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FEATURE



INVESTIGATION

A pill too hard to swallow: how the NHS is limiting access to high priced drugs

A joint investigation by The BMJ and Cambridge and Bath universities uncovers how NHS England tried to limit access to expensive new drugs for hepatitis C. **Jonathan Gornall, Amanda Hoey, and Piotr Ozieranski** report

Jonathan Gornall *freelance journalist*¹, Amanda Hoey *consultant*, Piotr Ozieranski *lecturer*³

¹Suffolk, UK; ²Department of Sociology, University of Cambridge, Cambridge, UK; ³Department of Social and Policy Sciences, University of Bath, Bath, UK

Highly priced medicines are challenging health systems around the world in unprecedented ways. And none more so than the new sofosbuvir based antiviral drugs introduced by Gilead Sciences in 2014. Offering greatly reduced treatment durations and high cure rates, these medicines hold out the real prospect of eliminating hepatitis C in countries where they are widely administered, with all that implies for long term savings in healthcare costs.

But launch of these drugs has ignited a global debate about high priced medicines. With launch prices ranging from around \$90 000 (£69 000; €82 000) per patient in the US to almost £35 000 in England and €41 000 in France,¹ they have sparked a US Senate investigation (box), been raised at both the G7 and G20 summits, and has been a major consideration for to a UN high level panel on access to medicines.

The hepatitis C medicines have intensified tensions between drug companies' duty to put shareholders' interests first and governments with limited health resources. Sofosbuvir is not the first high priced medicine. Many novel cancer medicines provide only marginal benefits but cost over \$100 000 per patient a year. But because hepatitis C affects so many people it has become a pill too hard to swallow for budget planners. Rationing, in their view, became inevitable.

Now there is new evidence about the extent to which hepatitis C treatments have challenged one of the most developed systems for assessing the value of new therapies and delivering them to patients: the NHS and the National Institute for Health and Care Excellence (NICE) in England.

In a joint investigation, *The BMJ* and researchers from the University of Cambridge and the University of Bath, show how NHS England, unable to budget for broad access to these drugs, tried to alter the outcome of the NICE process and, when it failed, defied NICE's authority by rationing access to the drugs.

Our investigation finds that NHS England was unable to adopt innovative funding mechanisms to reduce the price because of NHS procurement law.

In interviews with clinicians, patient groups, and drug company representatives, a picture emerges of how NHS England failed to plan ahead for expensive drugs it knew were in the pipeline, exaggerated the numbers likely to come forward for treatment and the financial burden for them in its submissions to NICE, and, in a "shroud waving" exercise, claimed thousands of other NHS patients would die if NICE gave the go ahead to the hepatitis C drugs.

The case shows how high prices for high prevalence diseases places huge stress on health systems and reveals the limitations of conventional cost effectiveness analysis. Although NICE may deem such medicines to be cost effective, the NHS is ill equipped to deal with the budgetary allocations required. This leads to conflict and damaging delays for patients. It also reveals an urgent need for reform to allow better deal making, transparent pricing, and new payment models, such as the one used to make the hepatitis C drugs available in Australia.

Hepatitis C medicines

By the end of last year, NICE had issued a series of guidelines, including approval for widespread use of two Gilead drugs for hepatitis C. First came sofosbuvir (Sovaldi),² in February 2015, followed by the oral combination ledipasvir-sofosbuvir (Harvoni) in November.³ Competitor treatments from drug companies AbbVie and Bristol-Myers Squibb were also approved.⁴

These drugs should have been widely available to NHS patients after a statutory 90 days.⁵ But for the first time, this has not happened.

Before the NICE process was complete, NHS England took care to ensure that the sickest patients—people with liver failure who might die before the guidelines were issued—were treated. In 2014, it set up an early access programme for patients with advanced liver disease,⁶ followed by a new £150m fund in June 2015 to treat patients with cirrhosis of the liver caused by chronic hepatitis C—nearly 5000 people in total.⁷

But according to Public Health England an estimated 214 000 people have chronic hepatitis C infection in the UK, 160 000 of whom are in England.⁸ Most of them are still waiting for treatment with the drugs that NICE has approved.

In apparent panic over high prices and affordability, NHS England deployed many delaying tactics to block timely access to the hepatitis C drugs. It delayed acting on NICE recommendations on sofosbuvir by requesting a three month extension to implement the guidance, on top of the mandatory 90 days, saying it needed time to set up a proper database to audit patients and use of the new drug.

NHS England went on to try to completely block Harvoni and two other competitor drugs by questioning the level of evidence for the new treatments. NICE prevailed and eventually, in November 2015, published guidance recommending these drugs for the most patients with hepatitis C. But NHS England has restricted use of the new drugs by imposing quotas on clinical teams around the country.

