence (NICE) was launched in 1999 to reduce unwarranted variation in clinical practice across the UK, encourage fast diffusion and uptake of medical innovations, and to ensure that money is invested in the NHS so that overall health benefit is maximised (Chalkidou, 2009). NICE began with two health technology assessment (HTA) programmes: the Technology Appraisal Programme (TAP) and Clinical Guidelines (CG). since then, several additional programmes have been launched: the Interventional Procedures Programme (IPG), Public Health guidance (PH), the Medical Technologies Evaluation Programme (MTEP), the Diagnostics Assessment Programme (DAP), the Medical Technologies Guidance (MTG) programme, and the Highly Specialised Technologies Programme (HSTP). Most recently, in 2013, NICE started producing guidelines for social care in accordance with the Health and Social Care Act 2012.

Methodological differences across international HTA programmes have previously been examined (Kavanos, Trueman and Bosilavec, 2000; Schwarzer and Siebert, 2009; Stafinski et al., 2011; Spinner et al., 2013) and country comparisons have also been undertaken within Great Britain between NICE and the Scottish Medicines Consortium (SMC) (Cairns, 2006) and the All Wales Medicines Strategy Group (AWMSG) (OFT, 2007). This demonstrates that there is great interest in comparing HTA processes and methods, and examining consistency in these across decision-makers. Yet, surprisingly, very little research has been undertaken to look into the differences in HTA methods within NICE itself.

Two papers that have carried out research in this area focus specifically on the methodological differences between MTEP and TAP. Chapman, Taylor & Girling (2014) draw on previous literature to explain why devices are different from drugs and highlight some of the methodological differences between MTG and TAP. The main focus of this paper is whether the original objectives for introducing MTEP have been met in terms of simplifying access, quickening the process of evaluation and increasing the capacity for the assessment of devices by NICE. Green and Hutton (2014) evaluate how MTEP compares to other HTA programmes, predominantly TAP. Their paper focuses specifically on two differences; measuring and valuing the effects of the technology, and synthesising the evidence for appraisal. This paper builds upon and broadens this research to identify further differences across a wider selection of HTA programmes, with the aim of investigating whether the processes and methods for five selected HTA programmes are consistent. We then explore how any differences identified may impact on efficiency and resource allocation within the NHS.

2. Methods

A mixed methods approach was adopted. Firstly, the HTA programmes were systematically compared. Following this, the differences were explored through discussions with NICE members of staff and committee members.

The manuals for the following programmes were reviewed: TAP (NICE, 2013a; NICE, 2013b), MTG (NICE, 2011a; NICE, 2011b), DAP (NICE, 2011c; NICE, 2011d†; NICE, 2011e†), HSTP (NICE, 2013c) and CG (NICE, 2015a; NICE, 2015b; NICE, 2015c), IPG (NICE, 2009a; NICE, 2009b).

The IPG programme was excluded from this study as its focus is on providing guidance on the safety and efficacy of a new procedure, and therefore takes on a different role to the other programmes and operates under a different agenda. Public Health Guidelines and Social Care Guidelines were also excluded as these programmes do not necessarily consider health technology interventions, and are therefore not strictly defined as HTA. Furthermore, although some of the guidance from these programmes may be funded by the NHS, the majority is funded by local authorities and therefore these programmes do not compete for NHS resources to the same extent as the other HTA programmes.

A set of data extraction tables were developed to capture the key aspects of the evaluation processes and methods; four themes were covered: 'Remit and Scope', 'Process of assessment', 'Methods of evaluation', and 'Appraisal of evidence'. Within each table, sub-headings were developed that would capture all of the relevant and fundamental information across all of the programmes. Finally, the data were extracted from the relevant manuals for each programme and entered into the tables. Information was also extracted from the NICE website if it could not be found within the manuals. Once all the data had been extracted, the differences across each of the sub-headings were assessed and noted for discussion at the interviews.

A total of five people participated in the interviews. Participants were initially identified through contacts of the Office of Health Economics. Some of these contacts recommended others, and further contacts were sought until representatives were obtained for all five appraisal programmes. None of those asked to participate declined. Two of the participants specialised in CG, one in TAP, one in MTG and one in HSTP and DAP, covering all of the HTA programmes compared. The interviews were semi-structured so as to elicit comparable answers to common questions, while also encouraging open responses and a reactive

discussion. The interviews were held with each participant individually; three in person and two by telephone.

3. Results

The key similarities and differences are shown in Tables 1-4. Detailed results tables can be found in the Appendix. Table 5 shows the programme of expertise for each of the respondents.

3.1. Remit and Scope

Table 1 shows that medical devices and diagnostics can be evaluated under either TAP, MTG or DAP, depending on the nature of the technology and its value proposition. Devices are routed by MTEP to TAP when the technology requires a cost-effectiveness analysis (benefits patients but at an increased cost) or to MTG when the product could be cost-saving. Diagnostic devices may also be routed for evaluation by MTEP if they are cost saving, otherwise they are routed to DAP.

Respondent 3 stated that there have been a few instances where TAP and DAP have overlapped due to the inclusion of companion diagnostics. In such scenarios the relevant diagnostic questions are referred to the diagnostics team for review.

All of the respondents stated that clinical guidelines overlap with every other programme due to the fact that they incorporate the whole care pathway. When this occurs the TA guidance is either incorporated into or cross referenced in the guideline.

