

**Report on NICE Citizens Council meeting**

# **Departing from the threshold**

**November 27-29, 2008**

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### **What we were asked to consider**

In what circumstances should NICE recommend interventions where the cost per QALY is above the threshold range of £20-30,000?

### **The conclusions we reached**

Two of the 29 Council members attending the meeting took the view that there were no circumstances in which NICE appraisal committees should depart from the established threshold. These two members took no further part in the voting.

Of the remaining 27 Council members, the numbers who favoured taking account of each of a list of various possible circumstances were - in order of support - as follows:

- the treatment in question is life-saving 24
- the illness is a result of NHS negligence 23
- the intervention would prevent more harm in the future 23
- the patients are children 22
- the intervention will have a major impact on the patient's family 22
- the illness under consideration is extremely severe 21
- the intervention will encourage more scientific and technical innovation 21
- the illness is rare 20
- there are no alternative therapies available 19
- the intervention will have a major impact on society at large 16
- the patients concerned are socially disadvantaged 13
- the treatment is life extending 10
- the condition being tackled is time-limited 9

- the illness is a result of corporate negligence 2
- the stakeholders happen to be highly persuasive 0

### **How we worked**

Twenty nine of the members of our Council were able to attend the meeting, held from November 27<sup>th</sup> to 29<sup>th</sup> at NICE headquarters in London. The first day began with an introduction to the question we had been asked to tackle. This was delivered by Peter Littlejohns, clinical and public health director of NICE. We then immersed ourselves in a refresher course (or a primer for new members) on health economics and the means by which NICE reaches its decisions. Once we had been reminded what the Citizens Council itself has said in the past about dealing with exceptional circumstances, we spent the rest of the day listening to - and discussing - various medical and commercial views on the issue.

On the second day we heard how NICE committees actually make decisions, and also tried making a typical decision for ourselves. The rest of the day was spent listening to and discussing more perspectives, this time including those of patient representatives and health administrators as well as doctors. The day's speakers then took part in a panel discussion.

Our final morning was devoted to discussing our ideas, reaching conclusions, and voting on what should go into the report.

We were able to question all the experts who spoke to us, and the meeting was punctuated with regular discussion: informally among ourselves; in pairs or small groups in the meeting room; and together in our plenary sessions.

During the course of the meeting we completed four questionnaires designed to track any shifts in our opinions.

### **What we heard, and what we did**

Professor Littlejohns began by reminding us of the circumstance that had led to the creation of NICE: "There just isn't, and never will be, enough money to provide every possible service." The question we had been convened to tackle on this occasion was clearly taking us to the very heart of NICE's activities: under what circumstances should its appraisal committees be prepared to depart from the organisation's guidelines regarding cost-effectiveness?

As Professor Littlejohns pointed out, when the Government created NICE in 1999 it left the new body to forge its own criteria for recommending whether or not procedures referred for assessment by the Department of Health should be made available through the NHS. This included setting its own economic threshold. NICE sought opinion and commissioned research - but to a great extent set its threshold in 2004 on the basis of the decisions that the appraisal committees had made. This eventually generated the familiar figures: £20,000 per QALY as the sum below which an effective treatment would normally be accepted; and £30,000 per QALY as the sum above which very good reasons would be needed to gain acceptance. The acceptance of interventions costing between these two figures would be subject to debate.

Final judgements can be influenced by the certainty or otherwise of the cost effectiveness calculations, by the innovative nature of the technology, by reference to previous appraisals, and by whether relevant societal costs and benefits have been captured. Particular features of the condition such as its severity, the uniqueness of the treatment, and the nature of the population to be treated are also factors that might be taken into account. These, Professor Littlejohns suggested, were among the factors that we would have to consider in reaching our decisions.

Responding to our questions, Professor Littlejohns said that in spite of inflation and increases in funds to the NHS, the NICE threshold had never been changed. But whether there was a need to do so, he added, was under review. He also conceded that the evidence on which NICE has to make up its mind may be incomplete. In many cases it can't tackle this by deferring a final decision until there is more to go on. Therefore an option is to authorise the drug to be used only in the context of a research project.

One of us wondered if NICE ever suggested that a treatment of lesser effectiveness be abandoned in favour of something else. We learned that dis-investment of this kind is a live issue – though while many people, including some politicians, believe that money is being wasted on ineffective treatments, very few of these have been identified. In most cases the problem is not that the treatment is ineffective, but that it works only in a minority of the patients receiving it. Another member chose to bowl a googly: what would happen if a company developed a drug that was *slightly* less effective than the existing agent, but a *lot* cheaper? Professor Littlejohns preferred to leave that for the next presenter.

### *Grappling with the QALY*

Our next presentation was from Joanne Lord, formerly of NICE but now a reader in health economics at Brunel University. She reminded us of the nature and process of cost-effectiveness analyses, how health outcomes are measured, the basis of the Quality Adjusted Life Year or QALY, the extent to which future QALY gains have to be discounted in comparison to ones gained immediately, and how harms, benefits and costs are balanced to reach an overall assessment of cost-effectiveness. Such assessments cannot always be made with total precision, she added.

She offered, for our consideration, some economic reasons that might justify a stretching of the threshold. The health gains of an intervention might, for example, have been underestimated; or its incremental cost might have been overestimated. Alternatively it might be felt that the health economic approach may not truly reflect societal preferences. The public may, for example, wish to put greater weight on length of life as opposed to its quality; or they might favour certain patient groups such as those with severe disease or some social disadvantage.

The intervention might also create extra costs or benefits outside the health arena: a reduction in crime due to drug misuse, for example. There is also a case to be made for rewarding treatment innovation and so supporting industry investment in the long term. All of these could be viewed as constituting a case for departure from the NICE threshold. She added that she saw no economic case for stretching the threshold because a disease was rare.

In subsequent questioning one of us asked her whether a NICE endorsement of an expensive drug that led to an increase in its sales would then bring about a fall in the price. Jo Lord confirmed that economic theory would point to the likelihood of this outcome, but said she had no empirical evidence.

She also responded to the question of less effective but significantly cheaper drugs put earlier to Peter Littlejohns. If the drug was only slightly less effective, she said, it might be acceptable. But people who'd been taking a more effective product would probably be loath to give it up.

