Appendix 1: Literature Review

A semi-systematic literature review was conducted between April and July 2017. The review focused on literature addressing the following question: 'How has the process, methods and ethical framework used by NICE in its technology appraisal programme changed over time and what are the implications for NICE's treatment of social and ethical values?'. Four databases—PubMed, Scopus, ProQuest and Web of Science—were systematically searched using search terms developed for a prior systematic literature review and a review of the terms used in pre-identified relevant papers. In addition, the Health Management Information Consortium (HMIC) and Social Policy and Practice Research (SPPR) databases were searched to identify relevant grey literature.

The search terms used across the review were as follows:

> Title/abstract/key (NICE OR "National Institute for Clinical Excellence" OR National Institute of Clinical Excellence" OR "National Institute for Health and Clinical Excellence" or "National Institute of Health and Clinical Excellence" OR "National Institute for Health and Care Excellence" OR "National Institute of Health and Care Excellence")
> AND
> Title/abstract/key ("technology assessment" OR "technology appraisal" OR HTA OR "cost benefit analysis" OR "cost effectiveness" OR "comparative effectiveness research" OR "economic evaluation" OR "healthcare rationing" OR "health care rationing" OR "resource allocation" OR "health priorities" OR "healthcare priorities" OR "health care priorities" OR "priority setting" OR "health technology prioritisation" OR "health technology prioritization" OR "reimbursement decision" OR QALY OR "quality adjusted life year" OR ICER)

The review identified several papers evaluating individual changes to NICE's methods and trends in NICE decision-making over time. However, it did not identify any empirical study of developments to NICE's approach as a whole or of the potential ethical implications of these changes.

Appendix 2: Documents Included in Systematic Review of NICE Policy

Year	Key policy documents*	Supporting documents
1999	Appraisal of new and existing technologies: interim guidance for manufacturers and sponsors	
2001	Guide to the technology appraisal process (1st ed.) Guidance for manufacturers and sponsors/ Guide to the methods of technology appraisal (1st ed.)[#] Guidance for appellants	Guidance for healthcare professional groups Guidance for patient/carer groups
2004	Guide to the methods of technology appraisal (2nd ed.) Guide to the technology appraisal process (2nd ed.) Technology appraisal process: guidance for appellants	A guide for manufacturers and sponsors A guide for healthcare professional groups A guide for NHS organisations A guide for patient/carer groups

Year	Key policy documents*	Supporting documents
2005	Social value judgements: principles for the development of NICE guidance (1st ed.)	
2006	Guide to the single technology appraisal process (1st ed.)	
2007		Single technology appraisal process: update
2008	Guide to the methods of technology appraisal (3rd ed.) Social value judgements: principles for the development of NICE guidance (2nd ed.)	
2009	Guide to the single technology appraisal process (2nd ed.) Guide to the multiple technology appraisal process (3rd ed.)	Supplementary advice: appraising life-extending, end-of-life treatments
2010	Appeals process guide	
2011		Clarification on discounting
2013	Guide to the methods of technology appraisal (4th ed.)	
2014	Guide to the processes of technology appraisal (4th ed.) Guide to the technology appraisal and highly specialised technologies appeal process	
2016		Addendum A—final amendments to the NICE technology appraisal processes and methods guides to support the proposed new cancer drugs fund arrangements Rapid re-consideration of drugs currently funded through the cancer drugs fund
2017		Fast track appraisal: addendum to the Guide to the processes of technology appraisal Cost comparison: addendum to the Guide to the processes of technology appraisal Procedure for varying the funding requirement to take account of net budget impact
2018	Guide to the processes of technology appraisal (4th ed.)—2018 update	

*Key policy documents include the methods guides, process guides and social value judgements documents. Versions of these guides that tailor the same information for a more specialised audience (e.g. patient/carer groups, NHS organisations), plus any amendment or addendums to these key documents, have been classed as supporting documents

#The 2001 guidance for manufacturers and sponsors document contained detailed information on the methods of technology appraisal, much of which went on to inform the development of the first formal methods guide in 2004. As such, it has been classed here as the first edition of the methods guide

Appendix 3: Initial Codes Generated Deductively During Familiarisation Stage of Thematic Analysis