Table 1: Remit and Scope of each NICE HTA programme

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Clinical Guidelines
What is appraised?	Medicines, medical devices, diagnostics, surgical procedures, therapeutic technologies, systems of care, screening tools.	Medical devices (active, active implantable, in vitro), genetic tests.	Diagnostic technologies/ tests, genetic tests.	Drugs for very rare conditions.	Condition specific care and services.
Referral	Primarily HSRIC; Formal referral required from Secretary of State for Health.	Primarily product sponsors; Also HSRIC.	Product sponsors, national clinical directors, medical royal colleges, professional bodies, national expert bodies, or HSRIC.	Primarily HSRIC; Formal referral required from DH.	Topic oversight group.
Selection/ routing	Must have been granted, or be soon to receive, marketing authorisation; Significant benefit to patients; new formulation at lower price; appropriate evidence available.	Have CE mark (or expected within 1 year); New or innovative technology; Cost saving or cost neutral technology.	CE marking (before publication); Potential to improve health outcomes, but at an increased cost to the NHS.	Criteria same as those used by AGNSS; Process similar to TAP.	Priority topics and those where existing NICE guidance does not cover the whole topic.
Prioritisation criteria	Significant health benefit; Significant impact on NHS resources and other government policies; Inappropriate variation in the use across the country.	Provide most benefit to patients and the NHS; Scoring system.	Particular urgency to the NHS.	Not stated.	Discussion between NHS England, DH and Public Health England.

Source: NICE (2011a), NICE(2011b), NICE(2011c), NICE(2011d†), NICE(2011e†), NICE (2013a), NICE (2013b), NICE (2013c), NICE (2015a), NICE (2015b), NICE (2015c).
Abbreviations: AGNSS: Advisory Group for National Specialised Services; CE mark: European Conformity mark; DH: Department of Health; HSRIC: Horizon Scanning Research & Intelligence Centre.

Table 2: Process of Assessment used in each of NICE's HTA programmes

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
Who prepares an evidence report?	STA: Company with review by Evidence Review Group; MTA: External Academic Assessment Group.	Sponsor with review by external assessment group.	External assessment group.	Sponsor with review by external assessment group.	Evidence Review Team.
Timelines (including scoping and not appeals)	STA: Min. 37 weeks; MTA: Min. 54 weeks (not including scope but including appeal).	38 weeks.	63 weeks.	27 or 17 weeks depending on whether here is a public consultation.	Between 52 and 117 weeks (reported as between 12 and 27 months).
Public consultation	✓	✓	✓	✓ (If marketing authorisation has been granted)	✓
Mandatory funding for recommendations	✓	×	×	✓	×
Appeals process	✓	×	×	✓	×
Review	Decided at publication.	No fixed review date; Considered by Guidance Executive if significant new evidence.	Every 3 years.	Decided on publication.	Usually every 2 years; Always every 4 years from date of publication.

Source: NICE (2011a), NICE(2011b), NICE(2011c), NICE(2011d†), NICE(2011e†), NICE (2013a), NICE (2013b), NICE (2013c), NICE (2015a), NICE (2015b), NICE (2015c).
Abbreviations: MTA: Multiple Technology Appraisal; STA: Single Technology Appraisal

Table 3: Methods of Evaluation used in each of NICE's HTA programmes

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Clinical Guidelines
Reference case	✓	×	✓	×	✓
Perspective					
Outcomes	Health effects for patients and, when relevant, carers.	Clinical outcomes and healthcare system outcomes.	Health effects for patients or, when relevant, other people (principally carers).	Health effects to patients and, when relevant, carers.	Health effects for those using services, and, where relevant, family and carers; Non-health benefits may also be included.
Costs	NHS and PSS.	NHS and PSS.	NHS and PSS.	NHS and PSS; Impact outside NHS and PSS.	NHS and PSS (health outcomes); Public sector and societal perspective (for non-health outcomes).
Clinical effectiveness	✓	✓	✓	✓	✓
Cost-effectiveness	✓	✓	✓	×	✓
Type of economic evaluation	CUA	CCA	CUA	n/a	CUA (CEA, CCA, CBA, CMA if non-health outcomes)
Discount rate (sensitivity analysis)	3.5% (1.5%)	3.5%	3.5% (between 0% and 6%)	Not stated	3.5% (1.5%)
Budget impact determined	✓	✓	✓	✓	✓
Sensitivity analysis	✓	✓	✓	Not stated	✓

Source: NICE (2011a), NICE(2011b), NICE(2011c), NICE(2011d†), NICE(2011e†), NICE (2013a), NICE (2013b), NICE (2013c), NICE (2015a), NICE (2015b), NICE (2015c).
Abbreviations: CBA: Cost benefit analysis; CCA: cost consequence analysis; CEA: cost effectiveness analysis; CMA: cost minimisation analysis; CUA: cost utility analysis; PSS: Personal Social Services

Table 4: Appraisal

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
Decision making criteria	Clinical effectiveness; Cost-effectiveness.	Benefits to patients over current technologies; Benefit to NHS in terms of reduced burden on NHS staff and resources compared with current management.	Quality of evidence; Diagnostic test accuracy; Clinical effectiveness; Cost-effectiveness.	Nature of condition; Impact of the new technology; Cost to the NHS and PSS (including budget impact in NHS and PSS); Value for money; Impact of the technology beyond direct health benefits; The impact of the technology on the delivery of the specialised service (staffing and infrastructure).	Quality of evidence; Trade-off between benefits and harms of intervention; Economic considerations; Availability of evidence to support implementation; Size of effect and potential impact on population health; Wider basis (e.g. ethical issues, social value judgements, equity and inequalities, policy imperatives, equality legislation).

