

# NICEimpact *cancer*



# NICE impact cancer

**One in 2 people** will be diagnosed with cancer in their lifetime, and the disease is responsible for more than a quarter of all deaths in the UK. This report considers how NICE's evidence-based guidance might contribute to improvements in the diagnosis and treatment of cancer.



## **Cancer referrals** p4

The annual number of people being urgently referred to a specialist has increased since the publication of the NICE guideline on suspected cancer: there were over 300,000 more urgent referrals in 2016/17 than in 2014/15. However, there is still wide variation across England in the percentage of people whose cancer is detected early, at stage 1 or 2.



## **Cancer medicines** p6

Prescribing data for medicines used for treating melanoma and prostate cancer show the same pattern: new medicines which are more effective, more convenient to take or with fewer side effects than existing medicines show increased prescribing following a NICE recommendation.



## **Access to new medicines** p12

The reformed Cancer Drugs Fund (CDF) gives fast access to cancer treatments, and makes promising new medicines available while more evidence is gathered. By November 2017, NICE had recommended 11 promising treatments for use within the CDF. We have also rapidly reconsidered 11 treatments in the previous fund and recommended them for routine use in the NHS.



## **Commentary** p17

Professor Chris Harrison reviews recent achievements and considers NICE's role in contributing to the further transformation of cancer care.

## Why focus on cancer?

Our new NICEimpact reports review how NICE recommendations for evidence-based and cost-effective care are being used in priority areas of the health and care system, helping to improve outcomes where this is needed most.

NICE provides evidence-based guidance and advice to improve health and social care services. The uptake of NICE guidance is influenced by close relationships with our partners in the system. The [NHS Five Year Forward View](#) identified that improving outcomes for people with cancer is one of the top priorities for the NHS and so, in this report, we have focused on what we know about the uptake and impact of our recommendations in this area.

The Forward View highlights that cancer survival in England remains below the European average and suggests that late diagnosis and variation in access to some treatments may be important issues to address. It sets out objectives to deliver better prevention, faster diagnosis and better treatment and care. This report considers how NICE guidance can contribute to the delivery of these objectives.

One of NICE's first technology appraisals was of taxanes for treating ovarian cancer. Published in May 2000, it represented a hugely significant move towards providing equitable access to new and innovative treatments across the NHS. Since then, NICE has produced over 230 evidence-based guidelines, quality standards and technology appraisals aimed at improving outcomes for the almost 300,000 people diagnosed with cancer each year.

We routinely look for data which give us information about the uptake of our guidance. In this report, we have focused on data which tell us about the uptake of the NICE guideline on suspected cancer and guidance published by our technology appraisal programme. These data help us understand how our recommendations might be making a difference to the care and treatment people with cancer receive. They also highlight areas where there remains room for improvement.

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## Cancer referrals

The annual number of people being urgently referred to a specialist has increased since the publication of NICE's guideline on suspected cancer: there were over 300,000 more urgent referrals in 2016/17 than in 2014/15.

More people with cancer reported being referred to a specialist without having to visit their GP 3 or more times.

There is wide variation across England in the percentage of people whose cancer is detected at stage 1 or 2.

Early referrals to a specialist are important because the sooner a diagnosis is made, the greater the chances of survival for a longer period of time. The number of urgent referrals has increased over the past 3 years, one of several important factors in the early diagnosis of people with cancer.

In June 2015, NICE published an updated guideline on [suspected cancer: recognition and referral](#). This guideline focuses on the symptoms that a patient might experience and go to their GP with. Data from the Office for National Statistics on [cancer survival by stage at diagnosis](#) for the 3 most common cancers in England show the importance of identifying cancer early. People who have their cancer diagnosed at stage 1 are much more likely to survive for a year than those diagnosed at stage 4. The identification of people with suspected cancer usually happens in primary care, and the NICE guideline clearly identifies those symptoms which should trigger an urgent referral.



**People who have their cancer diagnosed at stage 1 are much more likely to survive for a year than those diagnosed at stage 4.**