### *NICE appraisals*

Next it was the turn of Elizabeth George to give us more detail of the process of NICE appraisals. She described the make up of appraisal committees, how they go about their work and, with examples, how they reach their decisions. As she told us, to operate a rigid cost threshold with

no exceptions might make life simpler, but in practice this doesn't happen as it would deny any possibility of responding to the inherent uncertainty of some of the evidence and the need to promote therapeutic innovation. It would also prevent committees responding to the guidance incorporated in NICE's continually developing Social Value Judgement (SVJ) document, and might even create difficulty in coping with equality and fairness legislation covering matters such as race, gender and disability. She concluded by pointing out that since NICE had begun operating it had in fact recommended that most of the technologies put before it be made available either generally or for specific patient groups. Very few had received a blanket rejection.

At this point Peter Littlejohns took the microphone again to remind us that this was not the first occasion on which our Council had tackled the question of whether NICE should allow itself to breach its own threshold. One of our 2006 reports was on the "rule of rescue": the tendency to help people who are in imminent danger of death, even if to do so would deny resources to other people, possibly in greater numbers, whose longer term health might consequently be neglected or even damaged. Most of the then Council members had decided that, in exceptional cases, NICE should be guided by a rule of rescue, and listed a dozen or so circumstances in which it might apply. These included avoiding immediate loss of life, averting a threat to the public health, and fostering potentially valuable medical research. Members also added that they favoured a rule of rescue because it was one of the marks of a humane society, and one of the building blocks of social capital.

Another Council meeting had found a majority of members requesting that, under certain circumstances, the NHS should be prepared to pay premium prices for the treatment of individuals with very rare diseases. And yet another meeting, held earlier in 2008, had come down firmly in favour of taking the severity of an illness into account when making decisions.

At this point we split up into pairs for a five minute discussion on the choice of a question to put to a panel of the morning's speakers. The topics we picked included post code prescribing, possible conflicts of interest among appraisal committee members, and unlicensed medical treatments.

The panel reminded us that NICE does not scrutinise every technology. Much decision-making in the NHS, including which treatments to pay for, is still local; one trust may decide that the needs of its local

population will best be served by spending money in one way, another trust by spending in a different way. Geographical variation will continue.

### *Decisions, decisions*

The afternoon of the first day began with a presentation from Tony Hope, a medical ethics specialist from the University of Oxford. He told us the health authorities in his area, conscious that there had to be some way of resolving conflicting budgetary demands equitably, had set up a local NICE-type body even before NICE itself had been created. It too set a guide price for treatments, and also used QALYs in reaching its decisions. He then went on to discuss the circumstances under which the threshold might be breached: in particular with respect to need and equity.

Need can be recognised by urgency and by the high degree of harm that results from ignoring it. But need is not an all or nothing description; it comes in many degrees, with some patients having a greater need than others. Equity requires that people's needs be treated equally. But this isn't always possible. One can hardly spend an entire health budget on treating one (very expensive) condition, for example. And the cost of solving a particular problem may vary from patient to another. Thus dental treatment for people with a learning disability is more costly than for the rest of the community.

Tony Hope illustrated this by asking us to spend some minutes thinking about the conflict between cardiologists who wish to prescribe statins to prevent heart disease to a large but anonymous sector of the population, and renal physicians making a case for more dialysis for a smaller group of individually identifiable patients (see Appendix 4). Each of us then had five minutes to discuss the issue with our neighbour and try to decide which intervention we favoured, and why.

Although we didn't do a head count, there seemed to be more sympathy for the renal physicians than for the cardiologists. The latter might save more lives, but the improved quality of life for renal patients receiving dialysis would be measurable and demonstrable in particular individuals. It was also helping a group of people at greater need, and who had no other option. The cholesterol population, by contrast, might have recourse to other strategies including diet.

Following Professor Hope's presentation, one of us drew attention to the occasional media pressure on NICE following a decision. Professor Hope agreed that this is a problem, and commented that well thought-out and



robust procedures are an important safeguard in insulating NICE from such pressures.

Erik Nord of the Norwegian Institute of Public Health was next to speak. He pointed to differences between the Norwegian and the UK approaches. In Norway, he said, the legislation on entitlement to treatment requires three criteria – severity, benefit and cost – to be considered together. There is no primacy for cost-effectiveness in priority setting. And the guidelines say that “a small benefit may be compensated by a high degree of severity”. He devoted the rest of his talk to a detailed analysis of non-fatal illnesses in which there was priority setting according to severity, and equal access to treatment among patients with a different potential to benefit. He also considered some of the consequences of a trade off between these things when trying to make the most of available resources.

#### *A company view*

Our final presentation of the first day was by David Brickwood of the Johnson and Johnson pharmaceutical company. He outlined the process of drug research and development, and explained why it takes so long and costs so much. He illustrated the industry’s problem by reference to one of his company’s products: Velcade (bortezomib) for the treatment of patients with multiple myeloma. NICE rejected this as not cost-effective. In the end, though, the company struck a deal with the NHS which agreed to fund four cycles of treatment. In turn the company agreed to refund the cost of the drug if patients failed to respond in this time. Dr Brickwood described the scheme as “a time-limited, interim bridging arrangement to secure cost-effective market access ahead of new evidence”.

Talking of the QALY, David Brickwood echoed the familiar slogan: the cost per QALY should be seen as a tool, not a rule. He added that the current method of assessment takes no account of some of the treatment end points that patients themselves regard as highly relevant. He also offered an extensive list of factors which he himself thought should be taken into account when assessing decisions. These included the extent of unmet clinical need, the existence or otherwise of other therapies, whether this technology is a bridge to further therapies, the ease of obtaining patient compliance, and possible benefits to carers and to the wider community. He also complained that the current NICE threshold had taken no account of the growth in GDP or of inflation.

During the period for questions one of our members suggested that schemes of the “no effect, no pay” kind might be merely a clever

marketing scheme. Dr Brickwood denied that this was the case. He went on to describe other examples of this approach.

Other topics on which we questioned him included the choice of the comparators required in cost-effectiveness calculations, his industry's pricing policies, how products are priced in other countries, and what impact changes in the UK price can have internationally.

