



Dixon, P., Chamberlain, C., & Hollingworth, W. (2016). Did It Matter That the Cancer Drugs Fund Was Not NICE? A Retrospective Review. *Value in Health*, 19(6), 879-884. DOI: 10.1016/j.jval.2016.04.001

Peer reviewed version

License (if available):
CC BY-NC-ND

Link to published version (if available):
[10.1016/j.jval.2016.04.001](https://doi.org/10.1016/j.jval.2016.04.001)

[Link to publication record in Explore Bristol Research](#)
PDF-document

This is the author accepted manuscript (AAM). The final published version (version of record) is available online via Elsevier at <http://www.sciencedirect.com/science/article/pii/S1098301516300183>. Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research

General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
<http://www.bristol.ac.uk/pure/about/ebr-terms.html>

Did it matter that the Cancer Drugs Fund was not NICE? A retrospective review

Abstract

Background: The Cancer Drugs Fund (CDF) will have spent over £1bn between October 2010 and the introduction of reforms to its structure and operations in July 2016. There has been much more debate about the existence of the fund than about how it spent its substantial budget. It is important to undertake a retrospective examination of “where the money went” in light of the substantial reforms that will be introduced in 2016.

Objective: We review the means by which the CDF made recent funding decisions for cancer drugs in order to provide an assessment of the merits of the CDF “model” as a basis for allocation decisions. We assess the extent to which proposed reforms could overcome defects in the original CDF model of prioritisation, and lessons for other countries.

Methods: We provide a narrative commentary on the CDF’s methods and processes since 2014. We evaluate methods against best practice in cost-effectiveness analysis, and processes against the “accountability for reasonableness” framework. We comment on reforms to the fund.

Results: There are no grounds for concluding that the opportunity costs imposed on cancer patients were well evidenced, or the product of legitimate deliberative processes. We note that some of these issues will be addressed in the proposed next incarnation of the fund, but the rationale for the fund’s existence remains unconvincing.

Conclusions: It is important and timely to debate how cancer drugs appraisal ought to be conducted in order to confront the consequences of the CDF's model of appraisal. We conclude that it did matter that the CDF was not NICE.

Introduction

The Cancer Drugs Fund (CDF) was established by the UK government in 2010. It made available to patients in England cancer drugs not recommended by the National Institute for Health and Care Excellence (NICE) on the basis of cost-effectiveness, not yet appraised by NICE, and/or which were being used outside their marketing authorisation.

As of early 2016, 47 drug/indication combinations are funded (1). Annual fund expenditure in 2014/15 was £416m, amounting to a 48% overspend on the allocated budget for that period (2). The CDF was intended only as temporary solution (3) to a perceived deficit in access prior to the renegotiation of the Pharmaceutical Price Regulation Scheme, and the proposed but unfulfilled introduction of Value-Based Pricing (VBP).

The CDF's effects on population health are controversial (4-7). Calculations based on recent estimates of the National Health Service (NHS) cost-effectiveness threshold (8) suggest that the CDF caused roughly five times more Quality Adjusted Life Years (QALYs) to be lost elsewhere in the NHS than were generated by the fund's activities, (9, 10) leading to suggestions that the ethical basis for the fund is at best arbitrary (11), if not invidious (12).

There has been much more debate about the rationale for the fund's existence than about how the fund spent its substantial budget. A retrospective review of the fund's activities is important now that the fund is about to be reformed.

The review is made timely by the decision in February 2016 (13) to reform the CDF, and the risk that lessons from the CDF's approach to prioritisation will remain

unexamined against best practice in the transition to a new model for appraising and reimbursing cancer drugs. This review is also relevant to debates about the rationale for cancer-specific appraisal agencies in other countries e.g. (14, 15). We review the means by which the CDF made funding decisions for cancer drugs from late 2014, in order to provide an overall assessment of the merits of the CDF “model” as a basis for allocation decisions, and consider some of the lessons for other countries.

Methods

We evaluate the CDF's approach to prioritisation by assessing the *methods* and *processes* that combined to result in funding decisions for drugs.

We evaluate the methods of the CDF against best practice in relation to (a) measurement and valuation of outcomes, (b) cost-effectiveness and prioritisation. The approach adopted by the CDF to cost-effectiveness and prioritisation has led to circumstances where the opportunity costs of funding decisions are borne by some types of cancer patients but not others.

