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A TERRIBLE BEAUTY

A Short History of NICE

THE NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Nicholas Timmins

Sir Michael Rawlins

John Appleby

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This is not an official history of the National Institute for health and Care Excellence. It is not endorsed by NICE and it does not necessarily represent the views of NICE.

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Health Intervention and Technology Assessment Program (HITAP)

6th Floor, 6th Building, Department of Health,
Ministry of Public Health, Tiwanon Road
Muang, Nonthaburi 11000, Thailand
Tel: (66) 2590-4549 or (66) 2590-4374-5
E-mail: info@hitap.net
www.hitap.net

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FOREWORD AND ACKNOWLEDGEMENTS

This, as the title states, is "A Short History of NICE". It was constructed at considerable speed. In a matter of months from the initial idea to the final words.

Its origins go back a fair way. Some six years ago John Appleby and Nicholas Timmins agreed that someone should write a "History of NICE". Because we both believed this was one of the more important pieces of UK public policy, let alone in health, in the last couple of decades.

We talked to Sir Michael Rawlins and Sir Andrew Dillon about that and they offered their full co-operation, as at the time did the health department in providing access to at least some of the earlier files around the creation of the institute.

However, neither John nor Nick found the time, and the co-conspirators in the health department moved on.

A new trigger was provided by the commission from the Prince Mahidol Award Foundation as part of the conference material for the foundation's 2016 conference in Bangkok. In the middle of 2015 and after some preliminary conversations, it supplied both a deadline and a sum of money that would mainly meet research and travel costs. It was to be written in parallel with an account of HITAP, Thailand's own Health Intervention and Technology Assessment programme, a task that has been undertaken by Tony Culyer. (1) The result is this "short history". The authors, however, had day jobs to do, so this document is essentially a labour of love.

It is therefore important to understand that this account is based on interviews and memory (the memory of both the authors and interviewees which, as all historians will tell you, plays tricks) and on publicly available documents, whether from academic, media, or government and court sources, along with NICE's

own publications, none of which have been subject to what the academics would call "a literature search". It has dug neither into the unpublished archive of NICE, nor into that of the Department of Health, nor into the archive of the many life sciences companies that have been affected by NICE's work — were those ever to be available in the public domain. Too few people from the life sciences industry have been consulted. And while other parts of NICE's activities are addressed, it concentrates chiefly on health technology assessment. From the beginning the institute had a larger portfolio than that, and the range of its activities has expanded appreciably over the years.

To provide a complete account many more people, including some who played a central role in NICE's history, would have been interviewed, and many more documents would have been consulted.¹ That would doubtless have altered some of the judgements made here. But in the time available, and given other commitments, that was not possible.

So this is not just "A Short History of NICE" it is also almost certainly far from entirely right. It leaves out, in the interests of both time and length, some important events and controversies, and one day someone — either these or other authors — should write a longer, more accurate, more comprehensive and much more nuanced account of NICE.

We hope, nonetheless, that this "first rough draft of history" is one that others will, at the least, have to take into account. And either praise or destroy.

Even this account would not have been possible without help from a considerable number of people who found time for interviews or conversations or critiques, often at considerably short notice. In alphabetical order, and shorn of their formal titles, they include Ron Akehurst, Robert Anderson, Mark Baker, Richard Barker,

¹ We have, of course, relied on a range of others people's analyses which are referenced below.

A terrible beauty



Martin Buxton, Kalipso Chalkidou, Tony Culyer, Andrew Dillon, Frank Dobson, David Haslam, Patricia Hewitt, Andrew Jack, Trevor Jones, Alan Langlands, Andrew Lansley, Alan Maynard, Andy McKeon, Bill Morgan, Jenny Parsons, Mike Richards, Clive Smee, Andrew Stevens, Matthew Swindells, Adrian Towse and Graham Winyard. A small number of those still serving the current government also helped, some considerably, although by convention they have to remain anonymous.

Some of the above also read various stages of drafts and part drafts. They corrected errors of both fact and judgement, even if sometimes we stuck with our own judgement. To them, and to all of the above, we are immensely grateful. Any remaining errors of fact or judgement remain the responsibility of the authors.

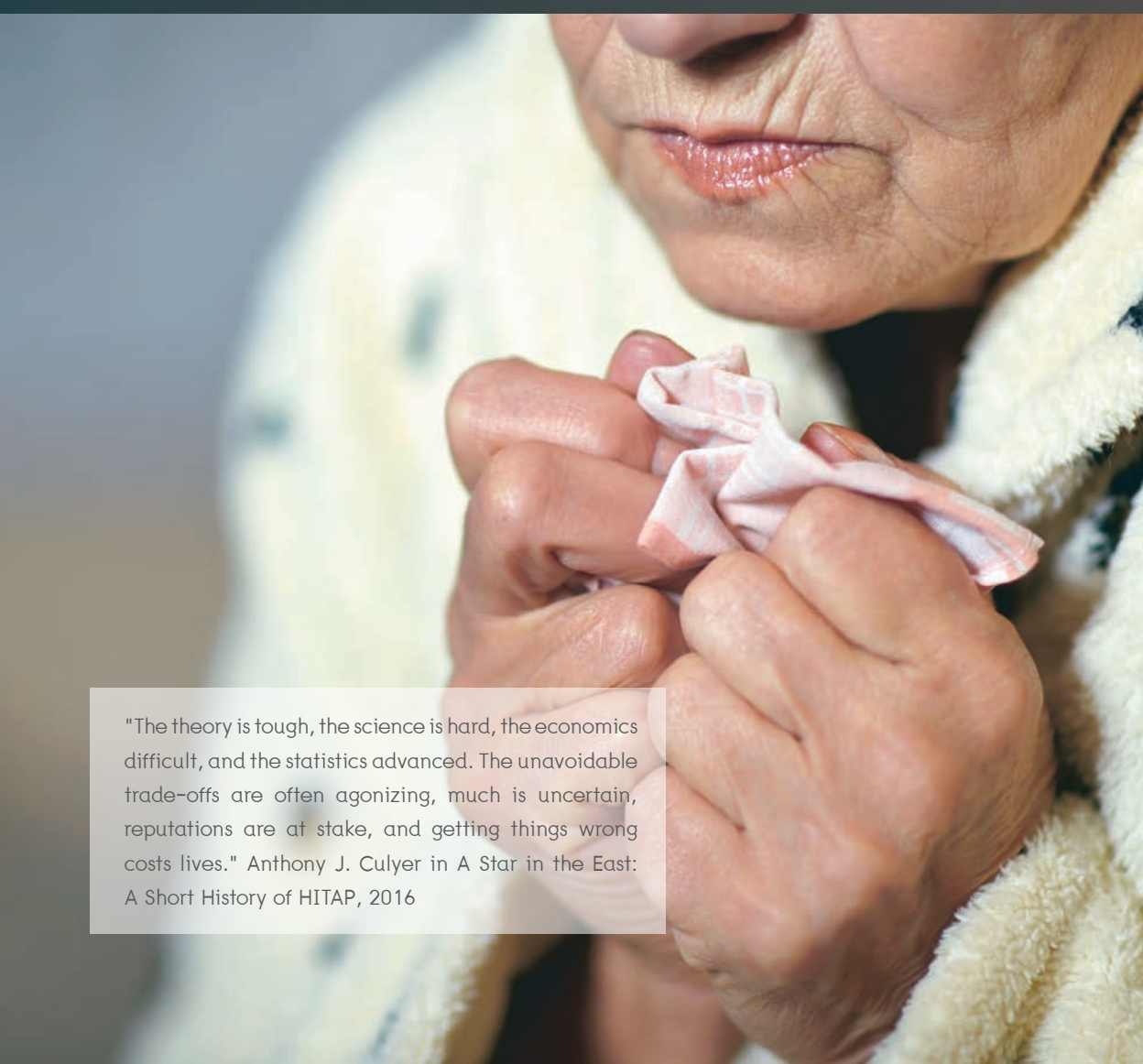
Those who want a yet richer understanding of the knotty issues that lie behind the work of NICE should read the first part of Tony Culyer's history of HITAP.

There is a short glossary at the end to help readers understand some of the peculiar NHS terms used here. It is there both for non-UK readers, but also for UK readers who have, entirely sensibly, not tried to understand the almost countless re-organisations of the superstructure of the National Health Service to which it has been subjected over the years.

Nicholas Timmins

THE FIRST SIXTEEN YEARS:

From Relenza to the Cancer Drugs Fund



"The theory is tough, the science is hard, the economics difficult, and the statistics advanced. The unavoidable trade-offs are often agonizing, much is uncertain, reputations are at stake, and getting things wrong costs lives." Anthony J. Culyer in *A Star in the East: A Short History of HITAP*, 2016

"THIS DECISION IS LUDICROUS"

In early October 1999, Sir Richard Sykes, the chairman of Glaxo Wellcome, then Britain's largest pharmaceutical company, stormed into No 10 Downing Street, the Prime Minister's residence and office. He was, says Trevor Jones, then the director general of the Association of the British Pharmaceutical Industry, "incandescent." (2)

A body that most people had not heard of — the National Institute for Clinical Excellence — had just recommended that the National Health Service in England and Wales should not prescribe Relenza, Glaxo's new treatment for influenza.

Relenza was given by an inhaler. If used within 48 hours of the onset of symptoms, the company maintained that it reduced the duration of a dose of flu — a condition for which there is a vaccination that changes annually as the virus mutates, but a condition that can also kill. In an epidemic year, millions of people in the UK catch it. Even in a non-epidemic year, many tens of thousands do so. If Relenza worked, it promised to reduce much misery and, perhaps, save lives. Given the scale of flu, it also promised to be a big money spinner for the company.

NICE, however, in its very first decision since becoming a legal entity on April 1, 1999 — and with a directly employed staff numbered in the tens — judged that there was insufficient evidence that Relenza in fact reduced the severity of the illness in those most at risk. Most notably the elderly, but also asthmatics and others.

A mere 70 patients out of the 6,000 in the clinical trial had been elderly. Relenza appeared to reduce the duration of symptoms from six to five days — but only if it was taken early enough when the initial symptoms differ little from a bad cold. There was no evidence that it reduced complications in the high risk groups. Furthermore, it cost £24 for a five day course of treatment. In an epidemic year, NICE calculated, the cost to the NHS might be close to

£100m at a time when the drug budget for the NHS, outside hospitals, was under £4bn. Even in a non-epidemic year, the additional load on Britain's family doctors — its general practitioners or GPs — for what might or might not turn out to be 'flu' would be considerable.² Relenza, NICE judged, was not cost-effective. It recommended that GPs should not prescribe it.

Sir Richard branded the decision as "ludicrous". He threatened that if it was not reversed Glaxo Wellcome would consider leaving the UK. In a public letter to the health secretary Frank Dobson, he said the decision "calls into question the suitability of the UK as a base for multi-national pharmaceutical operations." The recommendation was already causing problems for the product in other markets, he said, including the world's biggest, the United States. If the decision stood, "the UK can no longer be seen as a suitable market for the launch of innovative new medicines." This, he added, "is not Viagra [a recent new treatment for erectile dysfunction] but for a disease that kills people — 4,000 a year on average and 20,000 in a bad flu year."

Proof of efficacy in the elderly and other high risk patients would come as the product was used, he said, "otherwise you could be doing these studies [clinical trials to prove that] for 10 years". (3)

Blair, in October 1999, was still a relatively new prime minister. Just two-and-a-half years into the job. Glaxo Wellcome was a flagship UK company and a significant foreign currency earner. But Frank Dobson, the secretary of state for health who had set NICE up, had briefed Blair that he had to defend this new body's first decision. The prime minister did so, and firmly. Dobson later told Sir Michael Rawlins, NICE's chairman, that "I think we'd have had to back you regardless, whether you were right or wrong. Fortunately, you were right!" (4)

² For an explanation of family doctors and general practitioners, see the glossary.

Sykes' fury was in part — though only in part — caused by the speed of the process. NICE was still recruiting staff and was barely up and running. But the health department had known Relenza was coming and Dobson had asked NICE if it was willing to make an early rapid appraisal of the drug, ahead of the 1999/2000 flu season. "I put no pressure on them," Dobson says. "I only asked. I would have understood if they had said it was too early." (5)

But Rawlins says "the chief executive Andrew Dillon and I both felt this was precisely the sort of problem that we had been set up to sort out. We agreed without hesitation." (6) Glaxo too agreed to a speedy process as it expected to get a positive recommendation ahead of the winter. An ad hoc "rapid appraisal process" was set up. NICE reached its judgement at speed and then handled the appeal process, which Glaxo Wellcome took advantage of, in days. As it did so it made clear that the guidance was only for the forthcoming flu season. It would review the advice if further evidence emerged. Indeed, a year on, as evidence started to suggest that Relenza did reduce hospitalisation among the most vulnerable, the institute recommended limited use in high risk patients in years with a significant flu outbreak. Many years later, when a global epidemic of swine flu threatened in 2009, the NHS was to stockpile £136m worth of the drug.

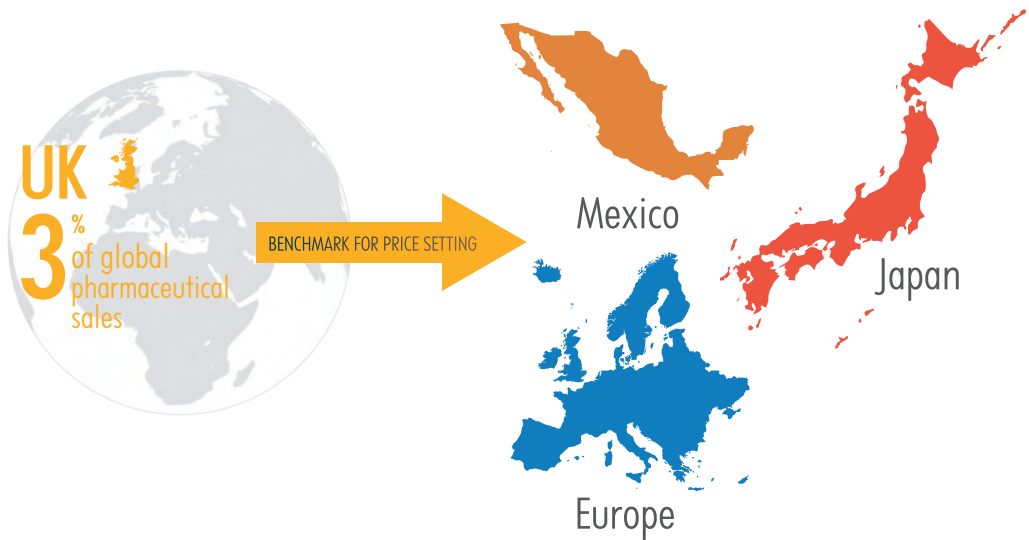
But that was in the future. At the time of the appraisal, the evidence for its efficacy in the patients who were most at risk was not there, while the bill, if Relenza was used indiscriminately, was potentially astronomic. NICE's decision took many in the industry aback. There were predictions of the "gloves off fight" that did indeed occur along with predictions of a likely judicial review of the decision. (7) As tempers cooled neither the judicial review nor the threat of the company's

withdrawal from the UK materialised. One gain the industry did make — a peace offering so to speak — was that the following month in the November Tony Blair agreed to set up a Pharmaceutical Industry Competitiveness Task Force which over the years took a series of steps to try to make it easier for companies to develop new products in the UK, not least by seeking to gear up the NHS better to help with clinical trials. (8)

The Relenza incident hurled NICE into huge media headlines and thus the public consciousness. But it also captured the essence of one of the key tasks for which the body had been created.

By world standards, the UK pharmaceutical market is a tiddler. It accounts for about 3 per cent of global pharmaceutical sales. It has, however, an influence appreciably larger than that. The price the NHS pays for pharmaceuticals is used as a benchmark by a string of other countries in settling their own prices for drugs — mainly in the rest of Europe but also elsewhere, including Japan and Mexico. The UK thus has an influence, though not necessarily a determining one, on prices in about a quarter of the global market. (9)

So here was a body which was to make recommendations not on whether a new product was effective — a pharmaceutical has to demonstrate efficacy in order to get a licence — but on whether it was cost-effective. In other words, did the benefits of a new pharmaceutical justify its costs? Its first judgement had been a "no". As Sykes complained, the effect in other markets was more or less instant, with a concomitant short term impact on Glaxo Wellcome's share price.



NICE had been set up to be an advisory body to the NHS. There was nothing in legislation that required the service to implement its recommendations. However, in a cash-limited service and with individual doctors and health authorities, in the main, poorly placed to assess the value-for-money of new treatments, the service and its clinicians were only too happy — certainly in this instance — to be advised.

In the debates leading to the creation of NICE, there had been concerns that the institute would limit "clinical freedom" — the right of the doctor to do what he or she thought was right for the patient in front of them. This was a concern that contributed to NICE's guidance being purely advisory even if, by 1999, it was more than 15 years since the cardiologist John Hampton had famously declared that clinical freedom "is at best a cloak for ignorance and at worst an excuse for quackery." Clinical freedom, he said then, was "dead and no-one need regret its passing." (10) He was, much later, to refine that view. (11)

Glaxo Wellcome placed advertisements in the medical press urging GPs to use the product. One GP practice in Devon declared publicly that it was going to pay no attention to this new kid on the block. But in the event, Rawlins notes, "just 212 prescriptions for Relenza were dispensed between September 1999 and January 2000 compared to the many hundreds of thousands that might have been." (12)

The Relenza incident also illustrated another key feature of the NICE arrangement. It worked because ministers allowed it to. Like clinicians and health authorities, ministers were not bound by NICE's recommendations. But as well as standing up to Glaxo Wellcome's fury, they in effect stood back, allowing their new baby to do the job for which they had created it. In the sixteen years since NICE was born, that principle — that having created NICE ministers would allow it fulfil its task without interference — has only been seriously challenged twice. A key reason for NICE's success and longevity.

Looking back many years later, Rawlins says "we were incredibly lucky with Relenza. It was the first big test, although I didn't realise at the time quite how big a test it was. It set the stage.

"It was blatantly obvious that the drug only reduced influenza symptoms by about a day, which wasn't a big deal. It cost an arm and a leg. And doctors were horrified at the prospect of finding themselves either running round everyone with flu to give them a prescription, or all the flu patients coming to their waiting rooms and spreading their germs around everyone else in the room. So the GPs were on side with the decision, and the newspaper leaders in the lay press were broadly supportive.

"It showed we were an evidence based organisation, and that we would make decisions on the available evidence, not on a wing and a prayer or a promise.

“*We were incredibly lucky with Relenza. It was the first big test, although I didn’t realise at the time quite how big a test it was. It set the stage.*”

Sir Michael Rawlins



General practitioners implemented our advice. And the industry learnt that there would be no political interference with our decisions, even when they involved a major UK company threatening to leave the UK. It was a tough few weeks. But we could not have had a better start." (13)

But if Relenza catapulted into the public domain an organisation whose acronym was to be the subject of many — not often very clever — jokes and puns over the years, where did NICE come from?



ORIGINS

Success has many parents. But the truth in that old aphorism makes tracing the precise origins of NICE far from entirely easy. Many seeds went into this particular acorn and many people, including many not mentioned here, can claim to have had a hand in it. One decidedly short and doubtless imperfect account of NICE's origins would, however, run like this.

In the period following the Second World War there was an explosion in the power of medicine in all its forms. The first pharmaceutical revolution — antibiotics — was followed by a second that included the anti-depressants, the contraceptive pill, and the first effective treatments for asthma and high blood pressure among many others. A whole host of other treatments also arrived — dialysis, hip replacements, and cervical smears to name but a few, along with first kidney transplants and then transplants for livers and hearts. Enabling much of that was a whole bunch of improved imaging and other technologies. A sense grew that the cost of health care was running away with itself. As early as 1966, Enoch Powell, the English health minister, spoke of an "infinity of demand". There was, he declared "virtually no limit to the amount of medical care an individual is capable of absorbing ... in short, the appetite for medical treatment *vientenmangent*". (14) That thesis is highly debatable. (15)

What is not debatable, however, is that particularly from the 1960s on, there was a parallel explosion in the medical research literature that accompanied all this. It progressively became impossible for any individual doctor to read it all and keep up, even within their own speciality, and even assuming they were equipped with the statistical skills to interpret the increasingly sophisticated data that started to emerge from clinical trials and other analyses. As Sir Miles Irving, professor of surgery at Manchester and director of the NHS's Health Technology Assessment Programme put it in 1998, "When I started medical school in 1954

the *Index Medicus* (the index of all medical research) was two thin volumes. By 1984 it was 16 fat ones. Today it comes four times a year on computer discs each the equivalent of 30 to 40 volumes. It is impossible for any one individual to keep up." (16)

In 1972, Dr Archie Cochrane published *Effectiveness and Efficiency: Random Reflections on Health Services* which stressed the importance of evidence based medicine — that treatments should be based on hard evidence, not just custom, tradition and hunch, and ideally that they should be subject to randomised controlled trials to ensure that they were indeed effective. (17) He also argued that "more and more requests for additional facilities" will have to be based not just on "the opinion of senior consultants" but "on detailed argument with 'hard evidence' as to the gain to be expected from the patients' angle, and the cost. Few can possibly object to this." (18)

In response to the growing mountain of evidence and the explosion in the research literature an industry of "guidelines" was spawned. These were attempts by medical specialists and others to provide guidance to clinicians on what constituted best practice. There was, however, no central authority for these. They varied hugely in who produced them, in their quality and in their evidence base — it being claimed at one point, for example, that there were 167 different guidelines for the treatment of asthma. (19) Which was a doctor to choose?

Alongside this concern about how clinicians were to know what amounted to best practice was the rising concern about cost — and thus, in time, about

cost-effectiveness. This was a world-wide phenomenon. In 1977, Milton Weinstein and William Stason from the Harvard School of Public Health were publishing papers on the foundations for applying cost-effectiveness analysis to medical practice. They argued that the inevitable limits on health spending that applied even in the United States — by far the world's biggest spender on health care — meant that "we, as a nation, will have to think very carefully about how to allocate the resources we are willing to make available." (20)

Decisions had to be guided "by considerations of cost in relation to expected benefits." There were, however, ways of doing that, they argued, including using "Quality-Adjusted Life Years" a concept that became known for short as the QALY. This was — at the time — an embryonic means of measuring the potential impacts of treatment by assessing not just the extra year or years of life an intervention might bring, but the quality of that life in terms of freedom from or reduction in pain, or the ability to perform basic activities of daily living such as feeding oneself or being mobile, or having a decent state of mental health. Crucially, it allowed a monetary value to be put on that in a way that provided a measure that could be used across all types of health intervention — whether from a new diagnostic, or a new drug, or new surgical, or new psychological treatment — thus allowing the comparison of the value of one treatment against another.

To put this very simply, a cheap, easily administered, highly effective oral vaccine for polio, a lethal disease that also leaves profound disability, has a very low cost per QALY even though millions of doses of it may be needed. In terms of cost-effectiveness it becomes obvious that a health system should fund it.

By contrast, a cancer drug that costs many tens of thousands of pounds or dollars for a course of treatment but which extends life for only a few months in only a proportion of those treated, and which comes with significant side effects, has a vastly higher cost per QALY. That brings questions about whether health systems should fund such treatments over more cost-effective interventions. In the UK, in the late 1960s and early 1970s, Alan Williams, a professor of health economics at the University of York, had already started on the development of the QALY — something that was to be a key part of his lifetime work.³

The underlying question behind all of this was 'is the health pound, or the health dollar, being spent in the best possible way'? In the UK in the 1980s, a string of developments addressed that.

In 1984 Bryan Jennett, a neurosurgeon from Glasgow, produced a highly influential book first aired for the Nuffield Trust as a Rock Carling lecture, entitled *High Technology Medicine: Benefits and Burdens*. It questioned not just the value in terms of health outcomes from some of the most recent high technology interventions, but also their cost-effectiveness. Entirely disconnected but almost in parallel, in 1983, Sir Roy Griffiths in his management inquiry into the NHS declared that hospital doctors needed to take responsibility for their budgets because "their decisions largely dictate the use of all resources, and they must accept the management responsibility which goes with clinical freedom". Implicit in that was the requirement to spend that money to best effect. Griffiths noted, disapprovingly, that the economic evaluation of clinical practice was "extremely rare". (21)

In 1985, the health department commissioned its first economic evaluation of the costs and benefits of treatment — first for heart transplants, an exercise undertaken by Martin Buxton at Brunel University, with that followed in 1986 with a similar

³ For a brief account of their development see: Alan Williams, *Discovering the QALY*
<https://www.york.ac.uk/media/che/documents/Williams%20on%20discovering%20the%20QALY.pdf>.

evaluation for breast cancer screening. (22) The two studies were a "breakthrough" in the development of the economic evaluation of cost-effectiveness in the NHS, according to Clive Smee, the health department's chief economic adviser for 18 years until 2002.

To strengthen that, and to address the increasingly overwhelming nature of the medical literature, a string of other initiatives followed. In 1991, the distinguished oncologist Sir Michael Peckham became the first director of research and development for the NHS, based in the department. One of his early moves was to establish in 1992 the Cochrane Centre, its task being to synthesise the results of clinical trials in order to provide the best available evidence on effectiveness — not yet cost-effectiveness, but effectiveness. The following year a Centre for Reviews and Dissemination at York University was established to push these and other findings out into the NHS through 'Effective Healthcare Bulletins', and in the same year a Standing Group on Health Technology Assessment was created. This saw the R&D programme investing in health technology units at a number of universities to undertake such work. The department also began talking to the drug industry about the issue, and in 1994, in conjunction with the Association of the British Pharmaceutical Industry, it issued joint guidance on the economic evaluation of pharmaceuticals. (23)

By now, the idea had taken root in both academic and policy making circles that there should perhaps be a "fourth hurdle" for the use of pharmaceuticals. To get a licence, drugs had long had to cross the three hurdles of safety, quality of manufacture and efficacy — although efficacy was defined by comparison to an inert placebo, a new pharmaceutical not necessarily having to prove its efficacy over an existing treatment. The proposed "fourth hurdle" was that the treatment should also be cost effective. There were powerful academic and indeed some consumer voices in favour of this. The move was supported "in principle" by

a report from the cross-party Commons Health Committee⁴ in July 1994, although the committee struggled somewhat to specify quite when and how this should be applied, whether during the licensing process or afterwards. (24) A key adviser to the committee was Alan Maynard, another of York University's many professors of health economics. Maynard had long been a strong advocate in the lay media, as well as in academic and policy making circles, of the need for cost-effectiveness studies in general and of the "fourth hurdle" in particular.