The day finished with questions to Peter Littlejohns and Sarah Garner, NICE's R&D leads. We learned that only on four or five occasions has NICE eventually authorised medicines that lie above the £30,000 threshold figure. These have included drugs for osteoporosis and motor neurone disease. We also heard about the choice of a comparator (normally whatever is current NHS best practice) and how different choices can radically affect the outcome of the comparison. Other topics raised by Council members were the prospects of an improvement to the EQ5D, the lack of change to the £30,000 upper threshold level over the years and the possibility that it needs to be changed, and America's current interest in creating a system not of comparative *cost*-effectiveness but of comparative *clinical* effectiveness. Neither panellist would be drawn on the suggestion that drug companies deciding how to price a drug in the UK might start from NICE's upper threshold and work backwards!

### *Appraisal in practice*

We began day two by completing a second tracker questionnaire, and then reflecting briefly on what we had already heard. One member commented on the difficulty that many of us experienced in trying to get to grips with health economics. It was, she added, her last meeting and only now had she really understood the basis of the QALY. Perhaps one of the central aims of the Council is, as much as anything, to look beneath the economic complexity and see if what is being done is common sense.

The first presentation of the day was a joint one by David Barnett, a practising physician, and Andrew Stevens, an epidemiologist. Both chair NICE appraisal committees and therefore have extensive first hand experience. They described the make-up of these committees and how they worked, especially in tackling the key questions: how well the new intervention performs in comparison with whatever is already in use (clinical effectiveness); and how much more life and/or quality of life we get for the extra money (cost effectiveness) compared to existing treatment. The sort of evidence provided to committees, and its quantity, varies from case to case - but in the end members have to balance clinical

effectiveness against cost effectiveness to reach their decision. Getting this balance right can be tricky, and it is not possible to please all the people all the time. As Andrew Stevens expressed it, “The information you have may not be what you want. The information you want may not be what you need. The information you need may not be what you can get. The information you can get may cost more than you want to pay!” While scientific evidence forms the core of the basis for decision-making, the evidence of patient experience also plays an important part.

They finished by listing some of the factors that lie beyond cost-effectiveness. Severity, for example. Cost-effectiveness calculations may make no distinction between one person making a big gain and ten people making a small one. But are these really equal? Then there is rarity; some diseases are so rare that you can virtually name the patients concerned. This makes it harder to say no...but should it? Likewise, some stakeholders are more persuasive than others. Anything to do with cancer tends to generate more emotion; an extra two months of life seem to matter disproportionately if that life is drawing to a close. Gains often seem to matter more if they’re likely to be experienced by children or people whose lives have been disadvantaged in some way; and so on. These and many other factors make the task of the appraisal committee extremely demanding. Such factors do influence decisions – though are not always captured in the clear and systematic manner of a cost per QALY calculation. Therefore the committee consider these issues alongside the cost-effectiveness information.

In the question session that followed the presentation we learned that appraisal committees frequently find themselves having to go beyond mere consideration of the cost per QALY in making their decisions, and that appeals against their initial decision are not unusual. Asked if he was happy with the current threshold Andrew Stevens replied that he was because he wishes to protect the NHS from the economically damaging consequences of a thoughtless prescription of extremely expensive remedies. In reality, he admitted, this is easier to say than to do. David Barnett added that it is not, of course, just what the committee itself thinks that matters; it’s what society thinks. And this was why the Citizens Council had been asked to consider the issue.

### *Trying it for ourselves*

Having heard from people directly concerned with the appraisal process we were given a chance to experience it for ourselves. We divided into two groups, each with a problem to tackle. One group had to decide on a policy for prescribing statins on the NHS for the prevention of

cardiovascular disease. The other was asked to provide guidance to the NHS on the use of pemetrexed for people with malignant pleural mesothelioma. After an hour we reconvened to report back.

The group who had worked on statins said that most of their discussion had been about the relative benefits of primary versus secondary use of the drug in preventing cardiovascular disease. There was some support for statins being available for primary prevention through the NHS in spite of the cost per QALY being much higher than when the drugs were used in secondary prevention. However, a majority of the group backed the secondary option. They also discussed the benefits of over-the-counter statins, but felt on balance that it was probably better to have them prescribed by patients' own GPs who could talk them through any difficulties. They also wanted men and women to be treated equally.

The mesothelioma group reported that it was extremely helpful to understanding the process of decision-making when you had to deal with a specific case rather than considering the issues only in principle. A majority concluded that they were in favour of treatment for one of the sub-groups of patients they discussed, feeling that the cost per QALY gain in this case could be justified. The cause of the illness - exposure to asbestos in the work place - prompted a feeling that society owed something to these individuals. This decision, we subsequently learned, was the one which the actual NICE committee reached – but only after its original decision had been appealed.

We began the afternoon of the second day by hearing from speakers who gave us several different perspectives on the consequences of a NICE decision to depart from the threshold. They came from a doctor, a health administrator and four representatives of patient support groups. Peter Clark, a medical oncologist who has himself sat on appraisal committees, told us that as many as half of future appraisals could turn out to feature cancer drugs, most of them intended solely for palliative use. He said that cost effectiveness in oncology was poorly understood, and added that in some of the industry trials presented to NICE committees the comparator had been poorly chosen. Moreover, besides the inherent difficulty of making a decision when data is (sometimes unavoidably) thin on the ground, committees have to cope with differing views and expectations among stakeholders. Patients with cancer often view matters differently to oncology nurses and doctors, and to healthy lay people. Both patients and their relatives tend to place extra value on the final months of life.

Having listed the drugs to which NICE committees have said no, and given the reasons why, Dr Clark outlined some recently revised guidance on the consideration of end of life medicines. Interestingly, his view was that in all but one recent case these new rules would not have affected the final outcome and allowed more drugs through the net. He finished by listing the consequences of varying the implementation of the cost per QALY threshold to patients (more equity of access, fewer private top-up payments etc) and to the NHS (less pressure on manufactures to reduce drug costs, discrimination against non-cancer disease etc).

Questions to Dr Clark included the reasons that prompt some patients to change their minds about wanting life-extending chemotherapy (first hand experience of its side effects), the difficulties of choosing comparator drugs, and the differences in decision-making among the UK's devolved administrations (less than usually claimed).

The next speaker, Rachel Flowers of the Newham Primary Care Trust, is concerned with the health and well being of about a quarter of a million people – for which she and her colleagues have a set budget. She has to consider clinical and cost effectiveness, risk, the acceptability to the patient of a treatment, and what alternatives are available. She reminded us that people's experience of illness, and their responses to it, are very different. More affluent areas, she noted, tend to make more demands for expensive treatments. PCTs have to take account of these and many other factors when deciding what to pay for and what not pay for. In short, they have to hold the ring when competing demands clash. When NICE tells them that something has to be delivered, they must decide what other things will not be done to keep the books balanced.