These are the classic issues of priority setting in constrained-resource settings to which the conventional tools of economic evaluation are one solution and, indeed, the predominant solution adopted by the NHS (via NICE) outside of the CDF. We therefore particularly emphasise implications for opportunity costs. Opportunity costs arise when scarce healthcare resources have valuable, alternative uses. Expenditure on a particular type of healthcare denies its application to other clinical areas for the benefit of other patients. The concept of opportunity costs is intended to measure the benefits that are foregone as a consequence of a decision, e.g. to fund particular types of cancer drugs.

We evaluate decision-making processes using the principles of "accountability for reasonableness" of Daniels and Sabin (16, 17). These principles require that allocation decisions in healthcare be public and transparent, be based on rules that "fair minded" people consider are relevant to the allocation at hand, allow for revisions and appeal, and be enforceable. We focus on relevance and transparency as being most relevant to a critique of the CDF's decision-making processes.

We begin by describing the CDF's "prioritisation tool", introduced in 2014, and used as the fundamental basis of funding decisions. We then consider the outcomes evaluated by the tool, and the approach to cost-effectiveness and prioritisation to which these outcomes are subject, before considering the processes of the fund. Finally, we comment on reformed structure and processes of the fund in light of our findings, and consider the implications for other countries.

Evaluation of methodologies and processes used in funding decisions

The prioritisation tool

The CDF's prioritisation tool is used to inform funding decisions. The provenance of the tool is not well documented, but is based on similar tools used by NHS commissioners (18) (19). The first version of the tool to include cost as a scored domain was introduced in late 2014, and it is this version (and subsequent amendments) that is the subject of comment below.

The tool evaluates each drug per indication under 4 clinical domains: survival encompassing overall survival (OS) and progression-free survival (PFS), toxicity, quality of life, and unmet need. The tool scores the quality of the available evidence with a letter grade (A, B, C, D, U1, or U2). An "A" grade is awarded where there are two or more quality, published Phase III Randomised Controlled Trials (RCTs), decreasing to a U grade where only unpublished data in abstract form are available. Median drug cost per patient is scored using one of 2 confidential scoring systems, the application of either of which depends on the rarity of the condition. The cost component focuses only on drug cost.

The clinical effectiveness score, based on a summation of scores from each clinical domain, is added to the (confidential) cost score. Drug/indication combinations are ranked by this final confidential score, and a funding cut-off is made to reflect available budget. If the cut-off falls across equally ranked treatments, a "triage" approach involving sequential rankings of one domain at a time is used (20). A representation of this process is provided in Figure 1.

The National CDF panel is a subgroup of the Chemotherapy Clinical Reference Group (CRG) of NHS England (20). Members of this CRG include clinicians, patients, carers, and professional organisations (21).

Evaluation of methods to measure and value outcomes: Survival

Survival relative to comparator therapies is scored on an ordinal scale. Both overall survival (OS) and progression-free survival (PFS) may be taken into account. Where both measures are available, they may contribute additively to the overall score.

A score of 0 is assigned to a drug for incremental survival < 2 months, a score of 2 for incremental survival of 2-3 months, 3 for incremental survival of 4-5 months, and so on to a maximum value of 13 for incremental survival of 24 months or more. Thus, the scale does not have interval or ratio properties: survival up to two months and beyond 24 months is not scored, and two months survival may attract the same score as one month.

There is no provision in the prioritisation tool to distinguish between measures of survival in curative and non-curative settings, unlike the overall distinction made between curative and non-curative therapies in the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) (22), or the distinction between advanced and potentially curative in the ASCO (American Society Of Clinical Oncology) framework (23). The use of PFS, and similar measures other than OS, are not reliable surrogates for OS in general (24, 25) (23) and specifically in non-curative settings (22). The usefulness of PFS as a surrogate for OS may depend, in metastatic or advanced cases, on cancer type. (26).

Unpublished data and non-statistically significant between-arm survival differences score zero. Statistical significance would be largely redundant in a more fully articulated decision-making approach, in which interventions would be recommended

based on expected net benefit, rather than on arbitrary statistical significance cut-off points (27).