In evidence to the committee, Charles George, professor of clinical pharmacology at Southampton University and one of the beneficiaries of the health technology units that the department had set up, told the MPs that "whether we like it or not, economic arguments are coming in, left, right and centre." All the large pharmaceutical companies were starting to employ health economists in numbers, he said, adding, with considerable foresight, that "they are going to produce these data even if they are not required because clearly they will be asked for it by somebody" — whether it be the Department of Health, or others — "as to what the evidence is in terms of cost benefit." (25)

If these events and initiatives were some of the tributaries that led to the creation of NICE, other streams were also flowing. In 1991 the then Conservative government introduced the "purchaser/provider" split into the NHS. In place of a more directly managed service, the core idea was that — in a sense for the first time — the NHS should consciously decide what health care it wanted to provide, and then purchase it from whoever seemed best placed to supply it — whether from competing NHS hospitals or from the private and voluntary sectors. To achieve this, NHS hospitals were turned into nominally self-governing NHS Trusts to bid

⁴ See glossary for explanation of the role of the Commons Health Committee.



*“Whether we like it or not,
economic arguments are
coming in, left, right
and centre.”*

Charles George

for the health service's business, while health authorities were given budgets with which to purchase the care, as were those GPs who volunteered to take on initially somewhat limited budgets with which to buy routine care on their patients' behalf — the so-called GP Fundholders. This new arrangement was dubbed, somewhat misleadingly, an "internal market".

These reforms were immensely controversial. By 1997, six years on at its peak, only around half of GPs had become fundholders, and bitter disputes remained over whether this was creating a "two tier" service where the patients of GP fundholders were advantaged over those of non-fundholders, many of whom objected in principle to this introduction of an element of economic competition into the NHS.

Over time, though mainly at the margins, health authorities and the GP fundholders made differing decisions about what they would buy. Patients, very occasionally quite literally on different sides of a street, might find they did or did not have access to certain treatments or procedures, depending on the decision of their fundholder or health authority. This led to complaints about "postcode lotteries" and "postcode prescribing."⁵ The fact that there had always in practice been variable access to the NHS by the simple reasons of geography and local capacity got lost in this debate. The issue of the "postcode lottery" became increasingly fraught politically.

That was compounded by the money. To ensure that the first version of the purchaser/provider split — the "internal market" — did not crash and burn on day one, the NHS had been given a record spending increase in 1991. Over the 1990s, however, the money got progressively tighter to the point in 1996/97 when there

⁵ In US parlance "zipcode prescribing"

“*Rationing in health care is inevitable.*”

was no real terms increase at all in NHS spending, and arguably a small cut — for virtually the first time in its history.

These two forces — the "postcode" nature of NHS purchasing and the money becoming ever tighter — produced not just a greater interest in whether the NHS was spending its money to best effect (were the treatments being purchased not just effective but cost-effective?) but to a debate about whether "rationing" was now an inevitability.

That was certainly the view of Dr Richard Smith, the editor of the influential *British Medical Journal*. Between 1990 and 1999, the BMJ published no fewer than 45 papers with "rationing" in the title. (26) Smith was a key figure in the founding of the Rationing Agenda Group. This body was so mainstream that the health think tank the King's Fund underpinned its funding. Its membership included health economists, political philosophers, consultants, GPs and senior King's Fund figures, none of whom would normally be judged to be on the right of politics. Its arguments were sophisticated. But its essential message was bleak. "Rationing in health care is inevitable," the group declared, and the public had to be involved in how that was to be done. (27)

There were significant semantic debates about whether "rationing" was the right word to use — its primary meaning, as in the Second World War ration book, being to give everyone an equal share of something regardless of need, something the NHS had never done. By contrast Alan Williams had long argued that "rationing" occurred "when someone is denied (or simply not offered) an intervention that everyone agrees would do them some good and which they would like to have." (28) Those who preferred the Second World War definition argued that what this was really about was priority setting — deciding which treatments the NHS should and should not provide and to whom, within any given budget — something the service in practice had always done but which it had rarely done with any degree of transparency. (29)

However, a growing part of that debate — deciding what the NHS should and should not provide — involved cost-effectiveness. The underlying argument was what the economists define as "opportunity cost". Namely that if you spend money from a limited budget on one thing, you do not spend it on another. Something else goes by the wayside. And, without analysis, the value of that might be greater than what you do decide to spend the money on.

Individual cases fired these issues into the media, sometimes on the newspapers' front page. In early 1995 Cambridge Health Authority refused to pay for a second bone marrow transplant for a 10 year old girl initially known as "Child B" on the grounds that clinicians at both Addenbrooke's Hospital and the Hammersmith judged there was only a 2.5 per cent chance of success. Given the pain and distress and the high chance of failure, they argued that the potential benefit did not outweigh the risks. The procedure would have cost around £75,000. The health

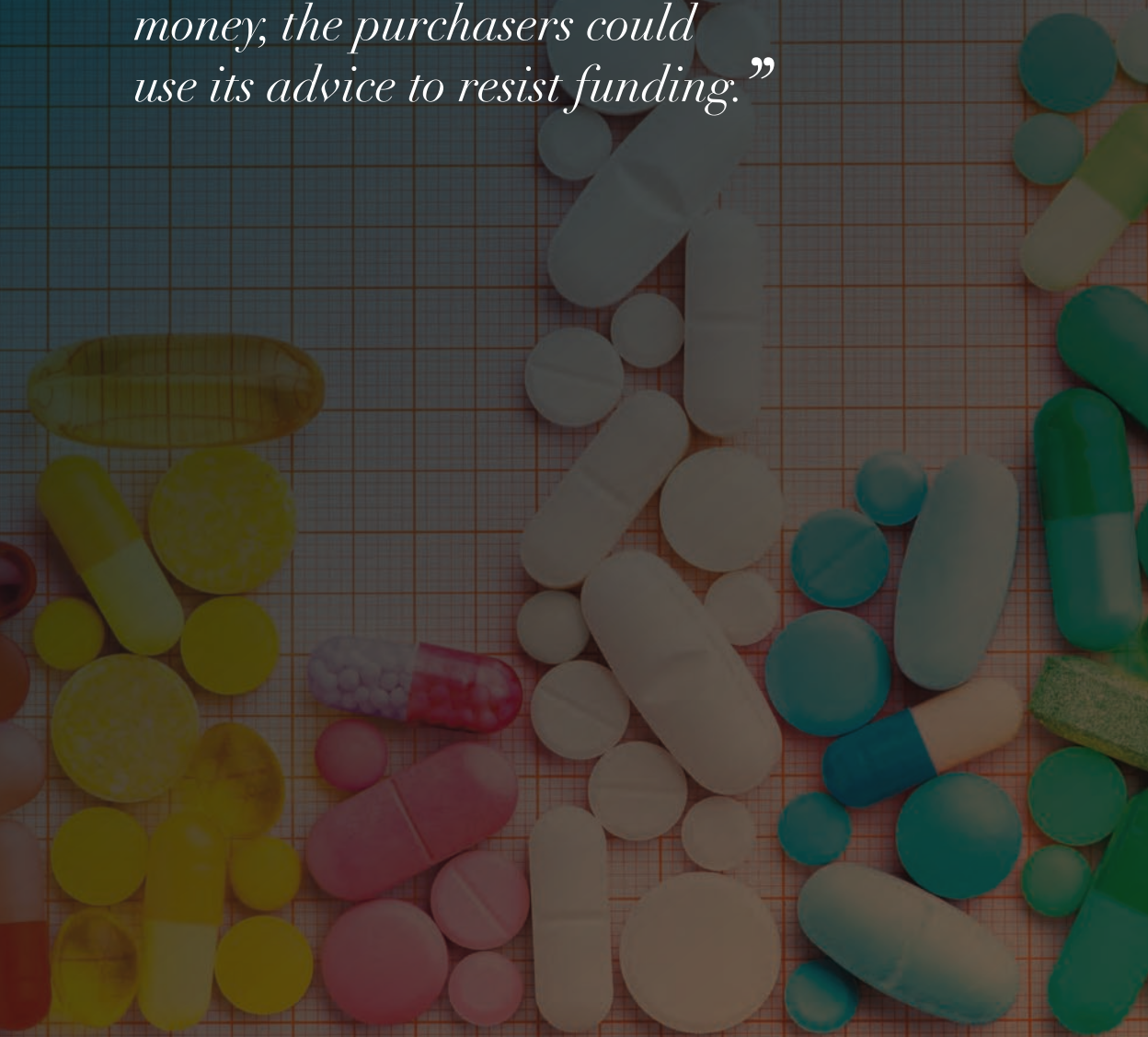
authority insisted that money was not the central issue, although it did also maintain that to spend it in this way would not be an effective use of its limited resources — so there was a financial "opportunity cost" involved, although the authority did not put it quite so bluntly. After court battles in which the authority's decision was ultimately upheld, Child B in fact received treatment in the private sector but eventually died in May 1996.

Equally, there were growing headlines as some health authorities refused to provide in-vitro fertilisation on the NHS while others restricted operations for conditions such as glue ear and varicose veins, and yet others considered scrapping ultrasound for low risk pregnancies or screening for brittle bone disease or for aortic aneurysms — a mix of decisions and proposals that encapsulated both the "postcode prescribing" and the "rationing" issues in one. (30)

It is difficult now to recall just how febrile the debate about the NHS was in the middle to late 1990s. John Major's fractured government had throughout his time in office a right wing element in his Conservative party that would gladly have scrapped the NHS in favour of some sort of insurance-based system. It was not, however, just the political right who had come to have doubts about the sustainability of a tax funded, largely free at the point of use, health system — or who had come to believe in the need for "rationing".

In September 1995, Rodney Walker, the retiring chairman of the NHS Trust Federation — the body that at the time represented most NHS hospitals — declared that in the face of an ageing population, medical advance and thus inevitably rising demand, the NHS would have to be reduced to "a safety net"

“When the Development and Evaluation Committee judged something to be poor value for money, the purchasers could use its advice to resist funding.”



for the old and weak. His comments were disowned by other NHS voices and indeed by ministers. (31) But later the same month, a group chaired by Sir Duncan Nichol, a former NHS chief executive, funded to the tune of £100,000 by the pharmaceutical industry, argued that the gap between resources and demand could not be closed by increased taxation alone, and that user charges and "a clearer definition of what services will be provided free at the point of use" were likely to be needed. (32) Its membership included Patricia Hewitt, the future Secretary of State for Health, and Chris Ham, a future chief executive of the King's Fund.

Sir Alan Langlands, the NHS chief executive, went public to attack these "doom and gloom" merchants, declaring that he wanted to distance himself from the "ration and privatise brigade." (33) The ministerial response came in a government white paper of early 1996 — *A Service with Ambitions* — produced by the then Conservative health secretary Stephen Dorrell. One of its most striking features was that it felt the need to open with a lengthy defence of the NHS and of its tax funded nature, arguing that the model was in fact sustainable. Not least because "there continues to be scope for funding desirable improvements in part by offsetting savings elsewhere, such as reducing expenditure on those treatments which are now recognised to be less clinically and cost-effective". (34) Indeed, Sir Michael Peckham, on his retirement as research and development director, bravely estimated that at least £1bn of NHS resources, more than 2 per cent of the budget, could be released for improved patient care if the NHS cut out unnecessary and ineffective treatments. (35)

Against this national background — a fevered debate about the sustainability of the NHS amid ever tightening budgets, alongside a growing interest in nationally driven cost-effectiveness initiatives within the health department — there was also bottom-up activity. The new purchasers or commissioners in the NHS — the health authorities and GP fundholders — felt the need for advice on what to buy. As early as 1991, the then Wessex region of the NHS had established

a "Development and Evaluation Committee" to provide just that, evaluating not just new technologies but some routine existing practice. The Wessex DEC was the idea of Dr Graham Winyard, the regional medical director. Its work programme was run by Dr Andrew Stevens, a senior lecturer in Public Health Medicine who a quarter of a century later was to be the longest serving member of NICE's appraisal committees. By the end of 1994, the Wessex DEC had made recommendations from 'strong support' to 'not proven' or 'not recommended' on well over 50 topics, including pharmaceuticals, devices, procedures and bits of service design, for example whether to introduce an "observation ward" into accident and emergency departments — a move it recommended. (36) When the DEC recommended something, the regional health authority would insist it went into contracts. When it judged something to be poor value for money, the purchasers could use its advice to resist funding. (37) The Wessex DEC was followed by others — most notably in the West Midlands and Trent regions — while most parts of the country developed at least some form of advice mechanism for purchasers on what was and was not worth buying. The north of England had a guidelines group while Oxford had a programme with the imaginative name of "Bandolier" which aimed to provide "bullets" of evidence for clinicians and commissioners on what was and wasn't worth doing. (38) The DEC's in particular began to co-operate to avoid duplication of their efforts.

Valuable though their work was, however, it had limited fire power. It remained well short of a nationally authoritative voice recommending what the NHS should or should not adopt, and it did not prevent the controversy over the so-called "postcode lottery".

Furthermore, for something like NICE — a national organisation — to come into existence it takes more than just academic interest, or the travails of health authorities and GPs trying to balance an ever tightening budget. It takes a political spark.

The first of these came in 1995. Gerry Malone, the minister of state for health between 1994 and 1997 was asked to take a decision on whether the NHS should provide Beta-interferon, a new treatment for multiple sclerosis which was about to get its licence. Over the years, how far and how generously it should be prescribed was to be a recurring issue for the NHS and later, indeed, for NICE itself. There were three problems. First, Beta-interferon was expensive. Second, while it appeared to reduce the number, and possibly the severity of attacks in patients with the relapsing-remitting form of the disease, it was far from clear that the effect was dramatic, or indeed lasting. And third while there were some 70,000 MS sufferers in England, the proportion with the relapsing-remitting form could only be estimated at around 45 per cent. There were fears that the NHS could easily face a £100m a year bill and possibly even a £380m one — 10 per cent of the then NHS drug budget — for a drug whose long-term impact was uncertain. (39)

Among Malone's other duties he had been revising the "limited list" — effectively a "blacklist" originally introduced in 1983 of ineffective or highly dubious remedies for which the NHS would no longer pay. "There I was, getting rid Old Mother Hubbard's remedies so to speak, including Gregory's Mixture [a laxative blend of rhubarb, magnesia and ginger] where I ended up on the Today⁶ programme arguing with the manufacturer about why we were no longer going to pay for it. I did think 'this is very silly. Why am I, the minister, doing this?' Malone says. (40)

"So there we were, scrabbling around getting rid of squibs in terms of the cost of these pretty useless remedies when this H-bomb called Beta-interferon comes flying in over us."

⁶ The Today programme is the BBC's flagship early morning current affairs radio programme which helps set the day's news agenda.

Malone was married to a doctor. But his own background was that of a lawyer and journalist — he was a former editor of the Sunday Times in Scotland. "My reaction when I was told I needed to take a decision on whether the NHS would provide Beta-interferon was 'how the hell am I meant make that decision?' The answer was 'because you are the minister.' But I pointed out that I was probably the least equipped person to make the judgement around its efficacy and its costs and benefits, even with the no doubt excellent advice of my civil servants."

Malone says he was acutely aware that if he issued an "ex-cathedra pronouncement that was likely to be very ill-informed" and which restricted its use, the likelihood would be a storm of controversy. His response was to get together "the great and the good among the neurologists and others who did know something about all this while bringing the MS Society into the frame. The Treasury had told me that they would only press me to ban the drug if it worked and was widely taken up — which was an incredibly daft position into which to get yourself! I basically said to this group 'I really don't want to ban this. But we are going to have to go fairly slowly to prove it, and to discover whether it is in fact effective'. Fortunately everyone was very reasonable, and they all bought into that." The result was an executive letter in late 1995 that permitted its use where NHS purchasers chose to adopt it, but did so in somewhat discouraging tones and carefully defined circumstances that limited the cost and stood some chance of providing better evidence of its efficacy.

Malone says, however, that "when that was over, I got together some of the key people in the department and said 'Look, we have got away with this on this occasion. But I never want a minister to be put in this position again. Go away and devise some scheme where ministers do not have to take these decisions. This is not something that in my view should ever again land on a minister's desk.'" (41)

The result was not the immediate creation of NICE. Whatever the reality of the "internal market", the rhetoric surrounding it was all about devolution. The politics were not sympathetic to the creation of a national body, and no similar potential crisis such as another Beta-interferon arose to force the issue over the next fifteen months of Malone's tenure, up to the 1997 general election. His intervention, however, did prompt at least some further thought about how a mechanism could be created that would distance ministers from such decisions. It also led the department to start a "horizon scanning" process, commissioned from others, aimed at spotting a future Beta-interferon well before it was licensed.

A couple of months later in February 1996, Clive Smee, the department's chief economist, persuaded Graham Hart, its permanent secretary, that he should take a sabbatical to spend six weeks in Australia and New Zealand, and six weeks in Canada and the United States "to see where the British health system was off the pace."

Although NICE these days may be the most famous globally of the NICE-like organisations, Australia had in fact got there first. Its Pharmaceutical Benefits Scheme had since 1993 included a "fourth hurdle" of cost-effectiveness in its decision about which pharmaceuticals would be publicly funded. The global impact of that was very limited given that Australia's share of the global pharmaceutical market was tiny, even compared to the UK's. But New Zealand and Canada too were dipping toes into this water while in the US the increasingly powerful, if much-loathed, Health Maintenance Organisations were also taking an increasing interest in cost-effectiveness when deciding which treatments they would fund for those they insured. "One of the lessons I brought back," Smee says, "is that we were off the pace in the use of cost-effectiveness criteria in evaluating new drugs." (42) His papers on the issue were circulating in the department by the autumn of 1996, and in early in 1997 Tony Culyer, another of the professors of health economics at York,

was asked to chair a DH Expert Workshop on Guidelines for Pharmaco-economic Studies — a high powered external follow-up to the guidelines the department had outlined with the industry in 1994. Its extensive membership included leading figures from the regional Development and Evaluation Committees as well as departmental officials and the two or three of the most senior figures from the pharmaceutical industry in the UK who were involved in such work. Its recommendations, completed in early 1998, were never published. According to Culyer, however, they form the basis of NICE's initial approach to technology appraisal. (43)

By now, the general election of May 1997 was looming and the issues around cost-effectiveness and evidence-based medicine were firmly in the public domain. In the February, Chris Smith, Labour's shadow health spokesman, made a speech on "Putting Quality at the Heart of Healthcare." His special adviser at the time was a young and fiercely bright health service manager by the name of Simon Stevens who would go on to be first Frank Dobson's special adviser, then Tony Blair's and eventually the chief executive of NHS England.⁷ Smith was also informally being advised by Alan Maynard. (44) The speech included a passage on "National Standards for Clinical Effectiveness." To provide "optimal quality care the NHS needs to ensure the speedy uptake of cost-effective innovations; the *non*-uptake of *ineffective* innovations; the regular assessment of current practice; and thorough testing of those not yet shown to be effective," Smith said. He added that "evidence based medicine, and active research programmes, can identify which treatments work; but you still have to persuade clinicians to use appropriate — and to avoid inappropriate — interventions." (45) There was no proposal in Smith's speech for a national body to undertake such work. So this was not yet NICE. But it was nearly there. And it was a concept that Stevens had helped create and would carry into government when he became Frank Dobson's special adviser.

So, to find a metaphor, over the years, both nationally and internationally, a host of tributaries — including doubtless some not identified here — had flowed to form a river that fed a lake.

⁷ For definitions of special adviser and NHS England see glossary



In the UK it had been fed by Archie Cochrane's advocacy of evidence-based medicine, by Bryan Jennett's questioning of its high technology use, by Alan Williams development of QALYs which provided a crucial tool — a measure of cost-effectiveness — and by the health department's growing interest and then investment in health technology assessment. An approach that the NHS's own regional health authorities were themselves beginning to apply from, so to speak, the bottom up. There was much debate, indeed argument, about the best way of doing this, and over how to get clinicians to adopt the findings. (46) But what was emerging was a bunch of methodologies that the as yet unformed NICE would be able to use. Allied to all that were a series of political and economic pressures on the National Health Service that played through into arguments about postcode prescribing and rationing, while, at ministerial level there was an incipient sense, as evidenced through Malone's experience over Beta-interferon, that ministers should not be taking detailed, individual, decisions about what the NHS should and should not provide — or, at the very least, they should not be taking them alone, or routinely. But while the lake was sitting there, it remained held back by a dam. It took a small political earthquake to break it.



The Department of Health

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Presented to Parliament by the
Secretary of State for Health
by Command of Her Majesty,
December 1997

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FORMATION

The earthquake was Tony Blair's landslide election victory in May 1997, ending eighteen years of Conservative rule. On the Sunday after the election, Blair rang Alan Milburn to confirm that he was to be the minister of state for health — the second rank position in the department. Blair told him: "We haven't got a health policy. Your job is to get us one." (47)

Blair's diagnosis was spot on. He had told the UK electorate on the eve of the poll that "We have 24 hours to save the NHS." But Labour's declared policy for the NHS was unconvincing and shallow. It consisted of little other than pretty much outright opposition to the Conservative's internal market. Robin Cook, Labour's health spokesman in 1991 when it was introduced, had made huge political capital from opposing it, highlighting the privatisation and fragmentation that it allegedly introduced, along with an explosion in contracting costs. But after his departure from the post in 1992 Labour's policy had barely moved on as the party went through a string of mainly short lived opposition health spokespeople none of whom was in post long enough to develop anything coherent as an alternative. Labour's election pledges on health consisted of cutting bureaucracy, abolishing GP fund-holding, and a badly phrased commitment to cut the numbers on the waiting list. Chris Smith and his adviser Simon Stevens had begun to form an intellectual framework for a policy — not least around improving quality as witnessed by the speech quoted earlier. But there had been no time to put detailed flesh on it. In remarkably short order, however — by the December of 1997 when the government had only been elected in May — a white paper on the future of the NHS was produced.

In retrospect, Blair's appointments to health — certainly when it came to NICE — proved pretty inspired.⁸ Frank Dobson, to his own as much as everyone else's

⁸ There is a case the other way on other aspects of Labour's health reforms.

surprise, had been made health secretary. A bluff and bearded Yorkshireman with a filthy sense of humour and a passionate commitment to the NHS, he had been the party's health spokesman in opposition in the mid-1980s. He was a far shrewder politician, and a much more effective manager, than his public persona sometimes portrayed. He proved to be a good delegator to a pretty impressive bunch of ministers. They included Milburn who was a dynamo of energy in creating the 1997 white paper. Like Tessa Jowell, the public health minister, Milburn would go on to be a Cabinet minister, in his case at health. The minister in the House of Lords⁹ was Baroness Jay. This is often a relatively lowly ministerial appointment but she held the rank of minister of state and brought to the task both a background in health and a brain to be reckoned with.

This ministerial team arrived to a department large parts of which were committed to the idea of cost-effectiveness in the NHS. Alan Langlands, [later Sir Alan Langlands], the NHS chief executive, was a science graduate from Glasgow University who had been a firm supporter and sponsor of Michael Peckham's R&D programme. Sir Ken Calman, the chief medical officer, "was always insistent that clinical effectiveness should include cost-effectiveness and had insisted that form part of the work of the National Screening Committee we had set up," according to Clive Smee, the department's chief economic adviser. Calman's deputy was Graham Winyard, the public health doctor who had set up the Wessex DEC in 1991. Aside from being deputy chief medical officer he was also the medical director for the NHS, sitting on the NHS Executive.¹⁰

Smee says that Milburn "was hungry for ideas. He lapped up anything new for consideration and from the start was very interested in cost-effectiveness".

⁹ The UK's second, and unelected, legislative chamber. At the time it was composed mainly of hereditary peers, leavened by a contingent of "life peers" whose title could not be passed on to their heirs and who were a mixture of party political appointees and "the great and the good". Many of the latter sat on the so-called "cross benches" – a position that aligned them with neither the government of the day nor the official opposition. The number of hereditary peers has since been massively reduced.

¹⁰ See Glossary for definition of NHS Executive.

“*Sir Kenneth Calman, the Chief medical officer, had always insisted that Clinical effectiveness should include cost-effectiveness and had insisted that form part of the National Screening Committee we had set up.*”

He and others say that after the huge political controversy around the fragmentation that the internal market had allegedly brought to the NHS, ministers were also very keen "to put the National back into the National Health Service." (48)

As evidenced by Chris Smith's speech and Simon Stevens continuing involvement as the special adviser to Frank Dobson, Winyard says that "Ministers wanted a strategy on quality, and of course quality sprawled into everyone's domain in the department, and all of this rather formidable bunch of ministers were interested in it.

"So the department produced a huge submission on quality — it was a pan-department effort — and it was too big. I doubt if anyone read it. We then had an initial meeting with all the ministers except Dobson — they all had to be there — and it was one of those dreadful meetings where no-one has really read the paper — it was too big — and there are lots of important people present who can

lob in questions, and it was all a bit shambolic and we were sent away to do more work. Which we did. And had another meeting. And the same thing happened.

"Before we had the third I decided, with some temerity, to try to grip it. So the night before I sat up with my wife doing overheads — this was before the days of Powerpoint — writing with a black pen on acetates and built up a schema, putting one acetate on top of another to build a story about what government could do about quality down one side and what the professions could do about it on the other. So one side had, for example, National Service Frameworks (guidance on how services should be organised) and how they could be performance managed. And the right hand was the more professional side of things along with the suggestion of an organisation, outside the department, that would produce audit tools and guidelines on clinical and cost-effectiveness. With that went some process to ensure these guidelines were implemented, which itself didn't have a name, but which fitted neatly into the concept of clinical governance being developed by Liam Donaldson [Ken Calman's successor as chief medical officer]¹¹.

"So with great trepidation I went through this presentation with the acetates projected on to a white wall in Milburn's office and at the end I turned the projector off. And Milburn said 'no, keep it on' and the rest of the discussion was about this big schema which basically was pulling together a lot of stuff that was already happening in one place or another, but included this new national body. And, as far as I am concerned, that was where NICE was born." (49)

There was still no name for this organisation, nor yet an entirely clear definition of what it would do, or who it should be.

