

Still elegantly muddling through? NICE and uncertainty in decision making about the rationing of expensive medicines in England

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Abstract

This paper examines the 'technological appraisals' carried out by NICE (National Institute for Health and Care Excellence) as it regulates the provision of expensive new drugs within the English NHS on cost-effectiveness grounds. Ostensibly this is a highly rational process by which the regulatory mechanisms absorb uncertainty but in practice decision-making remains highly complex and uncertain. This paper draws on ethnographic data – interviews with a range of stakeholders and decision-makers (n=41), observations of public and closed appraisal meetings, and documentary analysis – regarding the decision-making processes involving three different pharmaceutical products. The study explores the various ways in which different forms of uncertainty are perceived and tackled within these Single Technology Appraisals (STAs). Difficulties of dealing with the various levels of uncertainty were manifest and often rendered straightforward decision-making problematic. Uncertainties associated with epistemology, procedures, interpersonal relations and technicality were particularly evident. The need to exercise discretion within a more formal institutional framework shaped a pragmatic combining of explicit and informal, collective and individual, strategies and tactics to navigate through the layers of complexity and uncertainty in making decisions.

Introduction

The National Institute for Health and Care Excellence (NICE) which was set up in 1999 in England typifies the shift towards pursuing 'neutral' and 'objective' regulation which has recently characterised British governmental institutions.¹ Through systematic appraisals of the cost and clinical effectiveness (cost utility) of various expensive drugs for the NHS, NICE was designed to overcome the inconsistencies of the previously ad-hoc and implicit discretionary decisions of local clinicians² – replacing this with explicit, evidence-based decisions which regulate NHS prescribing. Though only one of several functions carried out by the institute,³ drug appraisals are the most prominent and publicly scrutinised.⁴ Decisions are considered, at least in part, in the public arena which is believed to enhance transparency and provide legitimacy to the policy process of rationing health care technology.⁵

From an ethical perspective, the role performed by NICE is intended to assure consistently equitable access for patients to drugs across the NHS and to facilitate the efficient use of public finances, by regulating NHS consumption of new and expensive drugs using cost-effectiveness criteria.^{4,6,7} Based on rigorous appraisals of scientific evidence, NICE seeks to manage uncertainty through a calculative and evidence-based approach, amidst increasing cultural expectations of a 'calculability of consequences'.⁸ This portrayal of the rationing process might be seen to reflect both instrumental and institutional forms of rationality.⁹ Yet behind this discourse or policy talk¹⁰ of objectivity and rationalism in the pursuit of explicit rationing, the influence of socially-constructed assumptions and subjectivity may still prevail.^{11,12}

Evidence from statistical analyses suggests that while the demonstration of clinical and economic value is central to NICE decisions, the variability in these decision-outcomes about

whether they recommend a technology or not can also be explained by other process and socio-economic factors.¹³ This may be due, at least in part, to the very nature of bureaucratic judgements amidst uncertainty, where reliance on – and correspondingly trust in – people and systems is unavoidable.¹⁴ Whether it is confidence in research paradigms and approaches, trust in expert panels, or weighing up the evidence presented by different expert patients, leading clinicians, or drug company representatives – a range of socially-constructed assumptions, might influence attributions of validity, competency and/or motives,¹⁵ which could bear decisively on appraisal decisions.¹⁶ There is explicit recognition by NICE that so-called ‘gut’ components might be important in disinvestment decisions¹⁷ and more recently NICE has formally introduced further prioritisation criteria, in addition to its threshold of cost- effectiveness based on social value judgements which include severity of underlying condition, unmet need, significant innovation, wider social benefit, disadvantaged populations and children.^{18,19} Such pragmatism might be a reaction to media pressure,²⁰ legal challenges²¹ unrepresentative minority interest group lobbying,²² and the challenging of NICE decisions by agreements made directly between the manufacturer and the Department of Health.^{2,3,4} This reactive behaviour by the regulator (NICE) makes evident the poly-centric nature of the regulatory regime and may also reflect the influence of interest groups such as NHS clinicians, patient groups and of the pharmaceutical industry with the associated claims of corporate bias and regulatory capture.⁴ The impact of these and related factors within the appraisal process, and their potential influence on the intuition based ‘gut components’ of decisions, might be obscured by the ostensible rationality of NICE as an institution which formally attempts to absorb uncertainty through its instrumental and institutional approach.

Conceptualising uncertainty

Uncertainty in this type of rationing and regulatory context has been portrayed in different ways, with one approach suggesting the need to recognise but minimise it²³ and another suggesting the exploration of uncertainty should be portrayed in a more positive light as a means of making rationing decisions more transparent, accountable and democratic.²¹

Uncertainty has been broadly defined as '*the normal determinant or unsettled quality of a statement or knowledge claim*'.²¹ The extent and the different forms of uncertainty faced by clinicians during medical training /socialisation²⁴ and how these are managed in clinical decision-making are well documented²⁵ and there are sociological studies which have examined how uncertainty in rationing decisions is negotiated.²¹ In addition, a number of ethnographic studies of rationing decisions have been carried at the local level^{26,27} which have identified the use of different forms of rationality although these studies have not specifically acknowledged the salience of uncertainty or the different ways it may become manifest. The aim of this paper is to fill this gap by unpacking the concept of uncertainty by focusing on two interrelated questions – pertaining to different forms of uncertainty and different strategies amid such uncertainties:

The first question aims to identify which forms of uncertainty are evident in NICE appraisal committee decision making? The conceptual approach adopted in this research was informed by a content analysis carried out on NICE documents (Authors) relating to technological evaluations. This analysis identified three distinct layers or forms of uncertainty which might be manifest within NICE appraisals which are epistemic, procedural and interpersonal or relational. The aim is to assess the explanatory power of this developmental framework based on documentary analysis and to see if these and other

forms of uncertainty are manifest and salient in decision-making analysed via ethnographic data.²⁸

Within this framework, *epistemic* uncertainty relates to the effectiveness of certain methods of investigation to provide knowledge about conditions and their treatment. This layer of uncertainty might involve at least two aspects: confidence in the system of bio-medical knowledge²⁴ and especially in the approach of randomised controlled trials²⁹ and confidence in the publication system of medical journals to differentiate reliable (published) studies from biased (non-published/manufacturers') data.^{30,31} The second layer of uncertainty is *procedural* – involving the various possible methods and approaches⁹ to considering/modelling quality of life and related features of effectiveness, the vast amounts of evidence which could be considered,²⁴ and the multiple contingencies and contestable outputs associated with these. The third layer of uncertainty is *interpersonal or relational* – regarding the competency and motives of those providing evidence and/or recommendations within the process. Uncertainty may exist due to diverse perspectives and relative expertise³² of an array of participants, but furthermore due to the interests that certain groups (eg manufacturers' representatives) have in the outcome of the decision-making process³².