NHS England says its delivery of the drugs is within NICE guidance. Expert clinicians do not agree and are angered by its tactics.

In April 2015, one member of NHS England's six person clinical advisory group, brought together from members of the hepatology and infectious diseases clinical reference groups, resigned in protest at NHS England's attempts to delay access to the treatments.

"I pulled out of the advisory group on principle, because of everything that was going on," said Andrew Ustianowski, a consultant in infectious diseases at Pennine Acute Hospitals NHS Trust. "I didn't want to be associated with what was happening."

There were, he says, "multiple things," but the final straw was an NHS England response to the NICE consultations on the hepatitis C drugs. "They said the advisory group was agreeing that the treatment centres around the country hadn't got the capacity and that's wrong—of course there's capacity to treat more people. I just got to the stage where I didn't want to be associated with delaying patients getting access to the treatments."

Steve Ryder, a hepatologist from Queen's Medical Centre, University of Nottingham, chair of advocacy organisation HCV Action, and a fellow member of the hepatitis advisory group, had other issues with NHS England's submissions to NICE.

"Its position was that the hepatitis C drugs were unaffordable and the figure they quoted in the NICE submission was something like £2bn, which was clearly fantasy," he said. "The assumption to come up with that figure was that you had no discounts on any of the drugs at all and that every single person with hepatitis C in England would come forward that year for treatment, so it was a completely ridiculous standpoint to take."

NHS England is also accused of pursuing the broader agenda of trying to hamper NICE's ability to impose budget busting drugs on the health service, and of having cynically chosen this battleground because most people with hepatitis C infection are from marginalised groups without a voice, such as people who inject drugs.⁸

"The difficulty is that NICE looks at cost effectiveness over a long period and says a drug is cost effective because it's saving people from dying or having problems years down the road," says Ustianowski, "and cost effectiveness is very different from budget impact, which is what NHS England is facing."

As a result, "I think some people in NHS England would love to clip NICE's wings and turn it into a kind of recommendatory rather than mandatory body. And if you are going to choose a fight then choosing this battlefield is quite a sensible thing to do—a marginalised population, very high cost drugs." Once people are infected with hepatitis C, progression of the disease can be slow and transition rates to cirrhosis and liver failure are hard to predict. "People don't have symptoms for years or cirrhosis for decades. So once you've treated the obviously sick and those with cirrhosis, who do you treat next?" says Ustianowski. "I think they've chosen this fight quite well."

Sofosbuvir appraisal—first struggle to delay access

Although NICE's technology appraisal guidance was published in February 2015, an unprecedented delaying tactic by NHS England ensured that sofosbuvir was not available until 1 August 2015, 10 months later than expected by doctors and patients.

This was largely because of NHS England obtaining exemption from its statutory 90 day obligation. In a letter to NICE, dated 19 November 2014, it claimed, in essence, that it wasn't ready to deal with the large numbers of patients expected to come forward for treatment.

Such a request for delay was almost unprecedented, but NICE bowed to it despite almost unanimous opposition from other consulted groups, including the British Association for the Study of the Liver and the British Viral Hepatitis Group, British HIV Association and British Association for Sexual Health and HIV, the British Liver Trust, Haemophilia Society, Royal College of Pathologists, and the Royal College of Physicians. The Department of Health alone thought that NHS England had "put forward a valid case for deferring the funding period."⁹

In its response to NICE, Gilead said NHS England's claims about the numbers of patients were "unsupported by evidence, and all information available to Gilead indicates that they are factually incorrect."

The Hepatitis C Trust pointed out to NICE that NHS England had known about the technology "for at least 18 months" and it would be "unconscionable that patients should be made to wait simply because NHS England has dragged its feet." "If we are going to change our healthcare resource allocation model to one based on the arbitrary consideration of this year's budget," it added, "then this should be debated nationally, preferably through an election manifesto. Either NICE has a mandate to decide resource allocation or it doesn't."

In a joint submission, the British Association for the Study of the Liver and the British Viral Hepatitis Group urged NICE to reject NHS England's plea for delayed implementation. Sofosbuvir was "less complex than existing therapies in many regards" with "significantly less toxicity and drug-interactions ... shorter course therapies [and] significantly better efficacies." Consequently, "we do not believe that any significant extra training, staffing or infrastructure are required for existing treatment centres to adopt this technology. We strongly believe that this technology could be safely and effectively adopted immediately within the structures already in place."

Ustianowski told *The BMJ* that, in his view, "the responses NHS England were giving were to try to delay the process, either to

give it more time to try to work out what to do or, if you're cynical, to push some of the costs into the next financial year." Regardless, NICE yielded. In its published guidance on 25 February 2015, it said that NHS England's request was "based on an arguable case."²

NICE told *The BMJ* that, though "we were not able to follow our normal appraisal timeline in this case, [the] extended process took account of legitimate requests for additional analysis and consideration."