¹¹ Dr Liam Donaldson. Later Professor Sir Liam Donaldson

Either just before or just after this meeting, Rawlins, who at the time was chairman of the Committee on Safety of Medicines, got a call from Baroness Jay asking him to go to see her on his own. "That caused a bit of consternation because no chairman of the CSM had ever been to see a minister on their own [without accompanying civil servants]. But I went along. And she said 'we are thinking of introducing an element of cost-effectiveness into whether or not we should fund drugs.

'Could the Committee on Safety of Medicines do that? Could it give advice to the licensing authority on whether a drug was cost effective?' I had no notice of the question. But I said I would not advise that. Either the licensing body or the CSM would confuse the two questions. The cost-effectiveness decisions would be awkward, and would at times be marginal. So if either the committee or the licensing body knew that cost-effectiveness was coming up in terms of the licence, it would say 'no'. You can always find a reason to say no to putting a new drug on the market, on grounds of quality, safety and efficacy, either on one or all three of them, if you have to take cost-effectiveness, which is the hardest decision, into account. It is only too easy to say, for example, that the safety profile has been inadequately studied. You can fudge it. So I said, 'no', it was best to make decisions about cost-effectiveness through a different body to the one asked to judge only quality, safety and efficacy." (50)

This different body, as already pointed out, had no name, and, still, no clear definition of precisely what it would do. But in Frank Dobson, the civil servants had a secretary of state who fully grasped what all this was about. He had had relatively little to do with NHS policy since his time as opposition spokesman in

the 1980s. But he knew about QALYs and Alan Williams's work from that time (51), and his parliamentary private secretary — an unpaid post that supplies an "eyes and ears" role for Cabinet ministers on the views of their back-bench MPs — was Hugh Bayley [later Sir Hugh], the York MP who had previously worked in the university's extensive health economics department. Dobson himself had a cottage just outside York. These were not issues that required explaining from the ground up to this new secretary of state.

Many others did the detail and donkey work. But NICE became very much Dobson's baby. It offered a potential solution to a bunch of disparate and at times conflicting problems — the proliferation of guidelines, too little assessment of the cost-effectiveness of treatments, the so-called postcode lottery, and at least some answer to the "rationing" debate, allied to the fact that the NHS was demonstrably slow in international terms in adopting new drugs and treatments.

"The whole situation was totally unsatisfactory," Dobson says, "and virtually everyone agreed it was unsatisfactory including the pharmaceutical industry. Trevor Jones, the director general of the Association of the British Pharmaceutical Industry, was endlessly pointing out that the companies would introduce a new drug that was clearly beneficial and it would only be used in half a dozen places instead of across the NHS. There was a clear issue over take-up. And from the industry's point of view, while something like NICE might give the thumbs down to some things, it was likely that more things would get the thumbs up, and once that happened, it would be used across the board. So there was something in it for the industry as well as for the NHS."

Dobson says, however, that the key issue for him was one of authority, something only a national body could bring. "I knew from when I had

been shadow health secretary that there was no national body advising on whether things were worthwhile. There were lots of bodies producing guidance, some local, some regional, some for particular conditions, and they all produced advice for the department and for doctors, but none of it had any authority. It was a perfect shambles. And if we were going to get a rational approach something like NICE was needed — particularly on innovation but also in terms of getting around to looking at a lot of stuff that was being done in the NHS that was not very effective.

"The whole issue needed some authority. And, on the Gerry Malone line, it would be insane to have ministers trying to take all these decisions" — a point shortly to be underlined when, ahead of NICE starting operations, Dobson had to decide whether or not the NHS should pay for Viagra.

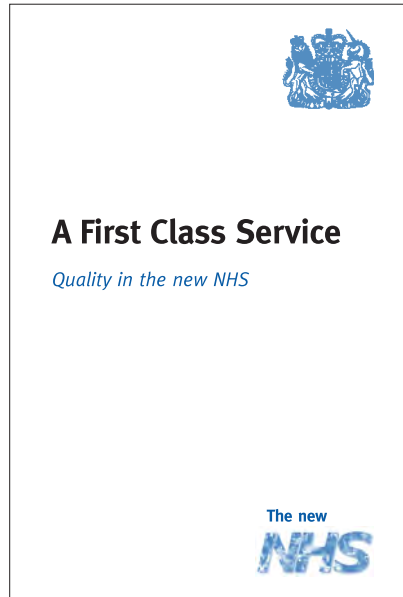
There was, however, a lot of work to be done to convert this idea into a reality and to decide precisely what NICE should do. There was some debate about what it would be called. An organisation for cost-effectiveness was felt too starkly challenging for both the life sciences industry and doctors. Clinical effectiveness was considered. But in the end, according to Winyard, it was Frank Dobson who came up with the name — the National Institute for Clinical Excellence, the use of excellence making it sound more positive than the alternatives, while its initials, of course, spelt NICE. At the same time the inclusion of the word "institute" gave it an academic, apolitical, ring.

Labour's first white paper in December 1997 announced NICE alongside many other things including the creation of the Commission for Health Improvement, an organisation to inspect the application of clinical governance in NHS bodies — in effect an NHS inspectorate, with the wits dubbing the two bodies NICE and NASTY.

But while the white paper, *The New NHS: Modern, Dependable* (52) talks a fair bit about cost-effectiveness, the specific tasks that were assigned to NICE were centred around producing clinical guidelines based on the evidence of clinical and cost-effectiveness, and on audit, bringing together the work done by the range of organisations that the department funded on behalf of the NHS, including the Medical Royal Colleges. There is no direct mention of health technology assessment in the paper.

"There wasn't a specific promise that it would be extended to include pharmaceuticals because there were doubts as to how large a work programme a new body like NICE could take on initially," Clive Smee says. "We looked at whether health technology assessment should go to the institute or some other organisation, and I remember preparing a paper on that for Baroness Jay. It was finally decided we would give it all to NICE."

The result in July 1998 was a document called *A First Class Service* which set out in more detail the outline of the quality framework that had appeared in *The New NHS*. Namely national service frameworks, the Commission for Health Improvement to inspect clinical governance, and NICE itself — a body which "will ensure authoritative national guidance is available for all health professionals on the latest drugs and technologies." In other words, health technology assessment was included. NICE was to bring together the work of some 26 organisations that the department in one way or another had come to fund.



The paper warned that the various industries which produce drugs and devices — the life sciences industry — "will need to enhance their capacity to produce evidence of clinical and cost-effectiveness" and that where that was not available "NICE may recommend that in the first instance the NHS channels its use through well controlled research studies."¹² Intriguingly, given later developments, it said that NICE would initially focus on clinical issues. But "we recognise that there are a range of other interventions, including screening programmes and other public health and health promotion programmes which could come within its orbit in the future." So the seeds of NICE's future expansion were present at its birth.

¹² NICE did indeed come to make "only in research" recommendations, though only rarely.

Thought had gone into how NICE should be structured, including the creation of a "partner's council" made up of "key stakeholders" from the Medical Royal Colleges, the industry itself, academics, patients and carers to help develop the organisation's work programme and report on its annual progress. That, Dobson says, was partly to encourage buy-in to NICE from the wide range of interests that its activities would affect, but also to ensure transparency. "It had to be out in the open," Dobson says. "I am not a loony about transparency. But there were too many people, chiefly clinicians but also patients and citizens whose experience and views had not been considered for one reason and another and who should have the opportunity to influence things."

There was, he says, some resistance in the department to the idea of a national body — "that it would over-ride clinical judgement, the argument being that what applied in Newcastle might not apply in Birmingham. That was a legitimate concern, although I must say it seemed to me to make no sense at all." It was essentially solved by saying that while purchasers and clinicians would be expected to follow NICE's guidelines and recommendations, neither would be mandatory. This was a crucial distinction to what was happening in Health Maintenance Organisations in the United States, for example, where doctors were required to follow protocols — an approach that tied them into a system of formulaic medicine, even though it was normally underpinned by bureaucratic appeal mechanisms, and which the critics dubbed "cook book medicine". In the NHS, by contrast, purchasers and doctors would be expected to follow NICE's guidelines and its recommendations on technologies. One element of clinical governance would be to measure how far they did. But NICE's pronouncements would not be mandatory on the NHS.

Furthermore, NICE would advise on cost-effectiveness but not on overall affordability within the NHS budget. That issue would remain with ministers. So the position could in theory arise where NICE would judge something to be highly cost-effective while still involving such a huge increase in NHS spending that ministers might decide it could not be funded. For most of NICE's life that never became a live issue. It may be becoming one now.

The affordability issue, of course, underlay the rationing debate and one key unresolved issue was whether NICE was likely to increase or decrease NHS spending. In the world outside the health department, some saw its task of recommending what the NHS should and should not buy as clearly being the "rationing" body that some had been demanding. (53) It would restrain or even cut costs by, in effect, ruling out cost ineffective treatments, or barring excessively expensive ones. Others saw it as likely to increase expenditure as it recommended the swift adoption of new and effective treatments. The debate flowed back and forth. (54) Richard Smith, the BMJ's editor, and a key advocate in the rationing debate, gave the institute a decidedly lukewarm welcome. He judged it to mark "the beginning of explicit, national, rationing" and the arrival of the "fourth hurdle" — changes he welcomed. But he judged its task to be too large and that it would struggle to solve the problem of variable performance throughout the NHS. (55)

Inside the department there was equal uncertainty about whether NICE would prove cost constraining or cost enhancing. "I remember saying very clearly when the papers on NICE went up that we were not clear whether it would increase or reduce overall expenditure because we did not know how much wasteful stuff it would be able to deal with," Clive Smee says. "What we did recommend very strongly

was that it should look at existing treatments alongside the new, and that was never quite given the priority, maybe because there were so many new ones." In the same vein, Graham Winyard says: "I didn't know whether it would increase or decrease costs. I just thought it would make expenditure more sensible — more rational. It was really about how we were going to make best use of whatever money was available, whether it was big or small. And we needed a NICE-like entity to do that."

With the organisation announced, the next job was recruiting for it. Dobson's first choice for chair was Naren Patel¹³, at the time president of the Royal College of Obstetricians and chairman of the Academy of Medical Royal Colleges. Unbeknown to Dobson, Patel had just agreed to an as yet unannounced post in Scotland from which he felt he could not withdraw. His second was Mike Rawlins, the retiring chairman, after six years in the role, of the Committee on Safety of Medicines. Rawlins, who had been appointed professor of clinical pharmacology at Newcastle at the then decidedly early age of 32, had been a member of the CSM since 1980. During his tenure, he had been something of an advocate of the CSM becoming more transparent in its operations. He also had experience as vice-chairman of the Northern Regional Health Authority, a position in which he had come to know Liam Donaldson who had been jointly its chief medical officer and general manager before Donaldson succeeded Ken Calman as the government's chief medical officer in 1998.

Rawlins records his arrival starting with the secretary of the CSM passing him a note at a September 1998 meeting which Rawlins promptly stuck unread into his pocket. Back in his office at the meeting's end the secretary asked him if he had called the phone number on it. "He said 'I think you ought to'," Rawlins recalls. "I found myself through to Frank Dobson's office and was told the Secretary of State wanted to meet me. I asked what it was about and they said 'don't know.' So I said 'when?'"

¹³ Now Lord Patel

"They said 'the Secretary of State is at Blackpool at the Labour party conference next week and then he's going to South Africa and he would like to talk to you before he goes'.

"So I said 'what you want me to do is go to Blackpool to meet him there' and they said 'thank you very much for putting it like that'. So I took the train back to Newcastle where I lived and on it by coincidence was Alan Langlands, the NHS chief executive. So I told him I had had this funny phone call and asked if he knew what it was about. He, very diplomatically, said he had no idea but that Liam would give me a call at the weekend, adding 'I think it might be about NICE'.

"Liam called me and said they were looking for a chairman and 'Frank Dobson wants to talk to you but he's not really allowed to do it [thanks to the formal appointments system]. So the conversation will be about the Committee on Safety of Medicines, though it may get round to NICE'.

"I'd of course vaguely heard about NICE, but over the weekend I read the documents [the white paper and its follow-up] and drove to Blackpool and as we were walking through the dining room to lunch Frank said 'we are supposed to be talking about you leaving the CSM and about any advice you've got for me.' And I said 'none at all. You've appointed my successor, a very good appointment, and I've got no advice at all.' Frank replied 'Good. We will talk about NICE'. Which we did. Over the meal. And it appealed to me. At the end he said 'you'll do. You will have to apply and be interviewed. But you'll do'. And then he added that 'you will probably hear it on the grapevine anyway but my first choice was Naren Patel but he wouldn't do it. And I'd rather you heard that from me than from anyone else'. And I must say I respected him for that."

Rawlins was indeed duly interviewed and appointed. "Quite simply one of the best appointments I ever made," Dobson says. "So much of NICE's success was down to him personally."

The instant reaction of much of the pharmaceutical industry was one of suspicion. Trevor Jones, director general at the time of the Association of the British Pharmaceutical Industry, said he first heard of NICE when Dobson's private secretary rang him to say "we are going to introduce a new body to look at the cost-effectiveness of medicines. We haven't decided on a title but Frank wants you to be one of the first to know. Can you come in?"

Dobson sold NICE to him as a mechanism to end postcode prescribing. "He said 'for too long your industry has worked hard at developing these products and it is unacceptable to me that patients are not getting the same access and I am going to bring that to an end.' He said he was going to ensure 'an end to postcode prescribing', and that became a bit of a litany."

The industry had, of course, been well aware that the pressure to measure cost-effectiveness was rising. But it was equally aware that effective new medicines were being introduced but not taken up at speed by the NHS. Here was a mechanism that might help with that.

Jones says he had three initial worries. First, what would be the measure of cost-effectiveness? QALYs, he felt, "were as good as anything going, but they came to be applied too rigidly." Second that cost-effectiveness might become a "fourth

hurdle" to a drug getting a licence in the first place. "My worry was that the price at which you want to sell it then becomes a negotiation in terms of it getting a licence — and that would mix up whether a drug is effective [which it has to be, against a placebo, to get a licence] with cost-effectiveness. That problem did not materialise because Mike Rawlins was very clear that the two should be kept separate. My third worry was what would happen if NICE approved new treatments and they still then did not get taken up. That got better, though I must say it remains something of a continuing problem."

His initial reaction to Rawlins appointment, he says, was "Oh my god! I knew Mike well and I found him a joy. But in his lectures at Newcastle, and when he was at the Committee on Safety of Medicines, he used to lambast the industry from time to time over its prices and other matters, and many people within it saw him as the enemy. So I knew there would be a bit of a reaction. But I knew he had huge integrity and intelligence. And I thought we would get a better judgement from him than from some lackey of the government who might simply have looked at the price, and not at the science. He and Andrew Dillon [soon to be appointed chief executive of NICE] were one of the key reasons for its success. The two are not similar people. But they are both tremendously enthusiastic, highly intelligent, and they listened to people's views and were not puppets of the system. And I thought one of the alternatives to NICE might well have been straight forward price cuts, which would have been the worst of all worlds. I always thought that while the industry would win some and lose some in NICE's assessments, overall it would increase spending because new and effective pharmaceuticals were simply not being taken up fast enough." Helping persuade the global industry of that turned into one of Trevor Jones own tasks.



Sir Andrew Dillion

Dobson says of Rawlins appointment "I knew the industry was wary of him. But they were also respectful. And I thought that combination was no bad thing. He was clever, charming and tough as old boots."

One of Rawlins first actions was to recruit Tony Culyer as vice-chair of NICE. "I thought I needed a health economist," Rawlins said, "and I knew Tony." Culyer recalls that Rawlins went to York to give a lecture and said on the way in that he "wanted a word" afterwards. Culyer was slightly unusual in not only being a top flight health economist but also someone whose economic analysis was underpinned by a firm grasp of philosophy. It informs so much of what he has written. (56) People are not allowed to use words like "equity" or "fairness" without Culyer forcing them to define precisely what they mean by that. So he

“*NICE constituted a threat to a lot of people – to politicians for whom this was a major piece of delegated decision making which some could reasonably argue should be for them or for a committee of the House of Commons.*”

brought a deep understanding of ethics and of social values to the judgements that would have to underpin so much of what NICE was to do, along with an understanding of process: what would be needed to make NICE's analyses both transparent and credible.

Once appointed, Culyer recalls, "Those early days were just huge fun — inventing NICE. Mike would get on the train at Newcastle I would get on the same train as it passed through York and we would sit right up in the front of the first class puffing away on our Hamlet cigars inventing NICE. And we had to invent pretty much everything.

"NICE constituted a threat to a lot of people — to politicians for whom this was a major piece of delegated decision making which some could reasonably argue should be for them or for a committee of the House of Commons. To the pharmaceutical industry — manifestly — who would not like some of what we were going to do. To clinicians who did not want to be told what to do — 'clinical

freedom' and all of that. To patients and patient groups who had an obviously vested interest in their own condition or disease. And so on. So we had to invent it all — the governance, how the technology appraisals would be done, how the guidelines would be created, working out who the stakeholders were and how to engage them. Just everything."¹⁴

The remainder of the board was appointed, thinned down from a list that was mainly supplied by Mike Rawlins. Its membership including Parveen Kumar, a distinguished physician who among many other achievements wrote one of the standard medical textbooks. Dobson, somewhat to the dismay of his civil servants, was sufficiently engaged in how NICE would function that he insisted on personally interviewing all the board members. "In practice," Dobson says, "she interviewed me. And at the end she asked 'do you think this will work?' And that was the moment, as both she and Mike have subsequently related, that I replied 'Probably not. But it's worth a bloody good try!'" (57)

Appointing a board of non-executive directors was one thing — crucial, first time round, for a nascent but already controversial organisation. Appointing someone to run it was quite another. With all the background outlined above and with NICE now announced, NHS managers clearly took the view that something significant might be happening here. There were scores of applications for the post of chief executive. (58) The one who emerged from this process was Andrew Dillon, at the time chief executive of St George's, the south London teaching hospital. Dillon had been interviewed and indeed had been approved by Dobson. The appointment, however, was technically a matter for the newly formed board, not for the Secretary of State.

¹⁴ A significant part of NICE's framework, including the Partner's Council, was, of course, already set out in the white papers. This, however, is what it felt like.

Rawlins relates: "So we had our first board meeting, on the eve of the official launch of NICE which was due at a press conference the next day. The first item on the agenda was the appointment of the chief executive. It was one of those times when you just throw yourself on the mercy of the board. So I said 'look, I am really sorry to say this, but we have got to appoint a chief executive and I've got Andrew Dillon sitting outside. He's been agreed by the Secretary of State, so give me a break and say you agree to appoint him. And they did. So that is how we started. A board. A chief executive. A laptop which Andrew brought, borrowed from St George's. And the official media launch the next day with the Secretary of State. At the launch, with Frank Dobson alongside, we clicked on the website. Only it wasn't real. It was a mock-up. But we were on our way."

Rawlins was to remain chair of NICE until 2013 while Sir Andrew Dillon is still its chief executive. Adrian Towse who throughout NICE's life has been the director of the Office of Health Economics, a think tank and consultancy partly funded by the pharmaceutical industry, says the longevity of the pair, and their complementary skills, have been an important part of the story. "Mike was very good at dealing with the politics. And he learnt, partly by experiment, that he could say provocative and sometimes very irritating things in public that highlighted the issues and sent signals, without the roof coming in. And in retrospect having a chief executive who had run a big teaching hospital was a stroke of genius. NICE is a much smaller organisation. But it is very complex and has become more so, while it is also very high profile and sensitive. Andrew is a brilliant manager but one who could also contribute personally to the very difficult judgements NICE had to make." (59)

A whole string of other, crucial, appointments followed. Dr David Barnett as Chairman of the Appraisals Committee who proved an expert at engineering through the committee, on time, the difficult decisions that NICE had to take. Dr Peter Littlejohns as clinical director and Anne-Toni Rodgers as the first director of communications who commissioned an easy-to-use website and who patiently helped explain NICE to its wide range of so-called "stakeholders" — not least to the media.

As Rawlins and the board were being appointed, and ahead of NICE becoming a legal entity in April 1999, one more event occurred that underlined the need for the institute. On September 15, 1998, Viagra was licenced. The first truly effective treatment for erectile dysfunction, it was rapidly dubbed a "lifestyle" drug by the media and it fell to Dobson — as Beta-interferon had fallen to Malone — to decide whether the NHS should pay for it. And if so, for whom? Again the potential bill could have run into the hundred million pound bracket at a time when spending on the NHS under the new Labour government remained heavily constrained. In January 1999, Dobson came up with an awkward, bridge-holding, list of conditions which could cause erectile dysfunction and for which Viagra could be prescribed on the NHS. His ruling made clear that Viagra would not be paid for as a recreational drug. The conditions for which it would be funded included prostatectomy, multiple sclerosis and diabetes. But he excluded for example hypertension and arterial disease. The list of conditions that were excluded and included made very limited sense. It caused "grave disquiet among doctors," according to John Chisholm, chairman of the general practitioners committee of the British Medical Association. He argued that Viagra was not only a "decidedly effective" treatment but that on a cost per QALY basis it was also "highly cost effective." The decision "makes no sense on clinical, equity, or cost-effectiveness grounds," Chisholm declared, making "cruel and unethical" distinctions between "acceptable and unacceptable" forms of impotence. (60)



Pfizer, the drug's manufacturer, was even less pleased. A senior executive came to see Dobson. "But we had done our home-work and established that no European country other than Sweden had agreed to fund it routinely. So I pointed out to him that we were about the only country in Europe that would be providing any taxpayer funded erections at all. It took him quite a while to see the joke and smile."

Dobson enjoyed that encounter. But even so, the Viagra decision had been a bruising one. The nascent NICE offered the possibility that this was the last time that ministers would have to take such a decision, and six months later, as Relenza arrived, Dobson asked NICE if it would make an appraisal of its cost-effectiveness.



BETA-INTERFERON BITES BACK

The Relenza controversy proved NICE's credentials, while also injecting it into the public eye. But the task of building the organisation and its methods was still under way. To do that, as Mike Rawlins has put it, it had "a rich heritage" to draw on. (61)

As outlined above in the origins of NICE, the QALY had become a useable tool for informing judgements about cost-effectiveness. The department paid for a number of guideline programmes run by the Medical Royal Colleges and others. There was the scattering of health technology units in universities that the department also funded. The expertise and the methodologies of the regional DEC's and similar bodies were available. And these in turn had helped inform the working party on pharmaceutical cost-effectiveness guidelines which Culyer had chaired in 1997 and 1998. All this fed into the initial version of NICE's technology assessments. (62) On top of that were the skills of a bunch of health economists, either part of, or independent from, the organisations already mentioned, at the universities of York, Southampton, Brunel, Birmingham, Sheffield and elsewhere.

Rather than try to draw all these into a single, central "institute" — which might, for example, have created a 1,000 person bureaucracy occupying some prestigious London site — NICE operated much more like a "virtual" institution.

Rawlins says it "had little choice". Its opening budget was tiny. While its initial work programme was by definition small — it was only just getting going — its direct turnover in its first financial year between 1999–2000 was a mere £600,000 and its full-time staff equivalent was just ten people. (63) A core of in-house expertise that built over the years was, of course, created. But, NICE essentially commissioned the work it needed from the people that already existed. For the technology appraisals it used the university

health technology units which were funded through the health department's R&D programme, with a chunk of that money cordoned off to support NICE. That helped ensure academic buy in. These units provided the assessment of new technologies which then went to the appraisal committee for the judgement on whether something was, or was not, cost effective. This independent funding gave them their own independence from NICE. That reduced the risk that NICE itself might, intentionally or not, lean on them to produce a particular result — a valuable safeguard given that NICE would always have debates, and even arguments, with the life sciences industry about how its appraisals were conducted. As one senior figure from the life sciences industry puts it, this arrangement "helped to reinforce the emphasis on science, rather than politics or bargaining down the prices being the key driver." (64)

For the guidelines, NICE was given no new money. But a lot of health department cash was going to the Medical Royal Colleges for research on clinical effectiveness. "We were told we would have to use that," Rawlins recalls. "I knew that taking it away from the colleges would cause trouble. So we settled on an arrangement whereby they would get the money back provided it was used to develop guidelines on topics we would decide, and using methods that we would prescribe. We would also quality assure their final products. The colleges were very decent about it." (65)

In addition, NICE gradually drew in an army of clinicians, patients, carers and others on a part-time basis to help inform its judgements.

One other crucial decision in the early days was to define and publish the principles on which NICE would operate — the mantra to which it still seeks to cling. Namely that it would be robust, inclusive, transparent, independent, contestable. (66)

THE PRINCIPLES ON WHICH NICE WOULD OPERATE INCLUDED:

ROBUST

INCLUSIVE

TRANSPARENT

INDEPENDENT

CONTESTABLE

These five principles underpinned the one word that Culyer repeatedly used, and uses, about NICE. "It had, and has, to be credible." (67)

These principles, however, came at a price that has haunted NICE throughout its existence, and which can be summed up in one word — time. Taking the guidelines first, it was clear that they had to overcome the criticisms of the existing ones that Rawlins neatly set out in evidence to the Commons Health Select Committee in February 1999, ahead of NICE's launch. (68) The existing ones were voluminous, indigestible, inconsistent and of highly variable quality. To be robust, NICE had to construct its versions by undertaking in some cases a dozen or more systematic reviews in order to ensure that all the appropriate evidence was considered. To be inclusive and robust it had also to consult leading clinicians in the field while taking into account the experience of patients. Unsurprisingly, this took time.

The same principles were of course applied to the technology appraisals. These covered

interventions and treatments other than drugs. But access to new pharmaceuticals was to become easily the most sensitive issue in terms of media coverage, and NICE initially took no action until a drug had acquired its licence.

The principles of being robust and inclusive, however, meant NICE had to assess all the evidence in published trials while also taking evidence from the manufacturer and considering unpublished data. Transparent, inclusive and contestable meant NICE handled technology appraisals by publishing its "preliminary" decision for consultation, taking whatever objections arose into account, before then issuing a "final" appraisal decision that was itself open to formal appeal. All this re-inforced credibility. But again, unsurprisingly, all this also took time. And even the "final" appraisal was potentially subject to judicial review.¹⁵

Post-Relenza, NICE scored an easy hit. In March 2000 in its first standard formal technology appraisal it recommended that impacted but otherwise healthy wisdom teeth should not be removed prophylactically — a move it estimated might save the NHS £5m a year. That was followed in May 2000 by an appraisal of the use of stents in coronary artery disease and by the use of taxanes in ovarian cancer, with an appraisal of proton pump inhibitors following in the July — its first two published decisions on pharmaceuticals post-Relenza. Gradually a portfolio of recommendations on new drugs built up. Some produced a 'yes' — i.e. the NHS should adopt it. Some a 'no' — the NHS should not pay for it. Others a 'yes but' — the 'but' varying but generally being that the service should only fund it for a particular sub-group of patients until further evidence emerged, or that it should be used "only in research".

