

The Cancer Drugs Fund of England: improving access to innovative drugs or bypassing HTA informed decision-making?

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List of abbreviations

AWMSG	All Wales Medicines Strategy Group
CDF	Cancer Drugs Fund
GDP	Gross domestic product
HTA	Health Technology Assessment
IFR	Individual funding request
MAA	Managed access agreement
NAO	National Audit Office
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NMF	New Medicines Fund
NTF	New Treatment Fund
OR	Overall survival
PPRS	Pharmaceutical Price Regulation Scheme
QALY	Quality adjusted life year
RCT	Randomized controlled trial
RWE	Real-world evidence
UK	United Kingdom
VBP	Value-based pricing

Abstract

Cancer is among the leading causes of death worldwide, with survival rates in the UK being significantly lower than in comparable countries. In order to address this issue, the government of the UK established the Cancer Drugs Fund (CDF) in England in 2011, with the objective of improving access to cancer treatments by funding drugs that are rejected by NICE for routine use in the National Health Service (NHS). The fund has been reformed into a managed access scheme in 2016, in which it only reimburses drugs for an interim period in between the draft and final NICE recommendation, as well as during a managed access agreement (MAA) period in which clinical uncertainty of promising drugs can be resolved. The fund has been subject to a considerable amount of criticism throughout its existence, i.e. for not properly collecting outcome data, prioritizing cancer over other diseases, and for rewarding the pharmaceutical industry for poor-quality drugs. The renewed CDF has addressed most of these key issues and has benefited over 168,000 patients during its existence. However, there remains criticism by researchers who state that using real-world evidence (RWE) to resolve clinical uncertainty is not reliable. We advocate other countries that wish to implement a similar funding policy to: 1) focus on high unmet clinical need rather than a specific therapeutic area; 2) maintain a holistic view and also invest in other health technologies besides drugs; 3) make use of financial control mechanisms to prevent overspending; 4) collect outcome data in order to determine the impact of the policy; 5) integrate the system in the existing HTA evaluation routine, while collaborating closely with all relevant stakeholders and making use of transparent entry and exit criteria; 6) adhere to robust clinical evidence on cost-effectiveness (e.g. RWE combined with evidence from randomized controlled trials (RCTs) in a conditional reimbursement system. Last, an important lesson that can be learnt from the CDF is to be careful when political actions interfere with reimbursement and regulatory processes, as ultimately HTA informed decision-making maximizes the added value of health technologies to society.

Layman's summary

In the UK, the number of new cancer cases grows strongly each year, and its performance on cancer survival is significantly lower than in comparable countries. Even though a considerable amount of new cancer drugs is being developed, many end up not being reimbursed by the National Health Service (NHS), as they are often determined not to be cost-effective, meaning that they do not demonstrate sufficient added benefit to the healthcare system in relation to the price that is set by the pharmaceutical industry. This has resulted in cancer patient groups in the UK to strongly criticize the methods of NICE, which is the agency that carries out these evaluations.

In 2011, the UK government established the Cancer Drugs Fund (CDF) in England to address these issues. With the former system of the CDF, all drugs that were not recommended by NICE for routine use in the NHS were eligible for funding, which was subject to a considerable amount of criticism; patients suffering from other diseases felt excluded, the fund overspent its budget, it did not collect data on the effectiveness of the funded treatments, and pharmaceutical companies were given an alternative way to market their expensive drugs that were determined not to be cost-effective. In 2016, the fund was reformed and introduced clearer entry and exit rules. In this renewed system, promising drugs that were associated with too weak clinical evidence to be recommended for reimbursement, were funded for a set period of time, while simultaneously the pharmaceutical company could submit supplementary evidence to prove its effectiveness. Additionally, a financial control mechanism was set up to prevent the fund from overspending its budget. Throughout its existence, the fund has helped over 168,000 patients to get access to a cancer treatment.

Some other countries in the UK and in Europe have employed similar policies to the CDF; England's neighboring countries Wales and Northern Ireland, for example, have recently introduced policies that allow access to the same drugs that have an arrangement through the CDF, whereas Scotland established a fund that reimburses drugs for rare diseases on an individual basis. We advocate countries that wish to introduce a similar funding policy to: 1) focus on high unmet clinical need rather than a specific disease to prevent the prioritization of one therapeutic area; 2) not solely focus on reimbursing drugs, but also other health technologies (prevention, surgery, diagnostics, etc.); 3) make use of a financial control mechanism to prevent overspending; 4) collect data on the effectiveness of funded treatments in order to determine the impact of the policy; 5) integrate the policy in the existing evaluation process of cost effectiveness, while collaborating closely with all relevant stakeholders and make use of clear and transparent entry and exit criteria; 6) adhere to robust clinical evidence. In that way, access to innovative drugs will be improved, while simultaneously maximizing the added value for society.

1. Introduction

1.1 Policy background

Cancer is among the leading causes of death worldwide, accounting for approximately 10 million deaths annually (1). In the United Kingdom (UK), survival rates are significantly lower than in comparable countries, which is most likely caused by later ages of diagnosis and poorer access to treatments (2). In addition, the number of new cancer cases in the UK is growing strongly each year, which is partly caused by the development of more advanced diagnostic and screening methods, but is also due to the growing and ageing population (2,3). Even though many new cancer drugs have been developed in recent years, access to these treatments is limited, as many are too expensive for healthcare systems or individual patients (4). Additionally, the added therapeutic benefit of novel cancer drugs is often uncertain, due to an increasing number of drugs being approved via pathways that require less comprehensive evidence (e.g. conditional market authorizations), as well as the increased approval of orphan drugs that are associated with small clinical trials (5–7). These uncertain and weak estimates of added therapeutic benefit restrict the reimbursement of cancer drugs, and thus limit availability in national healthcare systems even further (8). Moreover, treatments intended for small patient groups may fall outside the scope of national Health Technology Assessment (HTA) bodies, who are responsible for making reimbursement recommendations (9). As a result, only a limited number of treatments might be available for patients suffering from a rare (cancer) disease.

To improve access to cancer drugs, the Cancer Drugs Fund (CDF) was introduced in England in 2011. Patients living in other parts of the UK cannot access the fund and are restricted to the national policies in their own country. The purpose of the CDF is to provide a source of funding for earlier access to new cancer drugs, especially for rare cancer types (10,11). The fund was originally established as a temporary solution for patients and clinicians to improve access to cancer drugs that are not routinely available through the National Health Service (NHS). The CDF was supposed to act as a bridge to the proposed value-based pricing (VBP) system, however, when plans for this system were not pursued, the lifetime of the fund was extended. From July 2016, the CDF has changed into a managed access fund, meaning that it only pays for drugs during a set period of time in which they are not yet reviewed for routine use in the NHS by the HTA agency of the UK, the National Institute for Health and Care Excellence (NICE) (10). With this reformed system, patients are able to get access to novel cancer drugs up to five months earlier than previously (12).

Even though the CDF was established with the intention of improving access of valuable cancer treatments, the fund has always been subject to controversy. For example, the public criticized that other countries in the UK could not access the fund, the prioritization of cancer drugs above other

diseases, and the fact that money of taxpayers was used to enhance profits of Big Pharma (13–16). In addition, the CDF did not properly collect outcome data of patients whose treatments were funded by the CDF, meaning that the effectiveness of the fund could not be determined (17). This report addresses the developments of the CDF and explores the transferability of a similar policy to other countries.

1.2 Objectives and methods

This report analyzes the CDF policy in England, in which the content and developments of the policy, the role of stakeholders, and criticism and successes will be discussed. Furthermore, the CDF will be placed in international context by discussing similar policies in other countries, as well as exploring the transferability to other countries. A main source for this analysis was grey literature, such as governmental documents, investigation/evaluation reports, and news articles. Additionally, academic publications were used, which were mainly retrieved via Google Scholar and PubMed using (combinations of) the following keywords: ‘cancer drugs fund’, ‘CDF’, ‘cancer economics’, ‘cancer’, ‘oncology’, ‘NICE’, ‘uncertainty’, ‘cost-effectiveness’, ‘prioritization’, ‘access’. We retrieved literature dating from various years between 2010 and 2022 to ensure that all developments of the fund were captured.

Additionally, a data collection form on the policy is enclosed in the appendix, in which the policy context, policy design, rationale, governance, implementation, and impact of the CDF is concisely summarized. The purpose of this form is to track the developments of the policy regularly, which allows readers to easily understand the implementation and impact of the policy. Ultimately, this facilitates the analysis and discussion of certain policies, which allows exploration of the transferability to other countries.

