
Cancer Drug Manifesto

The Institute of Cancer Research, London

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- 1. NICE needs to prioritise the most innovative cancer treatments with the greatest potential to deliver step-change advances for patients. That means changing NICE's definition of innovation to promote treatments that tackle cancer in brand new ways.**

We will only make the dramatic advances against cancer that patients need by creating genuinely innovative new drugs with novel mechanisms of action, effective either on their own or in combination with existing treatments. There are approved drugs available for well under 10 per cent of the 500 or so cancer-causing proteins. If we want to make big advances in treating cancer – and to maximise our use of drug combinations – we need drugs against a wider range of targets. At the moment, we are not seeing sufficient numbers of genuinely innovative cancer treatments – too many of the drugs under development have similar mechanisms of action to others already on the market, and offer only incremental benefits. We need the drug evaluation system to properly recognise innovation, to incentivise companies to take on higher-risk projects that can deliver step changes in outcomes for patients. That means making it easier for the most innovative drugs to be approved for NHS patients.

Currently, NICE primarily sees innovation as a measure of how much more effective a drug is than existing treatments for a disease. This definition is too narrow and fails to encourage the development of genuinely innovative drugs that could help overcome drug resistance either on their own or in combinations that act against several different targets. We need a shared recognition of what a highly innovative treatment looks like, so regulators like NICE get better at assessing whether a cancer drug is innovative in its design, its target, the diseases it is effective against, or the way it is used or delivered. Drugs with a brand-new mechanism of action should be regarded as particularly innovative, and where possible fast tracked for NHS use.

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- 2. We need radical action to bring down the extremely high prices of modern cancer drugs, allowing as many patients as possible to benefit from advances in cancer treatment while not overburdening the NHS.**

We believe there are fundamental problems with the way that cancer drugs are priced – and as a consequence, many innovative new medicines end up being unaffordable for healthcare providers like the NHS. Drugs are commonly priced at the limit of what the market can bear rather than reflecting the true costs of development or the level of benefit they deliver. This is both unsustainable for healthcare providers and a bad use of taxpayers' money. We need pharmaceutical companies to come to the negotiating table with their best price early in discussions to avoid delays to patient access during disputes over costs. And we need to pilot new ways to price drugs that better reflect the benefits they have for patients.

The Government, NICE and the pharmaceutical industry must agree on a new approach to pricing, setting a fair price for each drug that takes into account the need for a return on investment without pushing healthcare systems to the limits of what they can afford. We need to explore new approaches to pricing that will deliver value for money for the NHS. One potential approach is outcomes-based pricing, where the NHS would pay for success in achieving a set outcome such as a defined delay in tumour growth. Another approach might allow the first drug that comes to market in a class of compounds to cap the price for that group of drugs. Any drugs developed later with a similar mechanism of action would then have to be priced lower, bringing down the cost of treatment over time and incentivising companies to develop novel treatments. Or companies could charge different prices for drugs when used in different diseases, which might give more flexibility to get drugs approved in multiple indications.

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- 3. We need to fully embrace personalised medicine by developing a test for every drug developed. Better access to ‘biomarker’ tests can ensure modern targeted drugs are directed at those who will benefit – which is better for patients and more efficient for the NHS.**

Precision cancer medicine relies on using tests to select the right patients for a new treatment or to give doctors early warning of whether or not a drug is working. We believe that these ‘biomarker’ tests hold the key to personalising medicine and addressing the spiralling costs of new cancer drugs for the NHS. We need to see regulations and funding mechanisms that encourage the development and use of biomarkers – in research, clinical trials and routine patient care. Ultimately, we believe that every new precision medicine should be accompanied by a new test to guide treatment – ideally developed alongside the drug, and if not as soon as possible afterwards.

The creation of tests to guide and monitor treatment is an exciting and constantly evolving area of science. We need clinical trial regulators, researchers and funders to keep pace with advances – to bring smarter treatment to patients as quickly and cheaply as possible. We want to make it as easy as possible to incorporate tests in the design of clinical trials. Researchers should be at least considering the use of a biomarker in every relevant new clinical trial for cancer. And we would urge pharmaceutical companies and funding bodies to fully recognise the essential role that biomarker tests play in targeting treatment effectively, and to ensure that their development is funded in grant awards for clinical trials.