¹⁵ For the history of judicial review Rawlins, section three. The need to as far as possible "bomb proof" appraisal decisions from judicial review in part explains their length. All the reasoning has to be set out.

“*Transparent, inclusive and contestable meant NICE handled technology appraisals by publishing its ‘preliminary’ decision for consultation, taking whatever objections arose into account, before then issuing a ‘final’ appraisal decision that was itself open to formal appeal.*”

As these early recommendations were being made, the attitude of the pharmaceutical industry to the institute was becoming clearer. According to both Trevor Jones, the ABPI director general at the time, and Andrew Jack, a long-serving and distinguished pharmaceutical correspondent on the Financial Times, the industry's views essentially split into three. (69)

The British based industry, which had been shaken as much as anyone by the original Relenza decision, was not wildly keen on NICE. It did not like the idea of a "fourth hurdle" any more than the rest of the industry. But it could see that, once approved by the institute, there might be a mechanism here for swifter uptake of new treatments, and it had lived through the developing demands

outlined above for cost-effectiveness to be taken into account. The European based companies — and all the large players in pharmaceuticals were by now global companies — were less sympathetic, but still prepared, grudgingly, to go along with the idea. The US companies were much more opposed. In 2000, the US still made up just over half of the global pharmaceutical market and they were used to free pricing in their home territory. "The Americans in general were much more hostile and Pfizer in particular," Trevor Jones says. "Pfizer were very opposed to this. They felt it was the thin end of the wedge and tantamount to a pricing policy when they came from a country that had always prided itself on free pricing. And at the time, aside from us [the ABPI] there were the UK offices of our European equivalent and of the American Pharmaceutical Group. And the American Pharmaceutical Group was very vociferous. I remember going to see the head of Pfizer for both the UK and Europe and saying 'I understand your concerns, but this is going to happen. And I believe that if we do this right and play the long game there is something in this for us and it could have a positive influence — although of course there are going to be times when we disagree with NICE. And, unwillingly I guess, Pfizer and the rest agreed.'" A by-product of the US industry's hostility was that Mike Rawlins and Andrew Dillon, sometimes with UK health and trade ministers, sometimes without, spent time in the US over the years, and indeed in Japan and elsewhere, seeking to calm fears and explaining NICE's role and mechanisms.

At the very beginning, NICE was created as a special health authority. That had two advantages. One it allowed NICE to be set up swiftly without primary legislation, and second it technically made NICE part of the "NHS family" — a friendly advisor — rather than it being outside it, or part of the Department

of Health. That carried a theoretical drawback. As a special health authority, it remained technically subject to ministerial direction, although, up to the time of writing, ministers at no point formally exercised that power. In its early years, however, it was the department which set NICE's work programme for technology appraisals. The department commissioned the "horizon scanning" which looked at what was coming up that looked likely to be costly and then asked NICE to do the appraisal. From March 2002 it became possible for stakeholders to propose topics for NICE's attention. From September 2006 NICE undertook the horizon scanning — "mainly because we thought we could do that better than the department, and persuaded them of that" Rawlins says — and itself proposed the topics to be covered which the department [and now NHS England as well] then reviewed and approved.

Early in NICE's life, in 2000, the department asked it to take another look at Beta-interferon and at glatiramer acetate, another treatment for multiple sclerosis. It was to be NICE's 32nd published health technology assessment. In August 2001, NICE produced its provisional ruling that "the use of these medicines cannot, presently, be justified, taking both benefits and costs into account." (70)

“One it allowed NICE to be set up swiftly without primary legislation, and second it technically made NICE part of the ‘NHS family’.”



The result was exactly the sort of storm that Gerry Malone had feared when he first tangled with the treatment back in 1995.

Newspaper advertisements were taken out attacking the recommendation. The Multiple Sclerosis Society condemned the decision. MS sufferers in wheelchairs descended on Parliament. "Both the industry and patient groups were up in arms," Trevor Jones recalls. "I went to Parliament with a group of them and I remember them sitting there saying to MPs 'what about our lives? This may not be the best treatment in the world but it is the only hope we have got. Are you telling us we are not worth it'?"

NICE took into account all the attempts to persuade it otherwise. But in January 2002 it reached exactly the same conclusion in its final determination which was then appealed, only for the recommendation, once again, to be upheld. Those already receiving the drugs should have the option to continue treatment until they and their consultant considered it appropriate to stop. But the NHS should not prescribe it for new patients. According to one long-standing, senior appraiser, the issue of the MS drugs was "a crucial test of the process and the appraisal committee's resolve." It involved "a very vociferous, public and at times quite nasty" assault from some of those campaigning for access to the medicines, he says. "The appeal left its scars on some of us who took part." (71)

In the background, however, other wheels had been turning. In its provisional decision, NICE had recommended to the manufacturers — Schering, Biogen and Serono — that they negotiate with the department of health to see if a lower price could be agreed which might make the treatments cost-effective. At the same time, according to Andy McKeon, the health department senior civil servant responsible for NICE between 2000 and 2003, "Tony Blair [the prime minister] did not like the heat over this. So the request, or the instruction, came across to the department asking could we not find a way of resolving this without undermining NICE?" (72)

The result was a deal with the manufacturers which agreed that many more patients would receive the treatments in return for a price cut, but, more importantly the success of the treatment in individual patients would be monitored over a 10 year programme. Where the drug performed as the manufacturers said it

would — reducing progression of the disease — the NHS would pay the full, newly agreed, price. Where it did not, payments would be reduced on a sliding scale. The numbers receiving treatment were expected to rise from around 2,000 to 9,000 in what both sides dubbed a "risk sharing" approach. And as part of the arrangement the manufacturers agreed to fund some 50 extra specialist nurses to develop the service, help administer the drug, and contribute to the monitoring of its effects. To put it very crudely, if the drugs worked the manufacturers got paid. If it didn't, they didn't — or more precisely they got paid less. Given the huge uncertainties over whether the two treatments in fact slowed progression, Alan Milburn the health secretary, declared, as he announced the deal, that Beta-interferon "has a unique history which requires a unique solution." (73) There were already strong hints, however, that this approach would not be a one off. (74)

Many years later the deal was to be attacked by some leading health economists as "a fiasco" and "a costly failure". (75) But while it did not carry the name at the time, it proved to be the first of what became known as "patient access schemes." It took until 2007 and 2008 for the second and third of these to arrive along with the title of "patient access schemes." But by 2015 there were to be well over 50 of them.

Their details varied considerably. (76) Some, as with Beta-interferon, were linked to patient response. Some provided the first treatment in a cycle free, with the NHS paying for subsequent cycles where there was evidence of efficacy in the individual patient. Others worked the other way around — the NHS would pay for the first cycles and the manufacturer for subsequent ones if they were needed. There were other forms of price cap, and the degree of risk sharing varied. Administering these more complex schemes which relied on

“*Patient access schemes, however, had the effect of providing NHS patients with access to high cost drugs which NICE had judged, at their submitted list price, to be cost ineffective.*”

patient response or outcome data proved a headache for the NHS, not least for hospital pharmacists who had to work out in the middle of busy days whether a particular drug at a particular time was free to the NHS or chargeable. Partly as a result, in the longer run the newer ones mainly involved a commercially in confidence discount on the headline price. All, however, had the effect of providing NHS patients with access to high cost drugs which NICE had judged, at their submitted list price, to be cost ineffective. For the manufacturers, patient access schemes were in practice a way of providing discounts without the headline price — which potentially affected the drug's price in other markets — being affected.¹⁶

Patient access schemes also proved a way round an issue that had been in the air from the beginning. Should NICE not just judge cost-effectiveness, but also negotiate price? Frank Dobson says the question was obviously there, "but I don't recall a debate about it at the time. It was certainly my view that you should keep the price negotiation separate from the approval. It would end up sullyng the cost-effectiveness decisions. They had to be utterly defensible against any suggestion of an interest around affordability on the part of the NHS. 'Worth it whatever it costs', so to speak, or 'not worth it however cheap it is'."

¹⁶ See page endnote 9 for impact of UK drug prices elsewhere.

Mike Rawlins too, certainly initially, was opposed to the idea. The issues of effectiveness (to get a licence), cost-effectiveness (NICE's judgement) and affordability for the NHS (still a matter for ministers) needed to be kept separate and pure. "I do remember when I was on the Committee on Safety of Medicines," he told MPs, "any time any member even opened their mouth and mentioned money I had to tell them to wash it out with soap. Safety and cost should not be mixed up, and it is absolutely right that the licensing process does not take cost-effectiveness into account." (77) Price negotiation was in any case not part of NICE's legal remit. And by now any company with their access to NICE's modelling could easily enough work out what the price would have to come down to in order to get under the £30,000 per QALY that had become the broad upper end of the threshold that NICE used to inform its judgements. There was the added risk that if NICE negotiated prices with the industry what was going on would not be transparent — it would muddy the waters when transparency was a key part of NICE's credibility. (78) The Patient Access Schemes were a way round all of that. In 2009 NICE established a liaison unit for such schemes to help manufacturers assess their feasibility, and to make sure that schemes submitted to the Department of Health did not impose the excessive monitoring or other burdens on front line staff that some of the earlier arrangements had done. The decision to agree a scheme remains one for ministers, not for NICE. (79)

With the Beta-interferon storm weathered, NICE was by now an established part of the NHS landscape. One of Trevor Jones's initial worries about NICE had, however, materialised — that even when it said "yes" the NHS did not always consistently take up the new treatments recommended.

A first attempt was made to address that in January 2002 with a "funding direction" — an idea several interviewees attributed to Simon Stevens. Both NHS hospitals and health service commissioners were told that they were now legally required

within three months of a positive recommendation from NICE to fund the new treatment, save where the institute itself said they could take longer. For example where a recommendation involved infrastructure of one sort or another that would take longer than three months to create — for instance, wider use of bariatric surgery. It was estimated that the funding direction would, overnight, boost NHS spending on NICE recommended treatments by £250m in a single year. (80)

This move undoubtedly helped make NICE's positive recommendations more enforceable. But on and off over the years the issue has never entirely gone away, its prominence in part depending on how generously funded the NHS was at any given time. As late as August 2012, and when the growth in NHS expenditure was more or less zero, Rawlins supported complaints from both patients and the pharmaceutical companies that some parts of the NHS were increasingly using "delaying tactics" to "circumvent" the law and postpone implementation of the institute's recommendations. He urged patients and patient groups to threaten to take their local NHS to court, arguing that cases would not get there because the service would be told by its lawyers that their delays were legally indefensible. (81)

By the end of 2002, however, NICE was not just an established part of the NHS landscape. It had acquired a global presence. Its website provided a window to the world. It was receiving a growing number of hits, soon to rise to a million a month. They came from all over the world, not least from the United States where insurers, Health Maintenance Organisations and others were drawing on its advice and judgements, not just for technology appraisals but for guidelines. Indeed there is a case to be made — which will be addressed later — that the guidelines, while receiving vastly less coverage in the mainstream media, have been at least as important a part of its work as the technology appraisals. Increasingly delegations from overseas were arriving seeking to understand what NICE did, and how the framework within which it operated allowed that to happen. Bodies

“*From April 2005, NICE became the National Institute for Health and Clinical Excellence, while keeping its short acronym.*”

similar to NICE were starting to be established elsewhere, in for example Sweden, Germany and France.

As if to underline that, in 2003 NICE was independently reviewed in glowing terms by the World Health Organisation which said that in terms of transparency, stakeholder engagement, decision making and innovation in technology appraisals, NICE had, in just four years set "a new international benchmark" for which it "can and should be congratulated." (82)

In July 2004, Richard Smith, the Editor of the BMJ, who noted, honourably, just how cautious he had been in welcoming this new body, published an editorial headlined '*The Triumph of NICE*'. His leading article declared that "NICE may prove to be one of Britain's greatest cultural exports, along with Shakespeare, Newtonian physics, the Beatles, Harry Potter, and the Teletubbies." Taken as a whole, the editorial was somewhat less glowing than that. And Smith published alongside this accolade a decidedly more critical, though in itself controversial, assessment of the institute's performance. (83) Nonetheless, it was clear by now that NICE was a concept and an organisation that was built on sound foundations.

It was that which helped it survive what might well have been a threat. Tony Blair's Labour government had become concerned about what might be dubbed the "regulatory state" a fair bit of which it had itself

created. This had produced a marked growth in the number of arms-length bodies or Quangos (quasi-autonomous non-governmental organisations) set up to inspect or regulate various parts of the public service. It announced plans for a "bonfire" of them. The original proposals included a plan to crunch 13 public sector inspectorates into just four. That bold aim was at least partially defeated when sanity prevailed and the plan was dropped to roll up into one the five inspectorates for criminal justice (police, prisons, probation, courts and the crown prosecution service). The NHS, however, was very much part of this review. The headline aim was simply to reduce the number of bodies and cut costs. The original NASTY — the Commission for Health Improvement — had already been re-cast and renamed once.

It found itself re-founded yet again, being yoked together with the social care and mental health inspectorates in a body to be known as the Care Quality Commission. Other NHS bodies, such as the Modernisation Agency, simply disappeared. But NICE prospered and survived, absorbing the five year old Health Development Agency which had itself been producing guidance in a range of areas intended to ensure healthier lives — on breast-feeding, falls prevention, smoking cessation and healthy schools, for example. In effect, NICE was to take on the brief for public health. In this area, the new responsibility subtly changed its role. It was no longer advising just the NHS. In the public health arena, it was advising ministers.¹⁷ The new responsibility produced a change of name. From April 2005, NICE became the National Institute for Health and Clinical Excellence, while keeping its short acronym.

Given that it had survived the quango-cull, it would be easy to think that its future was assured. Just a few months later, however, it hit the first crisis that — to the outside world at least — genuinely appeared to threaten its very existence.

¹⁷ And from 2013 local authorities as a significant part of public health expenditure was moved back to them.



November 24, 2009



The Mail, July 22, 2010



August 25, 2010



HERCEPTIN

It is mid-May 2005 in Orlando, Florida. The annual meeting of the American Society of Clinical Oncology. Some 25,000 cancer specialists are in town. They congregate in and around the huge, glass-fronted, Orange County Convention Centre. Among them is Sir Mike Richards, technically known as the national director for cancer for the National Health Service. Colloquially, to the British media, he is "the cancer czar".

To a packed hall, the results of three clinical trials of the use of trastuzumab in early breast cancer are flashed up on the screen. They look impressive. So impressive that the trials were stopped early on the grounds that they reduced the recurrence of tumours on such a scale that it was judged unethical for the trials to continue.

"Now the Americans can get over excited about new developments," Mike Richards says. "But this did look rather special. There were 20,000 people listening to these presentations and they were received to huge acclaim." (84)

Dr Gabriel Hortobagay, himself a breast cancer specialist and president-elect of ASCO, declared: "We have not seen anything of this magnitude in breast cancer research in 30 years," (85) and, according to some in the department of health, Richards himself returned as "something of an evangelist" about the treatment. One recalls him advising ministers that it "might save as many lives as breast cancer screening for about the same cost." (86) Trastuzumab, trade name Herceptin, was about to become a household name.

There is nothing more emotive in medicine than cancer in general, and if anything is, it is breast cancer. In Britain, as elsewhere, the pressure built for women to get it. Herceptin had originally been licensed in 1998 for end stage disease, and then in 2000 for metastatic cancer — cancer that had spread. NICE had approved its cost-effectiveness for these two uses in 2002. The new results showed it also

worked in early stage breast cancer, and the results were vigorously promoted by the companies involved — Roche and Genentech — while being seized on by breast cancer charities world-wide, some of whom took part of their funding from the pharmaceutical industry. (87)

But there were two problems. Presentation at an international conference is not the same as full publication of the results in a peer-reviewed medical journal. And, as they were being announced, Roche had yet to apply for a licence in the European Union for its use in early stage disease. As a result, NICE had yet to appraise it for such use.

Herceptin is of use in about one in five breast cancers, those with a high level of the HER2 protein. In the British arm of the trial it reduced recurrence from 17.2 per cent to 9.4 per cent, producing the headline that it "halved the risk of recurrence", though questions remained about long-term side effects, including heart problems.

In Stoke in the middle of England a group of women who became known as the Herceptin 7 campaigned for the right to get it while their primary care trust¹⁸, the body that at the time commissioned their health care locally, refused to fund a drug that was both unlicensed for this indication and which NICE had yet to appraise. In Somerset, Barbara Clark, a highly articulate, 49-year-old nurse, threatened her primary care trust with judicial review if it did not fund the treatment — the PCT backed down. (88) When another primary care trust in Swindon declined funding, it found itself with a high court case on its hands. At various times, as the issue mushroomed into the media, the Herceptin 7 and others were brought in to meet ministers. Those at the meetings attest to the power of their case as stories multiplied of people planning to sell their homes, or use their lifetime savings to get access to Herceptin.

¹⁸ See glossary for explanation of Primary Care Trust.

One of those present says "I remember one of the women saying to ministers that 'the good news for me is that I have a brother who will sell his house and downsize, because I know you won't approve this drug in time for me. So I will get the drug....' and the woman next to her saying, 'I am in exactly the same position, except I don't have a brother'." (89)

A 35,000 signature petition was delivered to Number 10 Downing Street, there was a march on Parliament and a media storm as The Sun, the Daily Mail and other parts of Britain's tabloid press demanded that this "magic bullet therapy" and "wonder drug" be funded immediately. The Sun was campaigning "to make Herceptin available to all on the NHS." (90)

Two further factors compounded the issue. One was that, quite remarkably given that it was enjoying record, sustained, increases in spending, the NHS had managed to overspend its budget and was having to make some (in practice very limited) cuts to get it back into balance. For many that left the impression that the refusal to fund the drug immediately was merely an issue of money. Not a question of cost-effectiveness, the absence of a licence, and the absence of peer reviewed published data. Not that the money was unimportant. The likely cost of Herceptin in the UK was put at £44,000 for a two year course of treatment.

The second additional factor was that concern had been growing for some time that — despite all the glowing praise heaped on NICE by the World Health Organisation — its technology appraisals for pharmaceuticals were taking too long. The sheer thoroughness of NICE's process, the degree of consultation and appeal it went through, and the fact that appraisals of new pharmaceuticals usually did not start until a drug was actually licensed meant that its standard appraisal process took at least 14 months to complete once the drug was licensed.

On occasion it took more than two years from a drug being licensed to NICE's final recommendation.

Furthermore, by now, much of the NHS was reluctant to pay for costly new products until NICE had approved them. The result was something that became known as "NICE blight" — that new products were being held up for too long while NICE studied them and the NHS refused, in the main, to fund them. According to Andy McKeon, the senior civil servant responsible for NICE between 2002 and 2003, the department had begun to agitate on that issue a good two years ahead of Herceptin. The institute, however, had taken "little effective action," he says. (91) By contrast, NICE felt the problem lay at least as much with the department, because, at this stage, it had no control over when a topic was referred to it, and could not start work until it was. (92) The fact that NICE and the department were discussing the issue with increasing intensity as the Herceptin headlines grew was not yet, however, in the public domain.

As the media storm raged and the legal threats multiplied, Patricia Hewitt, the health secretary, came under increasing pressure. Richards does not re-call being asked precisely what she should do. He did, however, advise Hewitt that the trial results were impressive and that his view was that they were unlikely to change as the data was peer reviewed and published. (93) In the view of more than one of Hewitt's political and clinical advisers, the position was becoming "untenable." (94)

On October 5, and depending on your point of view, Patricia Hewitt either did the decent thing or cracked under the pressure. She told the NHS to start testing all women with early breast cancer to see if they would be suitable for treatment

“*The drug,” Patricia Hewitt said, “has the potential to save many women’s lives and I want to see it in widespread use on the NHS.”*”

with Herceptin. Her message was that 'when Herceptin is ready, the NHS will be ready.' The drug, she said, "has the potential to save many women's lives and I want to see it in widespread use on the NHS." She wanted the licence to be granted "as quickly as possible" and the treatment "to be available within weeks of the licence being given." (95)

Fifteen days later, on October 20, 2005, the New England Journal of Medicine finally published the trial results. (96) They were accompanied by a glowing editorial from Dr Hortobaghy describing them as "stunning" and "maybe even a cure." That last judgement was a decidedly predictive one. The trials had been stopped early when Herceptin was shown to reduce significantly the recurrence of breast cancer. The effect of the early stoppage, however, was that there was very limited data to show that the treatment in fact reduced mortality in early stage disease. Dr Richard Horton, the editor of The Lancet, responded. Along with the New England Journal of Medicine and the British Medical Journal, The Lancet was one of the world's top three general medical journals. Horton's response included picking some holes in the published trials while accusing its American cousin of going way over the top. The excitement over the drug was "premature," he declared. "The best that can be said," is that the available evidence "is insufficient to make reliable judgements." (97)

Publication of the data, however, led Hewitt to go further. Five days afterwards she told PCTs that they "should not refuse to fund Herceptin solely on the grounds of its cost," while pointing out (quite correctly) that clinicians could use it off-licence. (98) PCTs should consider funding it because "it is the right thing to do," she said. (99) As if to underline the point, the Stoke primary care trust, in whose territory the Herceptin 7 had originated, was hauled in to see ministers. "On the basis of the published evidence, other PCTs have agreed to fund Herceptin for individual women with early stage breast cancer whose clinicians recommend that the drug is suitable for them providing they are aware of the potential risks," Hewitt said. The department said that Stoke was being called in "to discuss their approach to funding Herceptin" — a meeting which unsurprisingly led to a change of heart. The chairman of the trust, which at the time had a £7m deficit, declared it had had to fund the treatment "to satisfy the whim of the Prime Minister and the Secretary of State." (100)

Hewitt, to her credit, had called Mike Rawlins ahead of her original announcement to warn him and to ask if he would support her. He was on one of his trips building bridges with the US pharmaceutical companies. "I got the call around seven in the evening when I was in Boston airport," he says. "I explained that I couldn't support her. The drug did not have a licence and the trial data had not been properly published. She accepted that, and the conversation was entirely civil. My next phone call, however, was to Andrew Dillon [the NICE chief executive] warning him that, come the morning, and given what I had said, he might be needing a new chairman!"

Hewitt's pronouncements, needless to say, delighted the campaigners and those who, in some cases entirely reasonably believed that their lives were at risk in the absence of the product. Others saw it very differently. They saw the pressure by ministers

to fund an unlicensed drug as fundamentally undermining the role of NICE. The King's Fund, a leading health think tank, attacked the decision, as did The Lancet, the British Medical Journal and the Drug and Therapeutics Bulletin. The NHS Confederation, the body which represented all NHS interests, said its members were being put "in an almost impossible position by growing pressure to bypass systems established to protect patients." (101)

In public, Rawlins subtly defended not so much NICE's role in all this as the position of the licensing body. "I am worried," he said, "about the risk that the drug regulatory authorities will be short-circuited by the growing pressure from patients for new treatments to be adopted before they have been fully assessed. A couple of trials published in a medical journal are woefully inadequate for really assessing the safety and efficacy of a product." They would contain "only a fraction" of the data that the licensing authority would take into account. His comments, cleverly, made no mention of NICE's role which was to judge cost-effectiveness. It did not take a genius, however, to work out that his underlying message was that NICE was also under threat.

As the tabloid press celebrated "victory", the judgement in some of the broadsheet newspapers was somewhat harsher. By now, this had become something of a pattern.

The tabloids and the Daily Telegraph tended to be constant critics of any decision by NICE to say "no", or even "yes but". The Daily Mail, in particular, was unremittingly hostile. It routinely described NICE as "the government's drug rationing body" even when reporting a decision in favour of a new treatment. Its headlines over the years included "Fury as patients denied £2.50 a day drug", "Cancer Patients

Denied Better, Cheaper Cure" and "Sentenced to Death by NICE," (102) while a recommendation from NICE in favour of the use of injectable contraceptives was dubbed "A Charter for Promiscuity". (103)

By contrast some of the broadsheets — The Times, The Guardian and the Financial Times, for example, with their much smaller circulations — while reporting the controversies that NICE became embroiled in tended in their leader columns to support the case for cost-effectiveness that NICE had been created to deliver. On Herceptin, for example, the Financial Times judged that Hewitt's words "can only be seen as putting pressure first on the licensing authority and second on NICE. They set a profoundly dangerous precedent. These bodies are set up to distance politicians from such crucial decisions — taking them out of the political arena and into the world of evidence-based assessment. Her words severely undermine that process." Her actions, the FT added, "will simply encourage further campaigns for early adoption of new pharmaceuticals ahead of the evidence for or against them ... [that] is a door Ms Hewitt has opened — and now needs to close." (104)

As Hewitt made her pronouncements, both the department and NICE began to disclose that they had already been working on ways of reducing or ending "NICE blight", a key change being for the institute to start its appraisal of cost-effectiveness in parallel with the application for a drug's licence, using the same or any additional data. An approach that was dubbed "parallel processing".

Rawlins acknowledged that "both patients and primary care trusts tell us that PCTs will not pay until they have seen our guidance." He added that "the only answer to 'NICE blight' is starting earlier and moving quicker," though he warned that had to be done "without lowering the essential robustness of our process". (105)

“*In practice, however, while this new ‘fast track’ approach did indeed cut the time between a licence and NICE’s recommendation, it in the main failed to reduce it that spectacularly.*”

One senior figure in the institute at the time says of the problem of "NICE blight" that "we were all culpable" and of waking up to it too slowly — the "all" embracing the department and the institute. The department chose the topics and when they were referred, although once referred it was NICE which decided how quickly to work on them. "We needed to do four things," this figure says. "Have topics referred earlier, increase our appraisal capacity, start the appraisal earlier and introduce a new, shorter, appraisal process." (106)

Both the department and NICE were briefing journalists at the time that this might allow decisions to be made within weeks rather than months of a drug getting its licence.(107) In practice, however, while this new "fast track" approach did indeed cut the time between a licence and NICE's recommendation, it in the main failed to reduce it that spectacularly.¹⁹ The ABPI welcomed the "fast track" approach in principle. But it added a reservation. "There are sometimes limitations on what evidence is available on clinical and cost-effectiveness at the time of a medicine's launch." (108)

¹⁹ See page 126 below.