When we asked Rachel Flowers for an example of what she might decide not to do she (perhaps understandably) initially declined to give a direct answer. It would depend on so many other facts and influences. When pressed to say *how* she might decide, she said it would not be on cost alone, but would include other considerations such as cost per QALY. Most PCTs have a policy on these matters, but each approaches the task in its own way. One of us wondered if it might not be better to introduce more uniformity in PCT decision-making. Rachel Flowers was inclined to agree.

### *Patients' perspectives*

Each of the next three speakers put the patients' case for crossing the upper threshold limit. Penny Wilson Webb of the Rarer Cancers Forum represents 30,000 patients with 176 different types of tumour; for most of

them there are no treatments and a poor prognosis. The patients, she said, are looking for hope and help. She wanted to see greater flexibility, and a reconsideration of the existing threshold. Society places a premium on the last few months of life, and some of these drugs can offer those months – or even, on occasion, years. She went on to make an emotional plea that patients be given the time to do the things that can help them and their families make life compete. Even small extensions to life (and therefore small QALY gains) can mean a great deal to these patients.

Steve Winyard, head of policy and campaigns for the RNIB, began by listing his doubts about the QALY, and quoting a previous Citizens Council report suggesting that appraisal committees give more weight to the SVJ. He reminded us of the impact of sight loss – then pointed out how too heavy a reliance on cost per QALY calculations and a fixed threshold had led an appraisal committee to authorise a treatment for age-related macular degeneration only in the second eye to be affected. Or, to put it more bluntly, patients had to go blind in one eye before they were authorised to receive treatment to save the sight in the other. The public, he said, did not perceive this as “fair”. The cost per QALYs should be a guide, but not an immovable hurdle.

Jenny Snell of the National Rheumatoid Arthritis Society began by observing that the QALY and its valuation were controversial. She reminded us that people with arthritis have to learn to live with pain and disability and a significantly reduced quality of life, and may die prematurely. The disease places a burden not only on patients, but on their relatives, carers and society generally, and costs a great deal of money. Many sufferers have to give up work. Most of these indirect costs are not taken into account in NICE’s current economic approach. If the threshold was right eight years ago, she asked, how can it be right now when inflation hasn’t stood still? Like other patient representatives, she felt that more weight should be given to the SVJ.

Even if new drugs are expensive, early treatment to halt the progress of the disease will save later expense. Moreover, a refusal to pay for today’s drugs will obstruct progress in the development of tomorrow’s.

Our final patient representative was Alexis Willett of Breakthrough Breast Cancer. She began by describing what it was like to have this disease. She pointed out that while some patients would value a few extra weeks of life, others wouldn’t think it worth spending a lot of money that could be devoted to the treatment of others. In short, people vary. Nor, when it comes to the treatments themselves, is the issue an all-or-nothing

affair. A standard treatment may work in the sense of controlling the disease; a newer, more expensive one may bring about a similar result, but afford the patient a better quality of life while it is being used - for example because it has fewer side-effects.

She too emphasised that if newly developed treatments are not used, the likelihood of researchers devising even better ones will be diminished. Having assured us that she appreciated the difficulty of the question that NICE had set us, she suggested it might help to think about the question in reverse. That is, under what circumstances should NICE definitely not go above the cost per QALY threshold?

All four of the patient representatives came together in a panel to answer our questions. One of our members pointed out that all four were asking for money from the same pot. The NHS not being a bottomless pit of cash, giving money to one treatment meant, in effect, taking it from something else. She wondered how the speakers felt about this. One of them felt that it was a question for commissioners – who might even have more money if they could manage to disinvest from less effective forms of expenditure. She felt there was the potential to do this. A second panellist agreed but added that one must expect NICE sometimes to say no - which is why he favoured strengthening the system so that its decisions can be more rigorous. Under these circumstances it might be necessary to bite the bullet and accept the verdict. The third speaker suspected that the money was available in PCTs who had the will to find it. The remaining panellist felt it was unfair to set patient groups against one another.

Jenny Snell, responding to a query about her suggestion that the range of factors taken into account when assessing the costs and benefits of illness and its treatment is too narrow, conceded that the whole basis of doing these health economic calculations might have to be reassessed.

One Council member wondered if paying for expensive drugs which might raise hopes yet only prolong the life of someone with advanced cancer by a relatively short period was necessarily the best way of spending scarce resources. Maybe the effort should go into making their final days more peaceful. Antonia Willett thought this was a good point – but saw it as another argument for ensuring that the evidence placed before NICE is robust. Some drugs, she thought, had come before NICE too soon. Penny Wilson Webb added that if drugs aren't used at the end of life, they may not be used at all. Once the testing is complete, it may prove satisfactory to give them earlier in the illness. She felt that more

flexible pricing by the industry would also help. Steve Winyard, however, warned of the dangers of campaigning to reduce drug prices. The difficulty is to define an acceptable rate of return to a company. If a company doesn't feel it worthwhile spending on research, it won't invest in it. Either way, he said, the government should be tackling pricing issues, not patient groups.

Other topics discussed in the session were the feasibility of disinvestment. One Citizens Council member also challenged the panellists to come up with a way of establishing which of the groups represented by the panellists were most deserving! On the latter point the panellists wisely refused to be drawn.

#### *More questions to a bigger panel*

Following a further refresher session on the nature and role of the QALY from Sarah Garner of NICE, we broke into groups to formulate questions to put to a panel comprising most of the day's speakers. The first group raised the practical consequence of an increase in the number of factors that appraisal committees should be considering: an increase that might delay their eventual decision. Does this matter? Most panellists saw speed and thoroughness as a trade-off in which the important goal was to achieve a happy medium. But one panellist suggested that the current process appears to be unduly leisurely and could surely be speeded up. Another thought that certain organisational changes to the process now being considered would soon be accelerating it anyway.