### One-year survival by stage at diagnosis in England, 2015

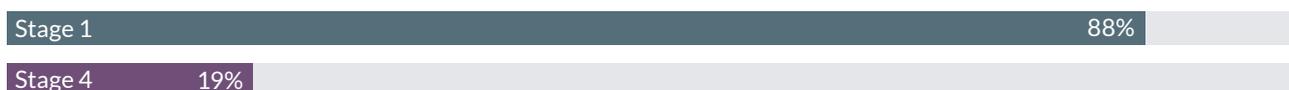
#### Breast cancer



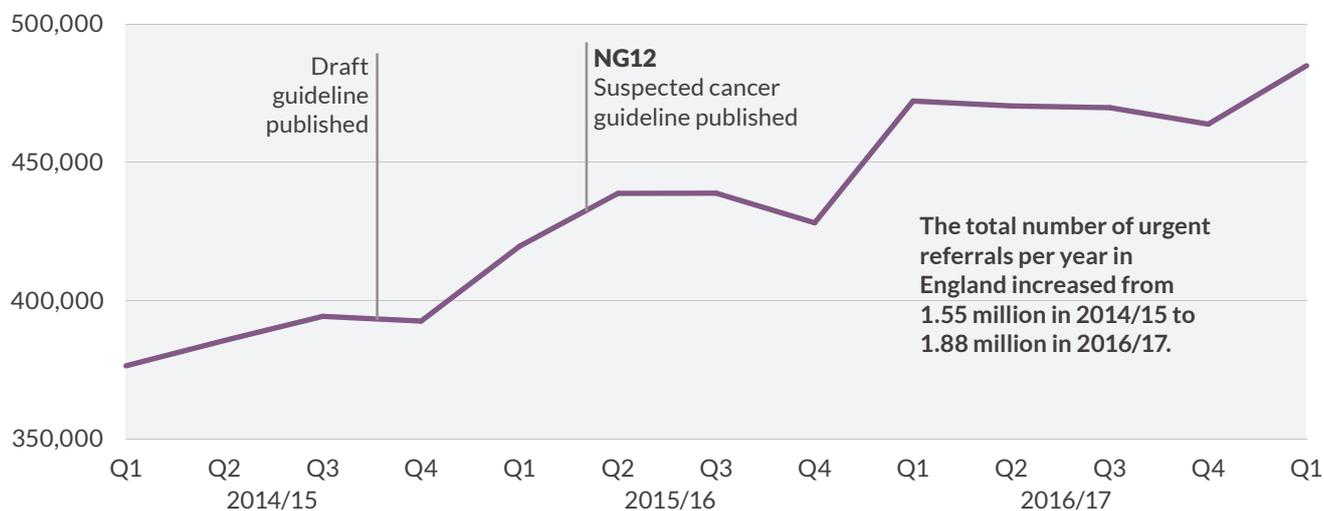
#### Prostate cancer



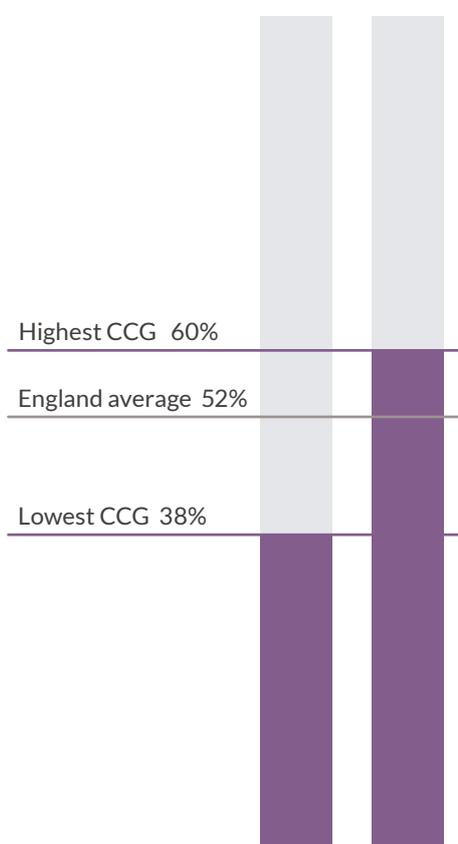
#### Lung cancer



### Urgent (2 week wait) referrals for suspected cancer in England



### Percentage of people whose cancer is detected at stage 1 or 2 in England, 2015



The [National Cancer Patient Experience Survey](#) records the number of people who say that they saw their GP only once or twice about the health problem caused by their cancer before they needed to go to hospital. Between 2014 and 2016 this increased slightly, from 75% to 77%. This suggests that fewer people with a cancer diagnosis visited their GP 3 or more times with symptoms which warrant a referral.

GP referrals are just one of the elements contributing to early diagnosis of people with cancer. The Independent Cancer Taskforce report [Achieving World-Class Cancer Outcomes](#) highlights other important elements, including access to screening and public awareness of symptoms. The report argues that late diagnosis is one of the major factors explaining England's poorer outcomes when compared to countries with similar wealth and universal health coverage such as Sweden, Australia and Canada.

Rates of early diagnosis are monitored in the [NHS Outcomes Framework](#). This records the percentage of people whose cancer is detected at stage 1 or 2, giving them the best chance of successful treatment. The national percentage has slightly increased overall, from 51% in 2014 to 52% in 2015. However, there is wide variation across the country. This suggests that there is room for improvement in early diagnosis in many parts of England.

# Cancer medicines

NICE has a vital role to play in ensuring that all patients have access to the most clinically- and cost-effective treatments. Patterns of prescribing for cancer medicines used for treating prostate cancer and melanoma show that access to new medicines increases after a NICE recommendation.

NICE recommendations are based on both clinical and economic evidence:



**Clinical evidence** shows how well the medicine works.

**Economic evidence** shows whether it represents value for money to the NHS.



The NICE [technology appraisal programme](#) assesses the clinical- and cost-effectiveness of new medicines, significant licence extensions and other health technologies. This is to ensure that all NHS patients have equitable access to the most clinically- and cost-effective treatments that are available.

The NHS is legally obliged to fund and resource medicines and treatments recommended by NICE's technology appraisals.

Since April 2016, it has been agreed that all new cancer medicines and significant new licenced indications will be appraised by NICE.

In 2009, growing concern about access to new cancer medicines led NICE, with the agreement of the Government, to introduce additional flexibility when appraising medicines that extend survival in patients with short life expectancy. This extended the cost-effectiveness threshold for 'end of life' treatments which was, and remains, controversial. As well as questioning whether a medicine can be regarded as cost-effective in the NHS at the increased threshold, critics argue that other life-limiting diseases and conditions, with which people live for long periods with very poor quality of life, deserve similar consideration.