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4. We need to test drugs in smaller, smarter clinical trials to generate findings more quickly and cheaply – giving the NHS fast access to drugs at affordable prices.

Drugs have traditionally needed to be assessed in large-scale phase III clinical trials before being approved for use – but these are extremely expensive to run and often take years to produce robust evidence. We now have the technology and expertise to conduct smaller, smarter clinical trials that target drugs at patients most likely to benefit. It is vital that we make use of these new types of trial as much as possible, to get new treatments to patients more quickly and at a price that healthcare systems like the NHS can afford.

Intelligent trial design, making use of predictive tests to direct new treatments to specific groups of patients, can significantly speed up the development of new cancer therapies. By selecting patients that are more likely to benefit from a new treatment, we can generate evidence that new drugs are beneficial more quickly and with smaller groups of patients. Adaptive trials can also be modified during the trial, depending on how well a treatment works in the early stages. Doctors can then change a patient's treatment and learn about the new drug as part of the same trial without having to invest time and money in getting a new trial set up.

We need academics, drug companies and regulators to work together to ensure as many new cancer drugs as possible are tested in smarter, personalised trials – and that the evidence from these smaller studies is allowed to be used in a drug's approval. When costs are reduced by using intelligent trial designs, it is essential that companies pass on these savings to the NHS, so that both industry and the public benefit from a more sustainable drug development system.

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5. We need to incentivise pharmaceutical companies to trial new medicines in novel combinations – including with other drugs manufactured by commercial rivals.

We need to make it easier to test cancer drugs in combination where they often have the best chances of being effective. Using combination treatments that attack cancer in multiple ways at once can make it harder for the disease to evolve drug resistance – just as is also the case with treatments for diseases such as tuberculosis and HIV. However, there are currently significant commercial barriers to getting drugs tested together in clinical trials.

Companies can be unwilling to collaborate in testing out combination treatments because of competition for profits and the reduced commercial benefits of providing a drug alongside a partner. Once a drug has been licensed on its own, its manufacturer will not always invest in clinical trials to prove that the drug can work even more effectively in combination with other treatments, leaving the burden of running these trials to academic institutions. Companies are legally unable to work together to price a drug combination sensibly, or to reduce the costs of drugs solely when used in combination. Given how expensive individual drugs are, it is unsurprising that combinations can prove unaffordable for the NHS.

We need to explore imaginative solutions to removing the barriers in taking combination treatments to patients – such as incentivising research through tax credits or introducing new pricing mechanisms for drug combinations. Initiatives such as these could help in bringing potentially life-saving combination treatments to patients more quickly.

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6. Drug regulators need to be more flexible in assessing evidence, so that innovative new treatments can reach patients as quickly as possible.

It takes much too long for the most innovative drugs to reach patients. In part, that is because drug regulators and bodies such as NICE have needed to see evidence of increases in overall survival from large-scale phase III clinical trials before approving drugs. More recently, these organisations have started to show more flexibility, but we can still do much better in ensuring the most innovative treatments are fast-tracked to patients.

We must increase the variety of measures that regulators can use to judge a drug's effectiveness – including evidence that can be gathered in earlier-phase clinical trials. Regulators should place more weight on measures such as patients' health-related quality of life and their progression-free survival – the amount of time a drug prevents the cancer from progressing. We support adaptive licencing approaches in which drugs are approved based on measures such as these and only analyse overall survival data at a later stage – allowing drugs to become available to patients much more quickly after the completion of smaller, phase II trials.

A more flexible approach to demonstrating a drug's effectiveness would be particularly beneficial for rare diseases such as children's cancer, where it is often difficult to find enough patients for trials to show a significant survival advantage. People with rare cancers suffer from a severe lack of new treatment options – so any improvement in bringing new treatments for these patients is likely to lead to major improvements in their outcomes. Survival data can then be provided later from patients being treated in a real-world setting.

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7. We need to ensure all cancer patients have access to suitable clinical trials at all appropriate stages of their disease, irrespective of where they are treated.

Clinical trials are essential to develop new treatments and ensure they are safe and effective. They provide cancer patients with access to the newest treatments ahead of their approval, and are essential to allow the NHS to innovate in the care it offers patients.