The next group wanted to know if PCTs could move their resources from treatment to prevention. The answer is yes – and it's what some PCTs are trying to do. But it can't be done overnight, said Rachel Flowers. The third group discussed the EQ5D and how QALYs are calculated. Some panellists thought certain issues would depend on the disease, but none had a simple remedy for improving the EQ5D. The next question concerned the best way of taking account of factors not satisfactorily assessed by the current EQ5D. One panellist with experience of appraisal committees stressed that their deliberations were not, as some of us appeared to think, slavishly bound by the EQ5D. He quoted the example of Alzheimer's disease where all sorts of ways had been used to get a more rounded assessment of the illness. Committees bent over backwards not to underplay the impact of the conditions they were considering, especially those like deafness or blindness that create sensory deprivation. However, criticism of appraisal committees could sometimes take a surprising form. Some deaf people, rather than claiming that their



problems are under-rated by NICE, have criticised it for presuming to view deafness as a disability!

Another group wondered if there should be an upper limit on the number of times each year that appraisal committees were allowed to depart from the upper threshold. The thought which had prompted the question was that as more and more expensive cancer drugs come before NICE in the future, there would be even more often an argument for crossing the threshold. Panellists agreed that there had to be limits on what could be paid for, but were not persuaded that a numerical limit of the kind suggested by our member would be the way forward. One drastic remedy would, of course, be to say that there should be no special cases at all.

The next group wondered if NICE was happy with schemes of the kind in which payment for new and expensive drugs is by results. If the patient does not benefit, the drug company receives no payment. One veteran of appraisal committees said that, in effect, it amounted to the manufacturer dropping the price, something that companies are generally reluctant to do more openly because it affects their international bargaining position on pricing. Another said that the lower the price to the NHS, by whatever the route, the better.

Another question sought clarification about the alleged budget surpluses within the NHS that had been mentioned from time to time. Rachel Flowers pointed out that these surpluses varied considerably from place to place – and this year's surplus might be followed by next year's deficit. It wasn't something you could plan around.

The panellists were then asked how they themselves would answer NICE's question! One panellist was insistent that departures from the threshold should be as infrequent as possible. In addition to the evidence that was given to them on a particular technology, appraisal committees had to remember the interests of all the people from other patient groups who were not represented in the room. Their interests too had to be defended. This was done by holding the line on expenditure – while not behaving totally inflexibly.

The final question was whether NICE had ever regretted a decision to depart from the threshold. No specific examples were offered, but one panellist pointed to the danger of creating precedents.

*Final day*

We began the final day by completing a third tracking questionnaire, and then reflecting on what we had heard so far. The issues that members chose to raise included the question of whether the principles spelt out in the SVJ were the right ones, and whether they were being properly or sufficiently implemented. One member felt it would be helpful to know more of those instances in which NICE had already been prepared to exceed the threshold. Someone else commented on the difference it had made hearing from a patients' representative (as opposed to reading a bald statement of facts) when learning why a particular treatment might be regarded as essential.

In support of having appraisal committees put more emphasis on the SVJ when making decisions, another of us pointed out that this component of the procedure should be taken seriously because it reflected society's values. He also suggested that to reject an intervention because it had found insufficient support in the SVJ might be more kindly received by those directly affected than being told that rejection was solely on economic grounds. The public too, he thought, would be more inclined to accept the decision. This might take some of the heat off NICE appraisal committees.

Another Council member said she felt that in this meeting she was being asked the same question as on previous occasions. Hadn't the Council already agreed that the QALY was a flawed instrument, and the EQ5D needed revision? Several others felt much the same way.

Responding, Peter Littlejohns conceded that the Council had indeed tackled this question before. He then referred back to the previous day's presentation from the RNIB's Steve Winyard about the NICE decision that allowed treatment for macular degeneration only to patients who had already been blinded by the condition in one eye. He said that although the decision made complete sense from a utilitarian, cost-effectiveness viewpoint, NICE had been well aware that it would prove controversial. Part of the point of this Citizens Council meeting, he went on, was to help NICE decide when it had to deviate from the cost-effectiveness approach.

There was little doubt that most of us on the Council felt that the macular degeneration decision was most definitely an instance in which pure cost-effectiveness should have been put to one side. "Inhumane" and "shameful" were just two of the words that members used to describe it. Either way, in spite of past debates about and revisions to the SVJ, the issue is still a live one. Hence the decision to ask us once again what NICE should be doing differently, and when.

Professor Littlejohns went on to remind us that both the EQ5D and the QALY valuation are under reconsideration by academics. In addition, the cost of drugs over the next five years is going to be dramatically different from the past five. Finally, policy cannot be decided purely on the basis of which advocacy groups make the loudest noise.

In response to a question about what happened before the creation of NICE he pointed out that there had always been debate and discussion, winners and losers, and arguments about “post code lotteries”. Some health authorities had chosen to use this or that drug; others had not. Some had even developed their own mini versions of NICE. The decision to create NICE itself was intended to help restore the importance of the word “national” in National Health Service.

Challenged to demonstrate that NICE was itself value for money, Professor Littlejohns pointed out how experience had shown that when NICE guidance is published, clinical practice often changes. As an example he mentioned the recommendation that people who have suffered a head injury should have a brain scan. In the long run, he believed, this was probably saving money. He also warned that every time you create a special case you take the pressure off the drug companies to keep prices down.

At this point we broke into seven small groups to discuss our preliminary thoughts on NICE’s question. We reconvened after half an hour to report back. There were many views - but most of us were inclined to have NICE take a more flexible, more liberal view of its responsibilities. Some thoughts:

- NICE is asking the public’s permission to breach the threshold, and on that we agree.
- Severity, orphan drugs, need and the desirability of innovation should all be reasons to breach the threshold.
- The SVJ should be the main basis of the decision.
- There should be a conscious decision to apportion relative weights to the QALY and the SVJ – perhaps 30 and 70 per cent respectively.
- Allowing an appraisal panel to depart from the threshold is one sign of a humane society.
- The SVJ might include a phrase along the lines that NICE should consider whether any decision it makes could be judged inhumane.
- It’s important to take account of patient groups that don’t have a loud voice.

- Cost effectiveness is important, but the EQ5D and how it is used to calculate QALYs need to be reformed.
- Whenever a committee feels it needs to go over the threshold, it should do so.
- Appraisal committees should have appointed members with a direct and relevant interest in the disease for which the intervention is intended.

A few of us took a more cautious or even restrictive view:

- Allowing too many special circumstances would reduce the pressure on manufacturers to control prices.
- Giving too much weight to the SVJ would tend to allow everything through the net.
- There should be no circumstances in which the threshold should be exceeded.