Evaluation of methods to measure and value outcomes: Toxicity and quality of life

Toxicity and quality of life are scored separately in the prioritisation tool. The distinction between toxicity and quality of life enables information on toxicity to be included in assessments, even if prospectively collected data from validated quality of life tools are not available. A similar distinction between toxicity and quality of life is made in the ESMO-MCBS (22).

Both toxicity and quality of life are assessed on 5 point scales ranging from -2 to +2 against comparators. Toxicity scale points range from “significantly worsened” to “significant improvement”, with a score of zero being awarded if toxicity is considered to be equivalent to comparator.

The criteria of the quality of life scale reflect the extent of change versus comparator, and the validity of the instrument. The scores used in each scale are largely arbitrary, are of unknown relevance to patients, and bear an unknown relationship to the underlying quality of life instruments.

Evaluation of methods for cost-effectiveness and prioritisation: Unmet need and rarity

A score of 3 is awarded if there is a first demonstration of efficacy for a systemic therapy, or the treatment represents a “step change”. If neither of these circumstances apply, and/or survival data are unavailable for the treatment, then a score of zero is awarded. In other contexts, innovation tends not to be privileged for its own sake, unless it happens to affect the estimated net benefit of the intervention concerned (28).

Median drug costs were assessed differently by the tool if a condition is “very rare”, defined as less than 100 patients per year likely to actually receive treatment when all drug indications are “considered and summated” (20). The manner in which rarity affected CDF assessments is not known because the scoring system is not published. In any event, there are compelling arguments against there being a sustainable basis for judging the cost-effectiveness of rare conditions differently from more prevalent conditions (29).

Evaluation of methods for cost-effectiveness and prioritisation: Focus on drug therapies and drug costs

The CDF is a fund for drugs, and drugs alone. The CDF is responsible for procuring drugs, but “NHS England is expected to meet the associated service costs related to delivery of medicines in the usual way” (20). Abiraterone, a therapy for the treatment of prostate cancer, is delivered orally, rather than intravenously. The costs of intravenous delivery to the health system (and to individuals) are avoided, but there is no mechanism for the CDF to reflect these wider cost impacts.

More generally, where non-drug therapies (e.g. surgery or radiotherapy) have been shown to contribute more to relevant outcomes than anti-cancer drug therapy (30), then some of the opportunity costs to which the fund gives rise fall on cancer patients receiving non-drug therapies (31).

Evaluation of methods for cost-effectiveness and prioritisation: The aggregate score

The only means of “weighting” the contribution of each domain was to alter the domain scoring systems. High survival gains dominated other domains, because the maximum value attributable to survival is 13 (and both OS and PFS can both enter additively to a theoretical maximum of 26 points for survival), and the maximum value of any other domain is 3. The trade-offs embodied in the prioritisation tool between

morbidity and mortality are not explicit, do not appear to have a basis in evidence, and have been the subject of little debate.

The pre-eminence of survival may bias cancer treatment, and industry priorities for development, towards drug therapies that extend life by small margins at high cost (32), and away from cancer prevention, early diagnosis, management, and palliative care (31).

The clinical score obtained by summation of each domain does not have a ready interpretation as a conventional cost-effectiveness ratio, or as the output of some form of multi-criteria decision analysis (33). Neither the full methodology for scoring nor the scores produced by that methodology are made known publicly.

The case of radium-223 for metastatic castration-resistant prostate cancer in patients with bone metastases illustrates some of the challenges in understanding how the clinical score actually influenced CDF decisions. In field testing of the ESMO-MCBS tool (22) radium-223 received the joint highest score for clinical benefit of any intervention for any indication, but was delisted from the CDF in September 2015 (34) and is subject to appeal at the time of writing. While the CDF and ESMO-MCBS tool may be measuring different constructs, the decision to delist radium-223 while retaining drugs of lower assessed benefit illustrates both the importance of cost to the CDF, and the difficulty of establishing the actual trade-offs between costs and benefits that inform the clinical score and influence listing decisions.

Evaluation of processes: Reprioritisation

The CDF reprioritises the “list” of available treatments on a periodic basis in order to ensure the fund remains in budget (35). A type of “grandfathering” is applied to prevent abrupt changes to treatment, and drugs that are the only systemic treatment

will not be removed (20). Manufacturers may engage in negotiation with NHS England if a drug is at risk of delisting.