Source: NICE (2011a), NICE(2011b), NICE(2011c), NICE(2011d†), NICE(2011e†), NICE (2013a), NICE (2013b), NICE (2013c), NICE (2015a), NICE (2015b), NICE (2015c).
Abbreviations: PSS: Personal Social Services

Table 5: Respondents' expertise

Respondent	HTA programme
1	CG and TAP
2	CG
3	HST and DAP
4	TAP
5	MTEP

3.2. Process of assessment

The main differences in the process of assessment are those of funding, appeal and review.

Only TAP and HSTP impose mandatory funding (within three months of publication); the other programmes do not. Both Respondents 2 and 3 mentioned that clinical guidelines are not mandatory to allow clinicians to use their clinical judgement for each patient. Respondent 3 also explained that device guidance is not mandatory but is recommended as an option because decisions for adoption should be taken at a local level. This is due to the variation in cost-effectiveness of the technology depending on the patient population and current clinical practice.

TAP and HSTP are the only programmes that have an official appeals process. However, Respondent 2 explained that even though there is not an official appeals process for CG, the team continually receive comments on published guidance which can be reviewed if deemed necessary. In addition, there is a rapid review process if concerns are raised that affect patient safety.

The review period, whereby a search is carried out to identify any new evidence, also differs. There is a predetermined review period for DAP and CG. However, for TAP and HSTP a review date is decided with publication and, therefore, may vary depending on the technology. MTG publish guidance with no fixed review date.

Respondent 3 stated that although the DAP manual states that review is undertaken every three years, there is the flexibility for earlier review if necessary. This respondent suggested that this flexibility in the review process is beneficial as it can be tailored to individual pieces of guidance.

Respondent 4 revealed that the default review period for TAP is usually three years. However, if it is known that new evidence will be available earlier then there is flexibility for the committee to decide on an earlier review period.

With respect to CG, Respondent 2 stated that there is difficulty in knowing what NICE can manage internally and determining the balance between the practicalities of the review process and keeping guidance up to date. CG have to be more responsive as new evidence becomes available at different rates for the multiple questions addressed within a guideline. This interviewee also mentioned there could be a possibility of introducing 'live' guidelines in the future, which involve constant reviews linked to registry data and literature.

Respondent 5 confirmed that there is currently no review process for MTG, but that this has been revisited and an update is soon to be published. The respondent also mentioned that such a review process for devices is likely to cause difficulties due to iterations made to devices that may change health outcomes and costs, plus the concern that prices often change over time.

3.3. Methods of evaluation

Methods of evaluation vary significantly across the different programmes.

Firstly, reference cases have been developed for TAP, DAP and CG, but not for MTG and HSTP. The reference case specifies the methods for analysis of the health technology, and is primarily used for economic analysis to improve transparency and consistency.

Respondent 1 explained that because TAP, DAP and CG use a cost-effectiveness threshold, these programmes need to be prescriptive.

In addition, Respondent 1 suggested that HSTP requires a more flexible approach; therefore a reference case may not be appropriate. This was confirmed by Respondent 3, and extended to apply to MTG, where the available evidence differs greatly by product. Respondent 3 also noted that although the definitions of a reference case for HSTP are formally absent they are still implied, partly due to the cross-over of staff between TAP and HSTP.

All programmes carry out economic analysis except for HSTP. However, the type of economic analysis undertaken varies. TAP, DAP and CG carry out cost-utility analysis (CUA), where health benefits are valued in quality-adjusted life years (QALYs), whereas MTG carries out cost-consequence analysis (CCA), in which health benefits are generally valued through a relevant clinical outcome or natural unit (for example falls avoided).

Respondent 1 explained that many companies in the device industry are small and cannot afford to carry out large clinical trials. Moreover, the nature of devices and their implementation can sometimes impede randomised controlled trials. Consequently the evidence base is often not compatible with a CUA approach. Furthermore, CCA may be important to incorporate metrics for non-health outcomes that are particularly relevant for devices and their implementation. Respondent 4 stated that MTG carries out CCA as any device found to require CUA is routed to TAP. The respondent also suggested that cost-effectiveness is not estimated for HSTP because there is a reluctance to apply a threshold for rare technologies.

Although HSTP does not undertake CUA it accounts for what is termed 'value for money'. This is defined as incorporating productive, technical, and allocative efficiency. However, it is not obvious what this means in practice. Respondent 3 agreed that this is not clear and is in need of clarification. Currently, the committee has to make a judgement on what it believes is value for money. The respondent added that this is being reviewed.

3.4. Appraisal of the evidence

The two main differences in criteria of appraising the evidence are the consideration of budget impact and infrastructure requirements.

Although the budget impact of a new technology is estimated for all programmes during the assessment process, it is only stated to be taken into consideration in decision making for HSTP. The manuals for both TAP and DAP mention that although the budget impact is not taken into consideration in decision making, the greater the impact the more certain the committee should be of the technology's cost-effectiveness (NICE 2011c, NICE 2013b).

Respondent 4 stated that implementation is not within NICE's remit and therefore guidance would be recommended regardless of the budget impact on the NHS. The respondent added that it could be possible to defer funding, but that this had not been actioned on the grounds of budget impact before.