2. Relevance and scope

2.1 Geographic background of England and the UK

The UK is located in north-western Europe and includes Great Britain (England, Scotland and Wales), the north-eastern part of Ireland, and several small islands in the British Isles, covering approximately 242,500 km² in total (18). Great Britain is surrounded by four seas: the Atlantic Ocean and Irish Sea on the western side, the English Channel on the southern side, and the North Sea on the eastern side. The CDF only applies in England, whereas Scotland, Wales and Northern Ireland make use of different policies to improve access to innovative drugs (see chapter 4.1.1).

The Office for National Statistics estimated the population size in the UK to be 67 million people in 2020, of which 57 million lived in England (18). In 2020, the population density in England was 434 people per km², making it one of the most densely populated countries in Europe. Furthermore, the median age of the population in 2020 was 40.2 years, with the life expectancy at birth in 2018 to 2020 to be 79.3 years for males and 83.1 years for females. The entire UK had a gross domestic product (GDP) of £2,043,373 million in 2020, of which 12.8% was attributed to healthcare (18).

2.2 Prevalence of cancer in the UK

With approximately 85% of the population in the UK living in England, the prevalence of cancer in the UK is representative for the situation in England. Even though progress on the prevention and treatment of cancer has been made in the past years, it remains to be the leading cause of death in the UK (2). The number of new cancer cases per year is estimated to be 514,000 by 2035, in comparison to 385,000 cases in 2018 (2,19). This increase is mainly due to a growing and ageing population, but also due to the development of more advanced diagnostic and screening methods. Ultimately, this will result in a strongly increased burden on the healthcare system.

Approximately 165,000 people in the UK die from cancer every year (19). Survival rates of cancer in the UK are significantly lower than in comparable countries, for reasons that are not completely known, but are thought to be associated with later ages of diagnosis and limited access to suitable treatments (2). Patients that are diagnosed at an early stage of disease have a significantly higher chance of survival. Early diagnosis is therefore crucial in improving the performance on cancer survival, however, it is a complex process in which many factors play a role, such as appropriate diagnostic methods, access to health professionals, but also public awareness and adequate referral of patients by GPs (2). The UK has set several targets to expedite diagnoses and improve waiting times after referral to a specialist or in between treatments. One of the targets states that 85% of patients should start their first cancer treatment within 62 days after urgent GP referral, and for patients who

are referred via an NHS cancer screening service this threshold is set at 90% (20). Figure 1 shows that the performance of both targets has declined over time, with the 85% threshold not being met since 2013/14, whereas the 90% threshold was last achieved in 2017/18.

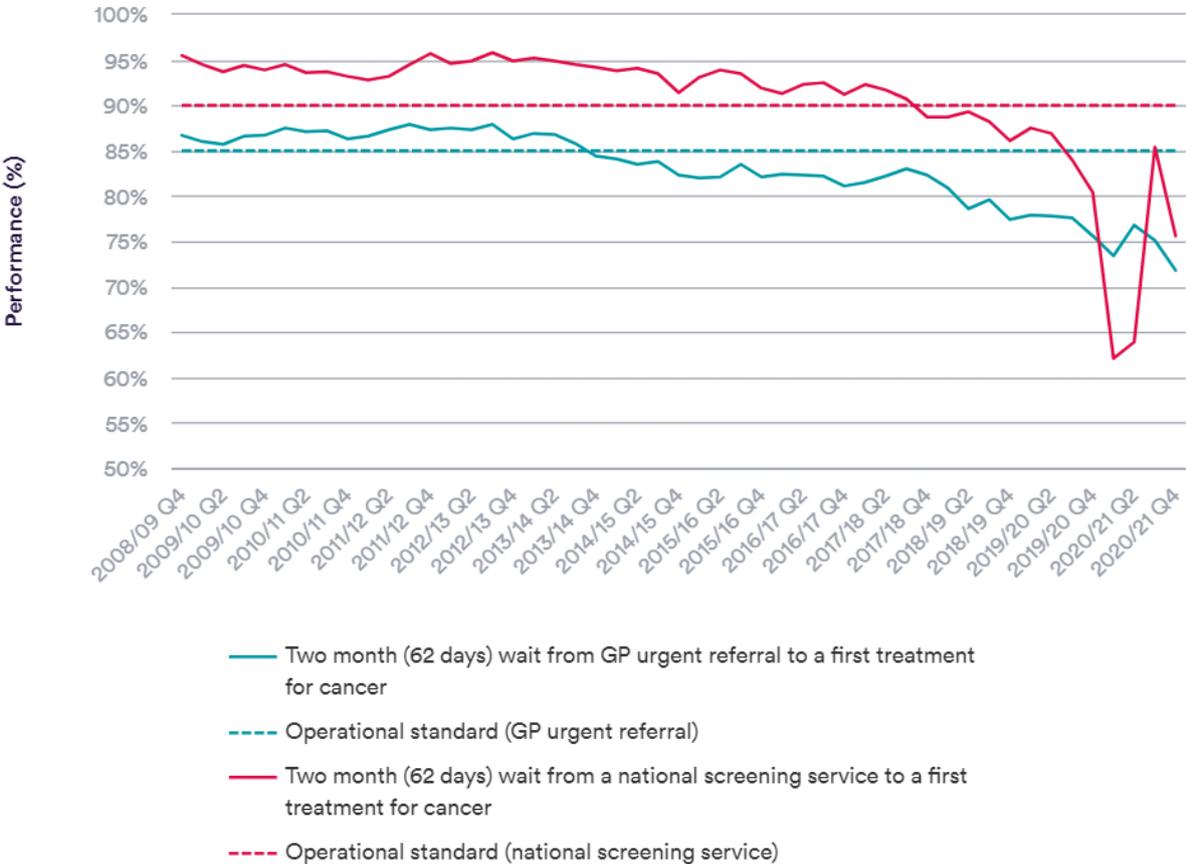


Figure 1: Waiting times for a first treatment after an urgent referral from the GP (blue line) or via a national screening service (red line) (20)

2.3 History of the policy

2.3.1 Former CDF

The CDF was established in England by the government of the UK in April 2011 with the ultimate goal of improving access to cancer drugs in the country. One of the driving forces for the establishment of the fund was a report that was published in July 2010 by the Department of Health’s National Clinical Director for Cancer, which had found the use of new cancer drugs in the UK to be significantly lower than in comparable countries (21). The report stated that the usage of novel cancer drugs in the UK was only 45% of the average of 13 similar European countries (22). In addition, there had been several campaigns at the time by cancer charities that advocated for improved access to cancer drugs, and several cases of patients that were refused a treatment had attracted media attention (21,23). With the Conservative Party winning the 2010 elections, the government of the UK made the commitment to establish a fund for cancer drugs in England (16). Until this proposed fund was officially established,

an interim system was set up for which £50 million was made available to help patients access innovative drugs (21). Meanwhile, a consultation report was published in October 2010, in which the final proposals for the CDF were outlined (21). This report emphasized the fact that numerous cancer drugs were not available due to them not being recommended by NICE because pharmaceutical companies were unable or unwilling to price them in such a manner that they would be regarded as cost-effective. Furthermore, it was also stated that the value of having access to end-of-life care was undervalued in the current system (21). The CDF was initially set up as a temporary system before the Pharmaceutical Price Regulation Scheme (PPRS) was replaced by a new VBP system in 2014, in which drug prices would reflect its value rather than an amount set by the pharmaceutical company. With this new system coming into effect, NICE would consider additional factors in its standard quality adjusted life year (QALY) assessment, such as burden of disease, therapeutic innovation, and wider societal impact (24).

The main principle of the CDF was to give clinicians and cancer specialists the possibility of providing patients access to treatments which were not routinely available through the NHS, if they believed it was their best treatment option. These may include (25):

- drugs that were appraised by NICE, but had not been recommended due to not being cost-effective;
- drugs that were only recommended by NICE to a subset of patients, even though the drug obtained market authorization for a larger patient group;
- drugs which NICE did not yet appraise or which NICE would not appraise at all.

Before 2013, the fund was managed by 10 distinct health authorities from different parts of England. Each of these authorities had its own list of treatments that were available through the fund, resulting in a lot of geographical variation in the degree of access to the fund (21). Since April 2013, however, the CDF became part of the NHS, which introduced a national list of drugs that would be made available through the fund. Besides this list, patients could also send an application for a drug that was not part of the list (21).

Initially, the CDF was assigned with a yearly budget of £200 million, however, it overspent £30 million by the end of 2014, resulting in the budget to be increased to £280 million in 2014/15 and £340 million in 2015/16 (21). Despite this supplementary budget, the CDF still overspent £136 million and £126 million, respectively (14,21). When the proposals for the VBP system were not pursued, the fund was extended further to 2016. From its establishment until March 2015, more than 74.000 cancer patients had received drugs through the CDF. Approximately 1 in 5 patients who started a new

chemotherapy were supported by the CDF, making it part of the conventional cancer care rather than an exceptional resource (21).