The second main question explores which mechanisms and/or strategies, if any, are used to address or bridge over these various uncertainties? Sociological research into rationing decisions at the national level appears to have paid rather limited attention to differentiating between different forms of uncertainty and how these are managed.²¹ More generally, however, Zinn³³ has described strategies such as emotion, rules-of-thumb, and intuition, as lying 'in-between' rational (calculative and probabilistic) and non-rational strategies (belief, trust, hope, faith and avoidance) for dealing with uncertainty.^{34,35} The aim is to explore the relevance and salience of

these various strategies for managing uncertainty within NICE appraisal decision-making as they are applied in the face of different forms of uncertainty.

Methods

Characterising the Single Technological Appraisal (STA)

The STA process for each technology is instigated by the Department of Health in negotiation with NICE and begins with the formulation/initiation of a decision-problem and decision-criteria followed by a review of evidence. The STA process relies on manufacturer-provided information¹³ so the modelling of clinical and cost effectiveness by pharmaceutical companies informs the formulation of an incremental cost effectiveness ratio (ICER or cost/QALY). Independent academic units or 'evidence review groups' (ERG) then appraise the drug manufacturer's (DM) submission along with official feedback statements from expert/professional organisations, patient groups and other interests. The committee is made up primarily of experts in medical statistics, health economics, epidemiology, public health, clinical specialisms (nurses and doctors), representatives from the health service, the pharmaceutical industry and the (lay) public. Each member (apart from the chair) is appointed on an unpaid voluntary basis. A number of open and closed sessions of committee meetings take place and decisions are (usually) explicitly agreed in the meeting, on the basis of the cost effectiveness threshold (the ICER must be £20,000-£30,000 or less). This threshold has become an explicit and formal norm but appears not to have a rational basis. Decision making is primarily consensual although on some occasions voting is used in the last resort.

Meeting outcomes are formulated into an *appraisal consultation document* (ACD) which, is further scrutinised and following further meetings (where necessary) a Final Appraisal

Determination(FAD) is published.¹⁷ Ideally, our study would have included all phases of the appraisal process, but this was not feasible (access, timing) so this investigation focused on a significant part of this process - following the various committee meeting stages through to the finalisation of the decision. However, an interview with the chair of the committee was carried out prior to the first committee meeting for each specific case but directly after the chairs' briefing meeting, to which we could not gain access. These interviews gave us important insights into the earlier stages of each appraisal.

Design: The study used a prospective design to follow three different pharmaceutical products through STAs involving three of the four NICE technological appraisal committees. Products were purposively selected for variation in the socio-cultural resonance of the condition they are designed to treat: a drug treating a common type of life-threatening illness, a drug treating a less 'prominent' but prevalent chronic illness, and a drug which treated a rare but life-threatening condition. Ten committee meetings were necessary to appraise the three case study technologies and the outcomes of the decision-making for the three technologies was one recommendation of a conditional 'yes' and two 'no's. None of these appraisals involved an appeal although one went through discussions regarding the discounting or patient access scheme (PAS).

Data collection: The research used an ethnographic approach to understand the decision making process from the perspective of those under study.^{36,37} Data were collected through three different but complementary methods: analysis of documents; non participant, unstructured observation of the meetings; and qualitative, semi-structured interviews with key informants involved in the appraisal process. These data were used in triangulation with one another, comparing how uncertainties and decisions were written about, and how they

were recounted in interviews, with what was observed in meetings – to cover different perspectives and features of the appraisal processes.³⁸

Analysis of documentary outputs of the appraisal process provided a detailed background for understanding the decision – and therefore facilitates comparison with the ‘back-stage’ process as elucidated through observations and interviews. Documents made publicly available by NICE were examined alongside those exclusively available to the committee, such as the drug manufacturers’ submissions. Observations were carried out at the public and closed sessions of nine of the ten committee meetings (alongside three pilot observations) where decisions were made - generating data for analysis in their own right as well as foci for discussion within the interviews. Ethical approval from the University of Kent was received in 2011 and those who consented were interviewed and/or observed. Pilot interviews and extensive observational work were carried out to refine the methodology. Across each drug appraisal, semi-structured interviews were conducted with a purposive cross-sectional sample (N=41) including the committee members (CM), representatives from the various interest groups, experts involved in the process and managers from NICE (see table 1), complemented by observations across the three case studies (N=9). Generally, the focus of the interview was on the structure and nature of the decision making process and what shaped it, with the salience of uncertainties and how these were managed being explored within the more general context. More specifically, the topic guide included broader themes associated with individuals’ history and experiences, social relations within the meeting and the social mechanisms and influences which might shape the decision-making from the wider social, cultural environment. The field work was carried out between 2012 and 2014.

Insert Table 1 here

Analysis: Analysis of uncertainty within and across the three cases can be described as abductive,³⁹ in that some of the themes had already been considered prior to the study as informed by the initial analytical schema but this did not preclude the identification of other forms of uncertainty. The themes which emerged from the qualitative data were used to refine, challenge and extend an awareness of the different aspects of uncertainty that are faced by actors within the appraisal process and moreover the strategies applied (explicitly or implicitly) in the face of these. Different dimensions of uncertainty were categorised into themes and sub-themes through a constant comparison approach.⁴⁰ The data were coded separately by two of the research team and samples of the data were double-coded and discussed to advance reliability and construct validity. Data from the observation and interviews were pooled and compared, with NVIVO being used to aid the analysis.