We need to make sure that suitable clinical trials are available for every cancer patient who wants to be included on one. That will not only speed up development of new cancer treatments, but should also ensure cancer patients are looked after as well as possible – since there is evidence that trials are the best way of offering state-of-the-art care.

Patients should be able to access suitable trials wherever they are treated – whether in a cancer unit or a specialist cancer centre, and whatever part of the country they live in. Collaborative networks are key to ensure this happens. We also need to make sure that all patients are aware of the clinical trial options available to them, and would urge the creation of a national, comprehensive, patient-friendly database of NHS trials.

We should be bolder too in trialling cancer treatments in patients earlier on in the course of their disease when they are more likely to respond. At the moment, new drugs are normally only trialled in patients with very advanced cancer, who are unlikely to see any major benefit. That can make it harder to spot the potential benefits of new treatments, and denies patients access to drugs at a stage in their disease when they could potentially gain significant benefits from them.

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8. We need to increase access to precision medicine for children with cancer – so they can benefit from the same kind of advances in treatments that adults have.

We need to do much more to ensure that children with cancer benefit from advances in personalised medicine for cancer. Few cancer drugs are developed specifically for children and drugs developed for adults are often only evaluated in children years later, if at all. There are far too few clinical trials being run for children with cancer, and that is preventing children from having access to the latest life-saving or life-extending treatments.

Under European regulations, companies are able to opt out of testing new adult treatments in children if the cancer type for which a drug has been developed does not occur in young people. But this is out of step with our current understanding of cancer – many drugs developed for adults act on mutations that are known to be present in other children's cancers. We are denying children access to medicines that could be effective for them. The current regulation is in urgent need of reform to make it much harder for pharmaceutical companies to opt out of running children's cancer trials.

We also need to provide greater incentives for companies to develop drugs for children. It is far less profitable for companies to produce treatments for children than it is for adults, because the numbers affected are much smaller. But we could persuade companies to prioritise children's cancer by offering longer periods of exclusive marketing time for children's drugs – as in the US – or tax incentives to favour paediatric research.

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9. We must be flexible on the age limits for clinical trials to avoid denying older children and young adults access to new treatments simply because they are judged too young or old.

Older children and younger adults with cancer are too often denied access to clinical trials because they happen to fall on the wrong side of the age cut-off for enrolment. We need to be much more flexible in the way we apply age criteria for clinical trials, so that patients are judged on their individual merits, and not arbitrarily denied access to potentially life-saving treatments.

Our researchers have warned that adolescents and young adults are a 'lost tribe' of cancer patients because cancer research and treatment are rarely tailored for their needs. We believe that once an adult clinical trial has shown that a treatment is sufficiently safe, adolescents and even children as young as 12 should have the option of being included without having to wait for a separate paediatric trial. We would also like to see more flexibility in increasing the age limit for children's cancer trials to include young adults who have paediatric types of cancers.

We believe that decisions to include patients in clinical trials should be made rationally and on an individual basis, based on a drug's mechanism of action and whether the drug's target is present in the patient's cancer. Patients must not be denied access to trials simply on the basis of their age.

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10. We need to incentivise companies, universities and charities to work together to turn research into innovative, medicines for patients.

Academic organisations and companies in the UK still don't collaborate enough to discover and develop cancer drugs. Collaboration between universities and companies is often the fastest and sometimes only way to bring the most exciting discoveries to patients. We need the Government to do more to create a favourable environment for academia and industry to work together and ensure that discoveries reach patients. Companies are less willing to conduct early-stage, high-risk research as they may not see a return on their investment. The lack of funding to bridge scientific research discoveries to the clinic has opened up a 'valley of death' for new therapeutic ideas.

The Government can encourage collaboration by offering tax incentives to companies that work with universities and charities to develop innovative products and encouraging translational research activities in collaboration with industry.

We also need to remove current barriers to universities working with companies. Current rules around tax credits and VAT on academic buildings need to reflect the increasingly collaborative nature of research and innovation. There are restrictions on when companies are eligible for tax credits when working with academic organisations, and VAT is currently charged on new buildings where academia and industry will work together but not on buildings only for academic use, which may disincentivise collaborations. Tax arrangements that remove barriers for businesses to work with universities would help speed up access to new discoveries.