HEALTH TECHNOLOGY APPRAISAL AND ACCESS TO CANCER DRUGS IN THE UK

CASMI SUMMARY REPORT JUNE 2018
SUMMARY REPORT

This report summarises the work completed between April 2015 and November 2017 under the Cancer Research UK - CASMI Fellowship.

Health Technology Appraisal (HTA) refers to the process of deciding whether a particular technology (including drugs) will be funded by the health service. Cancer drug appraisals in the UK have been challenging since the early days of the National Institute for Health and Care Excellence (NICE). High-profile examples of this include drugs such as trastuzumab (Herceptin) in breast cancer, imatinib (Glivec) in chronic myeloid leukaemia, and sunitinib (Sutent) in renal cell carcinoma. Initially rejected, these decisions were subsequently overturned following legal challenges and public campaigns.

Policy initiatives to resolve concerns over drug access have been similarly contentious. In response to sustained public concern, the Cancer Drugs Fund (CDF) was introduced in 2010, to provide drugs not routinely available on the NHS. However, it was challenged on its sustainability and its decision-making process. An alternative approach to pricing and reimbursement – value-based pricing – was developed, but shelved in 2014 due to implementation difficulties. Meanwhile, NICE appraisals of cancer drugs continued to be controversial, with no cancer drugs being recommended for use in 2013.

The Cancer Research UK - CASMI Fellowship was funded in the context of increasing public concern over cancer drug access, and a broad uncertainty about future funding mechanisms and HTA approaches.

The policy landscape has continued to evolve:

- In 2016, the CDF was reformed to create a managed access fund, which allows early access to innovative drugs while more evidence is gathered on their effectiveness from both clinical trials and real-world clinical use.
- The Government has accepted the recommendations of the Accelerated Access Review for a process to accelerate adoption of promising technologies, including therapies. From April 2018, five technologies per year will receive "breakthrough" designation and enter the Accelerated Access Pathway.
- The 2015 Cancer Strategy called for early access and additional flexibility in NICE’s appraisal process, an ambition which was recognised in changes made in April 2018 to the process of technology appraisal.

AIM

The aim of CASMI’s project was to inform Cancer Research UK (CRUK) policy positions on cancer drug access related to HTA. Specifically, we aimed to explore alternative approaches to HTA specifically for cancer, and to identify the key elements of a HTA process that would support increased and sustainable access to cancer drugs in the UK.
To evaluate potential alternatives and improvements to HTA processes in the UK, we studied:

- The impact Scotland’s HTA reforms had on access to new cancer drugs\(^1\);
- Sources of uncertainty in NICE appraisals of cancer drugs\(^2\);
- Pricing mechanisms to manage uncertainty\(^3\); and
- Trends in CDF and NICE decisions\(^4\).

To explore the justification for giving cancer special priority in HTA, we carried out a literature review of societal attitudes to funding cancer\(^5\). We extended our findings with qualitative research on public perceptions of cancer in comparison to other serious health conditions\(^6\).

The full CASMI Report, available to download from the CASMI website, provides detailed findings related to the four workstreams of the project focussed on the HTA processes. These workstreams were prioritised by CRUK as it was felt they had greatest immediate policy impact. This Summary Report provides an overview of the project as a whole.

All published papers are accessible via CASMI’s website, and links are provided in the Appendix to the main report.

**FINDINGS**

Here we provide an overview of our findings under two inter-related themes: HTA processes, and societal attitudes towards cancer.

**HTA PROCESSES AND PRIORITIES FOR REFORM**

**SCOTLAND’S HTA REFORMS**

NICE is not alone in facing challenging funding decisions for cancer drugs. We identified a variety of cancer-related adaptations to HTA processes worldwide. Following initial evaluation we chose to focus on HTA reforms in Scotland introduced in 2014. This would determine whether these changes provided a model for expansion across the other UK nations.

The Scottish reforms target drugs used to treat rare conditions, and drugs used to treat patients at the end of their life. They include a new mechanism for eliciting additional patient and clinician input (the Patient and Clinician Engagement (PACE) meeting). We found that the reforms achieved their aim of improving access to these drugs: over a two-year period up to 38 cancer drugs were accepted that would have been at risk of rejection pre-reform.\(^1\)

The PACE analysis highlights aspects of cancer treatments that have value to patients and which could be considered for formal inclusion in the appraisal process. However, CASMI concluded that we cannot advocate broad adoption of the PACE model as it remains unclear what specific contribution it made to funding decisions.
UNCERTAINTY IN NICE APPRAISALS OF CANCER DRUGS

The Cancer Drugs Fund (CDF) in England was originally created to provide patients with access to drugs that were not routinely funded in the NHS. In April 2016 it became a managed access fund, following extensive debates about its sustainability. It now provides funding for cancer drugs where there is:

1. uncertainty in the economic case; and
2. where that uncertainty can be resolved by generating “real-world” data (RWD) over two years’ use to inform a subsequent review and decision.