Harvoni—battle over cost effectiveness and budget impact

Gilead's combination treatment Harvoni was the next hepatitis C drug to pass through the NICE system, along with two competitor treatments, AbbVie's ombitasvir-paritaprevir-ritonavir (Viekirax) and Bristol-Myers Squibb's daclatasvir (Daklinza). They were approved in November 2015 but only after what other stakeholders describe as "extraordinary" attempts by NHS England to persuade NICE to reject them.

On 23 March 2015, NHS England responded to NICE's consultation on Harvoni with a document that rang alarm bells, not least with its conclusion that it didn't believe NICE's proposed recommendations were "in the best interest of the NHS at this time."

A covering email noted the response had been prepared by the specialist services commissioning team and, although it incorporates comments from NHS England's expert clinical advisory group, "those comments do not describe a consensus view from the clinical body as this has not been reached due to the variety of issues facing the decision making around hepatitis C."

NHS England tried to stop the appraisals and introduce an 18 month delay by saying a new appraisal was needed to compare all three oral drugs at the same time.

In further correspondence, on 1 April 2015, NHS England estimated that if access to the drugs was given to "all patients of all stages of disease," treatment numbers could range from 7000 to 32 000 patients, at an estimated cost of £285m-£772m a year. NHS England acknowledged the higher estimate of 32 000 patients was unlikely but the figures were based on "international examples" where 40% of known infected patients had accessed treatment.

NHS England commissioned an analysis of budget impact from the Centre for Health Economics at the University of York. This suggested that if £300m were diverted from the existing budget to pay for hepatitis drugs, 1542 lives would be lost across the rest of the NHS. For an investment in hepatitis treatments of £700m, the toll would be 3598 lives, with the biggest toll among patients with circulatory disease (1595), respiratory disease (936), and cancer (262).

These figures were disputed by the patient organisation and other consulted charities. In a joint submission to NICE, the British Society of Gastroenterology, the British Association for the Study of the Liver, the British Viral Hepatitis Group, and the Royal College of Pathologists, contested NHS England's claims about budget impact.

In fact, they wrote, "we contest that the true figures are highly affordable and represent excellent value for NHS England."¹⁰

The clinical bodies added that, in the face of overwhelmingly positive results from trials, NHS England's contention that the evidence for the interventions was inadequate was seriously

flawed, and "at odds" with the consensus reached by its hepatitis C clinical reference group and clinical advisory group.

The signatories clearly saw the subtext of the fight over the hepatitis C drugs as a struggle for power between NHS England and NICE.

"We believe that if upheld," they wrote, "this challenge to NICE by NHS England would fundamentally alter NICE's role and remit. This would potentially lead to a situation where NHS England's veto on the ground of potentially spurious claims of unaffordability would deny not only hepatitis C sufferers but people with other serious clinical conditions access to highly cost effective therapy."¹¹

It is NHS England's ambition, believes Charles Gore, chief executive of the Hepatitis C Trust, "to have NICE neutered. Clearly it wants to get rid of the system; it does not want to have its spend dictated by NICE."

New clinical infrastructure as rationing instrument

NICE eventually recommended Harvoni on 25 November 2015, with the drug in theory becoming available for all indicated patients by the end of February 2016. But NHS England had saved its most extraordinary manoeuvre until the end of its campaign to stall access to the drugs.

In an apparent attempt to build on the success of its early access programme, NHS England announced in March 2016 that it would be "doubling the number of treatments to 10 000 patients in 2016-17."¹² But what the celebratory tone of the press release concealed was that the "commitment" to treat 10 000 patients through 22 new "operational delivery networks" was actually a decision to ration the number of patients they could treat.

The new centres were given a "run rate," the maximum number of patients it would be allowed to treat each month in the financial year 2016-17.¹³ Exceed this number, they were warned, and "the dispensing provider will bear the financial cost of treatment." This approach, NHS England insisted, "will ensure hepatitis C treatment funding is used to maximise the benefit for patients."¹⁴

In fact, the rationing has left many clinicians facing hard decisions and difficult conversations with patients who have seen their treatments delayed several times.

"NHS England's view is that it is down to each network to prioritise patients and it envisaged it would be on severity of liver disease," says Ryder. "But once you've treated all the patients with cirrhosis, that's rather difficult, because by definition everybody else doesn't have serious liver disease yet. It's down to the individual physicians to prioritise and my practice has been pretty much 'Buggins' turn'— if you turn up to clinic early in the month you are more likely to get treatment immediately than if you turn up later."

The run rates, says Ryder, "are set entirely to hit NHS financial targets. For this financial year we are able to treat 10 000 people, which can be easily handled. My own experience is that we have about a third more people who meet the criteria every month than we have [funding] for."