“Herceptin was a poster child for the need to reform NICE’s appraisal process which was too slow.”



Roche, however, had no doubt it wanted a fast track for Herceptin, and co-operated fully. In late May 2006, the drug got its European licence for use in early stage breast cancer and a mere fortnight later on June 8 NICE approved it for NHS use.

The Herceptin crisis was over. Hewitt's intervention, however, had inevitably raised questions over whether ministers were again going to second guess or even over-rule NICE's judgements. Something that Hewitt had not, in a strictly literal sense done, but had come within a hair's breadth of doing.

In hindsight, those interviewed for this piece say that was not the intention. Herceptin was a one off. Mike Richards says: "You have to remember that the cancer lobby is an incredibly strong one, and if you put the word 'breast' in front of it, it is doubly strong. And this was one of those rare occasions when the evidence, even though it had not been officially published was extremely persuasive. I was not consulted over the details of what the Secretary of State did. But I understood why she did it. And I certainly did not see it as a precedent."

Matthew Swindells was Patricia Hewitt's special adviser at the time. "This was definitely not a case of ministers feeling they should be taking these decisions. It was much more 'we should definitely not be taking these decisions, but what are we going to do about this one?' And Herceptin was a poster child for the need to reform NICE's appraisal process which was too slow. To put it crudely, the real question was 'do you allow a bunch of people to die while you sort the process out, or do you make a one off decision on this drug so that bad things don't happen while you sort the process out?' The hope being that you will never have to do it again, because the new process will manage it better. It was definitely not 'we should be taking these decisions'." (109)

To the outside world, however, this all looked rather different. There appeared a real risk that ministers might reverse what might be called "the Malone/Dobson doctrine" — that they should not take these decisions. Or, conversely, if you disapproved of what NICE was doing and thought politicians should take these decisions, there was a real chance that in future that they would.

In the later, still unresolved, stages of the Herceptin controversy in January 2006, NICE revisited an earlier appraisal of a number of drugs used to treat Alzheimer's disease. Back in 2001 it had approved a fairly broad use of them. But in line with its policy of taking new evidence into account, in January 2006 it issued a revised preliminary appraisal which concluded that their use should be restricted to those with a moderate to severe form of the condition. It should no longer be prescribed for those with mild Alzheimer's because — on the face of it somewhat paradoxically — the treatments appeared to make little difference at that stage.²⁰ As ever, whenever NICE restricted something, this was unpopular.

Professor Clive Ballard, the director of research for the Alzheimer's Society, branded the decision not to continue access for those in the early stages as "unethical". The treatments cost a mere £2.50 a day, he argued. The society demanded — and got — a meeting with ministers. (110)

Those outside NICE who supported its decision made the case the other way. Alan Maynard, professor of health economics at York, acknowledged that Alzheimer's "is an awful condition that destroys individuals and their families". But the truth was, he said, "that the drugs have very limited impact." Furthermore, £2.50

²⁰ The treatments appeared to have a mild but broadly equal effect across all three stages of the condition when defined as mild, moderate and severe. For the later stages there was some evidence that they slowed, at the margins, growing reliance on care. Taking them early did not appear to enhance that effect, but added significantly to the cost. Hence, they were judged cost in-effective in early stage Alzheimer's. A neat example of the fine, and controversial, recommendations that NICE has had to make.

a day translated into a bill of nearly £70m a year for the NHS. "Just think" he said, "how many hip replacements you can buy for that money ... [or other treatments] ... that would make a real difference to people's lives." (111)

Those supporting people with Alzheimer's were outraged by such comments. (112) But — to take just two of the media views of the time — the Financial Times declared that in the wake of Herceptin, the recommendation to restrict the Alzheimer's treatments "will test ministers' resolve" to stand by NICE recommendations. The Daily Mail, by contrast, called on Patricia Hewitt to "over-rule" this "pettifogging body" and approve the drugs. It did so in a leader headed "What's NICE about drug rationing?" (113) In the event, ministers stayed silent. Eisai took NICE to judicial review on its recommendation — the first such legal challenge — with the institute winning on the substance of its recommendation.²¹

At ten year's distance[at the time of writing] it is probably impossible to judge whether this was because Herceptin was in fact a genuine one-off. A serious breakthrough in a highly emotive area of medicine, with articulate women whose lives were potentially at stake making the case for it, and all at a time when NICE was seen to be taking too long. Or whether ministers in fact recognised that they were playing with fire. That if they did this again — and certainly if they did it again and again — they would end up with every decision about cost-effectiveness coming back to them personally. Swindells is adamant that it was the former. (114)

²¹ See Rawlins, section three.

So is Patricia Hewitt. "No minister could ignore these women who were facing a possibly terminal illness and who were campaigning with great courage and determination to get the best possible treatment for themselves and others in the same position," she says. "But I was also crystal clear throughout about the need to respect NICE's independence and their crucial role. I remember often saying that 'decisions about drugs are for clinicians, not politicians' and I had absolutely no intention of changing that. So although Mike Rawlins felt I was getting too close for comfort, we were able to stay on good terms throughout.

"But I was shocked to discover that NICE waited for the licence to be granted before starting an appraisal when the information they needed was basically the same as that needed by the licensing body. So I saw 'parallel processing' as the real solution to the problem.

"Herceptin was a one-off. It didn't lead to me or other Health Ministers rushing round telling the NHS to prescribe particular drugs, and we held to that when, in my time, NICE made some decidedly difficult recommendations, both around Alzheimer's and macular degeneration." (115)

Whichever way, whether Herceptin was genuinely a one off, whether ministers realised they were playing with fire in terms of NICE's role, or whether it was a bit of both, the first big apparent threat to NICE's role and independence had passed.

The moves to speed up NICE's appraisal process involved not just starting ahead of a drug receiving its licence. A key change was moving from an approach known as "multiple technology appraisals" to a "single technology appraisal". MTAs looked at

“*The industry’s submissions came in remarkably often just below the threshold, even when that was plainly a pretty bizarre result. So our job became interrogating the detail in the economic model to get to what had been done within it.*”

a drug or new technology against all the other possible treatments for a condition, and/or at more than one possible use for it. Typically it was taking around 54 weeks to complete. Scotland's equivalent of NICE, the Scottish Medicines Commission, more normally used a single technology approach, looking only at one drug to be prescribed for a single purpose. It had thus been producing decisions (which only occasionally differed from those of NICE) faster. Without anything much by way of public acknowledgement, it was that approach that NICE adopted, producing a timetable that ran for 39 weeks from the start of appraisal, against the 54 weeks that the multiple technology assessments were taking.

With that, however, came a further change which many on the institute's appraisal committees felt produced a shift of power towards the pharmaceutical companies.



Instead of the university health technology units producing the initial assessment and the company responding to it, the companies, because they held most of the key information ahead of licensing, now produced the initial submission which was then subject to critique by the assessors. "Unsurprisingly," one senior appraiser says, "the industry's submissions came in remarkably often just below the threshold, even when that was plainly a pretty bizarre result. So our job became interrogating the detail in the economic model to get to what had been done within it. It became much more of technical battle around interrogating the model, and something of an arms race, with us challenging the industry rather than other way around." (116)

One effect of that was that while the process got faster because it started ahead of the licence, it was also slowed by the assessment and the work of the appraisal committee becoming one of challenging the industry's submissions rather than the other way around. Hence while there was in general a reduction in the time between the licence and the recommendation, the huge reductions that were being briefed when "parallel processing" was announced were not realised.

Significant though these changes were, however, the Herceptin incident was over. It was to be another four years before NICE faced further significant challenges to its role and existence.



THE ROAD TO THE CANCER DRUGS FUND

By now — six years in — it was possible for both insiders and outsiders to make some systematic assessment of NICE's impact.

James Raftery, Professor of Health Technology Assessment at Southampton University, reviewed the 117 technologies (which were far from exclusively pharmaceuticals) that NICE had assessed by April 2005 and divided the judgements into his own four-fold classification — "yes", "no", "yes with major restrictions" and "yes with minor restrictions."

On this analysis, it turned out NICE had said "no" in 19 per cent of cases, "yes" in 23 per cent, "yes with minor restrictions" in 26 per cent of cases, and "yes with major restrictions" in the remaining 32 per cent.

When NICE was launched, Raftery said, clinicians had "understandably feared blanket restrictions" but "these have been fairly rare. NICE continues to be best characterised not by saying no, but by saying yes but..." (117)

Raftery noted also that NICE was unique internationally in having an appeals system. Around a third of recommendations were in fact appealed, although that had led to a substantially different decision in only four cases. "Overall NICE must be judged to have succeeded in surviving some controversial decisions. Its appeal system has imposed consistency and has so far prevented appellants proceeding to legal challenge."²²

By now too, the threshold that NICE was using to inform its judgements on cost-effectiveness had become clearer. The issue of the threshold is dealt with in detail by John Appleby in section four. As Rawlins has said, initially it just "emerged."²³

²² They were to come later — see Rawlins, section three.

²³ A more detailed account of the threshold issue is in Appleby, section four.

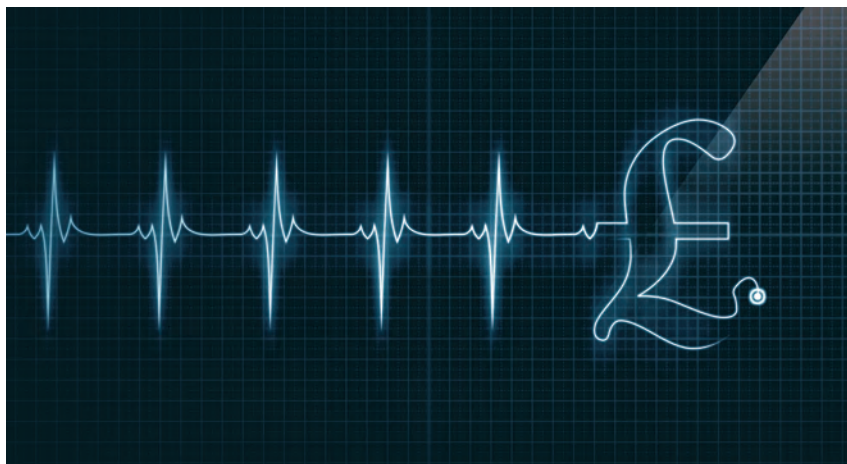
At this point it is important only to grasp that the threshold itself was never a single fixed figure. Furthermore, whether a pharmaceutical came in above or below, it did not produce an automatic ruling in favour or against. The threshold was an aid to judgement, not in itself the judgement. But it had become clear that NICE was operating in the £20,000 to £30,000 range in terms of the cost per QALY.

The institute came to explain it as follows. Where the cost per QALY was below £20,000, the institute would, more than likely, recommend adoption. Once it exceeded that figure, "judgements about the acceptability of the technology as an acceptable use of NHS resources are more likely to make more explicit reference to factors including the range of uncertainty surrounding the calculation, the innovative nature of the technology, the particular features of the condition and population receiving the technology, and where appropriate the wider societal costs and benefits. Above an incremental cost-effectiveness ratio of £30,000 per QALY, the case for supporting the technology on these factors has to be increasingly strong." (118)

To underline that last point, NICE had approved a small number of drugs with a cost per QALY of more than £30,000 a year — notably riluzole to treat motor neurone disease with an estimated cost per QALY of £39,000 and imatinib for chronic myeloid leukaemia where the initial estimate for the cost per QALY was between £22,000 and £56,000. Particular reasons for approving these were cited.

Also by now, the original question of whether NICE was likely to increase NHS costs, or decrease or restrain them, was becoming clearer. There is, of course,

“*Judgements about the acceptability of the technology as an acceptable use of NHS resources are more likely to make more explicit reference to factors including the range of uncertainty surrounding the calculation, the innovative nature of the technology, the particular features of the condition and population receiving the technology, and where appropriate the wider societal costs and benefits.*”



no counter-factual of what would have happened to spending without it. But by 2005 Rawlins was willing to estimate that its positive recommendations had added about £890m, or 10 per cent, to the NHS drugs bill. (119) At a time when NHS expenditure was rising at a record rate given Tony Blair's pledge to get England's health expenditure up to the European average, that was manageable — even if some of the appeals against NICE's recommendations were coming from primary care trusts who felt they could not afford to implement its recommendations.

NICE's next few years — controversies over the occasions when it said 'no' aside — were relatively peaceful. But a problem was building.

At the end of the 1990s there was growing concern in the pharmaceutical industry that the days of big "blockbuster" drugs were ending — those, for example, that reduced blood pressure and were taken by millions of patients to reduce the risk

of heart attacks and strokes. Research costs were rising, but the number of new chemical entities making it to market were not. The industry was becoming increasingly worried about its pipeline, and, in the US in particular, where cancer is an even more politically salient issue than in the UK, it switched much of its attention to new cancer drugs — charging highly for them. That came to apply not just to cancer treatments but to advances in other areas, for example, rheumatoid arthritis where the new drugs were potentially cost effective but decidedly more expensive than those they potentially replaced, without a dramatic improvement in the quality of life. As a result, the cost per patient year of treatment was rocketing. And the US companies, coming from an environment where there was, at least at the headline level, free pricing of pharmaceuticals, expected the UK and other countries to be a price taker for these drugs.

Not only were they expensive, there was the additional problem that many of the cancer treatments only prolonged life in people with advanced disease for a matter of months, and then only in a proportion of patients. A particular example arose over treatments for renal cancer. Several of them were in the pipeline. In a decision that Rawlins was later to regret, it was decided to wait for them all to reach market before appraising them.

"Everyone knew these were coming along, and rather than pick them off one by one. It was thought to be sensible to wait till they were all on the market and then have NICE look at them," he says. "Now, in a sense you can see the logic of that. They may vary in price and there may some advantages in one not the other. But what it meant was that the one that first got to market [Sutent] had to wait ages — in the end it was nearly two years — for its appraisal to start. And that was a mistake." (120)

Without NICE's appraisal, the NHS was reluctant to pay for Sutent, and would not pay for the other cancer drugs that NICE was judging to be cost ineffective. Patients, however, wanted them, and some started to pay for them privately. The NHS, however, had a rule that patients are not allowed to mix public and private in a single course of treatment, although precisely how that was interpreted varied around the country.²⁴ It resulted, however, in some patients who bought these drugs being told that they would have to pay for the whole of their cancer care — that they could not take the rest of their treatment on the NHS while paying for the drug and its administration. In lay language, they could not "top up" their NHS treatment by paying for the drug that the NHS would not fund.

The media — led by the Sunday Times and the Daily Mail — picked up the story. Again heart rending accounts emerged of patients selling their homes to fund treatment, and of spending their life savings to meet bills that ran to thousands of pounds a month — or, in other cases where people lacked such assets, simply going without. (121) The events that would lead to the Cancer Drugs Fund were underway.

The "top up" issue produced huge divisions. It split the medical profession, the NHS and commentators. Some argued that in such circumstances it was only humane to allow patients to pay the extra and keep the rest of their NHS treatment. Others believed that to do so would fundamentally undermine a principle of the NHS. If people could pay for expensive cancer drugs to "top up" their NHS treatment, where would that end? Would the better off also be able to pay for a better lens implant, or a better prosthesis, or some other piece of high-end, costly, technology that might have either a large advantage or even a small one over the standard

²⁴ See reference 123.

treatment? If that happened would it not only too clearly create a "two tier" NHS? To put it crudely, one for the rich and one for the poor? And once top-ups were allowed, would either the government of the day or the NHS itself be tempted to restrict what it provided, offering less and less as those who could afford it became able to "top up"?

Alan Johnson, the health secretary, resisted the pressure for months, declaring at one point that to allow "top ups" would undermine the "founding principles" of the NHS. It all became too much, however, and in June 2008 Johnson announced a four month review to be undertaken by Sir Mike Richards, the cancer czar. The market orientated think-tank Reform declared that "this marks the end of the NHS as a system based entirely on clinical need, not the ability to pay," with the NHS heading, in its view wisely, to a more mixed economy of care. (122)

Richards duly reported in the November. He produced a somewhat tortured if cleverly crafted compromise that allowed top ups so long as the private drug treatment was delivered separately from the patient's other NHS cancer care, and in a separate setting. That should only be permitted, Richards said, for "end of life" care — a definition that embraced the cancer drugs in question. (123) The immediate storm over "top-ups" died more or less overnight. But his report had implications for NICE.

First, he recommended that measures already under way to once again speed up the NICE appraisal process should be pursued. Second that the health department and NICE should assess whether, in an affordable fashion, a more generous threshold could be applied to "end of life" treatments. And third that

an upcoming renegotiation of the five-yearly Pharmaceutical Price Regulation Scheme should have more flexible pricing arrangements built into it — the PPRS being the scheme that in the UK indirectly affects drug prices by controlling pharmaceutical companies permitted profits. In other words could it be recast a little to make it easier to achieve the discounts that patient access schemes were providing? All three of these happened to varying degrees, with the number of patient access schemes rising rapidly thereafter.

NICE duly constructed a new "end-of-life" threshold, having to write formally to Alan Johnson to warn him that, it being more generous, it would increase NHS expenditure over and above the recommendations it would otherwise have made using the standard threshold — an example of the "affordability issue". Johnson accepted that and from January 2009 NICE introduced the new end of life criteria. As it did so, it underlined that only small numbers of patients a year — perhaps 7,000 — with a life expectancy of two years or less were likely to be affected.²⁵ Technically, it gave more value to the final months of life than to others, the effect being to push the threshold for these treatments up to about £50,000 a QALY. The shift was warmly welcomed by the industry which nonetheless warned that proving cost-effectiveness, even at the higher threshold would remain "extremely challenging in some cases." (124) That point was almost instantly underlined by NICE's ruling on the kidney cancer drugs.

During the Richards review, the institute had produced in August 2008 a preliminary appraisal on four of them. The products extended life in some patients by up to six months but their cost per QALY worked out at around six times NICE's normal top end threshold of £30,000. "Although these treatments are clinically effective,

²⁵ Technically, NICE did not "raise the threshold" for "end of life" treatments. What it did was put greater weight in the QALY to the last couple of years, or indeed the last few months, of life — compared to other lives. See Rawlins on the Citizen Council debates and Appleby on the threshold arguments.



regrettably, the cost to the NHS is such that they are not a cost-effective use of NHS resources," Peter Littlejohns, NICE's clinical and public health director, said as the preliminary appraisal was launched. (125) NICE found itself accused of "barbarism" and picketed by kidney cancer patients bearing placards declaring that they "deserve the right to life." (126)

Frustration was mounting all round. Rawlins gave an interview to the Observer in which he accused the industry of over-pricing its products. "We are told we are being mean all the time, but what nobody mentions is why the drugs are so expensive," he said.

Marketing costs, he pointed out, were twice the expenditure on research and development. Having been used to double-digit growth, the industry appeared to be facing "a very bad period" when many of its biggest earners were coming off

patent with little in the pipeline in terms of highly effective products for common conditions — the so-called "blockbuster" drugs. As a result a drop of 30 to 40 per cent in profits over the next few years looked likely, so the industry was pricing current products to cushion against that. And with the pay of senior management linked to share price "it is not in their interests to take less profit, personally as well as from the point of view of the business," Rawlins said. "All these perverse incentives drive the price up."

He added that the kidney cancer drugs could be produced for about a tenth of their current price. "Traditionally the pharmaceutical industry will admit that they actually charged what they think the market will bear," he said. "The wiser ones are recognising that that model is no longer available." (127)

As part of its support for what might be dubbed "the wiser ones", NICE started to develop and implement a scientific advice service for companies. This did not address the issue of price. But it helped companies by explaining more clearly the data that they could collect during clinical trials that would help with the assessment of cost-effectiveness.

In February 2009, following the Richards report and the new "end of life" approach, NICE produced its final determination on the kidney cancer drugs which allowed just one of them — Sutent — through. Even then it did so only because Pfizer agreed a patient access scheme which saw the company provide the first cycle of treatment, at a cost of about £3,000, free. Despite applying its new "end of life" guidance, NICE said, the other three products "do not represent a cost-effective use of NHS money." Thus the issue of expensive cancer products for advanced disease which provided only a limited extension of life, and in some patients only, had not gone away.

“*Traditionally the pharmaceutical industry will admit that they actually charged what they think the market will bear.*”

Two other sets of wheels were turning. The first was that in 2007 the Office of Fair Trading had taken a look at the operations of the Pharmaceutical Price Regulation Scheme. (128) It did not make comfortable reading for either the industry or the government. The OFT was unpersuaded that the scheme delivered value for money. Its core conclusion was that the PPRS did not deliver prices "that reflect the therapeutic value of the drugs companies are supplying to the NHS." Drugs that delivered the same value to a patient for the same condition could vary in price five-fold, it said. And the OFT's lead investigator later dubbed the scheme "no longer fit for purpose." (129) It recommended replacing it with something known as "value based pricing" — a seductively simple concept which essentially boiled down to companies being paid more for drugs that were highly effective compared to others for the same condition, and less for the less effective. It seemed a terribly simple and attractive idea. Though even in the OFT's own report there was some warning about the complexities of actually trying to do that. The report devoted dozens of somewhat uncertain pages to how variants of it might work.

Largely unspoken, but behind the idea, was an implication. That if this could be made to work, then there would be no need for NICE — or perhaps, more accurately, that NICE, if it survived, would become a very different organisation.

“Value based pricing – a seductively simple concept which essentially boiled down to companies being paid more for drugs that were highly effective compared to others for the same condition, and less for the less effective. It seemed a terribly simple and attractive idea.”

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Ministers and the industry started discussing the idea and the Commons Health Select Committee reviewed it. It found much support for the principle. But it noted, with considerable prescience, that many in evidence had voiced strong concerns "about how such a system would work in practice." (130) This wizard idea was, however, seized on by Andrew Lansley, the Conservative's long-standing opposition spokesman on health. It was to be the start of a six year journey down a long blind alley. It turned out that nobody could agree on how value based pricing would work. (131)

The second set of wheels was some unfinished business from the Richards review of "top ups". As part of the study, Richards had started to look at what the actual gap was in the use of cancer drugs in England compared to other developed countries. This was a more difficult piece of work than it sounds. So the decision was taken to put that to one side and treat it as a separate exercise.

"We very deliberately set up the study to involve pharma, so, for example, it was co-chaired by John Melville from Roche," Richards says. "We looked at 14 countries across the world for which we had reliable prescribing data and, again, very deliberately, we did not just look at cancer but at other conditions. And that did indeed confirm that we were low on the use of cancer drugs in terms of volume per head of population. We completed the work. But its publication got held up and did not appear before the 2010 election.

"As part of that work we had calculated that to bring spending up to the average of the other countries we had looked at would cost around £200m a year.²⁶ Now, because of the way it had been done, plenty of people outside government

²⁶ In fact the £200m figure does not appear in the final report, published after the election.

had access to that report. I've no idea whether it was available to people in the Conservative party, but I've every reason to believe it might have been. Whether it was or not, the figure that became the Cancer Drugs Fund just happened to be the one we had calculated." (132)

What is certain is that the idea of the Cancer Drugs Fund became a public reality on the 3rd of April 2010 when, a month before polling day and out of the blue, David Cameron, the Conservative party leader announced it. One of his constituents was Clive Stone who had been campaigning since 2007 over the availability of cancer drugs when he had been refused Sutent for his kidney cancer. He set up a group called Justice for Kidney Cancer Patients (133) and lobbied Cameron vigorously over the issue. (134)

The Labour government was planning an increase in employer's national insurance contributions to take effect after the election.²⁷ The Conservatives had promised to scrap that, producing a nominal £200m "saving" for the National Health Service. It was that £200m which Cameron said would go into the Cancer Drugs Fund, although just days ahead of the announcement, Cameron's aides were ringing around to ensure that £200m was a realistic figure. Bill Morgan had been a researcher on health at Conservative Central Office and after the election was to become Lansley's special adviser. At the time he was working for a lobbying company that had done some work for a charity that was then called the Rarer Cancers Forum. It had been looking at the "exceptional case" bids put in by clinicians to primary care trusts for funding for treatments not approved by NICE.²⁸ The charity had modelled what those requests added up to and had produced a figure of about £175m a year. (135)

²⁷ See glossary for definition of national insurance contributions.

²⁸ See glossary for explanation of exceptional case bids.

"I got a call, the first of several from Cameron's aides, asking if a £200m figure would stack up," Morgan recalls. "This was the first I'd heard of the Cancer Drugs Fund, and it was just days before it was announced. I do remember giving them the numbers and stressing that the figures were not bullet proof. It was those figures that were used in the Conservative Party press release.

"Once in government Andrew Lansley was perfectly happy to leave the introduction of the Cancer Drugs Fund until April 2011, which was what had been promised. But it was the Prime Minister (Cameron) who told us to introduce it as soon as possible which is why an initial allocation was made in October 2010." (136) Indeed, over the succeeding years anyone who tried to change the way it functioned without clearing that first with the Prime Minister found themselves in his firing line. (137)

Announcing the fund, Cameron declared that "other European countries are doing better than us at giving people longer, happier lives with cancer. We want to get more drugs to people more quickly and in the UK today there are some people — thousands of people — who want a certain cancer drug, whose doctors tell them they should have a certain cancer drug, who don't get it." (138)

Politically, the Cancer Drugs Fund was undoubtedly a success. Patient groups, charities and the industry warmly welcomed it, and for a time it put the issue of these cancer drugs on to the back burner.

The reaction in the Department of Health, among health economists and some commentators, along with NICE itself, was decidedly less enthusiastic. Clearly, the Cancer Drugs Fund, undermined NICE's role. Rawlins recalls that after the election

"Andrew Lansley summoned me and Mike Richards and Bruce Keogh who was the Medical Director for the NHS to his office, and all three of us said "don't do it" — including Mike who was the cancer czar. He, not Bruce and I, asked "Why just cancer? There are a lot of other rotten diseases out there." But it was obvious that Andrew had no alternative, because his boss had made a promise." It was also obvious that given an extra £200m to improve cancer outcomes, Richards would not have chosen to spend it in that way.

"It was," Rawlins says, "stupid. Not least because it stopped companies doing deals — deals under the Patient Access Scheme — and some companies simply stopped agreeing to undertake appraisals, and you can't undertake an appraisal without the company because they have the data."

Speaking in 2015, Rawlins says "I think everyone does now realises it was stupid and they are now just trying to get themselves out of the hole.