If uncertainty is an unwelcome consequence of this model of reprioritisation, the disinvestment that it represents is a task with which bodies such as NICE also struggle (36).

Evaluation of processes: Relevance and deliberation

Culyer (37) describes the ultimate product of a deliberative process as “guidance shaped by judgements”. A test of a deliberative process should account for its acceptability to those it affects. Different priorities are accorded by the CDF’s prioritisation tool to different types of cancer patients, and little is known about whether the public endorse the distribution of opportunity costs to which the tool gives rise.

Public consultations on changes to the prioritisation tool have been of short duration – for example, the consultation processes for the first SOP to include discussion of drugs costs was open only for the month of October 2014 (38). NICE’s “Citizen’s Council” provides one model, albeit subject to some criticism, in the search for rationales for prioritisation (39, 40), as do the structured public meetings and random telephone surveys conducted during Oregon’s experiments with using cost-effectiveness in prioritisation (41), and the “citizen juries” of Stafinski et al (42).

Evaluation of processes: Transparency

Drummond et al (43) note that cancer drug appraisals in France and England tend to reach similar assessments of value, but assessments in the former country are less transparent than those undertaken by NICE, partly because of institutional design and because of the more resource intensive process used by NICE. This suggests that conclusions of value can be the same under different levels of transparency.

However, a more extensive deliberative process than deployed by the CDF is appropriate if transparency is important in accountability for reasonableness. The body that assesses requests for reviews of CDF decisions stated in response to an appeal (18) that it "...did not accept that there is a requirement ... to explain how the scoring system has been derived or how the incremental scores have been developed and tested".

It is instructive, in this context, to compare a CDF "no" and a subsequent NICE "yes". It was possible to submit simultaneously to both bodies drugs for consideration. The CDF rejected the listing of nintedanib in combination with docetaxel (May 2015) (44) for patients with a form of adenocarcinoma of the lung, whereas NICE recommended its use for the same indication two months later (July 2015). A NICE appraisal (45) estimated a cost per QALY likely to be below £50,000, and which could be approved under end-of-life criteria. NICE noted that the company's model was well structured, similar to other economic models in the same disease area, adopted an appropriate time horizon, and used utility values collected during the trial. Few of these types of consideration would have ordinarily influenced CDF decisions.

Evaluation of processes: Speed of decision-making

An advantage of the CDF model was the speed of its decisions. Decisions of on-label submissions were to be made within 8 weeks of a drug being granted a licence by the European Medicines Agency (20). Re-evaluation of the list happened at least annually (20). Estimates of the time taken by NICE for a single technology appraisal suggest a median of approximately 48 and 74 weeks for a single and multiple technology appraisals respectively (46).

Proposed changes to the CDF

A reconfiguration of the CDF was announced in February 2016 (13, 47), following a twelve week consultation (48). The CDF will become a “managed access fund”, with an annual budget of £340m. A prospective contingency mechanism will be used as a budget control measure.

NICE will appraise all cancer drugs, and will normally issue guidance within 90 days of marketing authorisation. The CDF will provide access to drugs that may be cost-effective, but for which NICE has concluded there is insufficient evidence to support a recommendation for use in routine commissioning. A conditional recommendation will mean that the CDF could provide these drugs for a pre-specified period while more evidence was collected in order to inform decisions about the drug’s clinical and cost-effectiveness. Funding for evidence collection will be provided by the company holding a drug’s marketing authorisation. If subsequently approved, a drug will become available under routine commissioning.

Details on the nature of the evidence to be collected remain to be clarified, although there will be input from NICE with clinician and patient input, NHS England, the company involved and the Chemotherapy Clinical Reference Group. Cost-effectiveness would be assessed against NICE cost-effectiveness criteria, including, if applicable, “End of Life” criteria, which already offers a means of accessing high-cost cancer drugs not available to all other disease areas. Restrictions of drugs to the “smaller patient population” of the existing “End of life” criteria will not apply.

The use of NICE appraisal methodologies will overcome some of the problems with the use of non-standard outcome measures, the aggregate score, and some of the

emphases on rarity and unmet need. Appraisals will focus on all costs associated with delivery. These changes will support transparency, although details of implementation remain to be decided before the fund becomes operational in 2016.