Both Respondent 1 and 3 mentioned that HSTP takes budget impact into account because funding for these technologies comes from the NHS England Specialised Services budget. Respondent 1 added that as the technology is often a lot more expensive, there can be a large budget impact even though the technology only serves a small population. It was also suggested that there are different criteria for HSTP as the technologies are very unlikely to be cost-effective at the normal threshold.

Respondent 5 revealed that budget impact may be considered as additional information in recommendations in the next update of the manuals. This would highlight the extent of savings that the technology would bring to the NHS if it were to be used as standard practice.

4. Discussion

The vast majority of recommendations and guidance produced by NICE are to be delivered within the budget allocated to the NHS (key exceptions include public health and social care guidelines). Consequently, it is important that the way NICE produce guidance is consistent: inconsistencies and misalignment between guidance processes and methods that are not fully justified could potentially represent a substantial source of inefficiency for the NHS.

The efficient allocation of resources is that which "maximises the achievement of whatever objective we are setting" (Knapp, 1984, pp. 10). Therefore, in order to determine whether or not NICE's HTA processes are promoting efficiency, we must consider what the objectives are. Two potentially conflicting 'objectives' are highlighted by NICE: the first is to maximise the health of the population. An extra-welfarist approach (i.e. QALY maximisation) is taken to achieve this. This approach is consistent with the ethical theory of utilitarianism, which is concerned with maximising utility (see Dolan, 2001). The second objective is to ensure that resources are distributed to allow a "fair share of the opportunities available" (NICE, 2008, pp.9). This is consistent with an egalitarian approach. NICE state that they "do not subscribe fully to either approach" (NICE, 2008, pp.9) and incorporate both of these objectives into their decision making.

The utilitarian approach is considered when economic evaluation uses cost-utility analysis. The generic measure of health benefit preferred by NICE is the QALY. The incremental cost-effectiveness ratio (ICER) ('cost per QALY gained') is equal to the incremental[1] cost of the new technology divided by the incremental QALY increase. NICE state a "maximum acceptable ICER of £20,000–£30,000 per QALY gained" (NICE, 2013b, pp.54) when evaluating technologies.

The egalitarian approach is also considered when recommendations are made with respect to reducing health inequalities (NICE, 2008).

Therefore, two definitions of efficiency will be examined in this discussion; the first with the utilitarian aim of maximising QALYs for the whole population, and the second, with

[1] 'Incremental' refers to the difference between the technology under evaluation and a comparator.

an egalitarian aim to ensure "an adequate [...] level of healthcare" (NICE, 2008, pp.9) for all. For the purpose of the utilitarian definition, it will be assumed that any technology with an ICER above £30,000 per QALY is not cost-effective, and therefore represents inefficient use of resources.

The first topic where there are potential efficiency implications with respect to the first definition of efficiency (QALY maximisation) is in the methods used for economic evaluation; firstly with respect to carrying out different types of economic evaluation, and secondly from not carrying out any economic evaluation at all.

The four programmes that carry out economic evaluation (TAP, DAP, MTG, CG) all conduct CUA except for MTG, which undertakes CCA. MTEP will route a device to be assessed under MTG if it is believed that it will be cost-saving with the same clinical benefit, or cost-neutral with a greater clinical benefit. However, if the technology is believed to be cost-incurring it is routed to TAP. Therefore, under MTG any recommendation of a device should theoretically lead to improvements in the allocation of resources, as the cost savings made from the introduction of such devices can be redirected to other areas that will contribute to maximising QALY gains.

However, when undertaking CCA, the health outcomes are not measured using QALYs, but vary according to the specific device. This may lead to difficulties if one device shows equivalence or dominance for one or more outcomes, but is inferior in others. To be consistent with measures of health effect across programmes and optimise efficiency according to the definition above, clinical equivalence or dominance would need to be assessed in terms of QALYs, as the device would be if it were routed to TAP. Although one would expect quality of life to move in the same direction as the chosen clinical outcome, this may not always be the case. For example, an invasive device may prove to be dominant for clinical outcomes compared to a non-invasive device, but be inferior when measuring benefit using QALY scores due to the invasive nature of the device having a detrimental impact on the patient's quality of life. However, there are many issues which have been raised in the literature explaining why it is difficult to provide robust evidence to support a TAP-style economic evaluation for a device. The main issues are those associated with a lack of evidence due to the difficulties with carrying out randomised controlled trials (RCTs), e.g. blinding the trial, accounting for the learning curve effect associated with using the device and the cost incurred by the company (Drummond et al 2009, Taylor & Iglesias 2009, Sorenson et al 2011, Kiristis 2013, Chapman, Taylor & Girling 2014, Green & Hutton 2014).

HSTP, on the other hand, does not undertake any formal economic evaluation. This is likely to be because such technologies are rarely cost-effective at the conventional level. This is due to two main problems both related to the small population size. Firstly, it is impossible to carry out a controlled study on the effectiveness of a drug without significant uncertainty. Secondly, given the small market for drugs for rare diseases, pharmaceutical companies typically charge very high prices in order to recoup their research and development costs, and hence such drugs tend to be more expensive than drugs for common diseases (Drummond et al., 2007).

This demonstrates that recommendations made under this programme would lead to the inefficient allocation of resources under the utilitarian definition of efficiency and using NICE's maximum acceptable ICER. However, there could be an efficient allocation of resources under the egalitarian definition of efficiency if it is believed that such recommendations would lead to a 'fair' distribution of resources. The difficulty is in determining what society, as both funder and user of the NHS, determines as 'fair'.