Findings

The analytical purchase of the conceptual framework

The conceptual framework was based on documentary analysis but did it still have explanatory value given the different sources of data used in this analysis which were drawn from observation and interviews? The relevance and importance of uncertainty at a general level were recognised by all the informants, with those on the committee seeing it as central to the decision-making:

'There's lots of tension between the group because some will say, "No, this is really good.", "Look at the benefit it will bring to patients," and then others will say, "Yes, but it's far too expensive. How can we think about that and how do we know that the quality of life data is as accurate as the manufacturers say it is?" So, yeah, I found that there was lots of uncertainty.'
Committee member X07

The framework distinguished, however, between three different elements, epistemic uncertainty, procedural uncertainty and interpersonal uncertainty—each of which were evident in the data and salient to the participants, although other elements such as complexity were equally relevant.

Epistemic uncertainty:

Epistemic uncertainty relates to the basic effectiveness of particular methods of investigation to generate useful knowledge/data about illness experiences and treatment. Certainly the quality of the evidence base was a common theme of concern, the methods and status of randomised controlled trials were sometimes contested (eg the example of cherry picking below) and the quality of the trials was seen to be problematic. However, the lack of mature data was seen to be one of the key sources of epistemic uncertainty which is illustrated in the following extract drawn from observations made in one of the meetings for a TA which was being considered for the PAS (discount scheme) but where ‘newly surfaced uncertainties’, which had previously remained dormant, posed problems for the committee, such as the uncertainty regarding longevity:

Committee Member (CM) 1: we are asked to make a decision with inadequate data

CM 2: the original decision of £---- was made with so much uncertainty .. I would like more time

CM 3 : the age of the elderly patients is a big concern ...we are making extrapolations from 16 week data and we are now making decisions about 32 months. The uncertainty involved fills me with horror’. Open meeting Observation notes, case study Z

The data below are from later on in the meeting in the closed session:

CM 1: if its £--- and then we get away with a lot of uncertainty as it is so far from the threshold, but once it becomes closer to our threshold...’

CM 2 : what did we say about the comparability of the trial to the population to UK patients?

CM 3: refers to the article published about the trial .. maybe they cherry picked that population?

CM4: all trials cherry pick their participants, but normally it does not matter (for cost-effective calculations) but in this example it does’

Chair: we are very uncertain about benefit in the long term. Nobody wants to say yes ... the new ICER [incremental cost-effectiveness ratio] has new uncertainty and that the benefit is for fitter patients.' Closed meeting: Observation notes case study Z

Confidence in journal publication processes and the quality of data also spontaneously emerged within committee discussions, such as here in the context of a committee member discussing the role of the ERG who were also perceived to be influential:

'the quality of the critique by the evidence review group, bringing out points about the original clinical trial of the data that really could put into question the validity of some of the conclusions, and this has been an extraordinary eye opener to me because it makes me look at these very high impact factor, high profile publications in a different light; wondering even why these publications actually got through to be published'. Clinical expert Z06

The lack of quality data, but also understandings of the implementation costs, could also be seen to be problematic:

'There's often a poor understanding of the costs of the treatment and particularly of the sort of implementation costs, so there's always a huge uncertainty'. Committee member Y10

The limitations of the evidence base due to constraints in carrying out clinical trials was particularly evident in relation to certain social groups such, as younger children:

'I'm personally softer at the edges around childhood illness – whether the committee as a whole is I don't know. You know, there'll be people who argue for a very rigid approach. It's confounded by the fact that the evidence base for childhood diseases is usually weaker because randomised trials are much more difficult to arrange ...children are generally well and therefore only ill in smaller numbers isn't such a damaging thing for the NHS'. Committee member Z01

Thus, in response to the epistemic concerns, other social, cultural and logics of rationing judgements also came into play, reflecting the close link between epistemic and procedural uncertainties.

Procedural uncertainty and the problem of complexity

The preliminary conceptual framework indicated that procedural uncertainty involved the multiple contingencies associated with various approaches to modelling effectiveness, the contestable and conflicting outputs of many of these, alongside the sheer volume of evidence which could be considered.

The volume of information was a recurring and major issue for both committee members and for those who were invited to attend specific appraisals. Thus, doubts were expressed over whether the complete story could be comprehended given the sheer bulk of the information that needed to be digested.

‘undoubtedly what has happened in the ten years that I’ve been on the committee is, the reports have got much bigger. The serious point is that science is very complicated, there are an awful lot of uncertainties ‘. Committee member Y11

These challenges were compounded by the specialised and technical nature of the information provided, particularly the modelling for cost effectiveness or decision modelling. Thus, this issue appears to be related to both complexity (having too much information) and uncertainty (not knowing). The following observational extract illustrates this:

‘CM1: the evidence is remotely realistic. The modelling is so complex and difficult that I’m not sure if it does anything or not

CM2: this drug seems to work. It’s not that different from other treatments, but if we do a reality check. It’s not that expensive as current therapies

CM3: that’s a pragmatic approach. I don’t know what the cost effectiveness is.

