

# Making Outcome-Based Payment a Reality in the NHS

## *Phase 2: Practical Considerations*

Supplementary report

November 2021

Together we will beat cancer

Greater  
Manchester  
Health and  
Social Care  
Partnership



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# Reference

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# Authors

Cancer Research UK and Greater Manchester Health and Social Care Partnership commissioned the Office of Health Economics, RAND Europe and University College London to carry out the research underpinning this report. The research team also collaborated with colleagues from the University of Manchester.

The report authors are Amanda Cole<sup>1</sup>, Patricia Cubi-Molla<sup>1</sup>, Rachel Elliott<sup>2</sup>, Alexandra Feast<sup>3</sup>, Lucy Hocking<sup>4</sup>, Paula Lorgelly<sup>5</sup>, Katherine Payne<sup>2</sup>, Niels Peek<sup>2</sup>, Duncan Sim<sup>3</sup>, Jon Sussex<sup>4</sup>, Kyann Zhang<sup>1</sup>, Lotte Steuten<sup>1</sup>.

*1 Office of Health Economics*

*2 University of Manchester*

*3 Cancer Research UK*

*4 RAND Europe*

*5 University College London*

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We formed the Greater Manchester Health and Social Care Partnership to oversee the devolution of our health and social care services. Our aim is to achieve the biggest, fastest improvement to the health and wellbeing of our region.

The Partnership is made up of our local NHS organisations and councils, as well as people from NHS England and NHS Improvement, our emergency services, the voluntary sector, Healthwatch and others including the mayor of Greater Manchester.



<https://www.gmhsc.org.uk/>

# Research Team

This research was conducted by:



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# Appendix 1 – Outcome metrics and data in the NHS

## Objective

The main aim of this stage of the research was to identify the most appropriate measures, in terms of relevance and psychometric properties, and data to capture the effect of a cancer treatment on four core outcomes (derived from Phase 1).

Specifically, the objectives of this stage were:

- A. To identify previously validated **measurement instruments and metrics** to evaluate (specific aspects of the) the following outcomes: survival (S); disease progression, relapse or recurrence (DP); long-term treatment side effects (LT); and return to normal activities of daily life (RN).
- B. To identify relevant examples of **research and clinical data** on patient outcomes that are collected in the NHS and the health system more widely.
- C. To develop a set of **criteria** in order to categorise the measures and instruments, as well as the most appropriate datasets identified in relation to objectives A and B.

Based on the findings in objectives A, B, and C, we constructed a **pragmatic example** of how treatments outcomes could be assessed as part of an outcome-based payment scheme. This pragmatic example is detailed in the last section of this appendix.

## Method

The following sections summarise methods and approach followed for each objective.

### A. Measurement instruments and metrics

A Rapid Evidence Assessment (REA) was undertaken in order to identify instruments and metrics that align with the four core outcomes. REA provides a systematic approach to evidence gathering but places specific restrictions (such as timeframe, targeted databases) on the scope of the search to allow a focused review in a limited timeframe.

The search strategy was effectively tailored to two main sub-areas in the outcome literature: clinical measures (for S, DP and LT), and patient-reported outcome measures (for LT and RN). Note that LT instruments were identified using both approaches.

For clinical measures, we searched the following databases:

- [a] Recommended clinical outcomes or guidance documents by European Society for Medical Oncology (**ESMO**), American Society of Clinical Oncology (**ASCO**), European Federation of Pharmaceutical Industries and Associations (**EFPIA**), International Federation of Pharmaceutical Manufacturers & Associations (**IFPMA**), International Society For Pharmacoeconomics and Outcomes Research (**ISPOR**), National Institute for Health and Care Excellence (**NICE**), National Centre for Health Outcomes Development at the University of Oxford (**NCHOD**);

- [b] Clinical outcome requirements and guidance in European Medicines Agency (**EMA**), and the Food and Drug Administration (**FDA**);
- [c] Additional search of papers and citations in the following potential sources <sup>1,2</sup>

Limits applied: for **[a]** and **[b]**, the most recent list/guidance was reviewed; only literature in English.