"If the government, for political reasons, wanted to spend more on cancer drugs then they could have asked NICE, or indeed, instructed NICE to have a higher threshold for them — say £60,000 a QALY — and NICE would get you a better deal because of discounts through the patient access schemes. As it is, the Cancer Drugs Fund just took the manufacturer's price." Indeed the government's own impact assessment of the fund, ahead of it being introduced, was that the government might indeed get better value for money by spending the cash in other ways. (139)

The Cancer Drugs Fund remains an unfinished story. Andrew Lansley stresses that he was in favour of the fund and helped construct it, but that he always saw it as a stop gap until value-based pricing arrived, (140) a view that Bill Morgan confirms. Initially set up with a £200m a year budget it started out organised on a regional basis, which produced inconsistency, before being made national. It initially covered some 30 cancer drugs. It was intended to run until 2014 and

“*It was stupid. Not least because it stopped companies doing deals and some companies simply stopped agreeing to undertake appraisals, and you can't undertake an appraisal without the company because they have the data.*”

the arrival of value-based pricing. But as the government, the industry and all concerned struggled to make value-based pricing a reality, an announcement in 2013 extended the scheme until 2016. The fund, Cameron said, had been a "massive success". Some 34,000 patients had by then benefited, with the prime minister declaring that "people have lived longer and in some cases it has saved people's lives." He would recommend its extension if re-elected in 2015.

By 2015, however, the fund was breaking its budget. In the January of that year, faced with a projected overspend of £100m on its £280m allocation, the 84 clinical uses to which the 42 drugs now in the fund could be put were reduced to 59, although three new medicines were added. In the September, further cuts followed. These reduced the number of indications to 41 as final figures for 2014–15 showed it had overspent by £136m and was costing more than £400m a year. (141) Among the drugs excluded was Kadcyra for advanced metastatic breast cancer, which cost an eye watering £90,000 a year. This price was so high that NICE had not only recommended against its use but Sir Andrew Dillon, the institute's chief executive, had gone public to criticise it.

At that price it was "impossible" for NICE to recommend, he said. The discount its manufacturer Roche had offered was nowhere near enough to get under the institute's "end of life" threshold. Roche hit back saying that a 60 per cent discount would have been needed and that other countries were paying the list price. The decision was "symptomatic" of NICE's processes being "unfit for purpose", particularly when dealing with drugs for advanced cancer, Roche's head of health economics and strategic pricing, Jennifer Cozzone, said. Dillon replied that in 2014 NICE had in fact supported new cancer drugs for myeloma, prostate and lung cancer. That showed that "it was clearly possible for companies to present drugs which offer real incremental benefit to patients at a price that the NHS is able to support." (142) In the wake of the row Roche in fact eventually offered a substantial, though undisclosed, discount to NHS England to allow use of the drug, at least for as long as the Cancer Drugs Fund lasted.

Cancer charities reacted with anger to the cuts to the Cancer Drugs Fund. But even they recognised there was a mounting problem over the prices being charged. Karl Claxton, professor of health economics at the University of York, was blunter. "There is no doubt that the Cancer Drugs Fund has done more harm than good for NHS patients overall." By funding these expensive treatments, less costly but still effective treatments were more than likely being squeezed out of the NHS budget. "The real beneficiaries," Claxton said, "are manufacturers who have been able to sell their drugs to the NHS at prices that are unaffordable." The Association of the British Pharmaceutical Industry described the new constraints on the Cancer Drugs Fund as extremely disappointing, while stating that it was clear that the CDF was now "a sticking plaster" over a broken system. (143)

That was confirmed by the National Audit Office in September 2015 when it reported that 74,000 patients had been approved to receive drugs from the fund since its inception. Far from it being for relatively exceptional cases, the fund had become part of "mainstream services," the NAO said. In 2014/15 the fund

had supported almost one in five patients starting chemotherapy, with the costs shooting up by 138 per cent in the two years to April 2015. Half of that increase was due to a rise in the cost per patient, half to their being more patients. Data had not been collected in a way that allowed a judgement to be made on whether the fund was improving survival. "All parties agree that the Fund is not sustainable in its current form," the NAO said. (144)

In July 2015, NHS England²⁹ proposed that the fund should become something rather different — a 'managed access' fund that would pay for promising new drugs, and not just cancer drugs, for a set period, including a period that would allow further research on them, before NICE advised on whether the drugs should be routinely available on the NHS.

The implication of that was that the fund would no longer support the provision of drugs that had been appraised but not recommended by NICE. At the time of writing, that idea remained out to consultation, with further work underway to try to resolve what undoubtedly remains one of the thornier issues that the NHS, NICE, and the Prime Minister who created the Cancer Drugs Fund faces.

The arrival of David Cameron as prime minister and Andrew Lansley as his health secretary in 2010 brought one other threat to NICE and two other significant changes. The threat was linked to value-based pricing. Lansley proposed that NICE would continue to appraise the cost-effectiveness of new products whose "value based price" would be negotiated by the health department. Once that was done, however, it would be up to doctors whether to prescribe them. NICE would no longer make a formal recommendation for adoption or otherwise. (145)

GPs and others reacted with horror. They would no longer have NICE providing cover for decisions not to prescribe. Dr Clare Gerada, the president of the Royal College of General Practitioners, warned that "[individual] GPs will be exposed

²⁹ See glossary for definition of NHS England.

to lobbying by patients, patient groups and the pharma industry." Six months later, Lansley was forced into a U-turn, agreeing that NICE would still make a recommendation. Rawlins noted that both the industry and doctors wanted NICE's role retained.

"The industry wanted it because any negotiation about price involves a trade-off between price and volume, and without a recommendation from NICE the industry would not have a clear idea about volumes," he said. "GPs wanted our role retained because otherwise each commissioning group and GP would have to decide whether or not to provide any given treatment." They feared that having to make the decisions about cost-effectiveness themselves would damage relations with patients, some of whom would believe that doctors were personally profiting when they said 'no'. "They wanted a 'blame quango' to be responsible — i.e. NICE," he added. (146)

The ABPI confirmed his judgement from the industry's point of view. It stated that "we value the role of NICE and want it to retain a strong role." GP leaders declared themselves "very pleased".

The first of the two changes that the Cameron and Lansley did implement was that the institute was put on a new and more independent legal footing, turning it from a special health authority into a "non-departmental public body". This move, for example, made it less subject to ministerial direction.

The second was to extend its remit again. An existing body that provided guidance to the world of social care and social services — the National Institute for Social Care Excellence — was folded into it. Behind that lay the desire that is seen globally to integrate health and social care better, given the rising numbers of elderly patients with more than one condition whose quality of life often depends as much on the social as opposed to medical care they receive. There was a hope

“*The new responsibility brought a further change of name, though, again, no change to its acronym. It became the National Institute for Health and Care Excellence.*”

also that the rigour NICE applied to the construction of guidelines, and the health economic skills that it can command, would be brought to bear on social care — a part of the world not much subject to economic analysis. The new responsibility brought a further change of name, though, again, no change to its acronym. It became the National Institute for Health and Care Excellence.

These two changes took effect from April 2013. In September 2015, NICE produced its first piece of social care guidance, recommending standards aimed at eliminating low quality, very short, encounters between care staff and their clients and patients. (147) Yet again, that highlighted one of the continuing dilemmas that has surrounded NICE since its formation. It had taken two years to produce from the time NICE acquired the responsibility for social care guidance. So doing its job thoroughly takes time.

And neither NICE, nor central government, had a lever that would require that the guidance be followed. Local government, which in the main now commissioned this care from the private and voluntary sectors, theoretically had the lever to enforce it. It could have insisted on it in its contracts. But local authorities did not have the cash to pay for that requirement, given that the social care budget was being repeatedly cut as the government sought to eliminate the current budget deficit that had been caused by the global financial crisis of 2008. (148)

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BACK TO THE BEGINNING: THE IMPORTANCE OF THE GUIDELINES

This account has focused overwhelmingly on the technology appraisals — because that is where NICE's recommendations have been most controversial, where the political and media action has mainly been, and where, to be honest, many of the best of the stories that make an account like this readable lie.

But there is a case that technology assessment may not be the most important part of NICE's work. The guidelines were there in the arguments for the institute before its birth — they were a key reason for its creation. Indeed, according to Trevor Jones, the possibility that they would lead over time to more consistent use of newer and effective products was one of the attractions for an uncertain, if not downright hostile, life sciences industry.

"The technology appraisals get all the airtime and media attention," Rawlins said back in 2009. "But I think in many ways the guidelines have been more important. Drug therapy, after all, is only one part of managing patients with all sorts of different conditions. And the guidelines cover the whole pathway — from diagnosis, to the whole treatment, to who is responsible and all the other aspects of care. Our schizophrenia pathway, for example, one of the first we did, has had a very significant effect. It has been translated and adopted in Spain and Italy. It has been adopted in Australia and the state of California. The guidelines include cost-effectiveness, and they are put together with patient representatives. And whenever I talk to the Medical Royal Colleges, it is the guidelines they are most interested in. Our guidelines on the management of hypertension, for example,

“*During the first 14 years of its existence, almost all the National Institute for Clinical Excellence’s guidelines described the optimal management of individual conditions such as hypertension, heart failure, chronic obstructive pulmonary disease and so on.*”

will, we estimate save very considerable sums over the years because of the number of strokes and heart attacks it will prevent.” (149)

Measuring the impact of the guidelines in the UK is not easy. It raises two opposed questions. Are they taken up enough, or too much? Neither is easy to answer. Certainly some believe that they are not adopted with sufficient consistency.

No-one, however — not NICE, not NHS providers and commissioners, not the colleges — has the resources routinely and comprehensively to measure their uptake. As Professor Mark Baker, head of the directorate that produces the guidelines points out, each one can contain anything from 30 to 200 recommendations, ranging from the minor to the major. Furthermore, much of what a guideline will be recommending is already standard best practice. So what do you measure and how? “There is certainly anecdotal evidence of uptake,” Baker says, “and we do undertake some formal monitoring. Overall, we estimate uptake to be between 80 and 90 per cent, but for major changes in practice it might be only 50 per cent after two to three years. But it is only an estimate.

"The reason major changes take longer can be because they involve changes to infrastructure which take time. But the main reason is cultural — it takes leadership within organisations to get the new accepted and adopted. Furthermore, they are guidelines. They are not protocols or tramlines, and not every patient will fit into them. You would be rather worried if the uptake was 100 per cent." Indeed, he adds, some people harbour a counter worry — "that more junior doctors just follow the guidelines blindly without thinking. Not grasping that they are an aid to judgement, and that they won't fit every patient. They do not substitute for the responsibility of clinicians to make decisions." (150)

Measuring uptake — and the right sort of uptake — is one issue. But there is a further challenge. Producing a robust, evidence-based clinical guideline is no easy task for single conditions. But as the population ages, more and more patients have multiple conditions. "During the first 14 years of its existence, almost all the National Institute for Clinical Excellence's guidelines described the optimal management of individual conditions such as hypertension, heart failure, chronic obstructive pulmonary disease and so on," Mike Rawlins records. "Many, indeed most, patients over the age of 65 years have two or more co-morbidities. Those of us who are fortunate enough to reach the age of 80 are likely to have an average of five co-morbidities.

"The idea of trying to manage individual patients, especially those with chronic diseases, according to the advice in five guidelines is obviously impractical. On the other hand, producing a single guideline, covering all possible co-morbidities, is equally unhelpful.

"I am unaware of any guideline developers who have resolved this critical problem," although NICE is currently working on ways of resolving it. (151) By what electronic or other means that guidance is delivered to clinicians once it has been developed is also an issue.

“*In my view NICE is even more of an exemplar in its clinical guidelines work than it is for technology assessments.*”

The case for the guidelines being the most important part of the work lies in their overall impact on population health. Easy approvals for new health technologies have become rarer — in part because of the rising price of the products that NICE reviews. "All our decisions to recommend are now made at the margins," according to Andrew Stevens, who has been a deputy chair and now chair on the appraisal committees since the institute's inception. They increasingly tend to involve high cost treatments that affect relatively small numbers of patients. By contrast, and by way of example, the single guideline around the management of high blood pressure, and the pharmaceuticals to use for that has had a demonstrable impact in reducing heart attacks and strokes across a vastly wider population, as, for example, has the guideline on the prevention of venous thromboembolism in bed bound patients.

Adrian Towse, director of the Office of Health Economics, says "in my view NICE is even more of an exemplar in its clinical guidelines work than it is for technology assessments." Implemented more fully, he says, "they would have far more impact on the NHS and its patients than all the technology assessments put together. And for middle income countries, it is the development of evidence-based clinical pathways, and incentive schemes to ensure that clinicians implement them, that are the most interesting part of NICE's work. In other words, working out how best to manage patients and then ensuring that gets done." (152)



NICE IN “LA LONGUE DURÉE”

Sixteen years hardly qualifies for “la longue durée”. But that is NICE’s age at the time of writing and of the many organisations that the Labour government founded in the years after 1997 to operate in one way or another at arm’s length from ministers, it is one of the few to have survived. In health, it is the only one to have survived with its core remit — guidelines and health technology assessment — essentially unchanged.

If for no other reason, that makes it one of the more successful pieces of UK public policy in the past 20-plus years. Yet its life has been lived in ferment.

At various times it has been accused of being no more than “the marketing arm of the pharmaceutical industry” on the grounds that the threshold is too generous, and, in the United States of being a “death panel”. (153) In the UK it has been accused of “sentencing patients to death” by its decision not to approve a new technology, usually a pharmaceutical. (154) It has earned accolades — from the World Health Organisation and from academics, chiefly health economists, and from clinicians. It has also faced pickets and protests and condemnation, sometimes in brutal terms, including from other clinicians and academics, some of them health economists.

Furthermore the life sciences industry has always lived, at best, in uneasy and often resentful tension with NICE. One former senior figure in the Association of the British Pharmaceutical Industry complains not just about how it has handled cancer drugs, and about how few outright “yes” rather than “yes, but...” decisions NICE has produced, but also “of the disrespectful way the appraisal committees have dealt with the companies — ‘you can come but you have to sit over there, not speak and there won’t be any lunch for you’.” (155)

That criticism moves to the point, as one interviewee put it, that this account does not capture what it is like to be a member of, and inside, one of the appraisal committees where, he says, "it is always easier to say 'yes' than to say 'no'. You can write a short report and no-one much is going to challenge it. Say 'no' or a significant 'yes but ...' and you have to have every element of the appraisal right because it can go to appeal when it is the appraisal committee that is in the dock, faced with the company, the patient groups, their clinical experts, all backed by barristers who are trying to make a quasi-legal process go their way. And then there is the risk of judicial review which sees NICE picking up the bill if even one, minor, part of the judgement goes against it. That induces a certain conservatism." That also explains why the documents making a "no" recommendation run to such enormous length in an attempt to insulate their reasoning against judicial review.

"The appraisal committee," this interviewee says, "is a hugely satisfying task. There are not many jobs when you start at 10 and know you have to finish by 5 and reach a judgement with 25 or 30 other people in the room that is based on the evidence. But I sometimes joke that they should pull our fingernails out when we say yes to match the pain that comes our way when we say no. Every decision is tense."

The institute also faces, as always, a set of evolving challenges. In terms of scale, it is a very different organisation to the one that started out with three permanent staff and a lap-top borrowed from St George's hospital. From a staff of 10 and a turnover of £600,000 in 1999/2000, it has grown to employ directly more than 600 people with a core government grant in 2014/15 of just under £65m and

“*It is always easier
to say ‘yes’ than to say ‘no’.*”

a total turnover of around £71m. (156) It now has dozens of committees while the growth in health technology assessment means it now has four appraisal committees rather than the one it started out with. It has a website that was very to use in its early days that then became close to impossible to use, and is now appreciably easier.³⁰

The biggest headline additions to the institute's original remit of guidelines and health technology assessment have been public health and social care. But it also hosts many less immediately visible activities. These include commissioning and distributing the British National Formulary,³¹ providing advice to companies on how to build useful cost-effectiveness evidence into their trials, providing the evidence used to help negotiate the quality indicators used in family doctors' contracts and much else. The fact that what it has done has grown has been a vote of confidence by successive health ministers, regardless of party, who have plainly seen it as a competent organisation that can take on new tasks.

That very growth, however, has led some to worry about "mission creep". There is no shortage of English public bodies from the Audit Commission to the NHS Modernisation Agency to the National Policing Improvement Agency that have been undone by ministers loading new tasks on to them because they appeared to be effective organisations. (157) NICE has at times successfully resisted "mission creep" and at times has succeeded in moving to elsewhere some tasks it has been

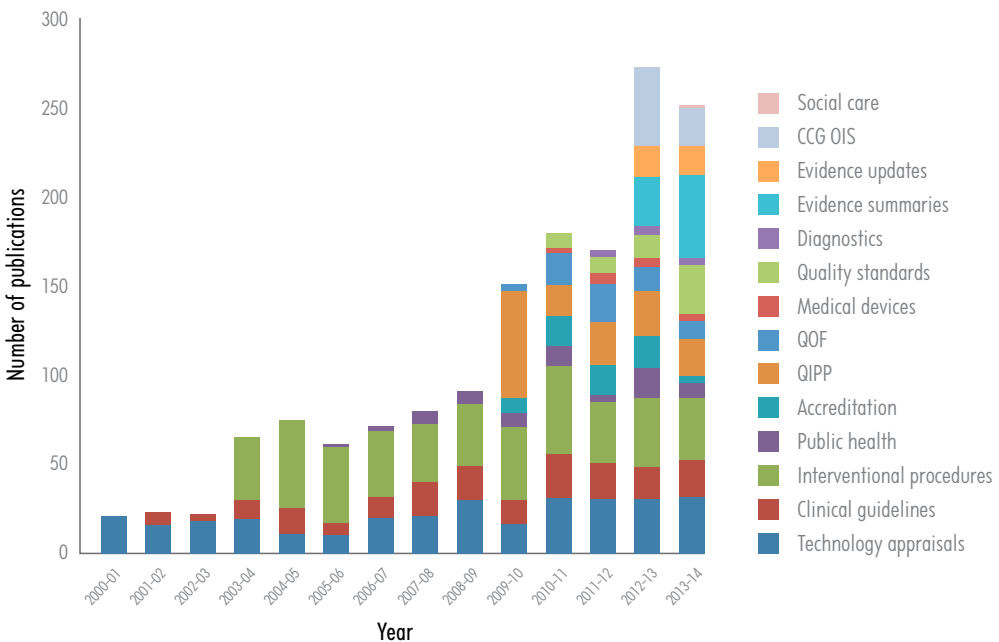
³⁰ Personal view

³¹ On behalf of the Royal Pharmaceutical Society and the British Medical Association

given — the Advisory Committee on Borderline Substances, for example, which deals with the prescribing of foodstuffs and toiletries. (158) But the risk must be there that too many additions to its role will dilute its original purpose, possibly to the point of emasculation or destruction. The board could lose focus on its original mission as the organisation becomes a more fragmented bureaucracy as its many different tasks have to be managed.

By mid-July 2015, the institute had produced more than 1,100 pieces of guidance, including more than 350 technology appraisals, more than 200 clinical guidelines, more than 500 assessments of interventional procedures, and 59 publications on public health — and even that list is a long way short of embracing all its activities (see Figure 1).

FIGURE 1 THE GROWTH OF NICE'S ACTIVITIES OVER THE YEARS



Source: Supplied by National Institute for Health and Care Excellence³²

³² Although not explained in detail, most of these activities can be grasped by their short name. Of the others, CCG OIS provides a set of outcome indicators that allow Clinical Commissioning Groups to benchmark their quality performance. QOF stands for the Quality and Outcomes Framework used in general practice. QIPP is support for the NHS's Quality, Innovation, Productivity and Improvement programme, aimed at improving the quality of care in ways that also increase the service's productivity and efficiency.

TABLE 1 AREAS OF NICE'S EXPENDITURE

| DIRECTORATE | 2014/15 GROSS EXPENDITURE (£m's) | COMMENTS |
|---|---|--|
| Centre for Health Technology Evaluation | 10.6 | Responsible for developing guidance on the use of new and existing treatments and procedures; including Technology Appraisals (£4.0m) and Medical Technologies & Diagnostic Guidance (£4.7m) |
| Centre for Clinical Practice | 13.0 | Responsible for developing guidance in the form of clinical guidelines |
| Medical Prescribing Centre (including British National Formulary) | 6.3 | Responsible for developing evidence summaries for new and unlicensed & off-label medicines. Also includes the publication of the BNF & BNFC (£4.8m). |
| Health and Social Care | 10.4 | Responsible for a range of products including the production of guidelines for Social Care (£2.7m) and Quality Standards & Indicators (£2.0m). Also provides resources to support the implementation and adoption of guidance. |
| Public Health | 4.3 | Responsible for the production of public health guidance |
| Estates, Infrastructure and Corporate | 8.5 | Infrastructure running cost and back office functions such as rent and rates |
| Communications and Publishing | 3.9 | Responsible for raising awareness of NICE products and services as well as engagement with key stakeholders, includes NICE website, Press & Public enquiries, Publication & Dissemination |
| Evidence Resources | 12.0 | Responsible for managing all of NICE's Digital Services (£5.6m) and delivering and information service for NICE internal guidance development programme (£2.6m). Also provides NICE Evidence Services and UK PharmaScan to external users. |
| NICE International | 2.5 | NICE International Income = £2.8m, Expenditure = £2.5m, Surplus = £0.3m |
| Scientific Advice | 0.8 | Scientific Advice programme Income = £0.8m, Expenditure = £0.8m |
| Depreciation | 0.9 | |
| | 73.2 | |

Source: Supplied by National Institute for Health and Care Excellence

The table of areas of expenditure in page 125 is somewhat distorted by the assessments that feed into the technology appraisals being done by some eight university units whose activities are funded by the NHS rather than NICE itself.³³ But of its own expenditure of some £70m, less than £11m goes directly on the technology evaluations, including medical devices and diagnostics. Some £13m is spent on producing clinical guidelines, something over £4m on public health, and approaching £3m on social care guidelines.

The outside world clearly draws on NICE's guidelines and technology appraisals, and indeed for some — to pick up Richard Smith's quote about NICE being one of Britain's greatest cultural exports — NICE's international influence may be the jewel in the crown. "The most important thing may be the influence on other countries," Andrew Stevens, the longest-serving member of NICE's appraisal committees says. "Particularly for those who are developing their health services and do not want to throw their money away on cost-ineffective spending."

From relatively early days, NICE received delegations from other countries, and in 2008 it formed NICE International, a division that provides advisory services, mainly to lower and middle income countries, on approaches to both guidelines and health technology assessment, although it tends to be the guideline development process that most interests them.³⁴ The funding for that has come mainly through contracts and grants from the World Bank and major philanthropic institutions.

Of the many challenges that NICE lives with, one has always been the trade-off between the robustness, inclusiveness, transparency and contestability of its work and the time it therefore takes to do. An assessment published in 2013 of completed appraisals up to 2010 showed that the single technology approach

³³ Technically these days by the National Institute for Health Research, the department's replacement for the original NHS+ R&D programme

³⁴ For a fuller account of the work of NICE International see Culyer et al., *A Star in the East: A Short History of HITAP*.

had reduced the time taken to a final decision by 36 weeks compared to multiple technology appraisals. But the median length of time for a single technology appraisal was still 48 weeks. (159) Guidelines — as the first guideline for social care illustrates — can take two years. The time technology appraisals take, however, is not entirely in the institute's control. Companies can seek to submit additional evidence, and appeals obviously lengthen the appraisal process. The gap between the licensing of a product and NICE's recommendation has reduced, thanks to starting earlier, building more appraisal capacity, and moving mainly to single technology appraisals. But the issue of "NICE blight" has never entirely gone away. In May 2015, the institute announced its latest initiative, an Office for Market Access to help the life sciences industry ease its way through NICE's processes and understand the complexity of the health service's adoption of new technologies and treatments. (160)

A current challenge is that with the growth in NHS spending now heavily constrained following the global financial crisis, there is little easy headroom for the service to fund the new technologies which NICE does recommend. Affordability, which to date has not been a headline issue, may become more important. Or, to put it another way, the issue of what in the current service has to be foregone in order for the new but cost-effective to be adopted may become much more acute than in the institute's earlier days. Furthermore, while that used to be an issue only for ministers and the department of health, from 2013 another voice can be involved in that discussion, given the creation of NHS England as a statutorily independent commissioning body for the service. It commissions specialist care which is the area of service most directly affected by the technology appraisals. In 2015 it delayed for a time approval of costly new treatments for hepatitis C on the grounds of affordability. A recent spat in which NICE was originally asked to draw up

guidance on safe levels of nurse staffing, only for it then to be asked not to publish them, apparently because the potential cost of their implementation was becoming clear, may be another straw in the wind. (161)

Indeed, following the recent five year settlement for NHS funding in November 2015, the chief financial officer for NHS England has warned that "we're going to have some serious discussions [with NICE] about the pace at which [an increasing volume of effective but expensive new drugs and devices] get adopted. (162)

The affordability issue has brought back to the fore the on-and-off argument over the years about what the threshold should be. Some of the health department's senior economists felt from the beginning that the £20,000 to £30,000 range per QALY was too high [see Appleby, section four]. Karl Claxton and a host of colleagues recently estimated — by undertaking some fairly heroic calculations around elements of the NHS's programme budget and PCT expenditure — that most of what the NHS does costs around £13,000 per QALY or less. That raises the question, they argue, of whether not just the Cancer Drugs Fund but NICE's own decisions are "doing more harm than good overall" by potentially crowding out more cost-effective treatments. (163) Back to the fundamental issue of "opportunity cost". Or as one health economist brutally puts it, "NICE is good idea badly implemented, indeed hardly implemented at all. (164) But the only problem is the overgenerous threshold, which could be corrected at the stroke of a pen."³⁵

³⁵ See Appleby pp for the challenges of adjusting the threshold either way.

The life sciences industry, needless to say, would greet that with dismay. As Sir Andrew Dillon put it in response to Claxton's paper, a £13,000 per QALY threshold "would mean the NHS closing the door on most new treatments" — unless that is "you believe the drug companies would be prepared to lower their prices in an unprecedented way." He added that "when you decide to move with the cutting edge of medicine ... there's a price to pay." (165) In other words, the National Health Service needs to balance the cost-effectiveness of individual treatments against the price of remaining at the forefront of new developments, which, initially at least, tend to be very expensive before becoming cheaper — think, for example, of scanners or the cost of surgical kit for laparoscopy. Or as Adrian Towse of the Office of Health Economics puts it, a £13,000 per QALY threshold would see "the NHS becoming a late launch, or never launch market. NICE would no longer be a leading health technology assessment body but would be sweeping up the dregs after everyone else around the world has reviewed the drug." (166)

One of the early hopes around NICE has not been fulfilled. Or at least not to the extent that its creators hoped. Namely, that it would find significant practices within the NHS that should cease, thus saving money to be spent on other things. In other words, in more technical language, "disinvestment".