CM4: I have concerns about the quality of the data which is poor as well as contentious

CM5: it is safe. It’s not our remit

Chair: we are in a position of great uncertainty. I don’t have any sense whether the model is correct. The Decision Support Unit (DSU) needs to be convinced that the numbers run correctly, then look at it again. Can we phrase a Minded No [Interim decision in that there needs to be more analysis carried out]] in that way?’ Observation notes case study Y

This last data extract raises the question of whether uncertainty was reduced during the course of the appraisal process. The contrary was found in some cases where epistemic uncertainties evolved into procedural uncertainty. For example, the following extract reflects the identification of additional sources of uncertainty from the experts during the discussion was perceived to have increased the uncertainties, resulting in a delay in the decision-making:

'In reality this drug probably should have gone through on the second appraisal [meeting] but we kept having this [newly emerging forms of] uncertainty thrown in'.
Committee member X14

The relationship between the independent assessment group (ERG) and the drug manufacturers was highlighted as a possible source of tension about access to information and uncertainty about what information should be available:

'The chair went on to discuss the ERG's comments on the manufacturer's submission and their re-analysis which led to an exchange and disagreement initiated by the chair between the manufacturer and ERG representatives over why the latter did not receive the analysis that they had repeatedly asked for and which the manufacturer said was not available'. Observation notes Case Study Y

Interpersonal or relational uncertainty

Interpersonal uncertainty was reflected in the perceived competency and motives of those providing evidence and/or recommendations within the process. This was relevant to a number of different interest groups who provided both written and oral submissions to the committee and, most commonly, the competencies and motives of the drug manufacturers, the nominated clinical experts and patient representatives. For example, in relation to the drug manufacturers' position, common themes included concerns about bias and whether

the drug manufacturers' analysis could be trusted, resulting in limited confidence expressed in the submissions from the drug manufacturers:

Manufacturer representative: We didn't understand the ERG's point. We did the adjustment.

CM1, So you haven't applied mortality from general life tables?

CM2, It's not correct

CM3, It sounds like the company does know what it's doing. I am mystified.

One CM went on to suggest that the drug manufacturer should 'give up and go home' given the weaknesses in analysis and that their representatives were unable to answer some of the committees' key questions. The representatives did not carry out the analysis themselves and were described by one member of the committee as 'fall guys'. Observation notes Case Study X

This case study illustrated a somewhat confrontational, becoming almost inquisitorial, interaction between the committee and the drug manufacturers:

'I think [the committee] were getting very irritated because they didn't have the answers that they wanted and at the end where they started really going for the manufacturers... I think the committee probably don't trust them'. Clinical expert X02

The reluctance to address at least some of uncertainties was perceived to be damaging for the drug manufacturers:

'I mean there's lots of evidence on uncertainty that should be provided but the manufacturers still don't give all of the information. I think one of the ways that we deal with that is that if there feels like there's a lot of unresolved uncertainty then we're more conservative in our estimate of what we think the ICER is going to be'. Committee member X08

Finally, it was suggested that committee members' uncertainty about and suspicion of the drug manufacturers had to be balanced against the level of criticism provided by the assessment groups:

'One thing that's really struck me about all of these appraisals, actually, is if you read the manufacturer's submission, well, you should definitely fund this. They must be really trained to write it in such a way that, you know, it's a done deal. But then you

read the ERG's critique of it and you think oh, wait a minute! And it makes you read it much more critically. But then, you know, sometimes they're over critical and it might be somewhere between the two'. Committee member Y12.

The committee members also expressed ambivalence regarding the testimonies of both patient experts and clinical experts to the committee. There seemed to be a perception that patient representatives tended to be narrowly focused on their own condition and therefore provided a less balanced or broader view. Moreover, concerns were expressed about potential conflicts of interest as these patients were drawn from interest groups which were sometimes supported or paid by the drug manufacturers:

'It appears that many of these companies support these groups and at the beginning of every meeting everyone declares a conflict of interest...I've certainly been aware of it once where it was quite clear that a company was heavily supportive of the particular sort of patient support group and I found that quite difficult to be completely objective about... maybe the patients might be a bit naïve about some of the motivation but I think it is something you can't really ignore. Committee member Z09.

Similarly, uncertainties and ambivalences were expressed about the importance, competence and motives of the clinical experts, with some seeing these experts as importantly influencing later discussion:

CM 'I was quite impressed at how the clinical expert was quite objective..'
Observation notes case study Y

while others suggested a more marginal role:

'The role of the clinical expert, I think, is more to confirm any doubts in the submissions that the appraisal committee have. So I don't think that clinical experts really would be 'game changers' under any circumstances'. Committee member Z05

As with expert patients, there was a potential for clinical experts to be seen to be 'evangelists', which raised the question of their independence as well as evidence of conflicted interests:

'occasionally you get some who seem to be very close to the manufacturer. [And so you question] the independence of the evidence.' Committee member X09

Navigating or muddling through?

Having considered the different types of uncertainty which appeared within the data, our analysis moves on to how these uncertainties were dealt with. A distinction can be made between explicit/formal strategies and/or mechanisms used by the committee and the informal strategies used by the committee both individually and collectively. The analysis shows how these personal practices used by individual members are organised into collective strategies adopted by the committee.

Explicit strategies included statistical and economic models available for denoting categories of uncertainty - particularly epistemic and procedural uncertainties - and thus attempts were made to technically measure and quantify the level and extent of confidence and uncertainty, although this did not necessarily solve problems of uncertainty. This perspective was evident in the following extract from an informant from NICE who suggested that they expected committee members to reflect on the epistemic and procedural uncertainties in the process:

'...we expect people to reflect on the uncertainty in the structure of the model, in the parameters used and the consequences of them. There's some different scenarios they could run and generally reflect on the timing at which the evidence has been created ...probably the difficulties in understanding the natural history of patients without technology – all that stuff which is in the evidence – so there's a technical way of expressing it. The challenge is to understand how committee deals with the uncertainty' NICE Employee,03

Informal strategies emerged due to the limitations of the explicit approaches.³³ There was a recognition that some parts of uncertainty cannot be addressed and therefore tend to be ignored or bracketed off:

'I mean if you would take it [uncertainty] fully into consideration you basically can never take a decision because you just have to acknowledge that you don't know, so every

decision's constantly taken on the best available evidence and what you think is most likely so, yeah, part of that uncertainty is just brushed under the carpet' Member of ERG Z02

Thus, one individual practice involved focusing on certainties as opposed to uncertainties reflecting a form of bounded rationality:

'Rather than concentrate on everything that's uncertain you say, "okay well what can we reasonably be confident about", otherwise you only end up in a sea of uncertainty.' Committee member.' X03