For patient-reported outcome measures, we searched the following sources:

- [a] Targeted databases: **COMET**<sup>i</sup>, **COSMIN**<sup>ii</sup>
- [b] Academic literature search: on Embase and MEDLINE (via Ovid). The search commands used for LT and RN are detailed in Table 1.
- [c] Selected set of papers known to be relevant <sup>1,3</sup>

**Table 1: Search commands for the academic literature review (via Ovid)**

Outcome	Search command	Filters
LT	<p>(cancer* OR neoplasm* OR tumor* OR tumour* OR carcinoma OR oncolog*)</p> <p>AND</p> <p>(medicine* OR pharmaceutical* OR drug* OR episode* OR treatment OR technology)</p> <p>AND</p> <p>((long term OR long-term OR long standing OR long-standing) adj3 (side effect* OR side-effect OR (adverse adj2 effect*) OR (adverse adj2 reaction*) OR complication* OR toxicity OR undesirable effect* OR unexpected effect*))</p> <p>AND</p> <p>(instrument* OR tool* OR scale* OR subscale* index OR indices OR rating* OR short form OR short-form OR score* OR measur* OR PROM OR PROMs OR (patient adj2 outcomes))</p> <p>AND</p> <p>(patient*)</p>	<p>MEDLINE: "all adult (19 plus years)"</p> <p>Embase: (adult &lt;18 to 64 years&gt; or aged &lt;65+ years&gt;)</p> <p>Other filters: English, human, humans, 2010-current (w3 September 2019)</p>
RN	<p>(cancer* OR neoplasm* OR tumor* OR tumour* OR carcinoma OR oncolog*)</p> <p>AND</p> <p>(usual OR normal OR daily OR everyday OR day to day OR day-to-day) adj3 (life OR lives OR activit*)</p> <p>AND</p> <p>(instrument* OR tool* OR scale* OR subscale* index OR indices OR rating* OR score OR measur* OR PROM OR PROMs OR (patient adj2 outcomes))</p> <p>AND</p> <p>(patient*)</p>	<p>MEDLINE: "all adult (19 plus years)"</p> <p>Embase: (adult &lt;18 to 64 years&gt; or aged &lt;65+ years&gt;)</p> <p>Other filters: English, human, humans, 2010-2019, Publication type: "Systematic Review"</p>

LT: long-term treatment side effects; RN: return to normal activities of daily life.

## B. Research and clinical data

A review of relevant websites and published papers related to data collection conformed the initial list of research and clinical data sources. In addition to identifying datasets, information was gathered on the data collection processes and linkage platforms. Preliminary findings were discussed, completed, and updated by expert input from members of the research team

<sup>i</sup> <http://www.comet-initiative.org/>

<sup>ii</sup> <https://www.cosmin.nl/>



(University of Manchester), as well as interviews to relevant researchers and data custodians along the project (see Appendix 3 for additional details).

## C. Selection criteria

An initial list of potential criteria to identify the best outcome measures, as well as the most appropriate datasets, was discussed by the research team. A survey was subsequently sent to members of the SG, in order to ratify or reject the suggested factors.

# Findings

## A. Measurement instruments and metrics

### Survival

Survival was usually included in guidelines with relation to recommendations for interventions in the treatment of cancer. The most frequent survival measures identified in the review were: *overall survival, all-cause mortality, and disease-specific mortality*. However, it was uncertain whether it could be assumed that the definitions were necessarily equivalent between documents or organisations. For instance, documents typically did not specify the start date used for survival (e.g. start of randomisation or treatment, or end of treatment), making difficult to compare across sources. A summary of the most common survival measures can be found in Table 2 (p.6).