Hughes, Tunnage & Yeo (2005) provide a comprehensive summary of the arguments. The first is that rarity should be taken into consideration on equality grounds as there is often no alternative treatment available for these conditions. The second is that it is not equitable to choose those with rare conditions over those with a common condition of equal severity. If in reality this means that a higher threshold is applied, then the opportunity cost of treating those with rare conditions is higher, implying that society must be willing to sacrifice QALYs from elsewhere to improve the health of those with very rare conditions. Studies to date do not suggest that society does value rarity (Desser et al. 2010, Linley & Hughes, 2013). However, NICE consulted the Citizens Council, 27 representatives of the general population brought together to inform NICE on different societal opinions, on the NHS paying higher prices for ultra-orphan diseases in 2004. Seven members did not believe that premium prices should be paid, whereas 20 members decided that paying premium prices was sometimes, or always, justified (NICE Citizens Council, 2004). The size of the premium that would be deemed acceptable is unknown. A similar scenario has previously been encountered for end-of-life drugs with ICERs greater than the threshold. In these circumstances NICE have developed supplementary advice for committees where they are to consider all of the potential benefits of the treatment which may not otherwise be included in the reference case. This often results in greater weight being given to the QALYs gained for these treatments. Again, although this may not maximise societal QALY gains and hence utilitarian efficiency, if this truly represents what society is willing to trade-off, resources could be efficiently allocated under an egalitarian definition.

Currently, two evaluations have been completed under HSTP, both of which have given positive recommendations. Given the nature of the conditions, the difficulties in obtaining sufficient evidence, and the struggle to develop firmer criteria to aid recommendation decisions, it appears unlikely that negative recommendations will be made for highly specialised technologies in the future. If this is the case, we question why such evaluation is currently undertaken and suggest that the resources currently used for evaluating orphan drugs could be allocated more efficiently elsewhere. For example, in France and Germany no formal economic evaluation is undertaken. Instead it is considered that additional clinical benefit is proven when marketing authorisation is granted, and if the annual budget associated with drug is below a certain threshold, the drug is reimbursed with no need for a formal evaluation. (Tordrup, Tzouma and Kanavos, 2014).

Another important area to explore is the potential efficiency implications for mandatory and non-mandatory funding for guidance. It was explained during the interviews that MTG and DAP do not impose mandatory funding because such decisions would be better made at a local level due to differences in practice and populations. Such considerations are important as resources will be allocated more efficiently if investment is made in the technologies that are most relevant for their local population. However, local decision makers are unlikely to have the capacity to undertake separate economic analysis for their individual regions and it is more likely that decisions are made in a 'business case' manner; primarily assessing costs and only marginally assessing outcomes (Appleby et al. 2009) and therefore such methods may not lead to the best allocation of resources.

Perhaps the more controversial issue that emerges with non-mandatory funding is that it is likely to result in different commissioning decisions across regions, leading to unequal access to technologies for patients across England and Wales.

A further topic for discussion is that of the review period set for the different programmes. It is important to note that there is support for flexibility in the review period for all of the HTA programmes when the release of new evidence is known at the point of publication. This is particularly beneficial if the new evidence finds that a technology is no longer cost-effective, as new guidance can be released early to avoid a continuation of an inefficient allocation of resources. As mentioned by one of the respondents during the interviews, it is also important to have a default review period to ensure that no evidence is missed.

This topic is particularly interesting for the MTG programme as devices evaluated under MTG do not currently have a process for being reviewed. This could be leading to the

misallocation of resources if device modification impacts its effectiveness and/or cost. There is particular concern relating to the changes in price of the device evaluated, as well as its comparators. Such price changes and their impact on cost-effectiveness would be discovered if the device were to have a fixed review period (as TAP does) and consequently the recommendation could be modified. Given the short lifetimes of medical devices, price changes are common and this may mean that MTGs (and the appropriateness of their recommendations) are soon outdated (Chapman, Taylor & Girling, 2014). This has occurred in practice with Ambu aScope2 where a newer updated version of the device (Ambu aScope3) was released during assessment. No official guidance was given for the updated version; however its price was mentioned in the costing statement for Ambu aScope2 for local decision makers to carry out their own evaluations (NICE, 2013d).

Importantly, during the interviews it was revealed that a review process may soon be introduced, which would ameliorate this effect. However, given the short lifetimes of medical devices and rapid technological developments, it will be impossible to avoid this problem completely.

Consideration of budget impact is not consistent between programmes: only HSTP explicitly takes budget impact into consideration. In practice, even if a new technology is cost-effective, given the constrained budget, it may not be affordable. The funding for highly specialised technologies comes from a smaller sub-section of the allocated budget for specialised services from NHS England. It is therefore likely to be more straightforward to determine the affordability of the new intervention as well as the services its implementation may displace.

Trueman (2001) argues that "..there is a role for both economic evaluation and budget impact analyses to independently inform healthcare decision-making" (Trueman, 2001, pp.610). Cookson et al. (2001) suggest that a "fixed growth budget for new technologies might be implemented […], within which NICE must prioritise its guidance" (Cookson et al., 2001, pp.744). This would involve ranking the guidance from the most to the least cost-effective and implementing the most cost-effective technologies first until the fixed budget is exhausted (Birch & Gafni, 2004). However, Birch & Gafni (2004) highlight that it may be possible that a combination of technologies that may not be deemed as cost-effective at a given threshold could produce a greater number of QALYs than implementing one intervention that is deemed as cost-effective but exhausts nearly all of the budget and does not leave enough resources for an additional programme to be implemented. Overall, these authors demonstrate the great difficulty in considering

budget impact, but also its importance for maximising health benefit. The challenge is determining how best to incorporate the two.