2.3.2 Reforming the CDF

Even though the Department of Health had acknowledged the importance of collecting outcome data of patients that received their treatment through the CDF, it was not mandatory for healthcare services until April 2014, resulting in large gaps in the obtained data (17,21). As a result, it was difficult, if not impossible, to evaluate the impact and effectiveness of the CDF in that period, which received a lot of criticism. Along with the fact that the fund continuously exceeded its budget, the Cancer Taskforce, which is part of the NHS, called for an urgent reform of the current CDF in July 2015, as they stated the fund to be "no longer sustainable or desirable [...] in its current form" (21). The former CDF closed in 2016, while NICE and the NHS jointly proposed to reform it into a managed access fund in which it would only pay for drugs during a set period of time before NICE finalized its appraisal, or until clinical uncertainty was resolved for promising drugs. The biggest difference with the former system is that it would no longer pay for drugs that had been appraised but not recommended by NICE. From 2016 onwards, the CDF reformed and became part of the routine NICE process of evaluating novel cancer drugs. With this new system, NICE aspired to speed up the evaluation process by providing a draft recommendation even prior to market authorization. In that way, a novel drug can become available immediately after market authorization, while previously NICE would first have to finalize its recommendation decision. Within 90 days after market authorization, NICE makes one of the following recommendation decisions (see Figure 2) (10,14):

- I. **Yes:** the drug is determined to be cost-effective and should be routinely available through the NHS. After a draft 'Yes' recommendation, the drug will first be available by interim funding through the CDF immediately after the drug has obtained market authorization. After NICE finalized its 'Yes' decision, the drug leaves the CDF and becomes available via routine NHS commissioning.
- II. **No:** the drug is determined not to be cost-effective and should not be routinely available through the NHS. Following a draft 'No' decision, the drug is not available through interim funding. After the final 'No' decision, the drug can only be accessed through an individual funding request (IFR), in cases where a patient is considered to be clinically exceptional.
- III. **Recommended for use within the CDF:** the drug shows promising clinical evidence, but not sufficient for a full 'Yes' decision. After a draft CDF decision, the drug gets interim funding through the CDF immediately after market authorization. If the drug obtains a final CDF decision, it will come into a managed access agreement (MAA) with the pharmaceutical company, in which the drug will be funded via the CDF for a maximum of two years, during

which clinical uncertainty can be resolved through the collection of real-world evidence (RWE). After that period, a final ‘Yes’ or ‘No’ decision must be made. In that way, patients still have the benefits of having quicker access to valuable treatments, while pharmaceutical companies are simultaneously encouraged to resolve the clinical uncertainty, as the drug would otherwise be excluded from both the NHS and the CDF.

These new arrangements introduced clear rules regarding the period that a drug stays within the CDF, which was lacking in the former system. Another important difference with the former model is that NICE now evaluates all drugs that are expected to obtain a market authorization, including treatments for rare cancers (14). In the period between 2016 and 2019, 31 MAAs were made between pharmaceutical companies and the CDF (12). Furthermore, the CDF now makes use of an expenditure control mechanism, meaning that the budget is fixed at an annual amount of £340 million. In the case that the CDF overspends its budget, a proportional rebate will be applied to all pharmaceutical companies that get their drugs funded through the CDF (12). Pharmaceutical companies have to accept the terms of the expenditure control mechanism in order to utilize the interim funding system or the managed access scheme of the CDF (14). If they are unwilling to accept this, they cannot make use of the funding systems of the CDF.

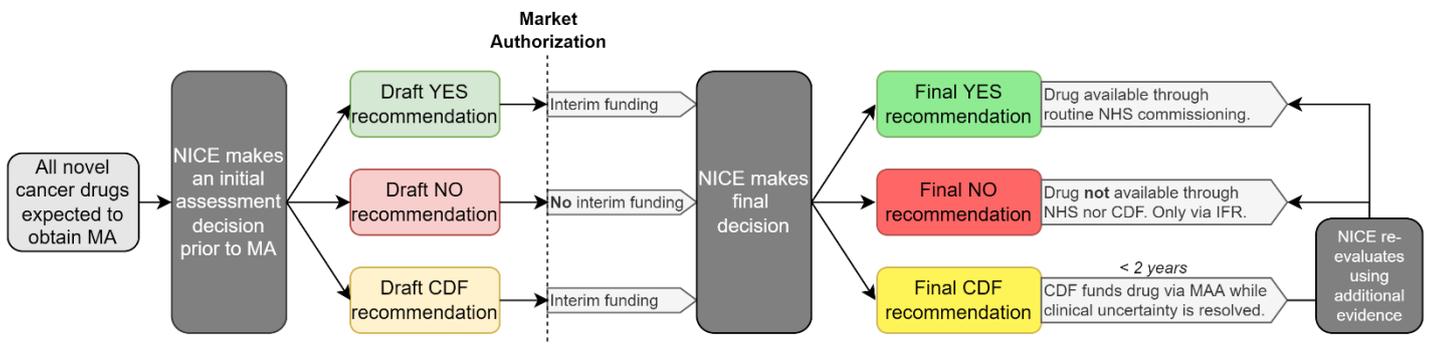


Figure 2: Schematic overview of the reformed CDF managed access process. CDF = Cancer Drugs Fund; IFR = individual funding request; MA = market authorization; MAA = managed access agreement; NHS = National Health Services; NICE = National Institute for Health and Care Excellence.

In 2019, the new Prime Minister Boris Johnson of the Conservative Party made proposals to extend the CDF into an Innovative Medicines Fund, which would aim at improving access to the ‘most advanced, life-saving treatments for conditions such as cancer or autoimmune disease, or for children with other rare diseases (26). In November 2021, the NHS and NICE launched an open consultation on the IMF to involve patients, clinicians, researchers, and the industry in the development of the IMF and gather views on their proposals. These stated that the new fund will run alongside, and not replace, the CDF (27). Furthermore, the proposal set out a budget of £340 million for both funds, resulting in a

total of £680 million per annum to be made available for funding early access of promising novel treatments. The IMF will operate in the same manner as the CDF, as it will give NICE the opportunity to recommend new promising drugs on a conditional basis, while simultaneously supplementary data is collected to resolve clinical uncertainty (27). The consultation on the IMF closed on 11 February 2022 and it is expected to be launched within the next few years. A full timeline of all important developments of the CDF is shown in Figure 3.