#	Code	Description
1	Fundamental principle	Any general principles identified by the document
2	Topic selection process	Process through which topics/technologies for appraisal are selected
3	Topic selection criteria	Criteria according to which topics/technologies for appraisal are selected
4	Outcomes	Health and non-health outcomes accounted for directly in the technology evaluation
5	Costs	Costs to the health service and elsewhere accounted for directly in the technology evaluation
6	Economic evaluation	Type of economic evaluation and methodology used to measure and value health effects. E.g. cost-utility analysis using QALYs based on EQ-5D
7	Acceptable evidence	The types of evidence considered acceptable in making an evaluation
8	Clinical effectiveness	Judgemental factors that can be taken into account in evaluating clinical effectiveness e.g. nature and quality of evidence, uncertainty, existing alternatives, patients views on outcomes
9	Cost effectiveness	Judgemental factors that can be considered in evaluating cost effectiveness e.g. patient perspectives on quality of life, wider societal benefit
10	Participants	Groups and individuals formally invited to participate in the appraisal process
11	Discounting policy	Discount rate(s) applied and the policy surrounding their application
12	Time horizon	Policy regarding the period of time over which costs/benefits can be calculated
13	Innovation	Any policy regarding how innovation should be treated and valued during appraisal
14	Social value judgements	Any social or ethical values explicitly regarded as relevant to appraisal and decision-making
15	Equalities considerations	Any specific considerations to be made regarding the potential for inequalities
16	Excluded considerations	Any considerations explicitly excluded from consideration during appraisal and decision-making
17	Threshold	Any explicitly stated cost-effectiveness threshold(s) or threshold range(s)
18	Resource impact	Any policy regarding the consideration of resource impact, budget impact or affordability during appraisal
19	Appeal criteria	Criteria according to which appellants may be heard

Appendix 4: Interview Guide

Note: This basic topic guide was adjusted as appropriate between interviews.

Topic	Questions
Relationship with NICE	*I'll begin by trying to understand a bit more about your relationship with NICE and the role that you played in the development of some of its key guidance documents* 1. As [role], what were your key responsibilities? What role did you play in the development of NICE's approach to technology appraisal? *For example, how involved were you in the various updates to the Process and Methods guides?* How would you describe your current relationship with NICE? Are you involved in any ongoing work to update NICE's *Process* guide, *Methods* guide or *Social Value Judgements* document?
View on key changes to approach	*This project is focusing on how the process guide, methods guide and SVJ document have changed over time and the implications of these changes for NICE's treatment of social and ethical values. As such, I'm now going to ask you some quite explorative questions about how you perceive NICE's approach to have evolved over time. Please don't worry if you're not able to provide detailed answers—a general perspective is absolutely fine* 2. Over the period of your involvement with NICE, what do you consider to have been the most important changes in its approach to technology appraisal? *By approach, I mean its process, methods or guidance on social or ethical values.* Can you identify any overarching patterns or trends in these changes? What do you think are the ethical implications of these changes?
Social value judgements document	*I'm now going to ask some questions focused on the social value judgements (or 'SVJ') document and its relationship with other key pieces of NICE guidance. I'll then go on to briefly consider SVJ's role in the practice of NICE's technology appraisal committees* 3. In your experience, what role has the *SVJ* document played in the development of NICE's *process* and *methods* guides? What role (if any) has the SVJ document played in the development of ad hoc amendments to these guides? *For example, the 2009 'End-of-life' addendum to the Methods guide and the 2011 'Clarification on discounting'* Can you think of any ways in which NICE's process and methods guides deviate from the principles set out in the corresponding versions SVJ? *I have a copy here of the eight principles set out in the most recent 2008 SVJ document if you would like to refer to them* *Moving on to consider the role of the SVJ document in the practice of technology appraisal:* Do you think the *SVJ* document has become more or less relevant to the practice of NICE's technology appraisal committees since the first edition was issued in 2005?
Citizens Council	*I'd now like to briefly explore the changing status of NICE's Citizens Council* 4. What role has the Citizens Council played in the development of NICE's *Process* and *Methods* guides? How have you observed this role to have changed over time? In your view, are there any aspects of NICE's process or methodology that conflict with advice given by the Citizens Council?