In this report, we have looked at the prescribing of medicines using data published in the [Innovation Scorecard](#). This reports on the use of medicines and medical technologies which have been recommended by NICE. We have considered appraisals published from 2012 onwards, because the Innovation Scorecard contains prescribing data from April 2012.

The Innovation Scorecard shows total prescribing for each medicine, and many cancer medicines have multiple marketing

## Medicines considered for this report

Cancer medicines appraised by NICE

92

Recommended since January 2012

62

Prescribing data available from the Innovation Scorecard

48

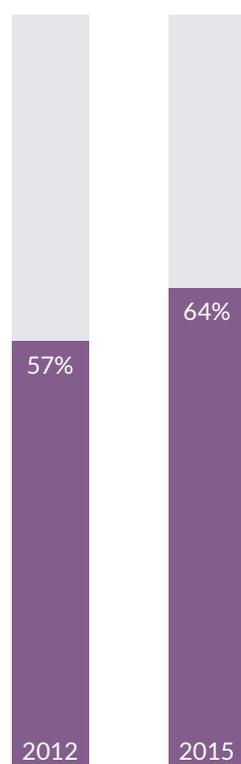
Marketing authorisation for a single indication

19

Enough prescribing data to analyse trends; at least 9 months

15

### Percentage of people with advanced non-small-cell lung cancer receiving systemic anticancer treatment



*The availability of newer, better tolerated medicines can sometimes mean that more people are able to receive treatment.*

authorisations. When medicines have been appraised more than once, or are licensed for indications which have not been appraised by NICE, it can be difficult to see if NICE recommendations have had an effect on prescribing. In this report we have focused on medicines which have marketing authorisation for a single indication, to make it easier to identify prescribing patterns.

NICE recommends medicines as an option for treatment. Looking at prescribing of an individual medicine can be misleading without considering the prescribing of other options for the same indication. We have therefore reviewed the 15 medicines which meet the above criteria and identified 3 groups of medicines for 2 conditions, melanoma and prostate cancer. This enables us to look at patterns of prescribing for a condition.

Many medicines NICE appraises are recommended because they are more effective or have fewer side effects than a current medicine, and sometimes both. The availability of newer, better tolerated medicines can sometimes mean that more people are able to receive treatment. For example, the [National Lung Cancer Audit](#) reports an increase in the percentage of people with advanced non-small-cell lung cancer who received treatment as new medicines with less toxicity became available. NICE has recommended 8 new medicines for this indication since 2012.

The medicines we have looked at in this report, used for treating melanoma and prostate cancer, show similar prescribing patterns in each group. Newer medicines which are more effective or have fewer or less severe side effects show an increase in prescribing when they are recommended.



### Prescribing of cancer medicines: prostate cancer

Prostate cancer is the second most common cancer in England, accounting for around a quarter of all male cancers. [Cancer registration statistics](#) show that there were over 40,000 new cases in 2015, and over 10,000 deaths.

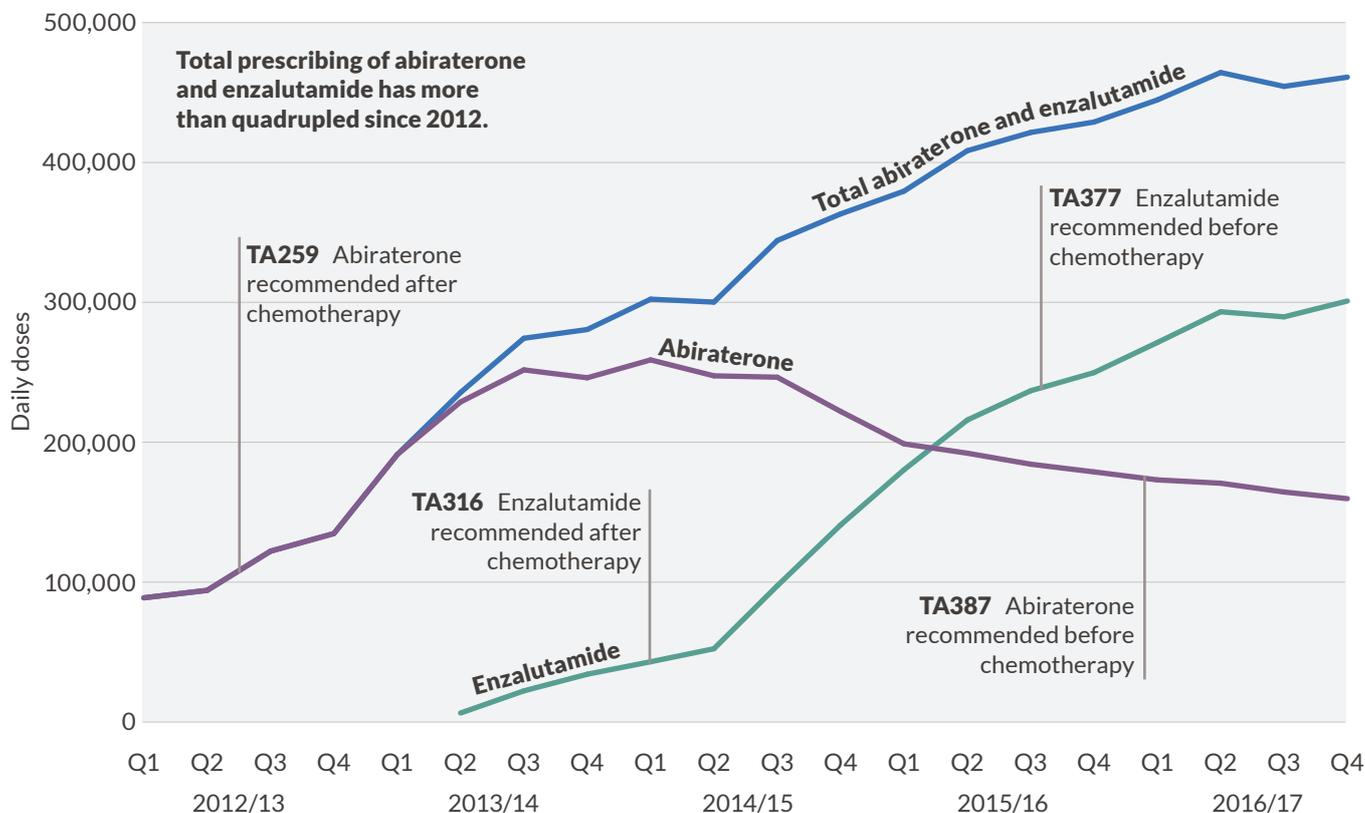
Abiraterone provided a treatment option for people whose cancer had progressed after chemotherapy when it was first recommended by NICE. Enzalutamide, which may be more convenient to take and is less likely to cause liver toxicity, has become more commonly prescribed than abiraterone since being recommended.