The proposals continue to give pre-eminence to cancer drugs, despite a lack of evidence of general population support (49). A better alternative to collecting evidence of unknown quality and relevance would be for negotiations to reduce price in order to meet cost-effectiveness thresholds, and/or the funding of independent, high quality RCTs.

The latter could arguably meet the CDF's needs at much lower cost than temporary funding of ineffective treatments. There is already evidence that the first incarnation of the CDF did expedite uptake of cost-effective drugs subsequently approved by NICE (50).

Proposed changes to the CDF and lessons for other countries

The new operating model amounts to a substantial and wide-ranging reform of the initial CDF model. This experience offers important lessons for other countries considering similar arrangements.

The initial incarnation of the CDF faced a severe structural defect in that the model did not readily support the delisting of drugs, despite a broader international context of rising prices for cancer drugs that were associated (in some cases) with limited benefit. (51, 52). The lack, until recently, of outcome data meant that the even the benefits to patients of funded therapies remains unknown, and should be a priority in any similar model introduced elsewhere (2, 53). The introduction of the prioritisation tool assessed in this paper was founded on a recognition that the initial system was unsustainable, while the move to the use of more conventional methodologies— as

adopted by NICE in other disease areas – under the reformed model amounts to tacit acceptance that conventional approaches to economic evaluation provide more reliable evidence for decision makers.

The reformed CDF will give rise to additional burden on NICE. An important message for other countries is that the burden to which expedited access gives rise was a topic raised during the consultation and recognised as a material issue by NHS England. In response, the capacity of NICE will be expanded in order to meet these additional obligations (47).

These considerations are also relevant to the relationship of a cancer-specific agency to a national appraisal authority. One consequence of the CDF was to reduce the incentive manufacturers would otherwise face to reduce prices or conduct further research in order to secure a favourable cost-effectiveness decision from NICE (4).

Ultimately, the decision to adopt a similar model elsewhere needs to reflect societal preferences, and a commitment to make funding decisions on the basis of the best available evidence in a transparent and accessible manner.