Topic	Questions
Perspective taken during assessment	*I'm now going to explore NICE's approach to several specific social or ethical values—this is so that you can help me to either validate or challenge some of the hypotheses that have emerged from this project so far. As a reminder, I am defining a social or ethical value to be any factor besides clinical- or cost-effectiveness that is taken into consideration, either directly or indirectly, during technology appraisal* *NICE has changed its stance several times on whether non-health impacts should be taken into consideration when assessing the cost-effectiveness new health technologies. For example, until 2004 both productivity gains and other non-NHS impacts—such as gains experienced by other government departments—could be included in the calculation of cost-effectiveness. By contrast, under current guidance productivity is explicitly rejected as a relevant consideration and non-NHS impacts can only be included in exceptional circumstances, with prior agreement from the Department of Health, and cannot be included in the main ICER calculation* 5. Do you agree that NICE's official guidance has increasingly delimited the types of costs and benefits that can be 'counted' during health technology assessment? *[If yes]:* What do you think are the reasons for this change? *[If yes]:* In your view, has this change in perspective also been reflected in the practice of appraisal committees? *In other words, are committees happy to take into consideration benefits presented alongside the reference case, or is the reference case analysis the main driver for decision-making?* Why do you think NICE has now singled out productivity as an inappropriate factor for consideration during health technology assessment?

Topic	Questions
Evidence and uncertainty	*I'd like now to briefly discuss how NICE's approach to evidence and uncertainty has evolved.* *Historically, the Methods guide has indicated a strong preference for data derived from RCTs. However, over time this preference has been less strongly expressed and the guide has provided more detailed advice on how alternative sources of evidence might be handled; for example, data derived from indirect comparisons and modelling* 6. Does this increased focus on non-RCT data indicate a greater willingness by NICE to make decisions based on less robust evidence? *Historically, committees were advised to take the degree of certainty into account when recommending technologies at high ICERs and to exercise more caution when there is significant uncertainty about clinical or cost effectiveness. This principle still exists, but appears to be in tension with amendments brought about by the end-of-life rules and the new cancer drugs fund, the wording of which seem to allow for a relatively high level of uncertainty at ICERs significantly above the usual threshold* *Another way of looking at this is that the 'benefit of the doubt' has shifted, for cancer drugs at least, from the unidentified NHS patient whose interests are protected by ensuring that technologies representing poor value for money are not recommended, to the particular group of patients whose interests are served by recommending a particular technology, even if this carries an opportunity cost for the NHS* Do you agree with this hypothesis? *[If yes]:* What has been the main driver of this shift? *[If yes}:* Do you think that this shift in the benefit of the doubt applies only to cancer drugs, or has it also been adopted for other technology types? If so, which? *[If no]:* What alternative hypothesis would you put forward for the wording changes referred to above?

Topic	Questions
Innovation	*I'm now going to move on to the topic of innovation* *Ever since its creation in 1999, NICE has had a statutory responsibility to support innovation. However, the tone of the statements describing this responsibility has arguably become stronger over time. (I've pulled together a few examples, here, for you to glance at, if you'd like to see some of the supporting evidence for this hypothesis.)* *Several recent changes to NICE's process have also been justified on the grounds that they accelerate access to innovation; for example, the introduction of the single technology appraisal process in 2009, which was intended to accelerate the appraisal process and enable it to be initiated closer to product launch* 7. Do you think it is fair to say that NICE has become more actively 'pro-innovation' in recent years? *[If yes]:* What do you think has been the main driver of this change? *[If yes]:* How do you think this change in attitude has been reflected in changes to NICE's process and methodology? *For example, in its appraisal timelines, topic selection criteria, evidence requirements, types of recommendation?* *The current version of SVJ states that "NICE should not recommend a technology if there is no evidence, or not enough evidence, on which to make a clear decision"*. Do you think that the desire to promote innovation has sometimes led to this principle being overridden? *[If yes]:* Do you have any concrete examples for this? *The current Methods guide suggests that the innovative nature of a new health technology should only be considered at high ICERs, and only when the innovation adds "demonstrable and distinctive benefits of a substantial nature" that have not been captured in the reference case calculation* Does this accord with your experience or perception of how appraisal committees respond to innovative products in practice?
Discounting	*I'm now going to move on to the subject of discounting and how changes to NICE's discounting policy may relate to its social or ethical value judgements* 8. What do you think were the factors driving the Supplementary guidance on discounting issued in 2011 and the subsequent change in recommended discount rates? Do you think that the reasons for these changes were purely technical or did social or ethical values also play a role? *For example, the desire to prioritise treatments targeting children and young people?*