Most prostate cancers are either localised or locally advanced at diagnosis. A number of treatments are available, including active surveillance and surgery. Hormone therapy is the usual primary treatment for metastatic prostate cancer. However, if the cancer continues to progress despite standard hormone therapy, treatment options are more limited.

In 2006, NICE recommended [docetaxel](#), a chemotherapy medicine, which became the standard treatment option for hormone-relapsed metastatic prostate cancer. In 2012, NICE recommended a new type of hormone therapy, [abiraterone](#), to be used when the disease had progressed after treatment with docetaxel. Prescribing of abiraterone increased until a new option became available.

[Enzalutamide](#) is similar to abiraterone, but it is less likely to cause liver toxicity and may be more convenient to take for some people. In July 2014, NICE recommended enzalutamide for use after chemotherapy and prescribing of this new option overtook that of abiraterone by early 2015. NICE has since recommended both medicines for use before chemotherapy and total prescribing has more than quadrupled since 2012.

**Prescribing of medicines for treating metastatic hormone-relapsed prostate cancer**





## Prescribing of cancer medicines: melanoma

In 2015, [cancer registration statistics](#) show that there were over 13,000 new cases of malignant melanoma in England, and over 2,000 deaths. Most cases of melanoma are identified early and treated with surgery, and the overall survival rates are among the highest of all cancers. However, for people with advanced or unresectable melanoma, treatment options are limited.



*There were over 13,000 new cases of malignant melanoma in England in 2015, and over 2,000 deaths*

Until 2012, the standard therapy for people with advanced melanoma was dacarbazine, a chemotherapy medicine. However, in the last few years, progress has been made in the development of new and innovative medicines. In December 2012, NICE recommended 2 new medicines for this population, ipilimumab and vemurafenib.