Finally, it must be noted that during the interviews it became clear that the new programmes which are generating many of these differences (HST and MTEP) were created to address the difficulties resulting from certain characteristics of the technologies they assess. It is also important to bear in mind that two further objectives of these programmes are to (1) ensure the HTA methods and processes are fit for purpose for those technologies and (2) to encourage research and innovation. Both programmes try to address the evidentiary standards that are practicable for devices and orphan drugs. In the case of HST, TA methodology could have been stifling innovation due to reduced incentives to industry to develop technologies that may not be deemed not cost-effective and consequently receive a negative recommendation. Once again this shows that, whilst there may be efficiency implications, society may still benefit overall, depending on the ethical standpoint which is adopted.

5. Conclusion

Although several differences between these NICE HTA programmes have been found, there are justifications for many of these differences and how they have evolved is apparent, particularly in terms of making sure methods and processes are practicable and relevant to the value proposition of the health technology under consideration. It should also be noted that NICE have other programmes such as Public Health and Social Care guidance which have fallen outside the scope of this paper, but for which the differences in processes and methods of evaluation may be having a significant impact on resource allocation. Further research into the efficiency implications of these programmes is needed. Overall, it is difficult to determine whether the differences found in this paper are likely to have a significant impact on efficiency of NHS spending. This is largely due to how efficiency is defined. From a strict utilitarian view there are several potential areas of inefficiency, many of which are eliminated or reduced if an egalitarian view is taken. The challenge is finding the balance between these two ethical theories of efficiency, and thereby determining where, and the extent to which, society is willing to trade health gains between different people.

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Appendix: Detailed results tables

Table A1: Remit and Scope

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Clinical Guidelines
REMIT					
What is appraised?	Medicinal products; Medical devices; Diagnostic techniques; Surgical procedures or other therapeutic techniques; Therapeutic technologies other than medicinal products; Systems of care; Screening tools.	Medical devices; Active medical devices; Active implantable medical devices; In vitro diagnostic medical devices; Genetic tests covered provided have medical purpose and fall within scope of Council Directive 98/79/EC.	Medical technologies; Diagnostic technologies that have the potential to improve health outcomes but whose introduction is likely to be associated with an increase in cost; Diagnostic tests; Genetic tests are covered provided they have a medical purpose and fall within scope of Council Directive 98/79/EC.	Drugs for very rare conditions.	Care and services suitable for most people with specific condition/need; Care and service suitable for particular populations in certain circumstances.
Notification	National Institute for Health Research Horizon Scanning Centre; Formal referral by the Secretary of State for Health before appraisal.	Product sponsors; National Institute for Health Research Horizon Scanning Centre.	Product sponsors; Suggested by National Clinical Directors, Royal Colleges, professional or expert bodies, national screening programmes.	National Institute for Health Research Horizon Scanning Centre; Referred to NICE by the DH and NHS Commissioning Board.	Topic selection oversight group.

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Clinical Guidelines
Selection/ routing	Must have been granted marketing authorisation (or equivalent) or there are plans to receive marketing authorisation (or equivalent) Topics are only considered if: • significant benefit to patients (admin, efficacy, side-effects) • new formulation or technology at significantly different price to current standard • appropriate evidence • relevant clinical questions can be addressed under this methodology.	Eligibility criteria: • Have CE mark or equivalent regulatory approval, or is expected within 1 year; • Within remit of evaluation programme and not currently being evaluated; • New or innovative technology; • Appropriate timing. Technology only routed to MTG if the technology: • is likely to be cost saving or cost neutral; • can be evaluated as a single technology; • can be evaluated on a short timescale. Selection criteria: • Claimed additional benefit to patient;	Potential to improve health outcomes, but the introduction of the technology is likely to result in an overall increase in resource costs to the NHS.	Criteria for topic selection same as those used by AGNSS; Process for selection similar to that of the process for the selection of technology appraisals; Will be based on five distinct decision points.	Chosen from a library of topics for quality standards and agreed with relevant commissioning body; Chosen based on: • whether there is existing NICE accredited guidance that encompasses whole topic; • the priority given by commissioners and professional organisations, organisations for people using services, their families and carers. Topic oversight group discuss these factors.

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Clinical Guidelines
		• Claimed healthcare system benefit; • Patient population; • Disease impact; • Cost considerations; • Sustainability.			
Prioritisation criteria	Significant health benefit, taken across the NHS as a whole, if given to all patients for whom it is indicated; Significant impact on other health-related Government policies; Significant impact on NHS resources if given to all patients for whom it is indicated; Significant inappropriate variation in the use of the technology across the country; NICE likely to add value by issuing national guidance.	Decisions based on a prepared briefing note including: • info provided by sponsor; • input from expert advisers; • input relevant to patient/carer organisations; • equality considerations; • scoring system.	A topic of particular urgency to the NHS could be prioritised for evaluation before other technologies already identified.	Not stated.	NICE discusses topics with NHS England, DH and Public Health England and create priority list.