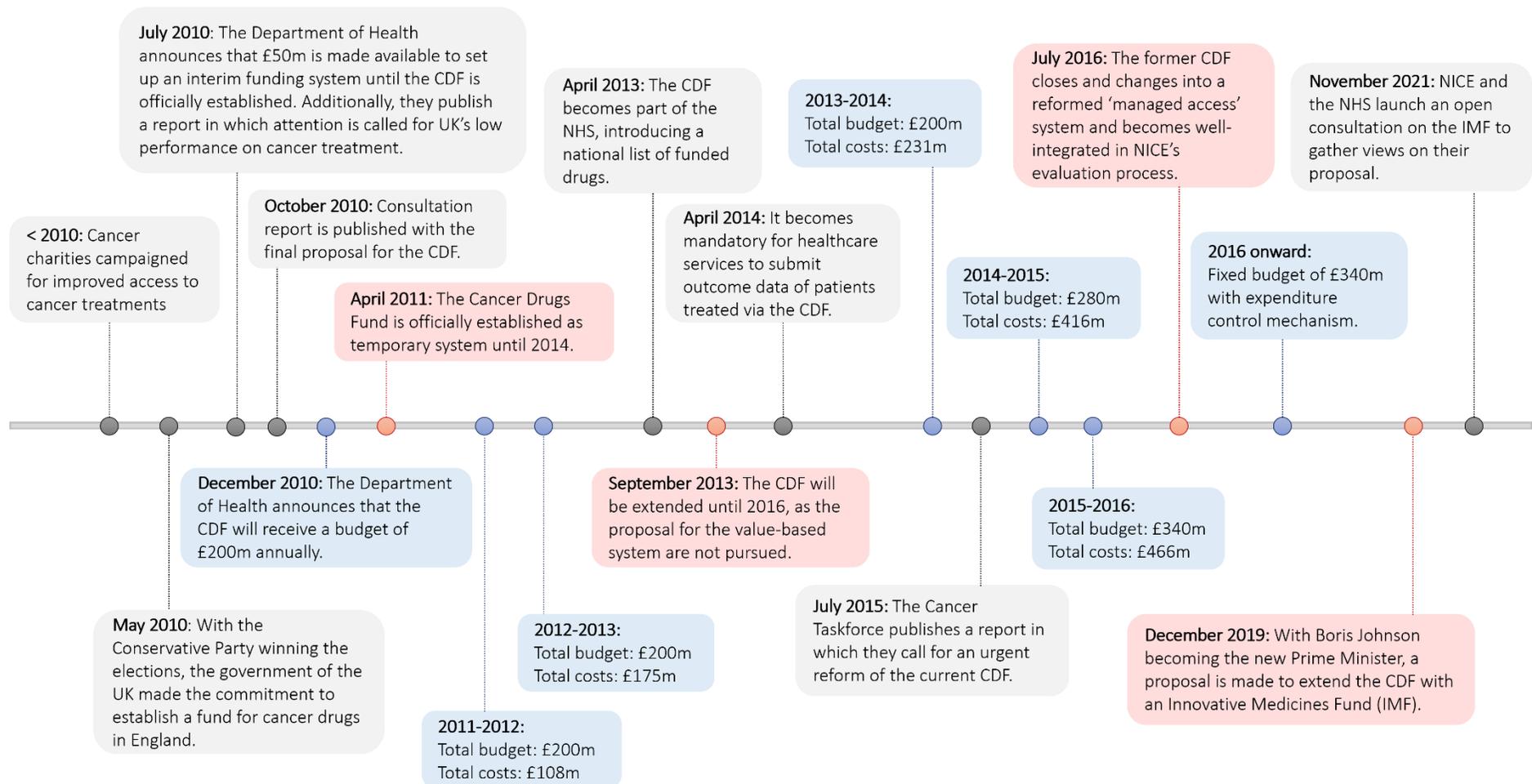


Figure 3: Timeline of all important developments of the CDF. Blue boxes show budget developments, red boxes show critical changes to the fund, and grey boxes show general developments.

2.4 Purpose of the policy

Prior to the reform of the CDF in 2016, its key objectives were as follows (25):

- Provide maximum support to NHS patients;
- Put clinicians and cancer specialists at the core of decision-making, congruent with the Government's wider objective of giving health professionals the responsibility and ability to use their professional judgement about what is right for patients;
- Act as an effective bridge to the proposed VBP system in 2014.

From 2016 onwards, the objectives were changed in order to cohere with the more sustainable direction that the fund was pursuing (14):

- Provide patients with faster access to promising novel cancer treatments;
- Ensure that taxpayers get better value for money in drug expenditure;
- Pharmaceutical companies that are willing to price their products responsibly, will be able to access a new, fast-track route to NHS funding for the most promising drugs, via the accelerated NICE evaluation process and the managed access scheme of the CDF.

In order to ensure that above objectives would be achieved, the CDF introduced several approaches, such as an expenditure control mechanism to prevent overspending as mentioned in chapter 2.3.2. Furthermore, more comprehensive rules were established regarding how and when drugs entered and exited the fund (14). The drugs that were included on the list of the former CDF were all re-appraised by NICE to ensure that they complied to the new rules. Additionally, the NHS acknowledged the importance of regularly reviewing the reformed operational mechanisms, and planned to do so on a yearly basis (14). Last, following the new rules of the fund, outcome data of patients who are treated through the CDF are now collected more properly, which enables the CDF to determine the effectiveness of the fund.

2.5 Political and economic context

2.5.1 UK's political system

England does not have its own parliament, but is subject to the UK government, which consists of three parts; the House of Commons, the House of Lords, and the Monarch (28). First, the House of Commons is the elected chamber of the parliament. Its main responsibilities include proposing new laws, changing existing laws, and debating important issues. The House of Commons consists of 650 Members of Parliament, who are elected by constituents of the area they represent. The UK primarily operates under two major parties: the right-wing Conservative party, and the left-wing Labour Party. The leader of the party that has the most Members of Parliament elected becomes the Prime Minister, who is the head of the government and selects a cabinet consisting of 20 Cabinet Ministers. The second-largest party forms the Opposition, who scrutinizes the actions of the Government. Secondly,

the House of Lords consists of approximately 800 members, who are mainly selected because of their knowledge and expertise. The role of the House of Lords is to question proposed legislations of the House of Commons and to investigate public policy. Last, the power of the Monarch has been reduced over the years, and is currently mainly ceremonial (28).

The establishment of the CDF was predominantly driven by a large public and political pressure to improve access to cancer drugs. Before 2011, NICE did not evaluate all novel cancer drugs that obtained market authorization, and nearly not all drugs that were evaluated were given a positive recommendation (29). Cancer charities and patient groups started campaigns to advocate for improved access to treatments, in which they criticized the methods of NICE and UK's poor performance on cancer survival (see Figure 4) (21,23). Furthermore, individual cases of patients who had been denied a treatment were highlighted in the media, which prompted political action. As a result, two cancer drugs were approved by NICE despite exceeding the £30.000 QALY threshold that it usually adheres to (30). In addition, NICE reviewed its policy for end-of-life drugs, eventually resulting in lowered approval criteria. At that same time, the Conservative party in the UK was led by David Cameron. One of the key promises of the Conservatives' health manifesto was to introduce a fund that provided money specifically for cancer drugs (16,29). With the Conservatives winning the elections in 2010 and David Cameron becoming the new Prime Minister, the proposals for the fund were pursued by the government (16). However, many people considered the promises of the CDF merely to be political expediency to attract voters (32). Furthermore, the government was blamed to treat cancer patients as more deserving in comparison to patients suffering from other diseases (see also section 3.2) (23,33). In 2015, the National Audit Office (NAO) published its findings on an investigation into the CDF (21). The NAO is an independent parliamentary body in the UK who scrutinizes public spending. The NAO stated the CDF was not sustainable or desirable, which was in agreement with findings of the Cancer Taskforce who called for an urgent reform of the fund (21). As a result, the NHS and NICE jointly proposed to change the fund into a managed access system from 2016 onwards, which it currently still is. In 2019, the government even proposed to extend the CDF with an Innovative Medicines Fund (IMF), which was mainly driven by the Prime Minister Boris Johnson (27). The IMF is expected to be established within the next years and allows access to drugs from other therapeutic areas that are associated with a high unmet clinical need (see also chapter 2.3.2).

2.5.2 Drug pricing in the UK

Up until 2018, the UK made use of the PPRS, a system in which drug prices are determined through a voluntarily agreement between the government and pharmaceutical companies (34). The PPRS was supposed to be replaced by a VBP system, however, the pharmaceutical industry criticized the VBP

system, claiming that it would undervalue innovative drugs, which eventually resulted in the proposals for it to be abandoned (24). Thus, after the PPRS came to an end in 2018, the Voluntary Scheme for Branded Medicines Pricing and Access (Voluntary Scheme) came into force instead, a collaboration between the government, NHS, and pharmaceutical industry (35). The Voluntary Scheme includes strict measures that set a limit to the rate of which drug prices are allowed to increase during the next five years, therefore providing stability and predictability with regard to UK's branded medicines prices and expenditures (35).



Figure 4: Left: protests by cancer charities; right: headlines that express strong criticism on negative reimbursement decisions by NICE (33,36–38).

3. Opinions and perceptions

3.1 Stakeholder positions

Figure 5 gives an overview of the stakeholder positions concerning the establishment of the CDF in 2011, as well as the reform of the policy after 2016. Each of the stakeholder groups will shortly be discussed below.