### Immunotherapy

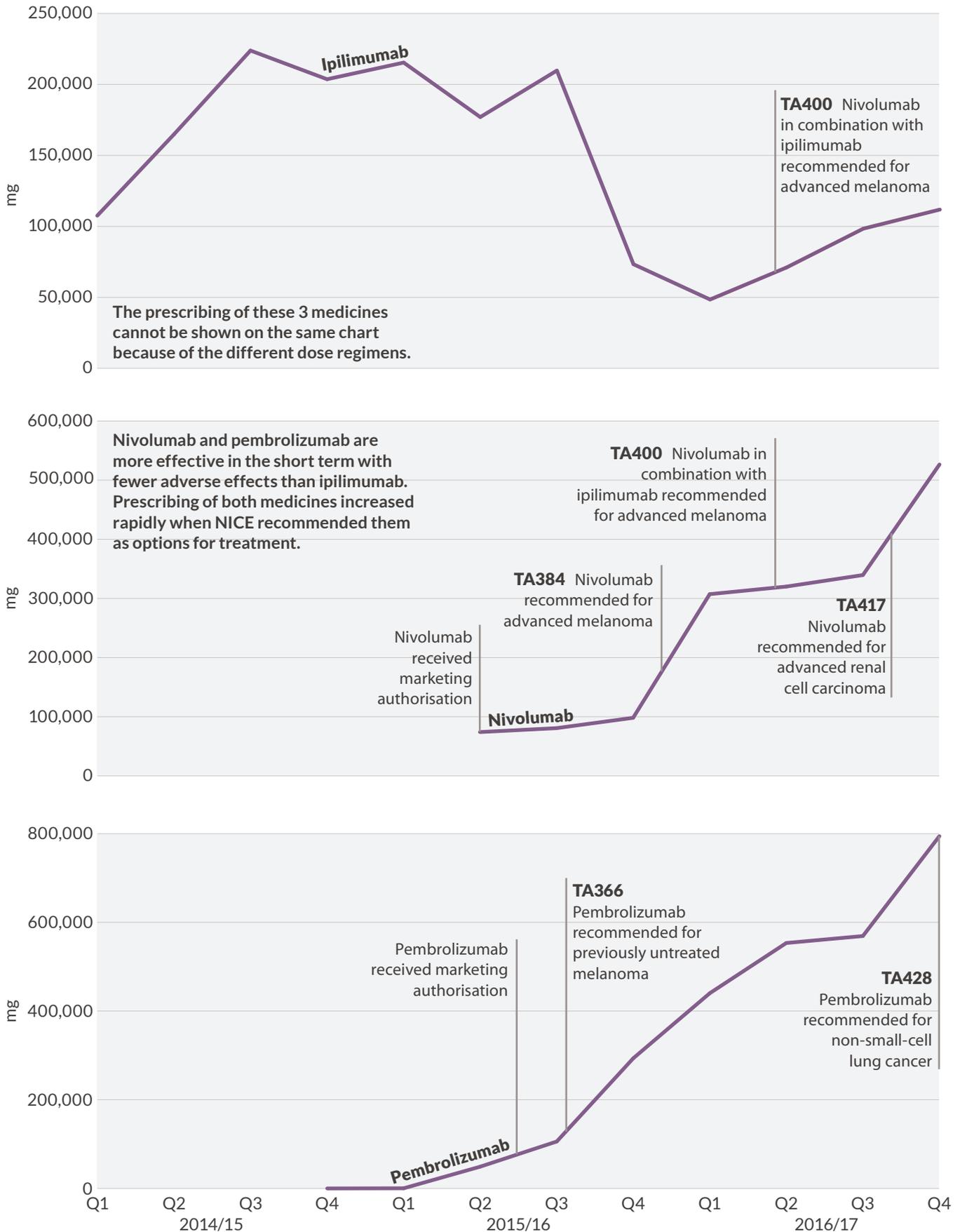
[Ipilimumab](#) triggers the immune system to fight cancer cells. It was recommended by NICE in 2012 for people with advanced, unresectable melanoma after chemotherapy. When the medicine's marketing authorisation was widened, NICE recommended it for use in people who had previously untreated advanced melanoma. Prescribing increased rapidly, from around 87,000 mg a quarter before the NICE recommendation to a peak of more than 215,000 mg between April and June 2015.

In 2015/16, NICE recommended 2 alternative immunotherapy medicines, [nivolumab](#) and [pembrolizumab](#). These medicines are more effective in the short term than ipilimumab, with fewer adverse effects. As can be seen in the prescribing charts, both of the newer medicines saw rapid increases in prescribing as ipilimumab began to decrease. However it should be noted that both were also recommended for other indications towards the end of the time period shown in these charts.

In July 2016, NICE recommended [nivolumab in combination with ipilimumab](#). This option is more effective in the short term than ipilimumab alone for people who can tolerate the combination. Following this recommendation, the prescribing of ipilimumab has once again increased.

*Ipilimumab and vemurafenib were step-changes in the treatment of advanced melanoma when they were launched. Newer alternatives, which are more effective or with fewer side effects, showed rapid uptake when NICE recommended them as options for treatment.*

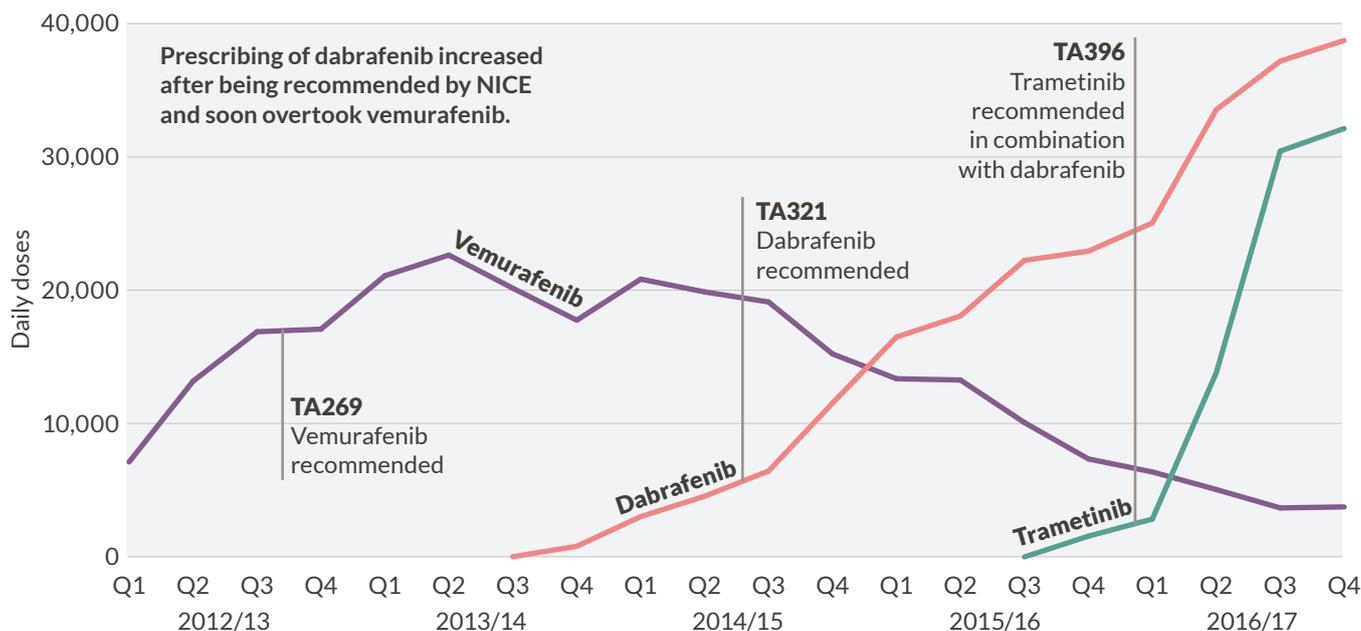
**Prescribing of medicines for treating advanced melanoma**