Discussion and conclusion

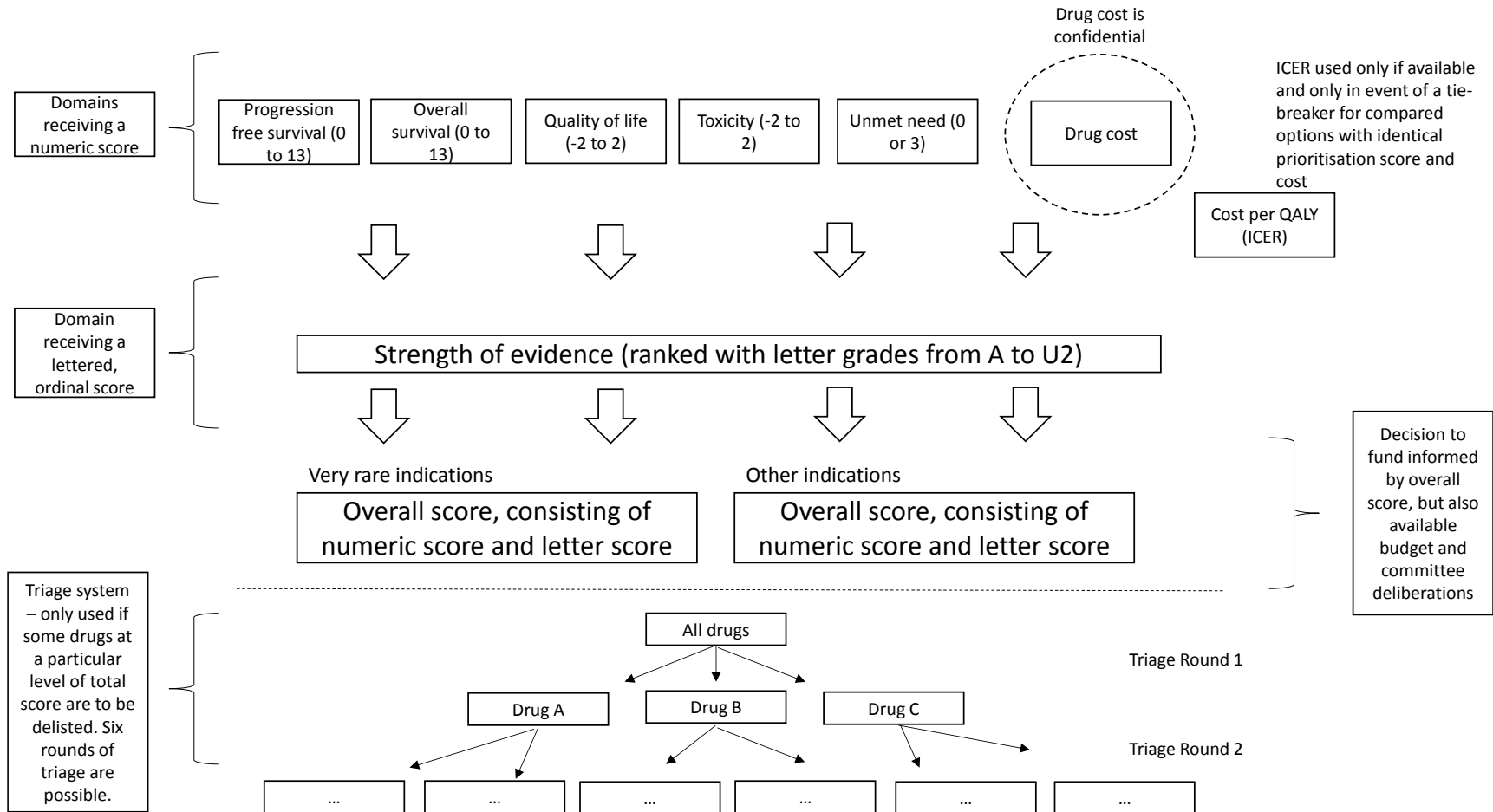
We maintain that it did matter that the CDF was not NICE. There is little or no evidence that the criteria used for prioritisation and the processes that underpinned them, which departed in many respects from the principles of economic evaluation and from existing practices and policies of technology appraisal in the UK and elsewhere, were relevant and acceptable to cancer patients or the wider public. Even a narrow consequentialist assessment of the CDF's impact on the health of individual beneficiaries of the scheme confronts the problem that little or no evidence is available to establish these effects (53) (54), primarily because important elements of relevant data did not begin to be collected until April 2014 (3).

The initial CDF imposed opportunity costs fell on different groups of cancer patients according to the criteria used in the CDF prioritisation tool, whereas the principle of a "QALY is a QALY is a QALY" that NICE applies (with exceptions) reflects the notion that each QALY has an equal value for different individuals (55). Arguments that the "hopeful outcomes" (56) of the CDF offered a bridge between cost-effectiveness analysis of bodies such as NICE and the views of patients are incomplete unless the opportunity costs of decisions so made are confronted. These findings are relevant both to the "reformed" CDF, many important details of which remain to be resolved at the time of writing, and to policymakers in other countries considering the introduction of cancer-specific appraisal and reimbursement authorities.

The reforms to the CDF are likely to improve decision-making within the fund, but the rationale for the fund's existence remains unconvincing. If there is something "special" about cancer – that it is indeed the "emperor of all maladies" (57) – such that the moral principle of treating equivalent suffering equally should be abandoned,

a debate will continue to be needed in order for economic evaluation to be conducted in a way that reflects an accepted ethical basis for allocation decisions.