We aimed to identify the sources of uncertainty that we might expect to see leading to entry into the new CDF, and the data collection required to resolve the uncertainty.

Analysis of NICE appraisals of cancer drugs during 2014-16 identified the main sources of uncertainty as immaturity of survival data and use of comparator treatments not relevant to England. These will not readily be resolved within the reformed CDF, although the CDF can provide early access whilst ongoing clinical trials mature.

Other key sources of uncertainty are costs, quality of life data, and trials not perfectly reflecting UK patient populations and treatment practices. These uncertainties are more readily resolved through RWD collection in the CDF and they are the ones we expect to see using the CDF route. This expectation was confirmed in the first year of operation of the new CDF.

PRICING MECHANISMS TO MANAGE UNCERTAINTY

HTA is a multifaceted process. It makes greatest sense in advocating for reform to focus on the aspects expected to have the greatest impact on patient access to drugs. During the summer of 2016, CASMI worked with CRUK to identify a wide range of potential targets for reform and prioritise key areas for future advocacy work.

Pricing mechanisms were selected as a priority. This would enable us to increase the effectiveness of a fixed health care budget, while managing uncertainty by enabling pricing to adapt to an evolving evidence base.

Our case studies confirm that pricing mechanisms can be used to enable access, manage uncertainty and, in some cases, link to the value provided by the technology. Key requirements for a successful scheme are: minimising the administrative load; unambiguous definition of data requirements; allocating rebates or credits to the specific provider; and ensuring any deferred decisions can be upheld once data are available.

IS IT NICER IN NICE?

CASMI monitored decisions made by NICE and by the former CDF, with the aim of identifying trends or process elements of relevance to future policy. In particular, we explored concerns at the time of reforms to the CDF that returning all cancer drugs funding decisions to NICE would be a backwards step in access terms.
We found this concern does not appear to have been realised. Overall, the proportion of cancer drugs recommended for routine or "optimised" (i.e. recommended for a subset of the population covered in the marketing authorisation) access has increased from an average of 45% over the period 2010-2015 to an average of 78% across 2016 and 2017.

All eleven drugs from the former CDF that had previously been rejected by NICE have now been accepted for funding following reconsideration. CASMI suggests this is driven largely by commercial negotiations, as we see limited use of additional data to support acceptance.

The vast majority of other drugs from the former CDF have also been accepted. We also observed eight examples of drugs that had been rejected by the former CDF being accepted by NICE. This is perhaps unexpected as NICE had been considered a tougher hurdle than the CDF. This reflects the fact that NICE’s process has capability to assess and debate uncertainty.

**SOCIETY’S ATTITUDE TO CANCER**

**SYSTEMATIC REVIEW**

To determine the basis for cancer being treated differently by HTA processes, we carried out a systematic literature review of studies of societal attitudes to cancer. We focused specifically on its relative priority among other uses of healthcare resources. We found that when respondents are asked to make a trade-off in health for other patients, they do not show a preference to fund cancer treatments at others’ expense. However, they do show a preference to fund “severe” conditions. Therefore, the evidence does not support extending special funding arrangements for cancer.

However, where no trade-off is required, or where respondents are thinking only about spending their own money, we found cancer to be a high priority. This is consistent with perceptions of cancer as a feared disease, strong support for cancer charities, and public and policy response to cancer drug funding decisions.

To resolve this inconsistency, CASMI suggests that the (tangible) concept of “health” might not capture the broader and perhaps subjective aspects that matter deeply to the public. We proposed to identify such attributes across diseases, so that they could be used explicitly in funding decisions, not only when they occur as a named condition, but in any other condition where they might apply. Our emphasis was on generalising important attributes, rather than on advocating special approaches for cancer. The outputs of this work are explored immediately below.

**UNDERSTANDING PERCEPTIONS OF ILLNESSES: QUALITATIVE RESEARCH**

Focus group research among members of the public identified five themes common to a range of serious health conditions: fear, impact on family, hope, detection and prevention.
Each condition had its own combination of specific concerns that shape public perceptions. Cancer was characterised by fear of death and of aggressive treatment, the all-consuming effect on family, a strong focus on hope and a sense of a fight against a vindictive, relentless and “sneaky” enemy. Importantly, concerns about missed treatment opportunities due to late detection, as well as limited awareness of lifestyle-related risk factors, fully support CRUK’s focus on early detection and prevention.