## BRAF V600 targeted therapy

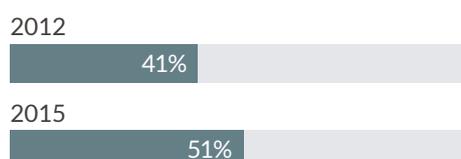
[Vemurafenib](#) was recommended by NICE in December 2012 for treating people with locally advanced or metastatic melanoma with a BRAF V600 mutation. In October 2014, another BRAF V600 inhibitor, [dabrafenib](#), was recommended by NICE. These medicines do not differ in clinical effectiveness, but dabrafenib has a lower incidence of photosensitivity, which may be a major problem for some patients.

### Prescribing of medicines for treating advanced BRAF V600 mutation-positive melanoma



Data from the Office for National Statistics on [cancer survival by stage at diagnosis](#) suggest that the survival of people with advanced melanoma has improved since 2012 when immunotherapy and BRAF V600 targeted medicines were first recommended by NICE.

### Percentage of people diagnosed with melanoma at stage 4 who survive for 1 year after diagnosis



Following the NICE recommendation, prescribing of dabrafenib increased rapidly, and by January 2015 had overtaken vemurafenib. The combined prescribing of these medicines has steadily increased.

Most people with advanced melanoma are now initially treated with immunotherapy, regardless of their BRAF V600 mutation status. However, for patients with rapidly progressing disease, a short life expectancy or poor prognostic features, a BRAF V600 inhibitor may still be the most appropriate medicine. New treatments continue to be developed.

In June 2016, NICE recommended [trametinib in combination with dabrafenib](#). This combination therapy is more effective than therapy with a single medicine, without any increase in adverse effects. Prescribing of trametinib has since increased rapidly. In October 2016, NICE was asked to appraise this combination for treating people with non-small-cell lung cancer with a BRAF V600 mutation.

# Access to new medicines

Through working in partnership with NHS England Specialised Services, NICE is ensuring that new medicines can be accessed more quickly. The Cancer Drugs Fund (CDF) gives fast access to cancer treatments, and makes promising new medicines available while more evidence is gathered.

*By November 2017, NICE had recommended 11 promising treatments for use within the CDF while more evidence is gathered.*

*NICE has rapidly reconsidered 11 treatments in the previous fund and recommended them for routine use in the NHS.*

*Interim funding for cancer medicines which have been granted a marketing authorisation is now available based on a draft recommendation from NICE, before final guidance is published.*

The data in this report show an increase in prescribing of new medicines following a NICE recommendation. However, data from the Office for Life Sciences (OLS) [Life Science Competitiveness Indicators](#) suggest that the overall uptake of new medicines may be slower in the UK than in comparator countries. The OLS compared uptake of a selection of medicines first granted marketing authorisation between 2011 and 2015. The data show that, in the first year of launch, the median relative uptake in the UK compared to the selected other countries was 18%, rising to 79% in year 3.

There are many reasons why uptake of new medicines may vary, and OLS urge extreme caution when performing any analysis of their data because of this. NICE can contribute to faster uptake by more closely aligning the timing of our decisions with the marketing authorisation and launch of new medicines. Over recent years, NICE has made significant improvements in the speed of production of draft and final guidance following a marketing authorisation. In April 2017, a new [fast-track appraisal process](#) was introduced to give faster access to the most cost effective new treatments. For cancer medicines, early access has been made possible by reforms to the [Cancer Drugs Fund](#).

## The Cancer Drugs Fund

In 2011, the UK government set up the CDF, intended to help patients gain access to cancer medicines not routinely available on the NHS. However, the fund came under unsustainable financial pressure and political scrutiny. NICE and NHS England worked in partnership to develop a new model and the reformed CDF was launched in July 2016.

NICE now has the option of recommending medicines for use within the CDF. Previously, if a medicine looked promising but there was not strong enough clinical evidence to show it was cost-effective, NICE had to say no. Now the medicine can be made available through the CDF, with a managed access agreement between the company and NHS England, while more evidence is gathered to help resolve the key areas of clinical uncertainty.



***Promising new cancer medicines can now be recommended for use within the CDF while more evidence is gathered.***

By November 2017, NICE had recommended 11 treatments for use within the CDF. Some of these medicines had previously been recommended for treating different indications, but NICE would not have been able to recommend them for use in the NHS for these new indications without the option of the CDF. However, these recommendations are too recent to allow us to look at any patterns in prescribing.

For most medicines, when NICE recommends a treatment 'as an option', the NHS must make sure it is available within 3 months (unless otherwise specified) of the final guidance publication. As part of the changes to the CDF, interim funding for medicines which have been granted a marketing authorisation is now available based on a draft recommendation, which means faster access to cancer medicines.