1 Figure 1 Schematic representation of prioritisation tool



2

References

1. NHS England. National Cancer Drugs Fund List 6.0. 2015.
2. National Audit Office. Investigation into the Cancer Drugs Fund. London, 2015.
3. Kmietowicz Z. No evidence that £1bn Cancer Drugs Fund has helped patients, says watchdog. *BMJ*. 2015; 351.
4. Buxton M, Longworth L, Raftery J, et al. Reforming the Cancer Drug Fund. *BMJ*. 2014; 349.
5. Hughes D, Duerden M. Ring-fencing a budget for cancer drugs: Is it fair? *Against. J R Coll Phys Edinb*. 2011; 14: 226-28.
6. Chamberlain C. Access to Non-Curative Anti-Cancer Therapies on the NHS: The Role of the Cancer Drugs Fund. School of Social and Community Medicine: University of Bristol, 2015.
7. Graham J, Cassidy J. Ring-fencing a budget for cancer drugs: is it fair? *For. J R Coll Phys Edinb*. 2011; 11: 224-26.
8. Claxton K, Martin S, Soares M, et al. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technol Assess*. 2015; 19.
9. Claxton K. Methods for the Estimation of the NICE Cost Effectiveness Threshold. Science Media Centre press briefing, 2015.
10. Hawkes N. NICE is too generous in approving drugs, analysis says. *BMJ*. 2015; 350.
11. John Appleby. The Cancer Drugs Fund: inequitable and inefficient? : The King's Fund, 2014.
12. Claxton K. The UK's Cancer Drugs Fund does more harm than good. *New Scientist*, 2015.
13. Mayor S. New "managed access" process for Cancer Drugs Fund to go ahead, NHS England confirms. *BMJ*. 2016; 352.
14. McDonald H, Charles C, Elit L, et al. Is there an economic rationale for cancer drugs to have a separate reimbursement review process for resource allocation purposes? *Pharmacoeconomics*. 2015; 33: 235-41.
15. Hoch J, Beca J, Sabharwal M, et al. Does it Matter Whether Canada's Separate Health Technology Assessment Process for Cancer Drugs has an Economic Rationale? *Pharmacoeconomics*. 2015; 33: 879-82.
16. Daniels N, Sabin J. The ethics of accountability in managed care reform. *Health Aff (Millwood)*. 1998; 17: 50-64.
17. Daniels N, Sabin J. Limits to health care: fair procedures, democratic deliberation, and the legitimacy problem for insurers. *Philosophy & public affairs*. 1997; 26: 303-50.
18. NHS England. Eisai A Decision Record. Undated.
19. Public Health England. Making the case for investment in prevention and early intervention: tools and frameworks to help local authorities and the NHS. London: Public Health England, 2014.
20. NHS England. Standard Operating procedures: The Cancer Drugs Fund (CDF). Guidance to support operation of the CDF in 2015/16. London, 2015.
21. NHS England. National Programmes of Care and Clinical Reference Groups Cancer – Group B15. Chemotherapy. 2016.

22. Cheryn NI, Sullivan R, Dafni U, et al. A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: The European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). *Ann Oncol*. 2015.
23. Schnipper LE, Davidson NE, Wollins DS, et al. American Society of Clinical Oncology Statement: A Conceptual Framework to Assess the Value of Cancer Treatment Options. *J Clin Oncol*. 2015.
24. Kim C, Prasad V. Cancer drugs approved on the basis of a surrogate end point and subsequent overall survival: An analysis of 5 years of us food and drug administration approvals. *JAMA Internal Medicine*. 2015: 1-2.
25. Prasad V, Kim C, Burotto M, et al. The strength of association between surrogate end points and survival in oncology: A systematic review of trial-level meta-analyses. *JAMA Internal Medicine*. 2015; 175: 1389-98.
26. Davis S, Tappenden P, Cantrell A. A Review of Studies Examining the Relationship between Progression-Free Survival and Overall Survival in Advanced or Metastatic Cancer. Report by Decision Support Unit. Sheffield, 2012.
27. Claxton K. The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies. *J Health Econ*. 1999; 18: 341-64.
28. Claxton K, Longo R, Longworth L, et al. *The Value of Innovation*. 2009.
29. McCabe C, Claxton K, Tsuchiya A. Orphan drugs and the NHS: should we value rarity? *BMJ : British Medical Journal*. 2005; 331: 1016-19.
30. Morgan G, Ward R, Barton M. The contribution of cytotoxic chemotherapy to 5-year survival in adult malignancies. *Clin Oncol*. 2004; 16: 549-60.
31. Davis C. Drugs, cancer and end-of-life care: A case study of pharmaceuticalization? *Soc Sci Med*. 2015; 131: 207-14.
32. Fojo T, Mailankody S, Lo A. Unintended consequences of expensive cancer therapeutics—the pursuit of marginal indications and a me-too mentality that stifles innovation and creativity: The John Conley lecture. *JAMA Otolaryngology–Head & Neck Surgery*. 2014; 140: 1225-36.
33. Baltussen R, Niessen L. Priority setting of health interventions: the need for multi-criteria decision analysis. *Cost effectiveness and resource allocation : C/E*. 2006; 4: 14.
34. Cancer Drugs Fund. Radium-223 in metastatic castrate resistant prostate cancer in patients with symptomatic bone metastases. In: NHS England, ed., 2015.
35. NHS England. Cancer Drug Fund decision summaries. 2016.
36. Beynon C, Hollingworth W, Rooshenas L, et al. Using clinical practice variations as a method for commissioners and clinicians to identify and prioritise opportunities for disinvestment in health care: a cross-sectional study, systematic reviews and qualitative study. *Health Serv Deliv Res*. 2015; 3.
37. Culyer AJ. NICE's use of cost effectiveness as an exemplar of a deliberative process. *Health Economics, Policy and Law*. 2006; 1: 299-318.
38. NHS England. NHS England consultation: Proposals for a sustainable Cancer Drug Fund. 2014.
39. Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. *BMJ : British Medical Journal*. 2004; 329: 224-27.
40. Daniels N. Accountability for reasonableness and the Citizens Council. In: Littlejohns P, Rawlins M, eds., *Patients, the public and priorities in healthcare*. Oxford: Radcliff Publishing,, 2009.
41. Dixon J, Welch HG. Priority setting: lessons from Oregon. *Lancet*. 1991; 337: 891-4.