This type of pragmatic rationalism was a common stance which encompassed a number of personalised strategies:

'...but being pragmatic about it as well and just realise, okay, we don't know but what is the objective here and try to keep sight of the goal...sometimes the economists on the committee lose this perspective'. Committee member X06

One of these strategies appeared to involve invoking a subjective 'gut' feeling:

'I think it comes down to a stance or gut feeling on how much you believe what's in front of you' Member of assessment group X05

There were also pragmatic strategies employed to manage the quantity of information:

'I mean the last [appraisal] was horrible. There were two thick volumes through each of the appraisals that we had which is why I think I've started working from the critique as it starts by summarising what they did'. Committee member Y12

The level of complexity regarding the technicality of the information led to a lack of participation in discussion by non-technical specialists on the committee in what might be perceived to be an intimidating setting:

'Many members of the committee did not participate in the discussion as it was very technical and at one point the chair told one of the members to "please speak in 'plain English'". One committee member commented: "I struggled today. there needs to be more education to help us feel comfortable"'. Observation notes Case Study Y

Trust relations becoming salient in this context of complexity, where one common type of strategy used was to defer to the expertise and judgements of the specialists and others on the committee who were seen to have greater understanding of the complexity of the modelling (authors):

'So I have to take my thoughts on what I understand from the papers with a pinch of salt. You need expert interpretation and guidance from the committee'. Committee member Y05

This influence of particular experts within the committee in driving decisions was also corroborated by the observational evidence, with the case below reflecting deference to clinical judgement when there was considerable uncertainty about cost effectiveness:

One committee member stated in the closed meeting that 'there is uncertainty about the cost effectiveness so, rather than say 'no' to cost-effectiveness, we could say 'no' based on clinical guidelines if the committee is envisaging a role for this [drug] maybe the decision should not be just on cost effectiveness'. Hence, the uncertainty with the economic analysis led to the strategy to leave the decision to the clinicians - 'let the doctors decide' - so the decision followed the clinicians' interpretation of NICE clinical guidelines. Observation notes Case study X.

Committee members described being influenced by the committee discussion itself but also through informal discussions with other members of the committee, as a way of managing particularly the level of technicality of the information:

'...at committee some of the really in-depth economic analysis modelling discussions, for me, there's that level of uncertainty...am I completely clear that I'm following everything that I should be? What does tend to happen is the people who sit around you ask questions to one another. "Did I hear that right? You know, so there is a bit of informal reinforcement'. Committee member Z09

One particular problematic area for the committee was dealing with the testimony of patient experts and contrasting collective strategies were used to manage these accounts and the related uncertainties:

'Often that's the last thing that happens at the end of part one [the public part of the meeting] is a speech by the patient group and I'm always a bit unsure of how I'm supposed to be processing that information and so it can sometimes be quite emotional... I think the committee members deal with it in two ways; one is to completely dismiss the emotional arguments, or [be] completely dominated by them if we really understand the burden of this and the unmet need of the treatment...so it's a tricky one'. Committee member Y12

The analysis furthermore found that individual practices for dealing with uncertainty were coordinated into more collective strategies. For example, shared understandings of norms of which uncertainties could be questioned which could not, alongside the importance of deferring to the navigating role of the chair in bypassing uncertainties (*'the fudge factor'*), were often referred to in interviews. These can be understood as a collective form of bounded rationality. For example, the chair could be seen to steer the committee towards what one committee member described as an efficient decision, as opposed to waiting for further evidence from the drug manufacturer or the specialist review groups which was seen as the easier option:

'a lot of that is to do with the experience of the Chair and the way of marshalling the contributions from the committee...there's probably quite a lot of opt-outs that the committee could have along the way in terms of we want more information before we make a decision or we will go back and will we stall and require the manufacturer to do more? Will we want the ERG to do more analysis?' Committee member Z12

Finally, a different collective strategy adopted by the committee took the form of an ongoing negotiating process with the drug manufacturers, involving demands for clarification over time. Hence, the latter depicted the appraisal process as a kind of game or strategy, whereby you initially submitted and were turned down and then resubmitted your work with the required outcome:

'I mean a 'game' probably makes it sound manipulative, but I suppose it's just how it is, isn't it, let's have a similar scenario where the cost is quite high, which it often is, and then the benefit, the uncertainty around the evidence is very uncertain... Equally

it's like getting your homework back and the teacher correcting it in the margin. If you resubmit it with the corrections then you'll get the A rather than the F you [were] predicted'. Drug manufacturer Z04

The effectiveness of such a strategy was confirmed by a member of the committee when discussing the analysis provided by a drug manufacturer:

'The only thing that that could reduce the uncertainty will be head-to-head comparisons with hard endpoints...And that basically forces the manufacturer to provide further information...something like over 70% of Minded No's become Yes when you get the information you actually want from them'. Committee member X01

This 'game' format appeared to enable the gradual working through of uncertainty - getting the manufacturer to reduce the uncertainty and work through the most problematic issues. For example, in case Z the willingness of the manufacturer to do this and 'play the game' appeared influential in their new data/submissions being taken seriously. This appeared to be a kind of reciprocated 'good will', by which reducing interpersonal uncertainty enabled epistemic uncertainty around the quality of the data to be partly overlooked.

Discussion

Sociological research into decision-making about rationing at the national level has to a limited extent focused on uncertainty,²¹ but not considered the different layers of uncertainty that might be embedded in these decisions and how they are managed. Thus, the focus of this analysis was on exploring the extent and nature of uncertainty in appraisal decision-making and how these uncertainties were addressed and managed in different ways. The data analysis suggests that various intractable uncertainties were a significant and somewhat defining issue recognised by the informants from the committee – hence, the identification of a range of strategies used by the committee for dealing or grappling with these various types of uncertainty.