In 2011 two senior figures at NICE produced a slightly defensive paper setting out the many difficulties the institute has encountered in seeking to encourage that plus some of the limited successes that have been achieved. As the paper makes clear, there is a question around how much investment should go into the work needed in order to produce what may, or may not, be a disinvestment recommendation. Would the costs outweigh the benefits even if the disinvestment was fully implemented? And as one appraiser put it, "with some of the pharmaceuticals we recommend, they are cost-effective but not massively better in terms of outcome than the cheaper drug that went before. You quietly hope that not everyone will adopt the new for every patient." (167) What is clear from the paper is that nowhere in the world has found the issue of disinvestment easy. (168)

Andrew Stevens argues that the easy hits — unnecessary tonsillectomies and over use of grommets for glue ear for example — were largely killed off by the evidence-based medicine movement from the 1980s on. Mike Rawlins points out that there is now little, if anything, in the British National Formulary that is actually ineffective. "There aren't, now, a lot of useless drugs," he says, "and very little is spent on the few that you could argue are pretty useless. So there are no big savings there."

But if technology appraisal does not lead to significant disinvestment, the clinical guidelines do contribute, he says. For example not routinely doing an ECG before an operation, and reducing routine use of antibiotics for sore throats, while some of the biggest savings may lie in reshaping the way services are provided. For example developing fewer, better, specialist centres, advice on which lies only partly in NICE's remit, and, perhaps, moving more services out of hospital and

closer to people's homes, although the economic evidence that will save money is at best, as yet, uncertain. Like the affordability issue, however, the disinvestment debate lives on.

Resolving the cancer drugs issue, and indeed the use of highly expensive drugs and treatments for very rare diseases, remain live concerns. And the way the Cancer Drugs Fund is finally resolved may offer NICE a new lease of life or seriously damage it. Further challenges include the emergence of gene therapy and more "personalised" medicine, and what that will do for the way NICE appraises new treatments. All these are matters that are central to what NICE does, but which are far from entirely within the institute's control.

Some worry that NICE no longer has a health economist on its board. (169) Others that as its own budget is squeezed amid limited growth in overall NHS spending, it will instinctively protect its in-house activities against those it commissions. (170)

Furthermore it is crucial to grasp that NICE has only worked because in the main ministers have stood back and allowed it to do the job for which it was created — as happened at its birth with the Relenza controversy. Linked to that is the fact that it will only survive if each new minister, regardless of party or government, has NICE's role and functions clearly explained to them — by the Department of Health, by NICE itself, and by NHS England. The need for new ministers to understand that is something to which this short history might just contribute.

Over the years, the industry, often grudgingly, has come to acknowledge and even, up to a point, value NICE. Occasional big bust-ups still happen — between

NICE and Roche over Kadcyca in 2014, for example. But, as Andrew Jack, the FT's long-standing pharmaceutical correspondent, puts it, "there is a pretty transparent process, and a set of rules and values behind that, which may get endlessly argued about and which have on occasion been modified, but which the industry understands and can live with — though, even now, it wishes, quite reasonably, that the NHS would take up the recommendations from NICE faster and more consistently." (171)

The way technology appraisals operate has, over the years, seen some swings and roundabouts. Some of the swings have favoured the industry and those patients who receive the most expensive treatments in terms of cost per QALY. The two most notable examples being the changes involved in the move to single technology appraisals and the new threshold that arrived for "end of life" treatments. The biggest roundabout has been the arrival of "patient access schemes" which involve the industry doing a deal to get a product adopted, even if the Cancer Drugs Fund has muddied those waters.

“*The biggest roundabout has been the arrival of ‘patient access schemes’ which involve the industry doing a deal to get a product adopted, even if the Cancer Drugs Fund has muddied those waters.*”

To sum up, NICE across its existence has sought to balance the unequal equation that lies at the heart of all this.

- The taxpayer's, or funder's, interest in cost-effectiveness.
- The interest of the individual patient who, when he or she is not paying direct, has little personal interest in cost-effectiveness. Quite simply, they want the treatment, whatever it costs. However, the individual patient and the taxpayer or funder both have a medium to long term interest in the cost-ineffective not driving out the cost-effective.
- The interest of clinicians who, by and large, welcome guidance but detest instruction and who are often only too glad to have someone else make the really difficult recommendation on what should and should not be funded.
- The interests of politicians who have overall responsibility in most countries for the provision of health care either for all, or for a large section, of their population — and who have come to recognise that they cannot possibly take every one of these decisions themselves.
- And not least the interests of the life sciences industry which needs a market for their products that will, ideally, encourage not just innovation but the best and most useful sort of innovation, while providing the best possible price they can obtain.

Throughout NICE's life, it has sought to balance these conflicts, not least those of the life sciences industry against those of the taxpayer or funder. It has been notable that on the two or three occasions when NICE's role has come under serious threat the industry has supported its existence. Better the devil you know, so to speak.

*NICE has been and is
“A Terrible Beauty”.*

To put it another way — and to steal, way out of context, a line from W.B Yeats that was itself stolen as a headline in the institute's early days by the Financial Times — NICE has been and is "A Terrible Beauty".

Terrible for those who have been denied treatments that offered hope, even if that hope — most often though not always — was for a few extra months of life for which the NHS declined to pay. Those with sufficient means could always circumvent that.

Terrible too for those in the life sciences industry who had invested their time and effort in new treatments that failed to meet NICE's thresholds — for whatever reason, including the cost of development, and the price at which their employer chose to sell. The "Beauty" element being the way NICE has sought to balance those interests against the multiple others outlined above, and in the way it has helped define and reinforce best medical practice through its guidelines programme.

As an end note, it is worth perhaps underlining that what NICE ultimately does is apply a judgement. The work that goes into the guidelines and technology appraisals is underpinned by huge numbers of numbers. But the weight applied to each of those numbers is itself a matter of judgement, and they do not then go into a dessicated calculating machine that produces a simple "yes" or "no" according to whether something comes out above or below a given threshold. What comes out is an aid to judgement to which NICE's declared societal and other values are then applied.³⁶ It is all a judgement, and thus a contestable one, and will forever remain so — just a better informed judgement than would be made in the absence of the calculations, and in the absence of the declared set of values that underpins the recommendations.

The final verdict on NICE to date may be that its biggest success is that if someone was daft enough to abolish or marginalise it, much, if not all of what it does, would have to be re-invented. Or, at least, ought to be.

³⁶ For NICE's social values and their development see Rawlins, section three.

NICE, THE LAW, ITS SOCIAL VALUES AND ITS STAKEHOLDERS



Health and Social Care Act 2012

CHAPTER 7

NICE was set up as an independent legal entity, separate from government, in 1999. It was originally established under so-called “secondary legislation” as what was then known as a “Special Health Authority”. This changed in 2012 when it became re-established under primary legislation in the Health and Social Care Act (2012) but with similar responsibilities. NICE’s remit, however, covers only England and Wales.

The independence of NICE from government was — and remains — critically important. Although ministers must agree the topics on which the institute should provide guidance the professions, patients and the public can be confident that NICE guidance is free from political interference. Indeed, the Health and Social Care Act in Section 237(4) specifically prohibits the Secretary of State from directing the institute about matters relating to the substance of NICE’s advice, guidance or recommendations.

NICE and the law

As a so-called “administrative body” NICE is required to act fairly, reasonably and according to the law. NICE’s processes and procedures, initially for technology appraisals and the development of clinical guidelines, were therefore designed so that interested parties (primarily the medical professions, patient advocacy groups and the life sciences industries) had appropriate opportunities to engage in the development of NICE’s guidance. Failure to do so could be challenged by an interested party in the Administrative Court by so-called judicial review. If successful, that could result in NICE being required to re-examine the specific piece of guidance under challenge, or could result in its being quashed.

NICE's legal advisors were therefore intimately involved, from the outset, in trying to ensure that the new Institute's processes and procedures met the requirements of administrative law. In particular the institute had to ensure that interested parties were aware that a particular technology appraisal or guideline development was to be undertaken; that there were opportunities for them to engage with the process including, if they so wished, the submission of evidence; and they would be able to "contest" the decisions that had been reached. We explained this approach as being one where all stakeholders are entitled to 'have their say — but not necessarily their way'.

The grounds on which NICE's guidance can be contested were, and still are, twofold. First, if the institute has either failed to act fairly or has exceeded its powers. In practice this means that interested parties can expect NICE to follow its published processes; that interested parties should be provided with sufficient information to be able to engage in the process; and that in reaching its conclusions NICE must take due account of any relevant legislation such as the Equalities Act (2010). Secondly, NICE's recommendations are expected to be "reasonable" in the light of the evidence that has been submitted. The standard legal test (172) for unreasonableness (or irrationality) is *"a decision that no reasonable person acting reasonably could have made"*. In terms of NICE it means that no reasonable technology appraisal committee or guideline development group, acting reasonably, could have reached the particular decision(s). To succeed at judicial review it also means that the guidance must be obviously and unarguably wrong and illogical; or so absurd that a reasonable advisory committee could not have reached such conclusions. It is possible, nevertheless, that two different committees could reach different conclusions, based on the same evidence, without either acting unreasonably.

FIRST 8 YEARS

NICE published 119 technology appraisals and 44 clinical guidelines without challenge in the courts.



2007 – 2009

NICE was taken to the administrative court on 4 occasions.

In the first 8 years of its existence NICE published 119 technology appraisals and 44 clinical guidelines without challenge in the courts. Between 2007 and 2009, however, the Institute was taken to the administrative court on four occasions.

Three of these involved technology appraisals (173), (174), (175) and one a clinical guideline. (176) In no instance did the courts quash the guidance. For one of the technology appraisals (177), and for the clinical guideline (178), the cases were dismissed in their entirety. For two technology appraisals the court dismissed most of the complaints but considered that NICE had acted in a discriminatory manner by failing to take sufficient account of the needs of those whose first language is not English and of those with disabilities. The courts required the institute to revise its guidance taking these issues into account. It did so, and the revised guidance was subsequently published without further legal challenge.

In 2014 the Institute was involved, albeit indirectly, in another case before the administrative court. A young woman with severe Crohn's disease had been advised to undergo bone marrow transplantation plus chemotherapy, under the NHS, which would inevitably cause her to become infertile. Her specialists therefore recommended her to have oocyte cryopreservation before the chemotherapy was started. The relevant Clinical Commissioning Group (CCG) declined to fund the oocyte transplantation despite the fact that the procedure had been recommended in a relevant NICE clinical guideline. In the course of his judgement the presiding judge (179) ruled that: *"...in reality the CCG could not lawfully disagree with the medical or scientific rationale for NICE's recommendation in relation to oocyte cryopreservation"*. This does not mean that the courts will invariably uphold a challenge to the authority of the institute because the judge continued: *"I am not ruling out the possibility that other reasons of a different nature could not lawfully be relied on. I should also make clear that my conclusion (on this alternative basis) applies only to this particular NICE recommendation"*. This judgement does, however, demonstrate the significance that the courts attach to NICE guidance.

These decisions demonstrate the exquisite care that NICE must take in preparing its guidance. For example, in its revision of the institute's 2004 clinical guideline on the treatment of infertility in 2013, it had to take account of the provisions of

“...in reality the CCG could not lawfully disagree with the medical or scientific rationale for NICE’s recommendation in relation to oocyte cryopreservation.”

the Equalities Act (2010) — enacted during the intervening period — which prohibits public bodies like NICE from discrimination on the grounds of age, gender, race or sexual orientation. The revised guideline therefore gave advice (as, arguably, it should have done in 2004) on the treatment of infertility in same sex couples.

NICE has, over the past 16 years, published over 1,110 individual pieces of guidance. The fact that there have been no further legal challenges since 2009, is perhaps testimony to the institute's assiduous approach to meeting its legal obligations.

NICE's relations with its stakeholders

From the outset NICE appreciated it had an obligation to earn, and retain, the confidence and respect of its stakeholders. These included professional bodies (especially the Medical Royal Colleges and Professional Societies), patients (particularly patient advocacy organisations), the life sciences industries and the staff of the National Health Service.

To encourage dialogue with such a disparate group the institute's original (1999) statutory instruments required it to establish a Partners Council *"...to advise the institute in relation to such matters as the institute may refer to them"*. The members were appointed by the Secretary of State, on the recommendation of NICE's Chair and Chief Executive, and included representatives from a wide range of organisations (see Table 1).

The partners council originally met quarterly and, in many respects, fulfilled a useful purpose during the first few years of the Institute's existence. It was consulted, annually, on the institute's business and corporate plans as well as on its annual reports. More specifically, the council was consulted on matters such as its emerging conflict of interest policy, whether advisory committee meetings should be open to the public, and on revisions to the technology appraisals process.

Over the years, however, it became clear that the partners council was becoming increasingly ineffective with attendance falling year by year. There were several reasons for this. First, the council was only "advisory" and with no "executive" role. Second, structured approaches to engaging with stakeholders had emerged over the years including:

- annual meetings between the chair and the presidents of the Royal Colleges, including the medical, nursing and midwifery colleges
- annual meetings between the chief executive and the British, European and American pharmaceutical groups as well as similar meetings with the representatives of the medical devices and diagnostics industries
- an annual programme of visits by the chief executive to the chief executives of the NHS regional bodies (the Strategic Health Authorities)
- the emergence of a semi-independent body — the "Patients Involved in NICE" Group (the PIN Group) — which is an alliance of patient advocacy and support groups
- the development, within the institute of a Patient and Public Involvement Unit.

In the light of these changes NICE's Board asked the Secretary of State for Health, in May 2010, to remove the partners council from the institute's statutory instruments (to which he agreed).

Although the council had outlived its usefulness, it had unquestionably been a useful means for engaging with stakeholders in the early years. It also allowed stakeholders to feel involved in NICE during its initial (and controversial) birth pangs as well as providing the institute with opportunities to explain its plans and report on its progress. It also helped diffuse antagonisms among different interest groups (such as between the professions, patient advocacy groups and the life sciences industries).

One additional way by which NICE interacts with overseas pharmaceutical and device industries is through visits that the chairman and chief executive (separately or together) have made to companies in Europe, the United States and Japan. Officials from the UK's Trade and Investment arm of the Foreign and Commonwealth Office usually arranged these meetings. The meetings were (and still are) intended to explain NICE's role in the NHS; the processes and procedures it uses; and the reasons why cost-effectiveness, as well as clinical effectiveness, are critical in drawing its conclusions. The meetings, mostly held at companies' headquarters, have been greatly appreciated by the life sciences industries; and have done much to dissipate initial hostility towards the Institute.

Social Values and the Citizens Council

From the outset, and particularly as a result of the influence of its vice-chairman Professor Anthony (Tony) Culyer,³⁷ the institute recognised that its advisory bodies should take account of social values, as well as scientific values, in reaching their decisions. NICE also appreciated that although the members of NICE's advisory bodies were well able to make judgements about the merits (or otherwise) of the underpinning science, they had no legitimacy to impose their own social values on patients and the public. The institute believed that such social values should be those of patients and the public.

The mechanism for eliciting public preferences was through the creation of the Citizens Council. The establishment of such a body was presaged in the "NHS Plan" (180) (of 2000) which merely stated: *"A new Citizens Council will be established to advise the National Institute for Clinical Excellence on its clinical assessments"*. As a member of the so-called "modernisation action team" that drew up the report I was able to ensure that no specific details were included thus allowing the institute to work out the detailed arrangements that would meet its needs.

³⁷ Tony Culyer, one of dozen of health economist as an academic discipline in the UK, is now Emeritus Professor of Economics at the University of York.

We had already concluded that trying to elicit the public's social values, through conventional opinion polls, would not meet our requirements. Polling would glean the instantaneous — "off the cuff" — views of interviewees without giving them the opportunity to consider, and deliberate with others, about the complex problems that they and we had to confront. Nor, for similar reasons, did we regard focus groups or public meetings as able to meet our requirements. We were, though, impressed by the experience of the Institute for Public Policy Research (181) in the use of citizens' juries as a means of involving the public in decisions about healthcare.



Conventional citizen's juries, comprising 14 to 16 members of the public, consider a particular topic over two to three days. They listen to the evidence of witnesses; they deliberate and discuss; and they then finally draw their conclusions. For NICE's purposes we felt that we needed a larger group and settled on a membership of 30 members as a compromise between a manageable size and an environment where a broader range of participants could participate.

We developed a set of principles to enable the council to fulfill its purpose:

1. The membership of the council was to be broadly representative of the population of England and Wales in respect of age, gender and socio-economic status.
2. Councilors should serve for only three years in order that its membership can be refreshed.
3. Healthcare professionals were excluded to avoid the possibility that they would be unduly influential in the council's deliberations.
4. The council meetings should be independently facilitated to ensure that the institute and its staff would not inadvertently influence the discussions and conclusions.
5. The question asked of the Council, at each meeting, was to be determined by the institute.
6. At the start of each meeting, a senior member of NICE's staff would explain the question and the reasons why it was important to the institute. The council would hear from witnesses (both internal and external) with expertise in the topic. Council members then had an opportunity to ask questions and deliberate among themselves.
7. A professional writer would be present throughout the meeting and prepare the council's report. This would be circulated, afterwards, to members so that they had an opportunity to agree the final version.
8. The final report was circulated widely so that interested parties (including the media) could have an opportunity to comment.
9. Two members of the council presented the report to the board of the institute at one of its public meetings.

In addition the institute commissioned an ethnographic study into the operation and workings of the first three council meetings by a team of academic social scientists. Their report was subsequently published as a book. (182)

The topics considered by the Council can be seen in Table 2. They covered a wide range of issues on which the Institute needed advice. The Council's conclusions from its first three meetings were encapsulated in a document (published in 2005) entitled *"Social value judgements: principles for the development of NICE guidance"*. The document was updated in 2008 to take account of the results of further deliberations by the council. (183) A further revision is currently in progress. As is explained in its introduction: *"All NICE guidance, and the procedures NICE uses to develop its guidance, should be in line with the institute's legal obligations and the social value principles set out in this document. If any parts of NICE's guidance do not conform to these principles, NICE and its advisory bodies should identify them and explain the reasons why."* A summary of the 8 principles within *"Social value judgements: principles for the development of NICE guidance"* is shown in Table 3.

The Institute learned three lessons from its experience with the citizens council. First, few members of the general public have ever been engaged in the type of deliberative approach needed to ensure that the institute is provided with appropriate conclusions. Expert facilitation is therefore essential if all members are to make effective contributions. Secondly, members of the public can make real contributions to the development of policy provided they are given sufficient time and that the issues are appropriately explained. At its 2011 meeting (Table 2), for example, councillors grasped the principles of applying discount rates in

assessing benefits and costs over long periods of time. Thirdly, the Institute has had to assume that the views and values of the 30 members of the Council resonate with those of the population of England and Wales. In defence of NICE and the council, however, the point has often been made (184) that the council's conclusions have rarely been seriously challenged in either the professional or lay media or, indeed, by parliament.

Concluding remarks

In its relatively short existence NICE has established processes and procedures that have only very rarely been challenged in the courts. The totality of published NICE guidance now totals over 1,100 items but only four have been considered at judicial review and the courts have quashed none. Its approach to engaging with stakeholders has evolved in a variety of ways leading to the disestablishment of the Partners Council. And it has developed a novel approach – the Citizens Council – to elicit the social values of the people who use – and own – the National Health Service.

TABLE 1 ORGANISATIONS REPRESENTED ON THE PARTNER'S COUNCIL

| | |
|---|---|
| A | Association of the Pharmaceutical Industry |
| | Association of the Healthcare Industries |
| | Academy of Medical Royal Colleges |
| | Arthritis and Musculoskeletal Alliance |
| | Association of Ambulance Services |
| | Association of British Insurers |
| | Association of Directors of Social Services |
| B | Board of Community Health Councils in Wales |
| | Black Health Agency |
| | British Dietetic Association |
| | British Dental Association |
| | British Medical Association |
| | British Psychological Society |
| C | British United Provident Association |
| | Carers UK |
| | Chartered Institute for Environmental Health |
| | Chartered Society of Physiotherapy |
| | College of Occupational Therapists |
| E | Community Practitioners and Health Visitors Association |
| | Equalities, National Council of Disabled People (BMEC) |
| F | Faculty of Dental Surgery |
| | Faculty of Pharmaceutical Medicine |
| | Faculty of Public Health |
| | Former member, Citizens Council |
| I | Independent Healthcare Advisory Services |
| | Institute for Quality Assurance |

N

National Consumer Council
National Federation of Women's Institutes
National Health Service Confederation

P

Princess Royal Carers for Trust

R

Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of Midwives
Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Ophthalmologists
Royal College of Paediatrics and Child Health
Royal College of Pathologist
Royal College of Physicians of London
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Speech & Language Therapists
Royal College of Surgeons of England
Royal Institute of Public Health
Royal Pharmaceutical Society of Great Britain

U

Unison
United Kingdom Public Health Association

TABLE 2 CITIZENS COUNCIL MEETINGS

| 2002 | 2003 | 2004 | 2005 | 2006 | 2007 |
|--|--|--|---|---|---|
| <i>Clinical Need:</i> What should the National Institute for Clinical Excellence take into account when making decisions about clinical need? | <i>Age:</i> Are there circumstances in which the age of a person should be taken into account when the National Institute for Clinical Excellence is making a decision about how treatments should be used in the NHS? | <i>Confidential Enquiries:</i> What is the Citizens Council's views on the use of patient information obtained from medical records by the National Confidential Enquiries? <i>Ultra orphan Drugs:</i> Should the National Health Service be prepared to pay premium prices for drugs to treat patients with very rare diseases? | <i>Mandatory public health measures:</i> What principles that should govern the imposition of public health measures on the UK population? | <i>Rule of rescue:</i> Is there a preference to save the life of people in imminent danger of dying? <i>Health inequalities:</i> Which of two broad health inequality strategies would be more appropriate for the National Institute for Clinical Excellence to follow? | <i>Only in research:</i> In what circumstances is it justified for the National Institute for Clinical Excellence to recommend that an intervention is used only in the context of research? <i>Patient safety:</i> How should solutions be developed to reduce or prevent harm to patients while under the care of the National Health Service? |

| 2008 | | 2009 | 2010 | 2011 | 2013 | 2014 |
|---|---|--|--|---|---|--|
| <p><i>Quality adjusted life years (QALYs) and severity of disease:</i> Should the National Institute for Clinical Excellence and its advisory bodies take into account the severity of a disease when making decisions?</p> | | <p><i>Innovation:</i> The National Institute for Clinical Excellence's Citizens Council met to discuss innovation in healthcare.</p> | <p><i>Incentives:</i> In what circumstances are incentives to promote individual behaviour change an acceptable way of promoting the health of the public?</p> | <p><i>Discounting:</i> How should the National Institute for Clinical Excellence assess future costs and health benefits?</p> | <p><i>Social Care:</i> What aspects of benefit, cost and need should the National Institute for Clinical Excellence take into account when developing social care guidance?</p> | <p><i>Societal values:</i> Societal values in trade-offs between equity and efficiency</p> |
| | <p><i>Departing from the threshold:</i> In what circumstances should the National Institute for Clinical Excellence recommend interventions where the cost per QALY is above the threshold range of £20–30,000?</p> | <p><i>Smoking and harm reduction:</i> The National Institute for Clinical Excellence's Citizens Council met to discuss smoking and harm reduction.</p> | | | | |

TABLE 3 SUMMARY OF PRINCIPLES IN THE INSTITUTE’S SOCIAL VALUES GUIDELINE

| | |
|---|--|
| <div>PRINCIPLE NUMBER</div> <div>01</div> | <div>STATEMENT</div> <div>NICE should not recommend an intervention if there is no evidence, or not enough evidence, on which to reach a clear decision.</div> |
| <div>PRINCIPLE NUMBER</div> <div>02</div> | <div>STATEMENT</div> <div>Those developing guidance must take into account the relative costs and benefits of interventions when deciding whether or not to recommend them.</div> |
| <div>PRINCIPLE NUMBER</div> <div>03</div> | <div>STATEMENT</div> <div>Decisions should not be based on the evidence of an intervention's costs and benefits alone. NICE must consider other factors including the need to distribute health resources in the fairest way within society.</div> |
| <div>PRINCIPLE NUMBER</div> <div>04</div> | <div>STATEMENT</div> <div>NICE usually expresses the cost-effectiveness of an intervention as the cost (in £) per quality-adjusted life year (QALY) gained. NICE should explain its reasons when deciding that an intervention less than £20,000 per QALY is not cost effective; and when an intervention of more than £30,000 per QALY is cost effective.</div> |

STATEMENT

Although NICE accepts that NHS users will expect to receive treatments to which their condition will respond, this should not impose a requirement on NICE's advisory bodies to recommend interventions that are not effective, or not cost effective enough, to provide the best value to users of the NHS as a whole.

PRINCIPLE NUMBER

05

PRINCIPLE NUMBER

06

STATEMENT

NICE should consider and respond to comments it receives about its draft guidance and make changes where appropriate.

STATEMENT

NICE can recommend that the use of an intervention is restricted to a particular group within the population but only in circumstances relating to fairness or a legal requirement to act in this manner.

PRINCIPLE NUMBER

07

PRINCIPLE NUMBER

08

STATEMENT

When developing guidance or supporting those who put its guidance into practice NICE should actively consider reducing health inequalities including those associated with gender, age, race, disability and socioeconomic status.

WHAT'S IN AND WHAT'S OUT? THE THORNY ISSUE OF THE THRESHOLD

John Appleby



Deciding what services and treatments should be part of a publicly funded health service is hugely important – and very difficult. Choosing ‘what’s in and what’s out’ quite literally involves decisions about life and death; the cost of getting a decision wrong can be measured not just in wasted resources, but in avoidable deaths and lower quality of life. Half a century into the existence of the National Health Service, during which time decisions about what it should provide remained fragmented and obscured, the creation of NICE was a watershed moment. For the first time there was an organisation required to advise the NHS in an explicit way on what it should offer to patients, drawing on evidence of the clinical benefits and the cost-effectiveness of the health care interventions it was to appraise.