Similar themes were found in our work on Scotland’s HTA reforms, which identified aspects important to patients that are not explicitly captured in the HTA process. Key themes included disease prognosis (long-term and recurrent conditions as well as life-limiting factors), independence and normality, unmet clinical need and sustaining hope.

Combining these findings with the focus groups, we designed a trade-off study to quantify the relative importance of these features. This work revealed aspects of hypothetical new treatments highly valued by the public included a lack or paucity of other treatment options (i.e. unmet clinical need), reducing care needs, where there is a better perceived prognosis for a person with the condition, and where diagnosis is easier or can be made more quickly. The results add particularly to the support for formal consideration of unmet need in HTA.

POLICY IMPLICATIONS

CASMI’s work has informed CRUK’s position and responses to consultations on a range of issues. This includes the changes to the CDF, response to the Montgomery report on HTA reforms in Scotland, patient involvement in NICE’s work, the Budget Impact Test, and NICE’s consultation on increasing capacity.

Findings from this work are also reflected in CRUK’s priorities for access policy. This focuses on:

- pricing mechanisms to manage uncertainty and reflect value;
- building on the UK’s real-world data collection capability as an enabler; and
- increased flexibility in the NICE process to accommodate value outside current definitions of health.

CRUK’s overall policy work (and forthcoming position paper) on access to cancer drugs reflects these priorities. Implications of CASMI’s work for informing ongoing policy activity fall under two main themes: additional aspects of value in cancer treatment and the role of pricing in managing uncertainty.

CASMI’s work on societal attitudes to cancer suggests there are aspects of cancer and its care that shape public perceptions. The themes identified are consistent with the broader aspects of value identified by the value-based pricing (VBP) initiative, which explicitly sought to include factors that patients and society value, such as impacts on carers.

This is the most recent approach in the UK to account for such broader aspects of value in HTA. From a policy perspective, the consistent emergence of common themes suggests that these are key issues that will continue to be reflected in public, patient and advocacy responses to negative funding decisions. CASMI recommends CRUK
continues to support discussions on incorporation of these broader aspects of value into HTA.

However, the VBP experience shows that integrating broader concepts of value is not without challenges. Examples of the difficulties include: determining the relative importance of the new parameters, defining the parameters such that we avoid inadvertently “double-counting” aspects of health benefit under more than one of them, and determining the appropriate cost-effectiveness threshold for such a “new QALY”. This is an active area of research, but is unlikely to find a quick fix – and long-term engagement will be needed from all stakeholders.

Uncertainty is an inevitable feature of decision-making. This will continue to increase as promising drugs seek accelerated approval at early stages of development. Where the uncertainty cannot be eliminated, two elements become necessary to support decision-making.

First, a mechanism to debate that uncertainty and understand its effect on the funding decision. Second, a pricing approach that moves away from a single point in time evaluation to an expectation of renegotiation as the evidence base evolves. The reformed CDF within NICE demonstrates both these elements and so provides an important step forward in our ability to handle uncertainty.

Such an adaptive approach is consistent with the aims of the Accelerated Access Review and the UK’s Early Access to Medicines Scheme. Linking the renegotiation directly to outcomes, rather than simply financial mechanisms, can act as an incentive for innovation. This will ensure drug spending reflects the real value of the technology.

CRUK recently launched a research programme, “Making outcome-based pricing a reality in the NHS”. The three-phase project aims to develop a new model for paying for cancer drugs, based on a combination of clinical trial data and evolving the evidence base on outcomes important to patients. This project neatly draws together the two threads of the CASMI work – broadening the definition of “value” in cancer care, and adaptive pricing mechanisms. The key challenge in progressing this work will be in determining how to combine the broader outcomes data, to arrive at a price that reflects the value provided.

Whilst we have made progress in understanding aspects of value and how to pay for it, challenges for HTA remain. Notably, these include the ability of the healthcare system to afford transformative technologies that may be very expensive. Examples include:

- cell engineering approaches to re-programme the patient’s own immune cells to attack cancer (CAR-T cell therapy);
- high-price drugs used in combination; and
- precision medicines at high prices that reflect the small target population.

Decision-making in these situations will require further development of our appraisal and payment processes. We expect these to include elements such as: considering radically different payment mechanisms; making sure we fully account for the benefits of avoiding treatment morbidity; and improving our ability to evaluate health outcomes across the whole of a patient’s complex treatment pathway.
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REFERENCES