The loose conceptual framework constructed from the previous documentary analysis which distinguished between epistemic, procedural and interpersonal provided some analytical purchase in that there was evidence in the analysis of these three different elements of uncertainty. However, this schema did not fully capture the nature and experiences of uncertainty as they appear in the observational and interview data. Sometimes there was an overlap or blurring of the boundaries between categories. For example, in relation to manufacturers' submissions, there were uncertainties about the data used, procedures for analysing the data, the presentation of the data and the general motives and competence of the drug manufacturers' stance by which epistemic, procedural and interpersonal uncertainty were interwoven with one another.

There was also some evidence of shifts from one form of uncertainty to another as decision-making processes evolved. For example, the data showed how issues of epistemic uncertainty evolved or were transformed into procedural issues as the committee deliberated on the evidence. Similarly, uncertainty about the quality of the drug manufacturers' analysis, a form of procedural uncertainty, seemed to evolve into issues around trust in the drug manufacturers' competence and motives - a form of interpersonal uncertainty. The types or layers of uncertainty identified in the analysis of publicly available, formal documents (Authors), tended to highlight issues around epistemic and procedural uncertainty rather than interpersonal uncertainty, which might reflect an emphasis within the front-stage policy talk about the instrumental and institutional approach of NICE. However, the evidence from this ethnographic study which looked more at backstage decision-making suggests that forms of interpersonal or relational uncertainty are important and prevalent, particularly in relation to uncertainties expressed about the independence and motives behind submissions and accounts presented by a range of interest groups.

Forms of uncertainty that the initial conceptual framework did not address included the level of technicality of the information provided, particularly in the modelling of the evidence, which led to the committee members being uncertain about its meaning and how to use it to come to a decision. This might be better described as complexity, whereby some authors⁴¹ argue that uncertainty is a residual of working with complexity, alongside related interpretative/valuing issues of *ambiguity*. Certainly, the extent of information provided seems to create further complexities rather than resolving uncertainty and straightforwardly facilitating rational decision making.⁴²

There was common recognition that some forms of uncertainty were ignored and not addressed, as they could not be managed and that, in order to reach a decision, deliberations ultimately needed to focus down on a relatively small number of issues, with wider potentially problematic uncertainties being bracketed off (Authors 2012). This reflected a form of reasoning characterised by bounded rationality and typifying a form of satisficing behaviour where this is seen as an acceptable, if not optimal, strategic solution⁴³ – although in this context the evidence suggested forms of bounded rationality manifested in both collective and individual strategies. Collective strategies included: emergent norms by which the committee members learned to openly question some uncertainties while overlooking others; forms of collective deference to the chair or specific committee members with particularly high levels of expertise; or shared (mis)trust of particular manufacturers as their performances were evaluated during the appraisal. These collective strategies were thus comprised of ‘embedded’ organisational understandings⁴⁴ which in turn involved an orchestration of many individual strategies,³³ such as individual committee members’ trust in the chair or their committee ‘habitus’ as this emerged over time.

There was evidence of a plurality of legitimate perspectives for evaluating evidence, decisions and outcomes but calculative approaches in NICE decision making were particularly emphasised

in the discussions on the strength of the evidence to support cost effectiveness¹³ and thus the uncertainties related to that issue were paramount. One primary concern was whether the drug manufacturers' analysis had been carried out using the most appropriate methodology and addressed the salient pre-agreed appraisal questions and whether the submission was transparent and accessible enough to be critically assessed. Much emphasis was placed upon the drug manufacturers' interpretations of the evidence and their tactics in presenting this, which might skew or shape the decision-making in favour of the drug manufacturer.¹³ However, the stance of the committees suggested that they were not passively accepting of this interpretation and could not be seen as simply aiding in so-called regulatory capture,⁴ at least at this micro-level of analysis.

The interpersonal uncertainty associated with a lack of trust in the drug manufacturers' competencies and motives led to a number of stances, strategies or tactics. One was a general scepticism adopted by the committee towards the drug manufacturers submissions requiring them to prove that their case was a genuine one. In response, the drug manufacturers pursued active strategies for dealing with the committee's approach, one of which was to adopt trial and error tactics, with the hope that at the second or third attempt the technology would be recommended.

A similarly critical or ambivalent stance was adopted by the committees towards the testimonies of the patient and clinical experts as there was concern about the latter's conflicts of interest, and possibilities of being 'captured' by the drug industry,²² or having too narrow an experiential focus rather than being concerned with what was best for the NHS patient population as a whole. The ambivalence or caution expressed about the opinions of these experts led their evidence to being used as supplementary or supportive information to the overall decision of the committee. The relative influence of the experts varied from case to case, thus

there was only limited evidence in this study to support the notion of co-production of knowledge argued to be evident in the case study of dementia drugs.²¹

The stereotype of NICE as a procedurally-rational evidence-based regulatory institution contrasts with the somewhat messy process of committee decision making above; Mechanic's description of muddling through elegantly is apposite here⁴⁵. This was exemplified by the informal strategies used by individual committee members for dealing with residual uncertainty and aspects of complexity, particularly in relation to the technicality and sheer volume of information provided. These strategies included developing rules of thumb, using 'gut reactions' based on intuitive/tacit knowledge and other ways of simplifying highly complex material. In some ways our findings reflected other ethnographic-oriented research focusing on rationing decisions at the local level which identified a related form of reasoning which is characterised as practical rationality and involves intuition and experiential knowledge⁹ and a 'case and judgement based' approach.²⁶ In both contexts the use of practical rationality was evident but appeared to be at odds with the dominant instrumental discourse. In these local contexts ethical discussions and informal modes of dealing with uncertainty related more directly to individual circumstances.