***Interim funding for cancer drugs is now available based on a draft recommendation, which means faster access to new treatments.***

NICE now aims to publish draft guidance for cancer medicines prior to marketing authorisation so that interim funding is available as soon as marketing authorisation is granted. For medicines which received a marketing authorisation in 2017, data to November 2017 show that the average time taken to release draft guidance after marketing authorisation for all new medicines was less than 2 months, and less than 1 month for cancer medicines.



### Cancer Drugs Fund: olaratumab

**Olaratumab** is a new medicine which NICE has recommended for use within the CDF. It is used for treating sarcoma, a rare type of cancer that affects tissues that connect, support and surround other body structures and organs. People with advanced soft tissue sarcoma having the current standard treatment, doxorubicin, alone are expected to live for 12 to 16 months after starting treatment. Evidence reviewed during the appraisal of olaratumab suggests that having olaratumab plus doxorubicin increases the length of time people live by a median of 11.8 months. This is potentially a step-change in treatment.



*Evidence suggests that having olaratumab plus doxorubicin increases the length of time people live by a median of 11.8 months. This is potentially a step-change in treatment.*

However, there are not enough long-term data to know the overall length of time people having olaratumab plus doxorubicin live compared with doxorubicin alone. An ongoing trial is expected to address the uncertainty in the data. NICE therefore recommended olaratumab for use within the CDF while further data are collected and around 450 people per year with advanced sarcoma will be eligible for this new

medicine. The company that markets olaratumab has agreed to make it available under special arrangements with NHS England, which will see the medicine funded at a discounted price while data collection continues.

**'I'm excited about being able to try olaratumab. You hear so much about new treatments for other cancers like immunotherapies coming through, and until recently we've had little in the way of new drugs come through for treating sarcoma. Doxorubicin has been used for over 30 years with sarcoma, so having olaratumab fills me with hope. The fact that it can be given for a lengthier period of time makes me hopeful it can keep my tumour under control for longer. My plan is to visit my grandchildren in Australia next spring, and I'm hoping olaratumab will play a part in maintaining a good quality of life and allow me to do this.'** Gill, sarcoma patient

## Medicines from the previous Cancer Drugs Fund

As part of the reforms to the CDF, NICE was asked to carry out 11 rapid reconsiderations of medicines in the previous fund. In many cases, companies were able to supply discounts or additional evidence, allowing NICE to reconsider an original decision that a medicine should not be recommended. All 11 treatments are now recommended for routine use in the NHS.



*NICE has recommended 11 treatments for routine use in the NHS after a rapid reconsideration process.*

The first CDF reconsiderations were of [bosutinib](#) for chronic myeloid leukaemia and [pemetrexed](#) for non-small-cell lung cancer. Pemetrexed is also recommended for many other indications, so we have looked at the prescribing of bosutinib in this report. Since these first reconsiderations, NICE has been able to reconsider and recommend medicines such as [everolimus](#) and [trastuzumab emtansine](#) for treating breast cancer, [crizotinib](#) for treating non-small-cell lung cancer and [cetuximab](#) for treating cancer of the head and neck. These medicines are now in routine use in the NHS, but the recommendations are too recent for prescribing data to be available for this report.



### Cancer Drugs Fund reconsideration: bosutinib

[Bosutinib](#) provides a treatment option for people with chronic myeloid leukaemia (CML) when other medicines no longer work or cause severe side effects. The CDF reconsideration process has allowed NICE to recommend this medicine for routine use in the NHS at an agreed discount. Prescribing has increased rapidly since the NICE recommendation.

Bosutinib was first appraised by NICE in 2013, when it was found to be not cost-effective and was not recommended. It was made available via the CDF until January 2015, when the fund decided not to retain bosutinib for treating blast phase CML. In September 2015 the CDF panel made a decision not to retain bosutinib for treating accelerated phase CML, or for chronic phase CML patients who were resistant to other treatments. However, when NICE reconsidered this medicine in 2016, a discount was agreed with the company which was

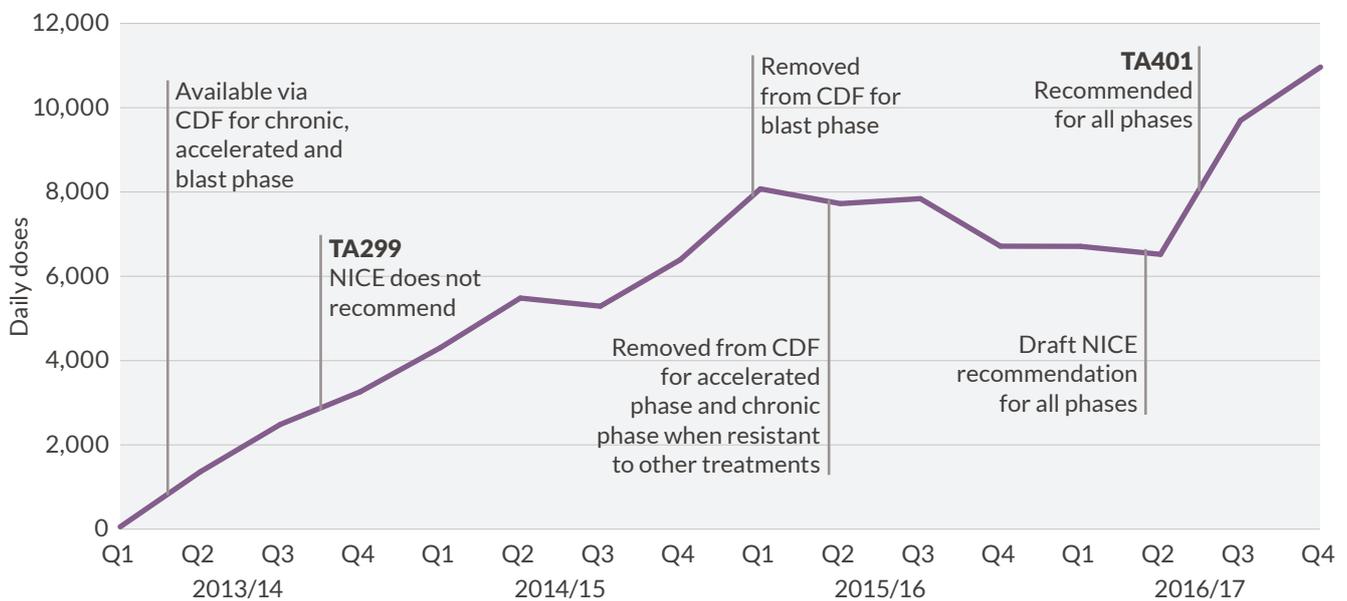
*Bosutinib provides a treatment option for people with chronic myeloid leukaemia when other medicines no longer work or cause severe side effects. The CDF reconsideration process has allowed NICE to recommend this medicine for routine use in the NHS at an agreed discount. Prescribing has increased rapidly since the NICE recommendation.*