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Clinical Guidelines
SCOPE					
What is included?	Framework and definitions of: • Disease/ health condition; • Population; • Potential comparators; • Potential subgroups; • Health outcome measures; • Costs; • Time horizon; • Patient sub groups; • Any other special considerations/issues e.g. equality and diversity issues, innovative nature.	Description of the technology and its benefits; Information about the disease, condition or clinical problem relevant to the technology; Regulatory status; Committee's rationale for developing guidance; Decision problem to be addressed: • population, intervention, comparator(s); • outcomes; • cost analysis; • subgroup analysis ; • any special considerations. List of professional and patient organisations involved, and societies or organisations to be invited to comment on the scope;	Definition of patient population; intervention (technology or test) to be evaluated and comparators; Description of care pathway; Defines key outcomes and costs; Selection of time horizon; May discuss special considerations – equality and diversity issues, or special implementation issues (topic specific).	Defines the disease, the patients and the technology covered by the evaluation and the questions it aims to answer.	Description of guideline topic; Context in which the guideline will be developed; Why guideline is needed; How it links to other NICE recommendations; Definition of population(s) and setting(s) that will and will not be covered; Describes what the guideline will consider; Key issues and questions; Economic perspective to use; Equality issues; Health inequalities associated with socio-economic factors, inequities of access, and

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Clinical Guidelines
		Technical questions raised by the Committee or Programme team.			opportunities to improve health.
Scope consultation?	✓	✓	✓	✓	✓
How are comparators chosen?	Established NHS practice in England; Natural history of the condition; Existing NCIE guidance; Cost-effectiveness; Licensing status of the comparator; Branded and generic drugs and biosimilar products.	Standard intervention; Usually similar or equivalent technology; Used as part of current management; Can be no intervention.	Most commonly used; Recommended in current NICE guidance for functions in the evaluation.	Can consider those that do not have a marketing authorisation for indication defined in scope when considered to be part of established practice for the indication in the NHS.	Current best practice.

Abbreviations: AGNSS = Advisory Group on National Specialised Services; DH = Department of Health.
Source: NICE (2011a), NICE (2011b), NICE (2011c), NICE (2011d†), NICE (2011e†), NICE (2013a), NICE (2013b), NICE (2013c), NICE (2015a), NICE (2015b), NICE (2015c).

Table A2: Process of assessment

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
Who submits the evidence?	The company; NHS commissioning experts; Patient experts; Consultees & selected clinical experts.	The sponsor; Programme team or other working groups; Expert advisers; Patient and carer organisations.	The sponsor/ manufacturer; Specialist Committee members.	Manufacturer/ sponsor; Supplemented with external review group explorations; Patient/carer groups; Other consultees.	Evidence Review Team through systematic literature searches; Stakeholders (through 'call for evidence').
Who prepares a review of the evidence?	STA - Evidence Review Group; MTA - External Academic Assessment Group.	External assessment group.	External assessment group.	External review group.	Evidence Review Team.
Timelines **Scope to publication (not appeals)**	STA: Min. 37 weeks (including appeals but not scoping); MTA: Min. 54 weeks (including appeals but not scoping).	38 weeks (no appeals).	63 weeks including resolution period (no appeals).	27 weeks or 17 weeks depending on whether there is public consultation.	Between 52 and 117 weeks (reported as between 12 and 27 months).
Public consultation	✓	✓	✓	✓ (If marketing authorisation has been granted)	✓

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
Mandatory implementation	✓	×	×	✓	×
Appeals process	✓	×	×	✓	×
Review	Suggested when guidance published; Varies depending on likely availability of evidence; If transferred to static list, reviewed every 5 years.	Guidance is not published with a fixed review date; Considered by Guidance Executive if significant new evidence becomes available.	Every 3 years; If transferred to static list, reviewed every 5 years.	Suggested when guidance published; Varies depending on the availability of evidence.	Less resource intensive checks performed 2, 6 and 10 years after publication, with more thorough checks at 4 and 8 years; If transferred to static list, reviewed every 5 years.

Source: NICE (2011a), NICE (2011b), NICE (2011c), NICE(2011d†), NICE(2011e†), NICE (2013a), NICE (2013b), NICE (2013c), NICE (2015a), NICE (2015b), NICE (2015c).

Table A3: Methods of evaluation

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
Reference case	✓	×	✓	×	✓
Perspective					
Outcomes	All direct health effects for patients and, when relevant, carers.	Clinical benefits to patients; Healthcare system outcomes ("A non-clinical outcome, typically impacting on resource capacity, resulting from a clinical (patient-level) treatment episode").	Health effects for patients or, when relevant, other people (principally carers).	All direct health benefits to patients and, when relevant, carers; Significant benefits outside NHS and PSS; Benefits of research and innovation.	Direct health effects for those using services, and, where relevant, family and carers; Non-health benefits may also be included.
Costs	NHS and PSS; Non-NHS and PSS costs in exceptional circumstances if agreed by DH.	NHS and PSS costs.	NHS and PSS; Non NHS/PSS costs considered in "exceptional circumstances" but are reported separately.	NHS and PSS; Outside NHS and PSS.	NHS and PSS (interventions with health outcomes); Public sector and societal perspective (intervention with health and non-health outcomes).
Evidence					
Types accepted	RCTs most appropriate for	Published evidence; Unpublished evidence;	End-to-end studies; Prospective cohort or cross-sectional studies;	Not stated.	Published studies;

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
	measures of relative treatment effect; Non-randomised and non-controlled evidence; Qualitative research; Economic evaluations; Unpublished and part-published evidence.	Contributions from expert advisers – theoretical outcomes.	Retrospective case-control studies; RCTs; Case studies; Patient registries; Systematic reviews; Existing models.		Conference abstracts (if evidence is limited); Legislation and policy; Unpublished data and studies in progress; Grey literature.
Clinical effectiveness					
What is taken into account?	Nature and quality of evidence; Uncertainty; Differential benefits or adverse outcomes; Impact of above from patients' viewpoint; Position in pathway of care; Existing alternatives.	Effectiveness outcomes (not explicit).	Nature and quality of the evidence; Uncertainty; Differential benefits or great risk of adverse effects; Risk (adverse events) and benefits from patient's perspective; Position in overall pathway care; Available alternative treatments.	Nature and quality of evidence; Uncertainty; Differential benefits or adverse outcomes; Impact from patients' viewpoint; Position in overall pathway of care; Existing alternatives.	Quality of evidence; Uncertainty; Tradeoff between different outcomes.