In contrast, within NICE appraisals there appeared to be less space for individual discretion and a greater coordination of informal approaches through reference to norms and previous decisions, alongside a reliance and trust in those with specialist expertise, particularly senior clinicians and economists, to steer them in the right direction. These influential players on the committee were the clinicians, economists and statisticians, supported by the evidence review groups, who were most able to make sense of the technicality of the data analysis. Central to the coordination of informal approaches was the navigating role of the chairs and their ability to steer the committee through the complexity and even circumnavigate different aspects of

residual uncertainty - a form of collective bounded rationality, towards a collective decision within the time and space allowed in the institutional framework. However, such influences of intra-group dynamics and power relations, as well as (dis)trust, time limitations and a related bypassing of uncertainty, were invisible within the official, disembodied account of the FAD.^{10,27}

At a more global level, there is the general question about whether regulatory agencies operating in other countries with different health and welfare systems and cultural contexts approach their tasks in a similar or different way to how NICE works in England. Comparative analyses of how different regulatory agencies⁴⁶ make recommendations about the provision of expensive medicines in the context of uncertainty are in short supply. However, at a more general level it appears that NICE might be more vulnerable to the influences of the pharmaceutical industry, compared with other regulatory agencies found in other contexts. For example, in New Zealand, PHARMAC (the equivalent of NICE) has become a Crown Entity, meaning that it is a standalone body and is independent from the influences and directions of government ministers, coupled with a set budget that it cannot legally exceed appears to make it less vulnerable to corporate bias⁴⁷. More generally, there seems to be this apparent paradox that regulatory agencies operating in the context of neoliberal health systems may be more able to resist the influences of the drug industry (regulatory capture) than those working in the context of more communitarian health systems.⁴⁸

Limitations: This study explored the decision-making across the three of the four committees which might be significant as it became evident that each of the committees appeared to have its own 'style' of decision-making heavily influenced by the chair, suggesting that there may be variations in recommendations by committee. Cerri and

colleagues¹³ found in their statistical analysis that a large majority of technological appraisals recommended 'yes' but the three cases followed in this current study involved two *no*'s and one conditional or restricted *yes*, suggesting that the appraisals included in our study might not be typical. However, in the pilot and feasibility stages of this research a number of other technological appraisal meetings were observed and the process, at the least, appeared to be similar to those that were observed in the main study. Moreover, statistical evidence¹³ suggest that the proportion of restrictions and non-recommendations issued by NICE are increasing although referral to discounting (via Patient Access Schemes and the recently abolished Cancer Drugs Fund) may have been increasing too²³

Conclusions

Vast complexity and many uncertainties were central to these rationing decisions and the difficulties of dealing with the various levels of uncertainty were manifest. Decision-makers adopted a mixture of collective and individual, explicit and informal strategies in making decisions as there was a need to exercise discretion and pragmatism within a more formal institutional framework. Thus, rather than the decision-making process being neat and procedurally-rational, it was also characterised by a process of negotiation with the use of pragmatic methods to navigate through complexity and layers of uncertainty.

The findings suggest that certain 'social' approaches to the appraisal process are gradually becoming institutionalized,³⁷ either as unspoken norms within committees or more formally within the 'methods' guide for NICE appraisals. Not all categories of uncertainty have been fully recognised in current policy and this study showed the salience of uncertainties associated with interpersonal relations and particularly the relations between the committee and the drug

manufacturers, clinical experts and patient experts. These relations tend to be characterised in terms of trust or the lack of it.⁴⁹

Potential solutions to some of these problems raised by this study might include giving the committee a further decision outcome, such as 'intolerable uncertainty' or insufficient data which would assist in placing an onus on manufacturers to make their submissions as clear and transparent as possible. In addition, committee members might be given enhanced training in economics and statistics and more time for discussion, deliberation and preparation, the adoption of tighter controls on the conflict of interests of expert clinicians and a broader selection criteria for expert patients, rather than relying solely on recruiting from patient organisations.

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References

1. Moran M. *The British Regulatory State: High Modernism and Hyper Innovation*. Oxford: Oxford University Press; 2003.
2. Crinson I. The Politics of Regulation within the 'Modernized' NHS: The Case of Beta Interferon and the 'Cost-Effective' Treatment of Multiple Sclerosis. *Crit Soc Pol*. 2014; 24: 30-49.
3. Timmins N, Rawlins M and Appelby J. *A Terrible Beauty: a short history of NICE, The National Institute for Health and Care Excellence*, Bangkok: Amarin; 2016
4. Abraham J. The pharmaceutical industry, the state, and the NHS. In: Gabe J, Calnan M, eds. *The New Sociology of the Health Service*. London: Routledge; 2009:99-120.
5. Faulkner A. Medical Technologies. In: Gabe J, Faulkner A, eds. *Key Concepts in Medical Sociology*. London: Sage; 2013: 128-132.
6. Harrison S, McDonald R. *The Politics of Healthcare in Britain*. London: Sage; 2008.

7. Shah K, Cookson R, Culyer A, Littlejohns P. NICE's social value judgements about equity in health and health care. *Health Econ Policy Law*. 2012; 8: 145-164.
8. Weber M. The Development of Bureaucracy and Its Relation to Law. In: Runciman W. ed. *Weber: Selections in Translation*. Cambridge: Cambridge University Press; 1978: 341–356.
9. Russell J, Greenhalgh T. Being 'rational' and being 'human': How National Health Service rationing decisions are constructed as rational by resource allocation panels. *Health*. 2014; 18: 441-457.
10. Degeling P. Health Planning as Context-Dependent Language Play. *Int J Health Plan M*. 1998; 11: 101–117.
11. Light D, Hughes, D. A sociological perspective on rationing: power, rhetoric, and situated practices. *Sociol Health Ill*. 2001; 23: 551-569.
12. Milewa T. Representation and legitimacy in health policy formulation at a national level: Perspectives from a study of health technology eligibility procedures in the United Kingdom. *Health Policy*. 2008; 85: 356-62.
13. Cerri K, Knapp M, Fernandez J. Decision-making by Nice: examining the influences of evidence, process and context. *Health Econ Policy Law*. 2014; 9: 119-141.
14. Power M. *The Audit Society: Rituals of Verification*. Oxford: Oxford University Press; 1997.
15. Poortinga W, Pidgeon N. Exploring the dimensionality of trust in risk regulation. *Risk Anal*. 2003; 23:961–73.
16. Milewa T, Barry C. Health Policy and the Politics of Evidence, *Soc Policy Admin*. 2005; 39: 498-512.
17. Guide to the single technological appraisal process. National Institute for Health and Clinical Excellence web site.
<http://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology->

[appraisals/Guide-to-the-single-technology-appraisal-process.pdf](#). Published October 2009.