NICE was faced with many fundamental technical and social value issues over how it would go about its work. (185) How, for example, was it to define and measure ‘benefits’? What evidence would it need to calculate the cost of achieving such benefits? How would it deal with incomplete and uncertain evidence? Crucially, how was it to make a judgement about whether a health care intervention was cost effective *enough* to merit inclusion in the NHS ‘package’ of care? And indeed, to what extent was the pure issue of cost-effectiveness to be qualified or amended by other criteria?

The empirical, theoretical and practical problems inherent in making the cost-effectiveness criterion a workable proposition has generated considerable debate since NICE’s creation. It has also focussed minds and research efforts on providing NICE not only with a practical solution but one which is acceptable to the public.

NICE's threshold dilemma

It is of course easy enough in theory to specify in general how cost effective an intervention needs to be to qualify for inclusion. In guidance on the principals underpinning its evaluative task first published in 2005 (186) and updated since, NICE has been clear that *'... a health care treatment is said to be 'cost effective' if it gives a greater health gain than could be achieved by using the resources in other ways.'* (187) And again, from its latest 2013 guide on technological appraisal methods, *'A technology can be considered to be cost effective if its health benefits are greater than the opportunity costs of programmes displaced to fund the new technology, in the context of a fixed NHS budget.'* (188)

This view of cost-effectiveness makes sense given the not unreasonable overall objective of the NHS to maximise the health of the population. Within a fixed budget, money is being spent on services that have a variety of levels of cost-effectiveness. So any new intervention should be more cost-effective than the least cost effective that is currently supplied. In other words, NICE effectively works to a threshold (the cost-effectiveness of the least cost effective treatment currently offered by the NHS) against which to test the cost-effectiveness of the intervention being appraised. At the same time this threshold implicitly represents the shadow price of the NHS budget.

Another view of what the threshold could (or should) represent is based not on what the NHS should give up (the least cost effective treatment) given a particular size of budget for the NHS, but on what the *public* are willing to give up in terms of non-health care consumption to gain more of the things that they value from health care — measured in lives saved, pain averted, Quality-Adjusted Life Years

(QALYs) etc. This interpretation of the threshold, however, leads to a problem. Starting with a threshold based on a willingness to pay for a unit of health benefit and applying it to decisions about which treatments fall below or above that threshold — in other words 'in' or 'out' — eventually leads to defining a budget or a total level of spend for the NHS. In other words, setting the threshold — even one based on the views and values of the public — implies setting the budget for the NHS. As Tony Culyer's³⁸ stylised representation of a health system shows (see Box 1), given the health interventions available, their cost-effectiveness and the total spend on each intervention, the relationship between the threshold and the overall health care budget is clear: setting the budget defines a threshold, and setting the threshold defines a total spend — which could be taken as an indication of what the budget should be. (189)

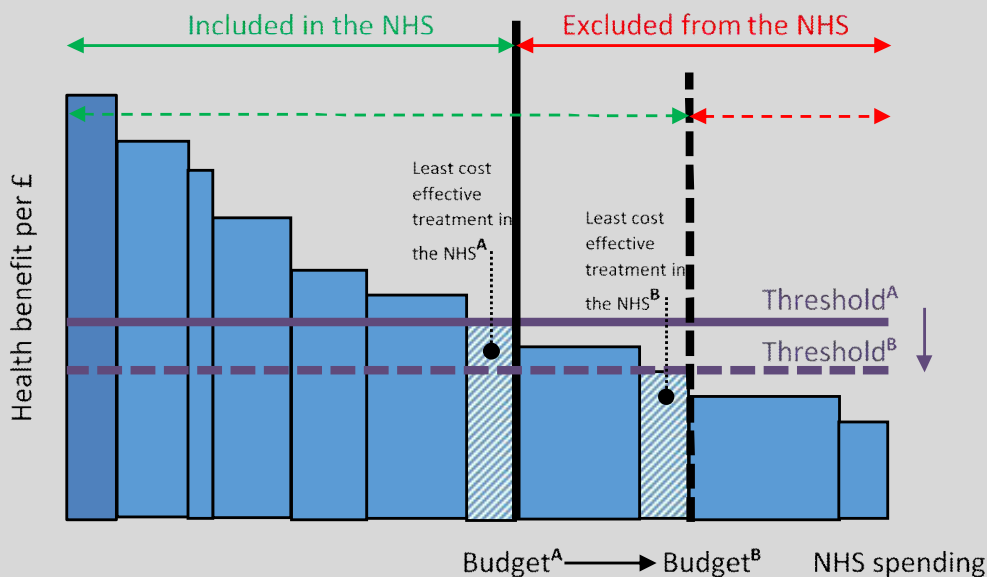
“A technology can be considered to be cost effective if its health benefits are greater than the opportunity costs of programmes displaced to fund the new technology, in the context of a fixed NHS budget.”

³⁸ Anthony Culyer, Emeritus Professor of Economics, Centre for Health Economics and Vice Chair NICE (1999–2003) and currently chair NICE International's Advisory Group

BOX 1 THE COST-EFFECTIVENESS THRESHOLD AND THE BUDGET (190)

Ranking all health care interventions in order of their cost-effectiveness — those producing the greatest effect per pound ranked on the left in the bookshelf-like diagram below where the width of the 'books' shows the total spend on each intervention — helps show the relationship between the budget for the NHS and the implied level of cost-effectiveness that acts as the threshold to decide what the NHS should and should not offer to patients.

In this stylised world where the cost-effectiveness of all possible health care interventions are known, increasing the budget for the NHS from A to B means that there is a new and lower threshold as the extra budget allows the NHS to offer new and effective (if not quite as cost effective) treatments.



Adapted from: Culyer

The inexorable logic that leads from NICE's stated definition of what constitutes a cost effective technology, through to the use of a cost-effectiveness threshold, and on to the link between the threshold and the NHS budget has created a paradoxical problem for NICE. As Culyer et al (191) and others point out, it is not NICE's constitutional position to set the NHS budget. But if it were to set a threshold (to make workable its cost-effectiveness decision criterion) it would in effect be setting the overall budget! No wonder perhaps that NICE states that it '*... has never identified an Incremental Cost-Effectiveness Ratio (ICER) above which interventions should not be recommended and below which they should.*' (192)

Solutions to the threshold dilemma?

So how has NICE managed to use cost-effectiveness as a criterion for making decisions about the worth of health care interventions when to do so seems to imply an impossible role for the organisation? Various solutions to this dilemma have been suggested. For example, it has been suggested that an independent panel set a threshold or threshold range for NICE to work to (not dissimilar to the Bank of England's Monetary Policy Committee tasked with setting the Bank's base rate of interest with the objective of ensuring inflation across the economy remains within certain limits). (193) Given an overall NHS budget set by the government, such an independent group would then have the task of deciding an appropriate cost-effectiveness threshold consistent with that budget which NICE would then use in its appraisals. A not insubstantial problem with this approach, however, is the dearth of evidence about the cost-effectiveness of all the possible interventions the NHS could supply. Given this, an alternative solution has been to recast the problem, with NICE not tasked with setting a threshold but instead adopting the strategies of a 'threshold-searcher'. (194)

In effect, this recognises the problem of the lack of cost-effectiveness evidence (such that it is impossible to rank all interventions as in Culyer's stylised bookshelf analogy) and suggests NICE engages in work and activities that are at least consistent with looking for the least cost effective treatment (which defines

the threshold). Importantly, such work would not just include appraisals of new interventions, but also those currently provided which may be candidates for disinvestment due to relatively poor cost-effectiveness.

In practice, for the technologies it has appraised, NICE has recommended their use, either for the entire licensed population or a subgroup, in around 80 per cent of cases. But as a paper in 2011 by NICE's associate director for research and development and its clinical director showed, in its first decade NICE identified some 800 potential disinvestments. (195) Many of these, however, appeared to be little used, or lacked clear cut evidence of no effect or harm, and the cost of producing the evidence might well outweigh the saving. Furthermore, while the institute has a searchable database of "do not do" interventions, it is ultimately the service itself — its clinicians and commissioners — who take the active decision to disinvest. The evidence of substitution of cost-ineffective interventions by cost-effective ones, driven by NICE guidance, is thin — and evidence of the implied threshold NICE is 'searching' for is only just emerging.

A NICE solution?

Nevertheless, the history of NICE and the threshold is in fact one of a journey involving a pragmatic search for a practical way to meet its objectives. While publicly denying that it referred to a single cost-effectiveness threshold, its own guidance and the decisions it has taken over the course of its existence have revealed a more nuanced approach driven in particular by the experience and the outcomes of NICE appraisal committee decisions.

And it was from the early decisions taken by NICE that, according to Sir Michael Rawlins, started to suggest a threshold of around £30,000 per QALY.

"The £30,000 emerged. I've always said that it's not locked in some empirical basis. It emerged. And it emerged during the first year or two of the appraisal committee meeting. It didn't become enshrined as a formal number until about 2002, 2003, but it was the figure that was emerging from the decisions they were making. There's no empirical research upon which to base it, but increasingly it looked as if this judgement, as you might call it, on behalf of the appraisal committees and particularly the health economic community, is probably around about the right ballpark." Sir Michael Rawlins (Interview with Nicholas Timmins, 2009)

Was £30,000 the 'correct' figure? Did it — going back to Culyer's bookshelf again — match the value of the least cost effective treatment currently on offer from the NHS? There was disagreement from the Department of Health at the time. The department's then chief economist, Clive Smee, thought the threshold was too high in comparison with other things the NHS was providing:

"..when we looked at things like breast cancer screening and tried to work out what a reasonable cost per QALY was, and when we looked at the national service frameworks, broadly we thought £15,000 to £20,000 looked to be all that the NHS in a sense could afford. We did have one or two exchanges about this with NICE in their very early days. We wondered if we should have gone much harder. But we were very keen to get NICE set up and for people not to rock the boat too much. So I didn't push it hard." Clive Smee (Interview with Nicholas Timmins, September, 2015)

On the other hand, as Sir Michael Rawlins points out, the figure seemed to triangulate with other estimates. For example, economists at the University

of York looked at spending on different disease groups — cancer, respiratory disease etc — across the NHS and linked spending patterns to health outcomes. They concluded that while their estimates of a 'cost per life saved' varied across different disease areas and had large confidence intervals, they appeared to be similar to the figure of £30,000 per QALY. (196) The 'emerging threshold' also seemed to triangulate with the alternative interpretation of the threshold based on the willingness to pay for a unit of health benefit. (197) Indeed, the threshold seemed even to align — albeit broadly — with international estimates of willingness to pay for a QALY [see for example, Bobinac et al's estimate of willingness to pay for a QALY for the Netherlands, 2010 (198)].

But the notion that NICE used or should use to a single threshold value was not a position that the institute was comfortable with — either empirically or theoretically.

In 2004 NICE published a guide to the methods it used to appraise health care interventions. (199) The guide — the first NICE produced — stated that

'Although the use of a threshold is inappropriate, comparisons of the most plausible ICER (incremental cost-effectiveness ratio) of a particular technology compared with other programmes currently funded are possible and are a legitimate reference for the Committee.'

As McCabe and colleagues pointed out in 2008, (200) while this sounds somewhat tortuous, — on the one hand eschewing the notion of a threshold while on the other suggesting comparison is inevitable (which it is of course) — the guide went on to define not a single threshold, but rather a range which at certain points would

trigger an appraisal committee to supplement the cost-effectiveness results with other criteria that could inform an eventual 'in/out' decision. (201)

The two trigger points on the range were at £20,000 and £30,000 per QALY. A technology with an ICER at or below the lower limit would in general be considered good value for money with the cost-effectiveness criterion dominating the decision. But above the lower limit an appraisal committee would have to bring to bear other possible justifications if they were to approve an intervention. These included the quality of the economic evidence, the innovative nature of a technology, the particular features of the condition or population receiving the intervention and the wider societal costs and benefits associated with the technology. And justifying the approval of technologies with a cost per QALY exceeding £30,000 would require increasingly strong evidence and arguments in these areas. In addition, while NICE does not formally take into account the budgetary impact of recommending a new health care intervention, in practice it is a consideration — but expressed in a way that gives appraisal committees some scope to make a judgement about what weight to give it in their decision making, viz:

"In general, the Committee will want to be increasingly certain of the cost-effectiveness of a technology as the impact of the adoption of the technology on NHS resources increases. Therefore, the Committee may require more robust evidence on the effectiveness and cost-effectiveness of technologies that are expected to have a large impact on NHS resources." (202)

These guidelines, with a move to a more explicit set of decision criteria in addition to the cost-effectiveness evidence have largely remained unchanged since 2004.

How are decisions actually made?

Over its first few years and since it has become increasingly clear that NICE could not (and did not want to) operate what would amount to a mechanistic approach to its guidance to the NHS. There would be no 'cliff edge' threshold deciding the fate of treatments NICE appraised as it cranked the cost-effectiveness handle. Rather, there would be a range which would invoke the need for NICE to consider the strength of the cost-effectiveness evidence. Importantly, other criteria could also be brought to bear on appraisal committee judgements about the worth of health interventions. But how have these committees actually reached the decisions they have? And what other criteria and information have they considered alongside evidence about cost-effectiveness?

An early attempt to analyse what factors influenced NICE appraisal committee decisions based on 33 evaluations suggested that while cost-effectiveness was the most important factor explaining why a technology was either accepted or rejected, other criteria were also important. In particular, Nancy Devlin and David Parkin found two important things: First, that the probability of *rejecting* a health intervention *increased* as more factors were considered. These included a measure reflecting the uncertainty of the accuracy of the cost-effectiveness evidence and the burden of the disease across the population. Second, they found little evidence to support NICE's threshold 'trigger' points (at £20,000 and £30,000) for considering additional criteria. (203)

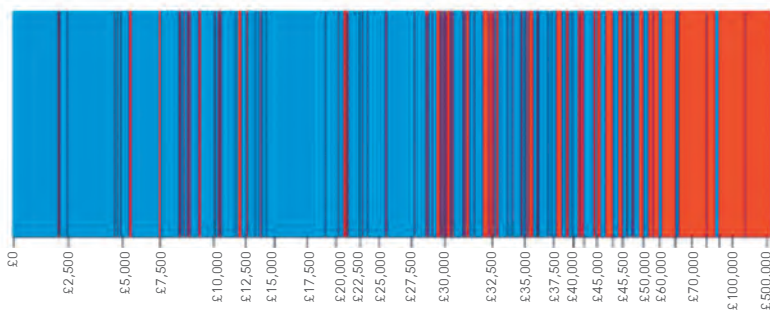
The latest update to this analysis in 2013 has looked at 190 NICE appraisals involving nearly 500 decisions that affected the use of treatments by patients. (204) Once again the research found that cost-effectiveness was the most important criterion driving decisions to reject or accept; over eight out of ten decisions were correctly predicted by cost-effectiveness alone. But this time it seems that the 16 other factors tested were less significant — adding only a few percentage points to the chances of rejection.

However, the research did find that there was a higher probability of acceptance if the intervention being appraised was for musculoskeletal problems or cancer (although these only added a small percentage to the probability of acceptance).

But as Figure 2 shows, while there is a general pattern of increasing probability of rejection as cost per QALY increases, there is little indication of a significant change in the pattern of rejection/acceptance at the trigger points of £20,000 and £30,000 per QALY. On average the threshold point at which there is a greater than 50% chance of rejection starts at around £40,000.

FIGURE 2 IMPACT OF INCREMENTAL COST-EFFECTIVENESS RANKINGS ON DECISIONS TO REJECT OR ACCEPT TECHNOLOGIES APPRAISED BY NICE

FACTORS INFLUENCING NICE DECISIONS



Source: Dakin et al. (205)

While this analysis of the plausible cost per QALY threshold range implied by the actual decisions NICE has made suggests a higher range than NICE state they use, analysis by Claxton and colleagues in 2013 of the threshold implied by the health the NHS generates by doing the things it does is, suggests a threshold value of around £13,000 per QALY. (206)

The implications of this finding are serious. Even at NICE's stated threshold range of £20,000 to £30,000 (although perhaps nearer £40,000 given Dakin et al's analysis of actual decisions) this would mean that some interventions recommended by NICE are less cost effective than existing treatments provided by the NHS. Given a fixed budget, the danger for the NHS is that in order to accommodate NICE's recommendations, some more cost effective interventions may be ousted. Whether and to what extent this has actually happened is hard to tell. The link (if there is one) between the investment decision to adopt a treatment recommended by NICE with a specific *disinvestment* decision by the NHS, and one for which the cost-effectiveness is known, is extremely hard to establish.

Is the NHS budget influenced by the threshold?

Evidence of less cost effective interventions potentially replacing more cost effective treatments is complicated by the fact that the NHS budget has not been fixed but has risen substantially in real terms over most of the time NICE has been in operation. Between 1999 and 2010, spending on the English NHS has more than doubled in real terms. In such a financial environment it has perhaps been easier for the NHS to adopt NICE recommended technologies without having to actively disinvest in existing treatments. Indeed, for many years decisions about the additional costs the NHS would need to bear each year not only included estimates of items such as pay inflation, but also estimates of additional spending arising from the institute's recommendations. Typically, these additional costs were estimated to be around £200 million to £300 million per year — not insubstantial, although representing less than 0.3% of the total NHS budget each year. It would seem that, in a roundabout way, the threshold range used by NICE has influenced decisions about the budget for the NHS and helped attenuate or avoid disinvestment decisions.

But how has the growth in the NHS budget affected the threshold? In practice it has remained essentially unchanged, despite increases in the NHS budget, rising prices and improvements in productivity. In terms of Culyer's bookshelf analogy (Figure 1), other things being equal, it might have been expected that as the NHS budget rose the threshold would become more generous as increasingly less

cost effective treatments become affordable. But NICE's stated threshold range has remained at £20,000 to £30,000. And indeed, as Dakin et al's analysis of actual decisions suggests, the relationship they found between the probability of acceptance of a technology and its cost-effectiveness has hardly changed at all, despite changes in the NHS budget, prices and productivity.

The decision not to change the threshold is understandable however. In an ideal world where all treatments (and their total costs) could be ordered in terms of their cost-effectiveness the NHS budget would be spent first on the most cost effective treatment, then the next most cost effective and so on until the budget ran out (as in Figure 1). And in this world, it is easy to see how changes in the total budget can then justify changes in the threshold (again, as in Figure 1). But back in the real world much of the necessary information is lacking. Not only that, any decision to make the threshold more generous would also have implications for past NICE decisions where interventions were previously rejected. In the circumstances, it is not surprising that the threshold range has remained unchanged.

Are all lives of equal value?

One further factor tested by Dakin et al was the extent to which new "end of life" criteria introduced in 2009 influenced NICE's recommendations. The research suggests there was an impact, and that such interventions were over three times more likely to be accepted than other interventions.

The change in NICE's stance — the results of the recommendations from the Richards review on access to NHS medicines (207) — was controversial. Giving more weight to the benefits certain types of patients received at the end of their lives in effect valued some patients' lives more highly than others. This caused consternation among some appraisal committee members. Since its foundation NICE had taken the view that in the absence of any general agreement about what would constitute a desirable inequality in pursuit of some desired equity objective, then the most ethical stance was not to discriminate on the basis of age, sex, gender, condition or any other patient or condition dimensions.

Nevertheless, in setting out the principles which underpinned its work in its 2008 social values guide, NICE stated that they sought to apply the equity principles that underpin the NHS through an emphasis on 'procedural justice': *"This focused on ensuring that the processes by which healthcare decisions were reached were transparent, and that the reasons for the decisions were explicit."* (208) But as the most recent technology appraisal guidelines make clear, since the decision in 2009, appraisal committees have the discretion, in certain cases, to depart from the view that the value of an additional QALY should be treated the same no matter to whom it accrues. (209)

While in principle a different weighting of the benefits from health interventions to reflect views that certain patient groups or conditions should be treated more or less favourably could be acceptable, the problem is what exactly the discrimination should be. One of the significant criticisms of the cancer drugs fund, for example, is that it has introduced an arbitrary and un-evidenced inequality in the way the NHS and NICE make decisions about the use of scarce health service resources.

“This focused on ensuring that the processes by which healthcare decisions were reached were transparent, and that the reasons for the decisions were explicit.”

Conclusion

The ethical dilemmas and technical difficulties NICE has had to grapple with are not unique to the institute. Any country that decides to make transparent decisions about how to get the best value from their finite public health care system resources will inevitably face similar difficulties. And the creation of NICE did not create the problems and dilemmas that it has had to address over value for money. Rather, it revealed what has traditionally remained hidden, with decisions about what's 'in' and what's 'out' being previously taken by default, and in arbitrary ways which lead to inefficient and inequitable distributions of scarce resources. The actual impact NICE has had on efficiency and equity remains somewhat unquantified, but it is hard to argue that it hasn't helped the NHS at least move in the right direction.

If there is one lesson to be learnt from NICE's experience with the cost-effectiveness threshold it's probably summed up by the phrase, don't let the perfect be the enemy of the good. There is unlikely to ever be enough information and certainty to unambiguously identify the 'true' value for money threshold – and in any case, other things do and should matter than cost-effectiveness. But while NICE has recognised these realities, it has been criticised for being less than transparent about what other factors its appraisal committees consider and the weight they give to all the decision criteria – including cost-effectiveness – in assessing the value of a health care technology (see Dakin et al, endnote 200). Ultimately, while evidence-led, and with cost-effectiveness an important criterion, NICE necessarily needs to exercise judgement in its evaluations. The question for NICE and other such organisations is how to be explicit about these judgements not just in its methodological guidance, but in practice, for real decisions about real technologies.

GLOSSARY

A small glossary for non-English and Welsh readers and indeed for those in the two countries who have not wasted their time trying to follow, particularly since 1991, the endless restructuring of the way the National Health Service in England works.

By way of over-view, the NHS is a tax funded, largely free at the point of use, service. It is crucial to understand that its staff are not, and never have been centrally employed civil servants. Britain's general practitioners — its family doctors — are independent contractors, or employees of independent contracts, operating on an NHS contract while hospital staff have always been employed by the NHS itself, not by central government.

In 1991, a purchaser/provider split, which still exists, was introduced (see pp 10 – 11). Over the years the "purchasing" or "commissioning" has been undertaken, at various times, by health authorities, GP Fundholders, Primary Care Trusts and, now, by Clinical Commissioning Groups and NHS England. This glossary briefly explains their role and the meaning of some other terms used in the text.

Clinical Commissioning Groups. The bodies that currently commission or purchase local health care for their resident populations. Most of the more specialist care is commissioned by NHS England. CCGs are the successors to Primary Care Trusts.

Commons Health Committee. The elected House of Commons has a number of specialist, cross party, committees that undertake inquiries into their field of interest. They have the power to quiz ministers and civil servants, and to call other witnesses.

Employer's National Insurance Contributions. National insurance contributions are sometimes characterised as a "jobs tax" — employers and employees both paying into a system that provides a state pension and entitlement to some other benefits. A small element of national insurance also technically helps fund the NHS.

Exceptional Case Bids. Clinicians and patients have always had a right of appeal to their local funder for treatments that would not normally be funded or which NICE has not approved or recommended against.

GP Fundholder, or fundholder. General practitioners who volunteered to take budgets with which to buy elements of their patients' care between 1991 and 1999.

NHS England. The current commissioners of specialist care, and overseer of commissioning by Clinical Commissioning Groups. It is a body statutorily independent of the department of health which came into existence in 2013. Most the money for treating patients flows through it.

NHS Executive. A body that went through myriad changes of title and function between 1985 and 2013. It was essentially an attempt to separate the management of the NHS from politicians, so that politicians would cease to be responsible for the day to day management of the service.³⁹

Primary Care Trust, or PCT. The health authority-like organisation that undertook purchasing between 1999 and 2012. These evolved out of Primary Care Groups, which were the successors to GP fundholding which ran from 1991 to 1999.

Special Adviser. A personal appointment of the Secretary of State of the day. Special advisers can be civil servants but are more usually a political appointee whose tenure often ends with that of the Secretary of State.

³⁹ For a very brief but fuller account of this body and the way that the NHS had been managed since 1948 see *Glaziers and Window Breakers: The role of the Secretary of State for Health in their own words*. The Health Foundation. 2015. <http://www.health.org.uk/publication/glaziers-and-window-breakers>

POSTSCRIPT

Nicholas Timmins would in particular like to thank, and by way of dedication, Alan Maynard and Tony Culyer who over the years and mainly through conversation and the 'you ought to read this' approach, gave him most of what little grasp he has of Health Economics. And Mike Rawlins and Andrew Dillon who again, over the years, and often on days when they faced multiple media demands, found the time to explain what NICE was up to while always acknowledging the counter arguments. None of the above are responsible for any failure to learn from them.

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“*A blow by blow account of the creation of NICE. The dramatis personae are allowed to tell their own story, which the author reproduces with uncritical endorsement. Indeed, the tone is positively Panglossian – the very best chaps were chosen and they did the best of all possible jobs.*”

Former health economist,
Department of Health

“Injects the pace of a racy thriller into a tale of reform that was in fact taken at the health service’s usual glacial pace.”

Gerry Malone, Minister of Health
in England between 1994 and 1997

“NICE does a vital job in difficult circumstances ... [it] has changed in response to new challenges, and we are sure it can do so again.”

Commons Health Committee, 2008



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“The theory is tough, the science is hard, the economics difficult, and the statistics advanced. The unavoidable trade-offs are often agonizing, much is uncertain, reputations are at stake, and getting things wrong costs lives.”

Anthony J. Culyer in *A Star in the East: A Short History of HITAP*, 2016

“When [NICE] first started to flex its muscles in 1999, the drug industry would love to have exported it, preferably to somewhere like Mars. Ten years later, the influence of NICE, far from being blunted, is beginning to spread. Its methods and organisational model have become something of a beacon to governments wrestling with the issues of efficacy and fairness in healthcare delivery.”

British Medical Journal, 31 January 2009

“Captures not just the policy issues but some of the personal dynamics that lead to success or failure.”

A reviewer of the draft

Health Intervention and Technology Assessment Program (HITAP)

6th Floor, 6th Building, Department of Health,
Ministry of Public Health, Tiwanon Road,
Muang, Nonthaburi 11000, Thailand
Tel: (66) 2590-4549 or (66) 2590-4374-5
E-mail: info@hitap.net
www.hitap.net