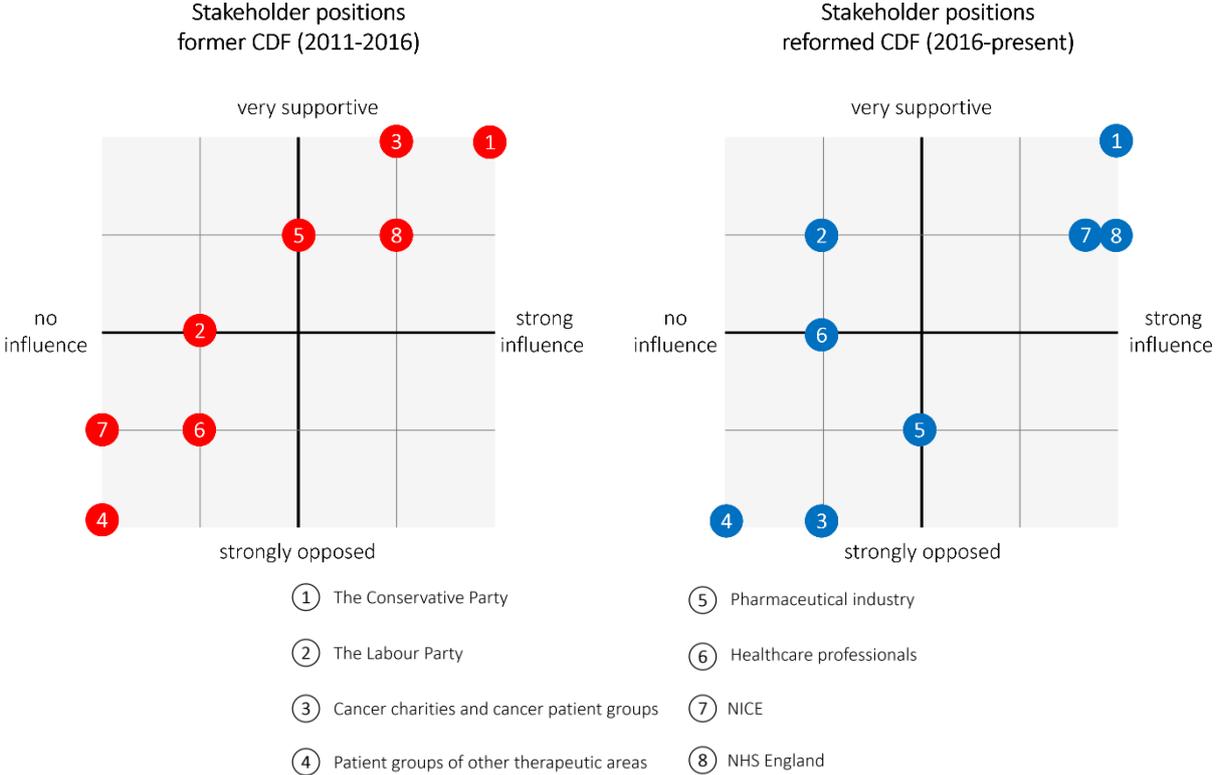


Figure 5: Stakeholder positions with regard to the former CDF (left) and the reformed CDF (right).

3.1.1 The government

The government played a key role in the establishment of the CDF, with the Conservative Party to pledge for a fund to improve access to cancer drugs during the elections of 2010 (23). After the Conservatives won, the fund was materialized by the government in 2011, who kept supporting it and investing in the fund throughout its existence (21,39). The other major political party, the Labour Party, also acknowledged the importance of improving access to cancer care, as they pledged to introduce an individual budget for everyone who suffered from long-term cancer (40). The Labour Party was not explicitly supportive of or opposed to the proposals of the CDF.

Prior to the reform in 2016, the Committee of Public Accounts, which is part of the House of Commons and is responsible for controlling public expenditure, published a report in which they discussed their conclusions and recommendations about the effectiveness of the former CDF (41).

They acknowledged that the former system was not managed properly and advocated for a reformed system. Two main changes that they recommended were to use a system to ensure that the fund would not overspend, and to keep better track of outcome data. Throughout its whole existence, the Conservative Party has always remained supportive of the fund and pledged to keep investing in it (39). The Labour party, on the other hand, expressed their concerns regarding the future of the CDF in November 2014, stating that it took away resources from other life-saving therapies and simultaneously pledging to axe the fund (39,42). Only weeks later, however, the Labour party changed their view and became supportive of the fund, but pledged to replace it by a similar 'Cancer Treatments Fund' under a Labour Government (39).

3.1.2 Cancer charities and cancer patient groups

Prior to the establishment of the CDF, cancer charities and cancer patient groups were actively advocating for improved cancer care, criticizing that many innovative medicines were not made available by NICE (21,23). This had received attention from the media, which eventually prompted political action. Thus, this stakeholder group played a significant role in the establishment of the CDF. However, cancer charities and patient groups were strongly opposed to the reform of the fund in 2016, as they expressed deep concerns about the availability of treatments (43). Fifteen cancer charities sent a collaborative letter to the prime minister David Cameron, in which they stated the reformed system to be flawed as it did not revise the evaluation methodology of NICE (43). This would, according to the charities, result in many clinically effective drugs to be rejected. Despite their efforts, it did influence the revision of the fund.

3.1.3 Patient groups of other therapeutic areas

Patients who suffer from diseases other than cancer have never been supportive of the CDF, stating that it is unethical to give priority to cancer over all other diseases (33). More information on the criticism regarding this 'onco-exceptionalism' can be found in chapter 3.2.

3.1.4 Pharmaceutical industry

Pharmaceutical companies have mostly been supportive of the former CDF, as they were given an alternative market access route for expensive products that were not recommended by NICE (16). However, not all pharmaceutical companies have benefited to the same extent as others. Roche, a major producer of cancer drugs, is one of the biggest beneficiaries, with 24% of the drugs that are available through the CDF being supplied by Roche (21). Other pharmaceutical companies, on the other hand, have not been equally content; under the terms of the PPRS at that time, pharmaceutical companies had to pay for the increase in the NHS bill, which affected some companies more severely than others (23).

The proposals for the reform of the CDF have caused pharmaceutical companies to express strong criticism, claiming that thousands of patients will lose their crucial treatment as a result of the revised system (33). A consultation report which addresses the perceptions of several stakeholder groups on the reform of the CDF showed that, for example, pharmaceutical companies strongly disagreed with (12% 'yes' responses) the proposal that drugs which are highly priced in relation to their clinical benefit should be removed from the list (44).

3.1.5 Healthcare professionals

Most clinicians and other healthcare experts have not been supportive of the CDF. Even though politicians have emphasized that the budget that is allocated to the CDF does not displace any other expenditures of the NHS, opportunity costs should also be taken into account (16,23). Some cancer specialists argue that greater impact on tackling cancer would have been achieved if the money was spent on improving early diagnosis, radiotherapy, and surgery, instead of expensive drugs with limited added benefit (23). Furthermore, experts state that the establishment of the fund was merely an action of political expediency, with the ultimate goal of making an end to media stories about denied treatments rather than actually improving cancer care (33). Even after the reform of the fund, there are still many researchers and clinicians who pledge to reform the fund even further, advocating it to rely on unbiased randomized controlled trials (RCTs) rather than unreliable RWE data to resolve uncertainties regarding the cost-effectiveness of novel drugs (45,46).

3.1.6 NICE and the NHS

The CDF was initially set up by the government as an independent organization that would operate parallel to NICE and the NHS. The former CDF was strongly criticized by NICE, who stated that it bypassed NICE and that the investments were not an effective use of NHS resources (47). Furthermore, NICE and the CDF did not collaborate efficiently and duplicated responsibilities. Despite its criticism, NICE did not have any say in the establishment of the fund nor its actions during its existence prior to the reform. The NHS, on the other hand, collaboratively worked with the Department of Health in developing the initial proposals and guidance for the CDF, making their influence considerable (25). Especially after the CDF became part of the NHS in 2013, its influence increased even more. The NHS and NICE jointly began the consultation on the reformed CDF, which eventually also gave NICE significant influence on the renewed system, as it became part of the routine NICE evaluation process (48).

3.2 Criticism on the CDF

Since its establishment, the CDF has always been subject to criticism. In the first place, the CDF was said to be undermining and bypassing NICE by allowing access to drugs that NICE had determined not to be cost-effective (23). Simultaneously, this attenuates the incentives for pharmaceutical companies to reduce drug prices; before the CDF was established, drug companies were stimulated to offer discounts in order to meet NICE's approval criteria. With the advent of the CDF, drug companies were given an alternative route for their expensive products, even though NICE did not recommend them. Pharmaceutical companies were therefore rewarded even if they had developed a product that did not meet the thresholds of cost-effectiveness. Peter Clark, the chair of the CDF, acknowledged that the fund has undermined NICE and has provided Big Pharma a 'get-out-of-jail card for reimbursement' (49). Research has shown that there was a significant decline in the NICE recommendation rate during the existence of the former CDF, suggesting that it provided an alternative market access route for expensive drugs which was preferred by pharmaceutical companies (50). After the CDF became integrated in NICE's evaluation process in 2016, the two agencies became more appropriately coordinated with each other, which also resulted in NICE's recommendation rate to increase again (50).