**‘Being given access to bosutinib, now through NHS funding, has meant that I am now able to live completely normally and, quite often, even forget I have leukaemia. Having had issues with four other medicines this was my last option but, four years on, my counts are stable and side effects minimal and the fact that I can pop those small pills every day means I can continue working and leading a full life.’** Karen, CML patient

included in the new cost analysis. This allowed NICE to recommend the medicine for routine NHS use in all 3 phases of CML.

Since the NICE recommendation, prescribing of this medicine has increased rapidly. Recommending this medicine for routine use appears to have made it available to many more people.

**Prescribing of bosutinib for treating chronic myeloid leukaemia**



# Commentary

Professor Chris Harrison, December 2017

Professor Chris Harrison is National Clinical Director for Cancer, and Medical Director (Strategy), The Christie NHS Foundation Trust.

The last 3 decades have seen remarkable improvements in cancer care across the UK. In 2016 and 2017 more people survived cancer than ever before. More focus has been put on prevention and many treatments have become less toxic and more personalised.

And yet, as the national cancer strategy for England based on the 96 recommendations from the national cancer task force sets out, there is a lot more to do. We have already been making improvements. Less than 2 years into the 5 year implementation programme we have, amongst other things, made good progress by setting up cancer alliances, replacing and upgrading radiotherapy equipment and designing new models for diagnostic services.

Against this background 2 questions come up a lot: how do we best address the persistently identified differences in cancer survival between UK jurisdictions and comparable countries, and how do we best tackle the persistent inequalities in outcomes and experience of cancer care within our own populations?



***The people leading cancer alliances will need clear, evidence-based information to help make decisions and tackle difficult choices.***

NICE has an important role in helping us to confront these issues and the current report is a significant contribution to this effort. In England, cancer alliances are designed to coordinate and lead service provision and commissioning in a way which ensures seamless care across the multitude of boundaries between organisations within the NHS and beyond into social care, commercial organisations and the third sector. The people leading alliances will need clear, evidence-based information to help make decisions and tackle difficult choices between the potential benefits of interventions for individuals against wider population considerations.

NICE guidelines have contributed to improvements in the identification, diagnosis, management and treatment of cancer. This report shows how guidance from NICE has helped to support GPs to identify those people with symptoms of

cancer and refer sooner than in the past. Fewer patients now have multiple GP visits before referral and more are referred for urgent assessment. Variations still exist and cancer alliances are building on innovations in the cancer vanguard to further support GPs and to develop models for multi-disciplinary diagnostic clinics which provide more rapid assessment for the many patients with less specific symptoms, often those with rarer and harder to diagnose cancers.

The time taken between licensing of new drugs and NICE draft recommendations being available has in the past created the possibility of variation in access where commissioners have had to make their own decisions whilst awaiting recommendations. Through cancer alliances we now have a mechanism for collective decisions to be taken by CCGs and other commissioners but speeding up the process as has been started through the new arrangements for the Cancer Drugs Fund and greater leverage of the purchasing power of the NHS is an important way of reducing inequalities.



***At a time of financial constraints on the NHS, the clarity and timeliness of NICE recommendations become all the more important.***

There is no doubt that NICE guidance is persuasive and this is seen by the increase in uptake of cancer medications following recommendations. At a time when the financial constraints on the NHS are widely acknowledged and choices have to be made, the clarity and timeliness of these recommendations become all the more important. At the coal face, commissioning decisions often need to be taken on the basis of imperfect or developing information. The examples in this report show how NICE can support this process.

The national cancer programme spans the interests and responsibilities of all the Department of Health's arm's length bodies including NICE. All sit round the national Cancer Transformation Board table as it oversees and coordinates implementation of the national strategy. The 19 cancer alliances are the key mechanism for real change to be made on the ground. They will continue to need timely evidence-based guidance on the relative cost-effectiveness of cancer treatments and service organisation if they are to succeed in the job of improving outcomes and reducing inequalities.

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