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
Cost-effectiveness					
Type used e.g. CEA, CUA, CCA, CMA	CUA.	CCA.	CUA preferred.	N/A: "value for money".	CUA preferred for health interventions; CUA, CEA, CCA, CBA or CMA for interventions that also include non-health outcomes.
Outcome measure	QALYs preferably using EQ-5D.	Clinical benefit; Resource consequences.	QALYs preferably using the EQ-5D (other measures may be needed if EQ-5D is insufficiently sensitive).	Not stated.	QALYs preferably using EQ-5D for health benefits; If non-health benefits, decided on a case-by-case basis.
Discount rate (Costs and benefits)	3.5%; Sensitivity analysis with 1.5%.	3.5%.	3.5%; Sensitivity analysis between 0% and 6%.	Not stated.	3.5%; Sensitivity analysis with 1.5%.
Budget/resource impact determined	✓	✓	✓	✓	✓
Sensitivity analysis	Probabilistic; Confidence ellipses; Scatter plots; Acceptability curves.	Scenario-based deterministic; Threshold analyses; Probabilistic.	Scenario-based; Probabilistic.	Not stated.	Deterministic; Probabilistic.

Abbreviations: CBA: Cost benefit analysis; CCA: cost consequence analysis; CEA: cost effectiveness analysis; CMA: cost minimisation analysis; CUA: cost utility analysis; PSS: Personal Social Services; QALYs = Quality Adjusted Life Years.
Source: NICE (2011a), NICE(2011b), NICE(2011c), NICE(2011d*), NICE(2011e*), NICE (2013a), NICE (2013b), NICE (2013c), NICE (2015a), NICE (2015b), NICE (2015c).

Table A4: Appraisal of evidence

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
Who appraises the evidence?	Appraisal committee consisting of: • People who work in the NHS; • Patient and carer representatives; • Lay members; • People from relevant academic disciplines; • Pharmaceutical and medical device industry representatives.	Medical Technologies Appraisal Committee consisting of: • Clinicians; • Scientists; • Lay people; • Experts in regulation and evaluation; • People with experience of the medical technologies industry.	Diagnostic Advisory Committee consisting of: • Clinicians; • Lay people; • Experts in regulation and evaluation; • People with commissioning experience; • People with experience of diagnostic technologies industry; • Additional specialist committee members for specific topics.	Evaluation Committee consisting of: • People who work in the NHS; • Patient and carer organisations; • Relevant academic disciplines • Pharmaceutical and medical devices industry representatives.	The Committee (either a standing committee or a topic-specific committee) includes: • Practitioners (specialist and non-specialist); • service/care providers or commissioners; • others working in the area covered by the guideline; • people using services, family members, carers.
Decision making criteria	• Clinical effectiveness; • Cost-effectiveness; • Non-health factors: Scientific and social value judgements.	• Measureable benefit for patients over current technologies; • Benefit to NHS: likely to reduce burden on NHS staff or reduce resource use.	• Quality of evidence; • Diagnostic test accuracy; • Clinical effectiveness; • Cost-effectiveness.	• Nature of condition; • Impact of the new technology: clinical effectiveness; magnitude of health benefits to patients and	• Quality of evidence; • Trade-off between benefits and harms of intervention; • Economic considerations;

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
				carers; heterogeneity of health benefits; robustness of evidence; treatment continuation rules; • Cost to the NHS and PSS (including patient access schemes); • Value for money; • Impact of the technology beyond direct health benefits (including long-term benefits of research and innovation) • The impact on the delivery of the specialised services.	• Extrapolation of evidence; • Availability of evidence to support implementation; • Size of effect and potential impact on population health; • Wider considerations: ○ ethical issues; ○ social value judgements; ○ equity and inequalities; ○ policy imperatives; ○ equality legislation.

	Technology Appraisal Programme	Medical Technologies Guidance	Diagnostics Assessment Programme	Highly Specialised Technology Programme	Guidelines
Additional considerations	Degree of need; Promoting innovation; Extent society may wish to forego health gain for non-health benefits.	Equality; Legislation on human rights; Eliminating unlawful discrimination; Scientific and social value judgements.	Relevant provisions of NICE's Directions, set out by Secretary of State for Health, legislation on human rights, discrimination and equality; Scientific and social value judgements.	Scientific and social value judgements – informed by Citizens Council, NICE advisory bodies, NICE's Board; Discrimination and equality.	"NICE social value judgements usually take precedence over economics"

Source: NICE (2011a), NICE(2011b), NICE(2011c), NICE(2011d†), NICE(2011e†), NICE (2013a), NICE (2013b), NICE (2013c), NICE (2015a), NICE (2015b), NICE (2015c).