A second point of criticism lies within the fact that the fund is solely intended for cancer drugs and not for other therapeutic areas, implying that cancer is seen as a bigger priority than other diseases. This 'onco-exceptionalism' has resulted in patients suffering from other diseases to feel disadvantaged (23). The preference for cancer is not a new phenomenon; cancer drugs have been the prime beneficiary of the end-of-life rule, which was set up by NICE in 2009 to give priority to drugs that are intended to extend the lives of terminally ill people, despite not being cost-effective (32). This rule contradicts NICE's own core principle that states that "a QALY is a QALY is a QALY", meaning that a QALY would always have equal value, irrespective of someone's age, gender, background, or condition (32). As a result, cancer drugs are often permitted with lower thresholds of evidence in comparison to drugs for other therapeutic areas, which also undermines the core principle of the NHS that states all patients to be equal (31,51). Prior to the initial establishment of the CDF, an impact assessment was carried out by the Department of Health, in which the following conclusion was drawn: "While there may be support in principle for greater weighting of QALYs provided to patients with severe conditions, there is currently no robust evidence in the literature to support a particular magnitude of weighting. It should also be noted that no evidence has been found for prioritizing cancer above other severe conditions, or for prioritizing drug treatments above any other interventions for cancer" (32). Nevertheless, the plans for establishing the CDF were pursued by the government. However, with the proposals for the new IMF, a wider range of patients will be affected by such funding policies, which

will partly address the issue. However, there still remain patients that fall outside the scope of these policies and cannot access the funds, as they are suffering from a non-cancerous disease that is not considered to be a high unmet clinical need.

Furthermore, the CDF has also been criticized for delivering poor value for tax payers (23,52). An analysis of the effectiveness of the CDF between 2010 and 2015 has shown that only 38% of the drugs within the CDF achieved statistically significant improvement in overall survival (OR), whereas only 18% met the thresholds for having a clinically meaningful benefit in accordance to validated scales developed by professional healthcare bodies (52). Thus, this means that the majority of the drugs that were available through the CDF did not offer any benefits with regard to improvements in Quality of Life (QoL) of prolonged survival. Furthermore, the welfare loss to society caused by the CDF should also be taken into account, as the total expenditure of the fund amounted up to £1.27 billion at the point of the reform in 2016 (53). Thus, this is a lost opportunity for spending a significant amount of money into other areas of the NHS. Additionally, the CDF initially claimed that it intended to target drugs used to treat rare cancers, however, 59% of patients treated through the CDF between 2013 and 2015 were treated for the most common types of cancer (breast cancer and colorectal cancer) (54).

Moreover, an important objective of the former CDF was to collect outcome data of patients who received treatment via the CDF in order to evaluate the effectiveness and impact of the fund (25). However, healthcare services were not mandated to submit outcome data to the CDF until 2014, making it impossible to evaluate the impact of the fund (21). This issue was also emphasized by the NAO who published an investigation report in 2015 in which they called for an urgent reform of the fund. In the proposals of the reformed CDF, elaborate measures are discussed to improve the collection of outcome data (14).

Last, the CDF only applies only in England, and not in other parts of the UK, which has been considered to be unfair. For a long time, Wales, Scotland, and Northern Ireland did not have a similar fund to pay for innovative drugs. Press coverage often advocated for the CDF to be extended to other parts of the UK, with stories appearing about people from Wales having to sell their homes and move to England in order to get access to optimal cancer treatments, as the Labour Government in Wales was not willing to establish a similar fund (42,52,55). The only way to access rejected cancer treatments in the remaining parts of the UK was through an IFR, a process that can take up months, wasting valuable time. However, Wales, Scotland and Northern Ireland have established similar policies since a few years. More information on this can be found in section 4.1.1.

3.2 Successes of the CDF

Despite the CDF having received a lot of criticism throughout its existence, there are also successes that should be highlighted. There is agreement on the fact that the fund has been successful in bridging the gap between a drug obtaining market authorization, and receiving its final recommendation by NICE (21). Prior to the CDF, there were no arrangements to access drugs in this interim period, which could delay the start of a promising treatment up to several months. Furthermore, the report of the NAO also emphasized that the fund has, despite there being no evidence, most likely contributed to the improvement in UK's performance on access to novel cancer drugs (21).

Since its inception until the reform of the CDF, it has benefitted more than 95,000 patients (14). After the reform of the CDF in 2016, 31 MAAs have been made between the fund and pharmaceutical companies (12). There have only been two drugs that had too much clinical uncertainty to make a final decision, making them available through the CDF on a conditional basis while additional evidence was collected. In both cases, the drug eventually got a positive recommendation (12). Thus, in those cases patients benefited from having earlier access to promising drugs, while simultaneously additional evidence was being collected to address clinical uncertainty. Since 2016, a total of 73,000 patients have benefited from one of the 91 CDF funded medicines treating 205 cancer types (27).

Last, NICE reviewed the cost-effectiveness of all treatments that the fund was paying for prior to the reform, of which 30 received full approval for routine use. Peter Clark emphasized the importance of this great achievement, who claims that NICE has developed a better understanding of cancer and corresponding treatments because of the changes to the fund (56). He also acknowledges that the reform of the fund has resulted in pharmaceutical companies to realize that they should aim for routine NHS approval of their novel products rather than alternative market access routes, which encouraging them to price their products more realistically.

4. International context

4.1 Comparison with other policies

4.1.1 *Scotland, Wales, and Northern Ireland*

For a long time, the CDF has been a unique model for funding innovative medicines that only applied in England. In the remaining parts of the UK, the only way to get access to treatments that were not recommended was via individual funding requests, which were only allocated in cases of clinical exceptionality. In order to get access to drugs from the CDF, you have to be entitled to routine NHS care and be registered with a GP in England (10). Thus, people from Scotland, Wales, or Northern Ireland are not able to access the fund and could not make use of a similar policy for a long time. In Wales, an online petition was started in 2014 to campaign for equal access to cancer drugs for patients in Wales as patients from England. Despite receiving 98.000 signatures, the proposal was rejected by Health Minister Mark Drakeford, who stated that the CDF was “neither ethical, lacked clinical support, was unpopular with the public and would deliver a lesser service in Wales” (57). However, since 2017, the Welsh Government established the New Treatment Fund (NTF), which requires Health Boards in Wales to make drugs that are recommended by NICE and the All Wales Medicines Strategy Group (AWMSG) available as soon as possible, but at least within two months (58). Furthermore, the fund also covers all drugs that have an MAA in the CDF. Due to the NTF, the average access time for novel drugs in Wales is decreased from 90 to 13 days (59).

In Northern Ireland, the Department of Health advises about health and social care, which decided in September 2018 to pay for drugs that are under an MAA in the CDF (56). Furthermore, the Scottish Government launched the New Medicines Fund (NMF) in 2014, which pays for some drugs intended for rare diseases or end-of-life patients on an individual basis (60). Similar to the CDF, the NMF also overspent its budget significantly during the first years of its existence. In addition, the NMF has also been criticized for its lack of collecting outcome data, making it difficult to determine its effectiveness (60).

4.1.2 *Other European countries*

In some other European countries, similar policies as the CDF are utilized. In the Netherlands, the Ministry of Health, Welfare and Sports introduced a policy in 2019 on conditional inclusion of specific drugs in the basic healthcare package that have a promising view to being positively reimbursed (61). The policy is intended for medicinal products that target a high unmet clinical need (e.g. orphan drugs), for which insufficient clinical evidence is available in order to obtain a positive reimbursement recommendation. During the conditional inclusion period, the market authorization holder of the product is given the opportunity to resolve the clinical uncertainty at its own expense, which is similar to the MAA of the CDF.

Afterwards, the supplementary evidence is reviewed by the HTA agency of the Netherlands (the National Health Care Institute), who makes a final recommendation on its reimbursement (61). Most drugs that are eligible for conditional inclusion are indicated for orphan diseases, of which small patient groups complicate the availability of comprehensive clinical evidence. Other countries, such as the US, Canada, Australia, Belgium and Sweden, have also implemented policies that allow conditional reimbursement (62). However, research shows that the reassessment procedure of conditionally reimbursed drugs is a complex and politically sensitive process (62). A drug that is conditionally reimbursed and subsequently rejected, is subject to a significant amount of social resistance. Furthermore, there is a general tendency to experience losses more severely than equivalent gains, a phenomenon known as 'loss aversion'. In the context of reimbursement decisions, this means that ending the reimbursement of a drug is generally perceived as more severe than not reimbursing a drug at all, in particular when the drug is proven to be effective but not cost-effective (62). In the light of decision-making, this could imply that policymakers might be willing to accept lower thresholds of clinical evidence (e.g. higher cost per QALY) for conditionally reimbursed drugs than for drugs that are not yet reimbursed (62).

5. Discussion and conclusion

The CDF has been utilized for more than 10 years and has been subject to some major changes during its existence. Initially, the fund attempted to make as many innovative drugs available as possible, without having clear entry and exit criteria, eventually causing the expenditures of the fund to exceed its allocated budget significantly. The reform of the CDF addressed its major issues; the fund became part of NICE's review process, which prevented it from undermining its methods. Furthermore, it changed into a managed access fund, meaning that it would only reimburse promising drugs for a maximum of two years during which the clinical uncertainty was expected to be resolved. In addition, the CDF improved its methods of collecting outcome data of patients that are treated through the fund, enabling it to accurately determine the impact that the fund has.