The group reports were followed by a more general discussion. Points made included: the difficulty of allocating resources to one condition when this meant taking it away from another, perhaps with less capacity to generate publicity; the danger that putting people with a direct interest in a condition on an appraisal panel would undermine its independence; the importance of having public acceptance for NICE decisions; the importance of encouraging appraisal committees to think in advance about the public response to their decisions; the role of the drug industry in influencing committee deliberations; and the risk of appraisal panel decisions being driven by pressure from the media.

At this point we were presented with a list of 13 circumstances in which it might be argued that NICE appraisal committees should consider waiving the usual threshold. These were all circumstances that had been mentioned during the previous two days by various of the people addressing us, or in our own discussions, or both. The list was as follows:

- the illness under consideration is extremely severe
- there are no alternative therapies available
- the intervention will encourage more scientific and technical innovation
- highly persuasive stakeholders have made a good case for it
- the illness is rare
- the treatment in question is life-saving
- the treatment is life-extending
- the condition being tackled is time-limited
- the illness is a result of corporate negligence
- the illness is a result of NHS negligence

- the patients concerned are socially disadvantaged
- the patients are children
- the intervention would prevent more harm in the future

Once again we split into seven small groups, each of which undertook to discuss two of these circumstances, and report our answers to the rest of the group.

The subsequent discussion included: the issue of whether or not children should be a special case; the impact on the wider family of childhood illness and death; the need to keep the list of relevant factors open to further modification; and the value of giving an appraisal committee the freedom to make an exception of a kind that might never previously have been considered.

#### *Final Vote*

To the above list of 13 circumstances which might prompt a departure from the threshold we added two more:

- the intervention will have a major impact on the patient's family
- the intervention will have a major impact on society at large

Before deciding on the circumstances in which NICE might breach its threshold, we first had to establish whether any of us now thought that there were actually no circumstances in which this should be done. We reached this and all other of our decisions by a show of hands.

**This initial vote revealed that two of the 29 Council members present felt that there were no circumstances in which NICE appraisal committees should depart from the established threshold.**

These two members took no further part in the voting. Among the remaining 27 members, the number of votes cast in favour of taking account of each circumstance were - in order of support - as follows:

- **the treatment in question is life-saving** **24**
- **the illness is a result of NHS negligence** **23**
- **the intervention would prevent more harm in the future** **23**
- **the patients are children** **22**
- **the intervention will have a major impact on the**

<b>patient's family</b>	<b>22</b>
- <b>the illness under consideration is extremely severe</b>	<b>21</b>
- <b>the intervention will encourage more scientific and technical innovation</b>	<b>21</b>
- <b>the illness is rare</b>	<b>20</b>
- <b>there are no alternative therapies available</b>	<b>19</b>
- <b>the intervention will have a major impact on society at large</b>	<b>16</b>
- <b>the patients concerned are socially disadvantaged</b>	<b>13</b>
- <b>the treatment is life extending</b>	<b>10</b>
- <b>the condition being tackled is time-limited</b>	<b>9</b>
- <b>the illness is a result of corporate negligence</b>	<b>2</b>
- <b>the stakeholders happen to be highly persuasive</b>	<b>0</b>

With the completion of a fourth and final tracking questionnaire the meeting closed.

### **A final thought**

It is clear from these votes that the great majority of us do not think that a view based solely on formulaic considerations of health economics is a satisfactory basis on which to make recommendations about the use of drug or other interventions by the NHS. Judgements also need to take account of other factors. (In addition, at various times during the meeting, a number of members repeated previously expressed concerns about the EQ5D and its use to calculate QALYs. We hope that the planned reviews of both, and any changes which follow, will serve to boost confidence in them.)

Our conclusions offer support to the current NICE procedure – which, through the Social Value Judgment document, already recognises that appraisal committees cannot work by health economics alone. The continuing uncertainty is over which additional factors should be taken into account, and what weight they should carry. Not surprisingly – as the

voting makes clear – within the Council there is a spectrum of opinion on these matters. But we hope that the pattern of our preferences may offer some guidance to appraisal committees as they do for real what we have done only in our imaginations.

### **In Memoriam**

The Council would like to express its sorrow at the death of Penny Wilson Webb. Although unwell at the time of our meeting she made a great effort to attend and express her views. We offer our condolences to her relatives – as we do also to those of one of our own members, Jonathan Barwick, who died before the meeting took place.

## **Appendix 1**

### **Results of the tracker questionnaires.**

The first question sought to illuminate our views of NICE. More than four out of five of us consider ourselves advocates of NICE's work, and this did not change substantially during the course of the meeting.

The first specific question (2a) was to assess our confidence that the current NICE threshold is set at the right level. While our certainty waned initially, it then increased. But even by the end of the meeting only a little over half of us felt that the level was correct.

As the replies to question 2b showed, we had severe doubts about the accuracy of the QALY as a method of measurement. The overall proportion of us with confidence in it changed little during the meeting; but opinion among doubters showed a definite hardening.

Questions 3a and 3b probed our views on whether or not NICE should be prepared to recommend interventions above the £30,000 upper threshold. Question 3a measured our response to the suggestion that NICE should never go above the threshold. Only a small initial minority (<10 per cent) agreed with this; this had increased by the end of the meeting, but only to 17 per cent. Not surprisingly, the findings in the second part of question 3 – do you agree that NICE should, in some circumstances, consider recommending interventions above the threshold? – mirrored those of the first part. A large majority of us felt that it should do so.

It was noticeable that here, as in all the questions so far discussed, the proportion of us who felt unable to give definite answers fell during the course of the meeting. What we were hearing was helping us to make up our minds.

The subsections of question 4 were all designed to assess our views on particular factors identified in advance as potentially likely to affect our thinking on whether or not NICE appraisal committees should recommend departing from the threshold. Our collective views moved back and forth without undergoing major change. The only question that seemed to show a discernible trend was 4f, designed to test our views on whether inequalities in people's chances to have good health should be a factor that influences decisions on departing from the threshold. We became more sympathetic to this idea as the meeting progressed.



**Appendix 2**  
**Question and briefing paper**

**NATIONAL INSTITUTE FOR HEALTH  
AND CLINICAL EXCELLENCE**

**Citizens Council**

**Question for November 2008 meeting**

**In what circumstances should NICE recommend interventions where the cost per QALY is above the threshold range of £20-£30,000?**

# **1 Background**

No country can afford all the health care interventions that might benefit patients. Clinical need will always outstrip available resources so priorities have to be agreed. How this prioritisation process takes place varies from country to country but the need to prioritise in some way is clear. There just isn't (and never will be) enough money to provide every possible service.