Accessed March 3, 2016.

18. Rawlins M, Barnett D, Stevens A. Pharmaco-economics: NICE's approach to decision-making, *Brit J Clin Pharmacol*. 2010; 70: 346 -349.
19. Lindley W, Hughes J. Societal views on NICE Cancer Drugs Fund and Value-based Pricing criteria for prioritising medicines: a cross-sectional survey of 4118 adults in Great Britain. *Health Econ*. 2013; 22: 94-964.
20. House of Commons Health Committee. *National Institute for Clinical Excellence*. Second Report of Session 2001-2 – Vol. 1. London: TSO. 2002; (HC515-I).
21. Moriera T. Health care rationing in an age of uncertainty: a conceptual model, *Soc Sci Med*. 2011; 72: 1333-1341.
22. Davis C, Abraham J. Desperately seeking cancer drugs: explaining the emergence and outcomes of accelerated pharmaceutical regulation. *Sociol Health Ill*. 2011; 33: 731-47.
23. Ferrario A, Kanavos P. Dealing with uncertainty and high prices of new medicines: A comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden, *Soc Sci Med*; 2014. doi: 110 1016/socsimed 2014.11.003.
24. Fox R. Medical uncertainty revisited. In: Bendelow G, Carpenter M, Vautier C, Williams S, eds. *Gender, Health and Healing: the public/private divide*. London: Routledge; 2002:236-253.
25. Calnan M. Clinical uncertainty: is it a problem in the doctor-patient relationship? *Sociol Health Ill*. 1984; 1: 74-85.
26. Hughes D, Doheny S. Deliberating Tarceva: a case study of how British NHS managers decide whether to purchase a high-cost drug in the shadow of NICE guidance. *Soc Sci Med*. 2011; 73: 1460-1468.

27. Russell J, Greenhalgh T. Affordability as a discursive accomplishment in a Changing National Health Service. *Soc Sci Med*. 2012; 75: 2463-2471.
28. Timmermnas S, Tavory I. Theory construction in qualitative research: from grounded theory to abductive analysis. *Sociol Theor*. 2012; 30: 167-186.
29. Busfield J. Pills, Power, People: Sociological Understandings of the Pharmaceutical Industry. *Sociology*. 2006; 40: 297-314.
30. Horton R. The dawn of McScience. *New York Rev Books*. 2004; 514: 7–9.
31. Smith R. Medical Journals are an Extension of the Marketing Arm of Pharmaceutical Companies. *PLoS Med*. 2005; 2: e138.
32. Britten N. *Medicines and Society: Patients, Professionals and the Dominance of Pharmaceuticals*. Basingstoke: Palgrave Macmillan; 2008.
33. Zinn J. Heading into the unknown: everyday strategies for managing risk and uncertainty, *Health Risk Soc*. 2008; 10: 439-50.
34. Gigerenzer G. *Rationality for mortals: How people cope with uncertainty*. 6 Oxford: Oxford University Press; 2006.
35. Möllering G. The Nature of Trust: From Georg Simmel to a Theory of Expectation, Interpretation and Suspension. *Sociology*. 2001; 35: 403 –420.
36. Ritchie J, Lewis J. eds. *Qualitative research practice*. London: Sage; 2006.
37. Davies D, Wetherell M, Barnett E. *Citizens at the Centre: deliberative participation in healthcare decisions*. Bristol: Policy press; 2006.
38. Bryman A. *Social Research Methods*. Oxford: Oxford University Press; 2008.
39. Meyer S, Lunnay B. The Application of Abductive and Retroductive Inference for the Design and Analysis of Theory-Driven Sociological Research. *Sociol Res Online*. 2013; 18:1.

40. Dye A, Schatz M, Rosenberg B, Coleman S. Constant comparison method: A kaleidoscope of data, *Qual Rep*; 2000: 4.
41. Renn O, Klinke A, van Asselt A. Coping with complexity, uncertainty and ambiguity in risk governance. *AMBIO*. 2011; 40: 231-246.
42. Tsoukas H. The Tyranny of Light. *Futures*. 1997; 29: 827-43.
43. Simon H. *Models of Bounded Rationality, Volume 1: Economic Analysis and Public Policy*. Cambridge, Mass: MIT Press; 1982.
44. Lam A. Tacit knowledge, organisational learning and societal institutions: an integrated framework. *Organ Stud*. 2000; 21: 487-513.
45. Mechanic D. Muddling through elegantly: finding the proper balance in rationing. *Health Aff*. 1997; 16:83-92.
46. Ozieranski P, McKee M, King L. The politics of health technology assessment in Poland. *Health Policy*, 2012; 2-3:178-193.
47. Dew K and Davis A. Limits to neoliberal reforms in the health sector: the case of pharmaceutical management in New Zealand. *International Journal of Health Services*, 2014; 44(1): 137-153.
48. Calnan M and Douglass T. The Evaluation of New Medicines in Geve B (eds) *Handbook of Social Policy Evaluation*, Cheltenham: Edward Elgar; Chapter 20, 2017 (in press).
49. Brown P, Hashem F, Calnan M. Trust, regulatory processes and NICE decision-making: Appraising cost-effective models through appraising people and systems. *Soc Stud Sci*. 2016; 46(1):87-111

Table 1: Type of informant interviewed

Committee members including chairs ¹	N = 23
Managers from NICE	N = 3
Patient organisations	N = 3
Drug manufacturers	N = 5

Experts from assessment group/clinical exper	N = 7
Overall Sample	N= 41 ^{2,3}

¹ Includes statisticians, health economists, clinicians, public health epidemiologists and lay members. ² Three with NICE staff plus 14 in case study X, 12 in case study Y and 12 in case study Z. ³ 15 face to face and 26 telephone interviews.