One of the main objectives of the reformed fund was to provide cancer patients with faster access to promising novel cancer treatments. Thanks to the interim funding that the CDF provides, patients can get up to five months earlier access to their treatments, which is a considerable improvement. Since the fund now only covers drugs that are expected to adhere to the thresholds of cost-effectiveness in the future, it also achieves its second objective – ensuring that taxpayers get better value for money in drug expenditure. Last, it also aimed at encouraging pharmaceutical companies to price their products responsibly. With the use of the conditional reimbursement period, in which supplementary evidence can be submitted, incentives are created for pharmaceutical companies to comply to the thresholds of cost-effectiveness and to adjust their prices realistically. Prior to the reform, pharmaceutical companies were not stimulated to do this, as the CDF provided an alternative market access route.

Overall, the CDF meets the objectives that it set. However, even after the reform of the fund, there remains criticism, which mainly considers the fact that clinical uncertainty is resolved through the collection of RWE. Many researchers state that this type of evidence is not as reliable as evidence through RCTs, which is deemed to have the highest credibility due to limiting bias and spurious causality (63). However, a disadvantage of RCTs is that the included patients might not fully represent the entire population, due to the strict inclusion and exclusion criteria. RWE on the other hand, is more prone to bias and requires a large amount of data to be collected in order to be analyzed correctly. However, RWE can provide data that is impossible to generate with RCTs, such as more elaborate data on actual clinical aspects and detection of less frequent adverse effects (63). A combination of the two types of evidence might therefore provide strong and robust evidence.

5.1 Transferability to other countries

Although the CDF was set up with good intentions, it has been inherent to complex issues and criticism. However, the CDF has made significant improvements throughout its existence. Below, some suggestions are made with regard to the transferability of a similar policy to other countries based on the lessons that can be learnt from the CDF (32).

- I. First of all, a similar policy should not give out the message that one therapeutic area is prioritized above others. This is especially important if national healthcare services express the principle that they treat patients of all diseases equally. We therefore suggest avoiding setting up a fund that is intended for one therapeutic area, but rather focus on drugs for patients with a high unmet clinical need. Examples are the conditional inclusion policy of the Netherlands and the prospective IMF.
- II. Moreover, the CDF has been criticized for being too narrowly focused on funding drugs, whereas researchers state that it might be better to keep a holistic view and also invest in improving access to diagnostics, prevention, surgery, and early diagnosis. Thus, we advise that these healthcare technologies and services are also included in similar funding policies. These technologies could be made available in a comparable managed access scheme as is applied in the CDF, as they can also be evaluated by HTA agencies on their cost-effectiveness.
- III. Additionally, a similar policy should make use of financial control mechanisms in order to prevent overspending. This is an important lesson that can be learnt from the CDF, which significantly and consistently exceeded its annual budget. Preferably, this financial control mechanism should be arranged in such a manner that it does not have to close for new entrants if the budget approaches to be exceeded. Instead, we suggest applying a similar mechanism as the CDF, in which pharmaceutical companies indirectly repay the money that is overspent on a proportional basis.
- IV. Furthermore, a lesson that can be learnt from the CDF is that it is crucial to gather outcome data of patients that are treated via such a policy in order to determine its effectiveness, especially since a significant amount of money is invested in certain policies.
- V. Moreover, a similar policy should be well-integrated in the routine reimbursement and regulatory processes of a country, by close collaboration with the national HTA agencies, the government, healthcare services, and the pharmaceutical industry. This will maximize the credibility of the policy and prevent it from undermining or bypassing the national HTA agency. Here, it is also important to make use of explicit entry and exit criteria, which should be clear and transparent to all stakeholders that are involved. This will prevent social resistance when

the reimbursement of a drug is ended, but also ensures that policymakers adhere to the same thresholds of cost-effectiveness as for drugs that have not been reimbursed at all.

- VI. Last, it is important to adhere to clinical evidence and corresponding cost-effectiveness. A policy that uses interim funding during a period in which clinical uncertainty can be resolved, is much more effective than a policy that provides a bypass for poor-quality drugs, as the latter eliminates the incentives for pharmaceutical companies to gather strong, comprehensive clinical evidence of a drug at a reasonable price. Here, we advocate to combine RWE with evidence from RCTs during a conditional funding period, as the two types of evidence generation can act mutually supplementary. In that way, a very powerful way of evidence generation can be achieved.

5.2 Future perspectives of the CDF

Now that NICE has control over the CDF, some think that the power of it will slowly be decreased, until it ultimately ceases to exist (32). However, as long as England is under a Conservative Government, chances of the CDF to disappear are slim (39). The Conservatives have always remained positive and supportive of the fund, and mainly emphasize the successes that it has had rather than acknowledging its flaws. Furthermore, with the prospective IMF that is planned to run parallel to the CDF, a wider range of patients will be able to benefit from funds that facilitate access to promising medicine. Thus, the advent of the IMF will address the criticism of cancer being prioritized over other therapeutic areas. Furthermore, we advise the CDF and IMF to make use of a combination of RWE and evidence from RCTs, as this will provide a very powerful way of generating evidence during the period of conditional reimbursement. Last, we also suggest the CDF, IMF, or similar policies to adopt a holistic view on the improved access of care, by also investing in improvements on health technologies other than drugs, such as prevention, diagnostics/screening methods, and surgery. A last lesson that can be learnt from the CDF and its developments, is to be careful when political actions interfere with reimbursement and regulatory processes. Ultimately, reimbursement decisions should not be influenced by political expediency, but rather be based on adequate HTA evaluations using credible evidence on cost-effectiveness, which will eventually maximize the value that novel drugs have for society.

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Appendix

Policy title		Cancer Drugs Fund (CDF)		
Administrative info				
Date of update		Reviewer name		Comments
25 February 2022		Francine Brinkhuis, Utrecht University		
Information				
Domain		2022	[Year]	[Year]
Context	Population	<ul style="list-style-type: none"> UK: 67 million (2020) (1) England: 57 million (2020) (1) 		
	Life expectancy at birth	<ul style="list-style-type: none"> UK: 79.0 years for males and 82.9 years for females (2018 to 2020) (1) England: 79.3 years for males and 83.1 years for females (2018 to 2020) (1) 		
	Total disease burden in DALYs	<ul style="list-style-type: none"> England and Wales: 8,605,362 DALYs due to cancer per year = 3,242 DALYs/100,000 population/year (between 2002 and 2006) (2) 		
	Per capita health expenditure (US\$)	<ul style="list-style-type: none"> UK: 3,278 GBP = 4,474 US\$ (2020) (3) England not specified 		
	Per capita pharmaceutical expenditure (US\$)	<ul style="list-style-type: none"> UK: 515 US\$ (2019) (4) England not specified 		
Policy design	Pricing intervention	Interim funding of cancer drugs in England that have obtained a draft 'yes' or 'CDF' recommendation by NICE, as well as conditional reimbursement of max. 2 years through a managed access agreement (MAA) intended for promising drugs that are associated with clinical uncertainty but have high plausibility to obtain full reimbursement in the future (5).		
	Pharmaceutical products concerned	Cancer drugs		

	Health service settings concerned	<ul style="list-style-type: none"> The NHS is the umbrella term for the healthcare systems in the UK, which are responsible for providing the majority of healthcare in England, Wales and Scotland. The NHS is mainly funded by the government from general taxation and National Insurance payments. The CDF became part of the NHS from 2013 onward (6,7). NICE is the independent HTA organization that serves both the English NHS and the Welsh NHS. NICE is responsible for conducting HTA evaluations of novel health technologies and subsequently make reimbursement recommendations to the NHS. From 2016 onwards, the CDF became integrated in the routine NICE evaluation process (7). Drugs that do not get recommended by NICE are not available through routine commissioning via the NHS (5). 		
	Supporting legislation or policy	n/a		
	Other relevant policies	<ul style="list-style-type: none"> Innovative Medicines Fund (IMF), which is a prospective extension of the CDF that will operate in a similar way to fund drugs for rare diseases (8). Individual Funding Requests (IFR) can be consulted on an individual basis for drugs that NICE has rejected in its final decision. Patients that are eligible for an IFR should be considered clinically exceptional (5). 		
	Technical methods description	<ul style="list-style-type: none"> MAAs between the CDF and the pharmaceutical companies, in which a drug that has a positive view on being reimbursed in the future gets funding for max. 2 years, while clinical uncertainty is resolved (9). Expenditure control mechanism prevents the CDF from overspending its budget by applying proportional rebates to the pharmaceutical companies that generate revenues through the CDF (9). 		
Rationale	What were the problems being solved?	Improving access to innovative cancer drugs, as the UK was criticized for its poor performance on cancer survival. Furthermore, cancer charities and cancer patient groups advocated for improved access to cancer drugs, which attracted media attention (7).		
	What were the main policy changes?	<ul style="list-style-type: none"> From 2011 to 2016, drugs that were eligible to get funded through the CDF included all cancer treatments that were not routinely available via the NHS. In this time, the fund received a lot of criticism, e.g. for not collecting outcome data and not having clear enter and exit criteria for funded drugs (7). In 2016, the policy was reformed into a managed access fund, which only funded drugs for a limited time while simultaneously NICE finalized its recommendation, or while clinical uncertainty was resolved by collecting supplementary evidence (MAA) (9). With the reform, the CDF also started making use of an expenditure control mechanism that fixed its budget at £340 million annually (9). 		
	What was the overall politico-legal environment?	<ul style="list-style-type: none"> The establishment of the CDF was driven by the Conservative Party, who have been in power in the UK government since 2010 (10,12). The Conservative Party was led by David Cameron at that time, and with him becoming the new Prime Minister (PM) in 2010, the proposals for the CDF were pursued (12). 		