In Britain, before NICE was established, these decisions were largely made behind closed doors. Although formal economic assessments were sometimes made they were rarely exposed (or explained) to the public, nor was the public involved in making the assessments. More often, decisions about how the NHS's money was used were based on other factors. These included historical patterns of health care, assumptions about where (and how) additional investment might most appropriately be made, pressure from special interest groups, political lobbying and perceptions about public preferences.

The creation of NICE, in 1999, made possible a fundamental change in how these issues were tackled by the NHS. For the first time, a national public body was charged with making authoritative recommendations about the availability of new and established treatments, and pathways of care, and doing so by formally taking cost-effectiveness (or value-for-money) into account. Few healthcare systems had tried to do this before; and in those that did, such as that in Australia, the process was mainly limited to new pharmaceutical products. Since 2005, NICE's remit has also been extended to public health interventions, again the first time this has been done.

## **2 How does NICE evaluate healthcare?**

In making its decisions on whether an intervention (e.g. a drug, device or health promotion intervention) should be available to the NHS, NICE compares interventions by using an economic approach called 'cost-utility analysis' to consider:

- the impact each intervention has on health compared to current care; and
- how much it costs again compared to the costs of current care.

Cost-utility analysis uses a measure or ‘yardstick’ called the Quality Adjusted Life Year (QALY). The QALY captures the impact of a treatment on both ‘quality of life (QoL)’ and length of life. One QALY is the equivalent of one year in perfect health, or two years in 50% of that health, or four years in 25% of that health, and so on. It provides a ‘common currency’ that allows different interventions to be compared for different conditions. For more explanation of economic analysis and QALYs please see the accompanying document ‘Health economics: the basics’. The cost per QALY indicates how much extra it costs the NHS to buy the equivalent of one QALY of benefit from a new intervention over and above what it pays now for the benefits from existing treatments. Economists also refer to this comparative ‘cost per QALY’ as the ‘Incremental Cost-effectiveness Ratio’ or ICER.

The aim of the cost-utility approach used by NICE is to use the budget of the NHS to ‘purchase’ the greatest number of QALYs possible i.e. to maximize the amount of health gained for the money available.

### **3 The threshold in theory**

In doing its job NICE has the challenge of having to decide what the dividing line is between health care interventions that are thought to be cost-effective and those that are not. Many people call this dividing line the “threshold” and it represents the maximum cost per QALY that is considered to be a cost-effective use of NHS money. When NICE was established it was not given a value for the “threshold” and NICE has never defined a single value, but instead has considered a range of values.

Obviously, because the law states that funding has to be provided for NICE recommended interventions, getting the level right is crucial. If NICE’s threshold is above that relevant to other budgets in the NHS (in other words if it is recommending interventions that would not be considered to be value for money by other parts of the NHS) then implementation of NICE decisions will ‘crowd out’ more cost effective services locally. If NICE’s threshold is too low,

NICE will reject health care technologies that are cost effective relative to others provided locally.

NICE's early experience demonstrates that NICE's advisory bodies and health economics advisors consider that the threshold lies within the range of £20,000 to £30,000 per QALY. If the Advisory Committees decide to deviate from this range (either by recommending an intervention with a cost per QALY more than £30,000 or by not recommending an intervention with a cost per QALY of less than £20,000) NICE asks them to explain their reasons in the guidance issued.

NICE requires its advisory bodies to be clear why they might be recommending an intervention that is above the threshold range i.e. is not considered to be cost-effective. This is important because in doing, the fixed health care budget means that the money spent will not be available to treat other groups. The advisory body seems to be implicitly saying that some groups of patients are more or less deserving than others.

## **4 The threshold in practice**

NICE's advice to its advisory bodies on how to apply the threshold is encapsulated in its technical manuals and the social values judgements document. The advice is based on NICE's legal responsibilities to promote equality and prevent discrimination, the Secretary of State's directions to the Institute, the views of the Citizens Council and the Institute's independent professional advisors. Each of these documents has been subject to public consultation.

The advice includes:

- Above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of the intervention as an effective use of NHS resources will specifically take into account the following factors:
  - The degree of certainty around the ICER. In particular, the Committee will be more cautious about recommending a technology when they are less certain about the ICERs presented. In other words, how certain are we that the QALY value calculated is the true one?
  - Whether there are strong reasons to indicate that the assessment of the change in HRQL has been inadequately captured, and may therefore misrepresent the health utility

gained. In other words, are there any benefits that are not easily assessed by the way that the Health Related Quality of Life was measured?

- The innovative nature of the technology, specifically if the innovation adds demonstrable and distinctive benefits of a substantial nature which may not have been adequately captured in the QALY measure. In other words is there something about the technology that the QALY does not take into account for example, is it the only treatment for that group of patients?
- As the ICER of an intervention increases in the £20,000 to £30,000 range an advisory body's judgement about its acceptability as an effective use of NHS resources should make more explicit reference to the relevant factors considered above. Above a most plausible ICER of £30,000 per QALY gained advisory bodies will need to make an increasingly stronger case for supporting the intervention as an effective use of NHS resources with respect to the factors considered above.

Further advice is presented in the Social Value Judgements paper as Principle 3: “decisions about whether to recommend interventions should not be based on evidence of the relative costs and benefits alone. NICE must consider other factors when developing its guidance, including the need to distribute health resources in the fairest way within society as a whole.”

The Citizen Council was asked to explore one of these other factors, disease severity, at its last meeting.

## **5 The Question**

NICE is asking the Citizens Council to advise on the circumstances in which NICE should consider recommend interventions where the cost per QALY is above the threshold range of £20-£30,000?

The Citizens Council has addressed these types of issues before and has usually concluded that some allowance should be made in some

circumstances. For example when the Council considered the rule of rescue, the age of the individual, and targeting the most disadvantaged people.

NICE is not asking the Citizens Council to re-visit all these previous issues but to take an overview and provide further advice on how and when the public would wish a case to be made for the threshold to be deviated from.

Examples could include uncertainty around the ICER estimates, the nature of the disease (for example the severity, disability, and treatments at the end of life), the previous health history of a typical patient, the innovative nature of the technology, inequalities in health status.