42. Stafinski T, McCabe C, Menon D. Determining social values for resource allocation decision-making in cancer care: a Canadian experiment. *Journal of Cancer Policy*. 2014; 2: 81-88.
43. Drummond M, de Pouvourville G, Jones E, et al. A Comparative Analysis of Two Contrasting European Approaches for Rewarding the Value Added by Drugs for Cancer: England Versus France. *Pharmacoeconomics*. 2014; 32: 509-20.
44. Cancer Drugs Fund. Nintedanib as part of chemotherapy for patients with locally advanced or metastatic adenocarcinoma of the lung progressing after 1st line chemotherapy. In: NHS England, ed., 2015.
45. National Institute for Health and Care Excellence. Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer. *Technology Appraisal Guidance*, 2015.
46. Casson SG, Ruiz FJ, Miners A. How long has NICE taken to produce Technology Appraisal guidance? A retrospective study to estimate predictors of time to guidance. *BMJ Open*. 2013; 3.
47. NHS England. Cancer Drugs Fund. NHS Board Paper - Board Meeting 25 February 2016, 2016.
48. NHS England & NICE. Consultation on proposals for a new Cancer Drugs Fund (CDF) operating model from 1 April 2016. 2015.
49. Linley WG, Hughes DA. Societal views on NICE, cancer drugs fund and value-based pricing criteria for prioritising medicines: a cross-sectional survey of 4118 adults in Great Britain. *Health Econ*. 2013; 22: 948-64.
50. Chamberlain C, Collin SM, Stephens P, et al. Does the cancer drugs fund lead to faster uptake of cost-effective drugs? A time-trend analysis comparing England and Wales. *Br J Cancer*. 2014; 111: 1693-702.
51. Howard DH, Bach PB, Berndt ER, et al. Pricing in the Market for Anticancer Drugs. *J Econ Perspect*. 2015; 29: 139-62.
52. Saltz LB. Perspectives on cost and value in cancer care. *JAMA Oncology*. 2015: 1-3.
53. Chamberlain C, Hollingworth W. Where is the evidence for the existence of the Cancer Drugs Fund? *BMJ*. 2014; 349.
54. House of Commons Committee of Public Accounts. Cancer Drugs Fund. Twentieth Report of Session 2015–16. London, 2016.
55. Paulden M, O'Mahony J, Culyer A, et al. Some Inconsistencies in NICE's Consideration of Social Values. *Pharmacoeconomics*. 2014; 32: 1043-53.
56. Lakdawalla DN, Jena AB, Doctor JN. Careful use of science to advance the debate on the uk cancer drugs fund. *JAMA*. 2014; 311: 25-26.
57. Mukherjee S. *The Emperor of All Maladies: A Biography of Cancer*. Scribner, 2010.