		<ul style="list-style-type: none"> The second-largest political party in the UK is the Labour Party, who have been expressing varying support of the fund (11). With Boris Johnson becoming the new PM in 2019, a proposal was made to extend the CDF with the IMF (see above) (8). 		
Governance	Role of government	The government, especially the Conservative Party, have played a key role in establishing the CDF, as they made the proposals for the policy and kept extending its lifetime through the years, even though the CDF was supposed to end in 2014 (12).		
	Role of non-government actors, incl. private sector	<ul style="list-style-type: none"> NICE: the CDF ran parallel to NICE for a long time, while many people criticized the fund for undermining NICE and duplicating its responsibilities (10). In 2016, the CDF became part of NICE's evaluation process, which significantly increased their influence (9). Pharmaceutical industry: pharmaceutical companies are responsible for demonstrating the efficacy of novel products and pricing their products in a responsible way, which is subsequently evaluated by NICE on added benefit and cost-effectiveness. This eventually yields a recommendation on the reimbursement of a novel products. Many drugs have often been priced too high to be considered cost-effective, resulting in the recommendation rate of NICE to be low, which has received a lot of criticism by patient groups (7). NHS: the NHS was collaborating with the Department of Health in developing the proposals for the initial fund (13). The CDF became part of the NHS in 2013, which gave them a significant influence on the development of the fund. The NHS and NICE jointly proposed to reform the fund to a managed access system in 2016 (9). Patient groups: cancer patient groups played a key role in the establishment of the fund, as their protests on improved access to cancer drugs prompted political action (10). 		
	Decision making process	The proposal of the CDF was mainly driven by a large public and political pressure to improve the access to innovative cancer drugs (10). A key promise in the health manifesto of the Conservative Party during the 2010 elections was to introduce a fund for cancer drugs (12). With the Conservatives winning the elections, the proposals for the CDF were pursued by the government.		
Implementation	Main steps of policy roll out	<ul style="list-style-type: none"> Proposal for CDF included in 2010 health manifesto of Conservative Party (12). Conservative Party win elections in 2010, proposals for CDF are pursued. From 2010 to 2011, an interim fund is set up, which is officially replaced by the CDF in 2011 (7). In 2013, the CDF becomes part of the NHS, who then manages it (7). In 2015, the National Audit Office (NAO) and Cancer Taskforce call for an urgent reform of the CDF, as it is considered not to be desirable nor sustainable (7). In 2016, the NHS and NICE propose to change the fund in a managed access fund with an expenditure control mechanism. Furthermore, the CDF will be integrated in NICE's evaluation process (9). 		
	Human resource	<ul style="list-style-type: none"> A joint NHS/NICE CDF Investment Group is established to manage the budget and approve of MAAs (9). Technology Appraisal Committee identifies CDF drug candidates during the evaluation process (9). 		

	Financial resource	The CDF is managed by the NHS, which is predominantly funded by the government from general taxation. Thus, the CDF is funded by tax, which has caused taxpayers to express strong criticism, stating that their money is used to finance expensive poor-quality drugs (10).		
	Infrastructure (e.g. IT)	<ul style="list-style-type: none"> if (chemotherapy) treatments are funded via the CDF, it is a requirement that chemotherapy e-prescribing systems are used to ensure safe and efficient delivery of the treatment (9). Furthermore, this system also facilitates the return of outcome data to the Systematic Anti-Cancer Therapy (SACT) dataset. The online CDF notification system is used by clinicians to prescribe a drug via the CDF. Data of patients treated via the CDF is also recorded on this system and includes the SACT dataset (9). The Minimum Dataset (MDS) is specifically used for high-cost drugs to collect outcome data and monitor expenditure (9). 		
Impacts	Policy uptake	Included in the 2010 health manifesto of the Conservative Party, who subsequently won the elections and came to power (12).		
	Price	<ul style="list-style-type: none"> 2011/12: budget £200m, costs £108m 2012/13: budget £200m, costs £175m 2013/14: budget £200m, costs £231m 2014/15: budget £280m, costs £416m 2015/16: budget £340m, costs £466m 2016 onward: fixed budget of £340m (7,9) 		
	Volume	<ul style="list-style-type: none"> Since its inception until the reform of the CDF, it has benefitted >95,000 patients (9). After 2016, >73,000 cancer patients benefited from having access to 91 CDF funded drugs, treating a total of 205 cancer types (8). 		
	Availability	<ul style="list-style-type: none"> The treating clinician of a cancer patient can apply for a treatment via the CDF by filling in a form on the online CDF notification system (5). If a pharmaceutical company agrees to the terms of the CDF, cancer treatments that are recommended by NICE (either for routine commissioning, or for use via the CDF) are available to patients immediately after NICE published its final recommendation (9). Up to five months earlier access to cancer treatments can subsequently be achieved (14). 		
	Pharmaceutical expenditure	The entire UK had a GDP of £2,043,373m in 2020, of which 12.8% = £261,552m was attributed to healthcare (1). Thus, with an annual budget of £340m, costs of the CDF corresponded to approximately 0.1% of total health expenditure in 2020.		

Stakeholder acceptability	<p>Since the reform of the CDF, main opposition originates from:</p> <ul style="list-style-type: none"> • Patient groups of other diseases, who believe the fund prioritizes cancer above other diseases (10). • Cancer patient groups were also opposed to the reform, as it resulted in a decline in the number of drugs that are reimbursed, which prompted a lot of resistance (15). • The pharmaceutical industry was initially very supportive of the fund, as they were given an alternative market access routes to sell drugs that were rejected for reimbursement (7). With regard to the reform of the CDF, however, the pharmaceutical industry was not supportive, as they would have to deal with stricter reimbursement rules and had to pay a rebate in cases of an overspent (9). They stated that many patients would be losing their valuable treatments due to the new managed access scheme (16). <p>More neutral stakeholders are:</p> <ul style="list-style-type: none"> • Healthcare professionals and researchers, who were supportive of the new arrangements in the reform, but state that the collection of solely real-world evidence (RWE) to resolve clinical uncertainty is not sufficient. They advocate to combine RWE with evidence from randomized controlled trials (RCTs) (17). • The Labour Party has taken on varying positions during the lifetime of the CDF. They do acknowledge the importance of improving cancer care, and even proposed to establish a similar fund under a Labour Government, but have also been expressing strong criticism, stating to end the fund (11). <p>Supportive stakeholders include:</p> <ul style="list-style-type: none"> • The Conservative Party, who have always advocated to extend the fund and increase its budget (15). • The NHS and NICE are also supportive of the reformed CDF, as the fund is managed by the NHS and is well-integrated in the routine evaluation process of NICE (18). 		
Other impacts	<ul style="list-style-type: none"> • Incentives and realizations are created for pharmaceutical companies to price their products reasonably. • Patients from Wales and Northern Ireland can now also access drugs that have a MAA with the CDF via their own national policies (19). <p>Suggestions for the transferability of similar policies to other countries:</p> <ol style="list-style-type: none"> I. Focus on high unmet clinical need rather than a specific disease; II. Keep a holistic view on other health technologies besides drugs; III. Make use of financial control mechanisms to prevent overspending; IV. Properly collect outcome data in order to determine the impact of the policy; V. Integrate the system in the existing HTA evaluation routine, while collaborating closely with all relevant stakeholders and making use of transparent entry and exit criteria; VI. Adhere to robust clinical evidence on cost-effectiveness (e.g. RWE combined with evidence from randomized controlled trials (RCTs) in a conditional reimbursement system. 		
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