It is obviously not possible to produce a definitive list and we are not expecting the Citizens Council to do so. There will always be need for flexibility in applying the criteria. However in order for NICE to meet its standards of explicitness, transparency and consistency it is important to establish in which circumstances the Citizen's Council consider discretion might be justified and why.

The results of this meeting will feed into other work that NICE is currently undertaking including a technical workshop on the threshold value. The Citizens Council recommendations will also be fed into NICE's current consultation on supplementary advice that NICE intends to give its Appraisal Committees when they are appraising life-extending medicines licensed for terminal illnesses affecting small numbers of patients.

## Appendix 3 Agenda

<b>NICE Citizens Council: Departing from the threshold</b>		
<b>Time</b>	<b>Title</b>	<b>Speaker(s)</b>
<b>Thursday 27<sup>th</sup> November 2008</b>		
<b>Theme of morning session: NICE's approach to making its decisions – the theory</b>		
9:00 – 9:15	Welcome from facilitators and some housekeeping information	Frances Chinemana, OLR & Clifford Middleton, NICE
9:15 – 9:30	NICE's question	Peter Littlejohns, NICE
9:30 – 10:00	Discussion of question	All
10:00 – 10:45	Recap on Health Economics (with discussion)	Jo Lord, Brunel University
10:45 – 11:00	<b>Break</b>	
11:00 – 11:30	How NICE makes decisions-the theory. <ul style="list-style-type: none"> <li>- Clinical effectiveness</li> <li>- Cost effectiveness</li> <li>- Social value judgements</li> </ul> (with discussion)	Elisabeth George, NICE
11:30 – 12:00	What the Citizen's Council has already said about exceptional circumstances  (with discussion)	Peter Littlejohns, NICE
12:00 – 12:30	Discussion	All
12:30 – 1:00	<b>Lunch</b>	
<b>Theme of afternoon session: other perspectives</b>		

<b>NICE Citizens Council: Departing from the threshold</b>		
<b>Time</b>	<b>Title</b>	<b>Speaker(s)</b>
1:00 – 2:00	The Oxfordshire experience (with discussion)	Tony Hope, University of Oxford
2:00 – 3:00	International approaches (with discussion)	Erik Nord, Norwegian Institute of Public Health
3:00 – 3:15	<b>Break</b>	
3:15 – 4:00	A perspective from industry (with discussion)	David Brickwood, Johnson & Johnson
4:00 – 5:00	Questions and discussion	All (Peter Littlejohns / Sarah Garner, NICE in attendance)
<b>Friday 28<sup>th</sup> November 2008</b>		
<b>Theme of morning session: NICE's approach to making its decisions – the reality</b>		
9.00 – 9:30	Recap	2 x CC volunteers Geoff Watts, rapporteur
9:30 – 10:30	How NICE committees makes their decisions  (with discussion)	David Barnett, NICE Andrew Stevens, NICE
10:30 – 10:45	<b>Break</b>	
10:45 – 12:30	Decision making in practice- The Citizens Council tackles a typical NICE question	All  (David Barnett and Andrew Stevens advising)
12:30 – 1:15	<b>Lunch</b>	
<b>Theme of afternoon session: consequences of varying from the threshold</b>		



<b>NICE Citizens Council: Departing from the threshold</b>		
<b>Time</b>	<b>Title</b>	<b>Speaker(s)</b>
1:15 – 1:45	A doctor's perspective (with discussion)	Peter Clark, consultant oncologist
1:45 – 2:15	A PCT perspective (with discussion)	Rachel Flowers, PCT
2:15 – 3:15	Patients' perspectives (with discussion).	Steve Winyard, RNIB Alexis Willett, Breakthrough Breast Cancer Penny Wilson Webb, Rarer Cancers Forum Jenny Snell, National Rheumatoid Arthritis Society
3:15 – 3:30	<b>Break</b>	
3:30 – 3:45	Developing questions for the panel	All
3:45 – 4:45	Panel discussion	David Barnett Andrew Stevens Erik Nord Steve Winyard Alexis Willett Penny Wilson Webb Jenny Snell Peter Clark Rachel Flowers
4:45 – 5:00	Any questions	All (Peter Littlejohns / Sarah Garner in attendance)
<b>Saturday 29<sup>th</sup> November 2008 – <u>Closed Session</u></b>		
9.00 – 9:30	Recap	2 x CC volunteers Geoff Watts
9:30 – 12:30	Drawing conclusions and deciding what goes into the report.	All

<b>NICE Citizens Council: Departing from the threshold</b>		
<b>Time</b>	<b>Title</b>	<b>Speaker(s)</b>
12:30	Close	Mike Rawlins / Peter Littlejohns
	<b>Lunch</b>	

## **Appendix 4**

### **Exercise on need set by Professor Tony Hope**

The renal physicians make a case to NICE to extend renal dialysis. They argue that they do not currently have sufficient resources to offer dialysis to all patients who could benefit from it. In particular there are two groups of patients who are currently not receiving dialysis: those with other chronic health problems and very elderly patients (over 80 years old) who, with dialysis, are likely to live for several years more. Dialysis in these groups costs about £40,000 per life year extended.

The cardiologists also make a case to NICE. They argue that some of the extra money should be used to broaden the criteria for people to receive cholesterol reducing drugs (statins). These drugs are used to reduce cholesterol in those with raised cholesterol levels. The evidence that this reduces subsequent chance of death from heart attack and stroke is good. The cost per life year extended depends on both the patient's level of cholesterol and other risk factors for heart disease and stroke. The greater the risk, the more cost effective is the treatment. Currently the NHS pays only for cholesterol reducing treatment in those patients at high risk. This is a cost per QALY of £10,000. The cardiologists argue that those at moderate risk should also be offered treatment – this would be at a cost of £20,000 per QALY.

The renal physicians on hearing of the cardiologists' case argue:

a) That they can identify precisely which patients, who need renal dialysis, are not currently receiving such treatment. They even offer to send, confidentially, the names of these patients to the NICE decision-making board so that the members of the board can know precisely whose deaths they will be responsible for if they do not advise the NHS to pay for these treatments. They point out that the cardiologists can never know whose lives are saved by the cholesterol-lowering drugs.

b) That because there are so many people in the population with cholesterol levels at the value that the cardiologists want to treat, the overall cost to the NHS will be far greater if NICE recommends funding the cholesterol-lowering drug than if it recommends funding the extra renal dialysis.

**Which intervention should have priority? Should neither, both or one of the interventions be funded under the NHS?**