Topic	Questions
Formalisation (appraisal)	*The case of discounting appears to be one of several instances in which social or ethical value judgements previously addressed through deliberation and the discretionary decision-making of appraisal committees are becoming more prescriptive and 'rule-based'. Moreover, the rules often tend to introduce quantitative criteria rather than providing guidance for deliberation. Other examples include the 'End-of-Life' rules (which introduced several quantitative 'cut-offs'), the increasingly stringent criteria concerning consideration of non-health benefits, and the proposed use of QALY weighting in the highly specialised technology appraisal process. [Expand on EoL example and/or mention BI test if necessary]* 9. Bearing our conversation so far in mind, do you think it is accurate to say that NICE has sought to make its social and ethical value judgements more 'rule-based' in recent years? Several of the recently introduced rules employ numerical ranges and cut-offs. Do you think that this reflects an emerging preference in NICE's approach for quantitative decision-making over deliberative approaches? *Technology assessment is described by NICE as a three-stage process, consisting of scoping, assessment and appraisal. This sheet summarises what each stage involves, in case a refresher would be useful* Do you agree that social and ethical value judgements are increasingly being made in the scoping and assessment phases, rather than the appraisal stage? [*If yes]:* Why do you think this trend has emerged?
Formalisation (assessment)	*A review of the five editions of the Methods guide indicates that aspects of NICE's methodology other than its social and ethical value judgments have also become more prescriptive, or 'rule-based', over time, particularly since the introduction of the reference case in 2004. A general indicator of this is the increasing length of these documents: from 12 pages in 1999, to 54 pages in 2004, to 94 pages in 2013* 10. The 2001 *Guidance for Manufacturers and Sponsors* states that it "should be seen as an aid to thought during the process of submission rather than as a substitute for it". Do you think that this advice still applies to the current Methods guide, or has NICE's methodology become less flexible over time? *The number of NICE appraisal programmes has increased over time, from two core programmes in the early 2000s [technology appraisal and clinical guidelines] to six today, several of which also have multiple process variations (e.g. MTA, STA, FTA)* Is it accurate to say that this expansion in the number of NICE programmes and processes has been necessitated in part by the reduced flexibility of the core technology appraisal programme? In your experience, how does NICE address technologies that cannot easily be appraised through its standard methodology?

Topic	Questions
Political landscape (relationship with government)	*I'm going to finish by asking two sets of questions concerning NICE's role in the political landscape. These are much more explorative than the last few questions, so they could be a little challenging to answer on the spot. My first question concerns NICE's changing relationship with government and the extent to which it is able to act independently in developing its approach to technology appraisal* 11. How would you characterise NICE's relationship with the most recent government and how do you think this compares with its relationship with previous governments? How do you think that government priorities are reflected in the way that NICE conducts technology appraisal? *For example, in the process of topic selection? In NICE's approach to innovation? In its consideration of wider societal impacts?* *Several of the more controversial recent changes to NICE's approach have been issued by NICE's Board, rather than through a full methodology review. [For example, the End-of-life rules, supplementary advice on discounting, budget impact test.]* Do you think that this reflects an increase in the political pressure NICE is now exposed to?
Political landscape (NHS)	*My last question focuses on the relationship between NICE's methodology and the financial pressures faced by the NHS* *12. NICE's cost-effectiveness threshold hasn't formally changed since 1999, but financial pressure on the NHS has increased significantly during this period.* What techniques, if any, do you think NICE has employed over the years to maintain the overall affordability of its advice for the NHS? Would you say that the budget impact of individual technologies has become more or less relevant to decision-making as NICE's methodology has evolved over time? *In a public health system funded by finite resources, tension inevitably arises between the needs of the individual and the needs of the population. This tension arguably becomes more acute as the system experiences greater financial stress. Principle 5 of the current SVJ document states that "although NICE accepts that individual NHS users will expect to receive treatments to which their condition will respond, this should not impose a requirement on NICE's advisory bodies to recommend technologies that are not effective, or are not cost effective enough to provide the best value to users of the NHS as a whole"* Do you think that NICE's methodology, overall, remains compliant with this principle?
AOB	13. Is there anything else you'd like to add or discuss that we haven't covered?