NHS England acknowledged that it considered its "planned roll-out" of the new treatments to be "in line with the NICE guidance," which required networks to prioritise patients with the highest unmet clinical need. Its "commitment" to 10 000 treatments in 2016-17 reflected both modelling used by NICE and "the advice of clinical experts to the NICE committee that

a realistic estimate of patients accessing treatment each year is between 7000 and 10 000.”

Ustianowski, who runs the operational delivery network for Greater Manchester and East Cheshire, says NHS England's “logistical limits” are overstated. His group of five hospitals have been given a total monthly run rate of just 50 patients, which “is hardly anything,” he said. “We could easily do the 50 just in our hospital every month, if not a bit more, but we're better off than some regions ... For example, Sussex and Brighton have something like 180 patients for the whole year, which is absolutely ridiculous. We're grumbling but I think other people should be grumbling even more.”

There is now growing evidence, says Ryder, that some frustrated patients are turning to overseas “buyers' clubs” to source the drugs at their own expense. In November last year one anonymous poster on the NHS website explained that, having been refused access to treatment, “I will now purchase my medication from fixhepc.com which is a legal way to import Harvoni from China, where the drug is sold [for] considerable less cost).”¹⁵

But according to Ryder, some NHS operational delivery networks have been told they should not supervise the treatment of people who do this, “which seems ridiculous and rather spiteful. For one thing it takes the cost off the NHS, so if you're trying to get as many people treated for as little as possible and patients are willing to pay for their own drug, why wouldn't you support them? Co-payment is allowed in cancer treatment, why is it any different in hepatitis C?”

Confronted with this question, NHS England said the issue was “being looked at from a policy perspective.”

Is company pricing to blame?

Faced with the intensifying criticisms, the NHS England highlighted Gilead's pricing as the key reason why treatment was being delayed. A press release issued in March 2016 said that while the NHS had made “the tough prioritisation choices necessary to free up funds to invest significantly in new treatments [drug companies] also need to play their part; quite simply, making faster progress for patients in eliminating this disease will depend on pharmaceutical companies making them more affordable.”¹²

This echoed major criticisms of Gilead's pricing strategy, perhaps best documented in an 18 month investigation by the US Senate Committee on Finance into the pricing and marketing of sofosbuvir and Harvoni in America. The US legislators concluded that the company had adopted a strategy “designed to maximise revenue with little concern for access or affordability.”¹⁶ This was made evident by the company's income jumping from about \$10bn in 2013 to over \$32bn in 2015, a year in which its revenue from Harvoni alone amounted to \$10bn in the US and \$2.2bn in Europe.

So why didn't NHS England strike a better pricing deal with Gilead? It refused to disclose how much it had budgeted for the new hepatitis drugs in 2016-17, “to avoid prejudice to the ongoing tendering processes and commercially confidential prices agreed.” Nor would it say how much it was paying Gilead for the drugs as “the publication of discounts and prices might inhibit reductions that pharmaceutical suppliers to the NHS are prepared to make given their commercial interests in other markets.”

NHS England wasn't able to enter into a risk sharing deal similar to that agreed between Gilead and the Australian government in December 2015. The Australian government announced it

was investing \$A1bn (£600m) over five years “to give all Australians with hepatitis C [estimated at 230 000 people] access to breakthrough cures that could all but eradicate the deadly and debilitating disease within a generation.”¹⁷

A spokesperson for Gilead said such a deal in England had been rejected “on the basis of NHS England's view that it is unable to negotiate with pharmaceutical companies as this sits within the remit of the Commercial Medicines Unit, reporting directly to the Department of Health, which runs regionalised tenders of different time periods.” This is correct. NHS England is unable to broker specific deals with individual drug companies. A spokesperson for NHS England declined to say why it had deemed a deal on the Australian model inappropriate for England but hinted that this could change. Over the next eight months, following discussions with the Commercial Medicines Unit, it was “exploring the potential for a longer term strategic procurement for a supply agreement with the industry to improve the affordability of and access to treatment further.” The organisation would not comment in further detail “to avoid prejudice to the outcome of these discussions.”

“Time, however, is not on the side of many patients and last month the Hepatitis C Trust launched legal action seeking a judicial review of the decision to limit access to the new drugs—a decision which, it says, could have repercussions for other patient groups as increasingly expensive drugs become available.

“It is truly ironic that NHS England should choose to start rationing drugs that are so effective they cure almost everyone who is treated,” said the charity in a statement. “It feels like people with hepatitis C are being picked on.”

Legal action, said its chief executive, was “a very significant financial risk for us but we absolutely have to stand up for the people we are here to support. We do not want to fight the NHS but we will fight for a fair NHS.”¹¹

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