### Disease Progression, Relapse or Recurrence

A variety of measures were reported to evaluate outcomes in this category (see Table 2 for a summary of the most frequently identified). Measures of disease progression were observed to be dependent on the nature and location of disease. For example, response of patients with solid tumours may be measured using x-rays, CT or MRI scans to detect and report change in size of tumours.<sup>4</sup>

As *disease progression* was commonly considered a surrogate endpoint, we found that different measures often used different reference points. For example, ***time to progression*** was usually measured from randomisation to objective tumour progression (not including death); ***progression-free survival*** was typically defined as from randomisation to objective tumour progression or death; ***whereas time to treatment failure*** is normally defined from randomisation to discontinuation of treatment for any reason (including disease progression, toxicity, and death). Other clinical measures identified in our search were: *response evaluation criteria in solid tumours (RECIST), overall objective response rate, duration of response, time to next treatment, treatment duration, relapse-free survival, and time to objective response*. In some cases, a measure of patient symptoms (as opposed to an objective measure) was used, however it was noted that symptoms of disease may be difficult to differentiate from those relating to treatment (toxicity).

## Long-term treatment side effects

'Side effect' is a colloquial term often used to refer to a drug's unintended effects that occur within the therapeutic range<sup>iii</sup>. In particular, the NHS<sup>iv</sup> defines side effects as unwanted symptoms caused by medical treatment, which are also called 'adverse effect' or 'adverse reaction'. In the literature review, we identified 'adverse drug reaction' as a type of toxicity.

While side-effects are an important consideration in guidelines, most of the focus appeared to be placed on those that were relevant either during treatment or in the short-term following treatment. In some cases it is noted that some side effects from the treatment – either during or immediately after – may persist into the long-term, however it is not usually specified what length of time constitutes 'long term', and whether these require follow-up (e.g. to note frequency or severity).

The review of the literature on clinical outcomes also signalled that side-effects of treatments are highly varied depending on the location of disease and the treatment prescribed. It may be advisable to identify either the most common long-term treatment side-effects; and/or the side-effects that are most important from the patient's perspective (e.g. due to impact on quality of life).

Figure 1 provides a graphical representation of the literature identified in the search focusing on patient reported outcomes and patient reported experience, as well as the results of each stage of the sifting process. Similar to our findings from the clinical outcome literature, long-term treatment side-effects were not typically a focal point in studies. Some effects may be captured through questionnaires on quality of life or in relation to daily activities<sup>5-7</sup> (for example, Radiation Therapy Oncology Group *Late Radiation Morbidity Scoring Schema* is used to report long-term quality of life and late side effects after adjuvant chemoradiotherapy);<sup>8</sup> however, these are not specifically linked to treatments or treatment pathways.

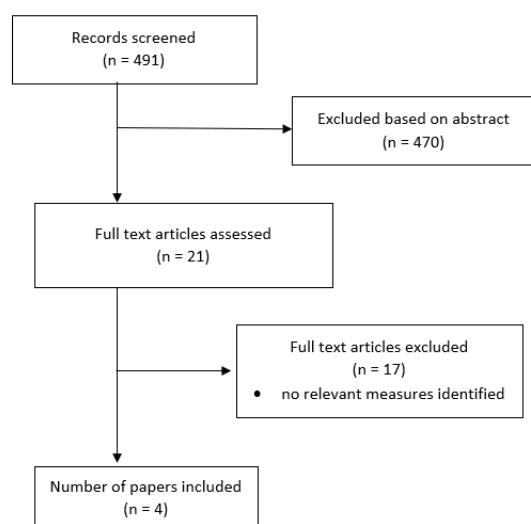


Figure 1: PRISMA Flow Diagram for long-term treatment side effects (LT)

<sup>iii</sup> <https://www.msdmanuals.com/professional/clinical-pharmacology/adverse-drug-reactions/adverse-drug-reactions>

<sup>iv</sup> <https://www.nhs.uk/common-health-questions/medicines/what-are-side-effects/>

In general, we found that due to the wide range of side effects relating to different disease areas and treatments, it is highly unlikely that they can be captured with a single instrument. The search did not provide any reliable measure to capture the overall impact of long-term treatment side effect. Table 2 (p.6) reports the most common side-effects identified across cancer types, for illustrative purposes.

## Return to normal activities of daily life

Figure 2 provides a graphical representation of the literature identified in the search focusing on patient reported outcomes and patient reported experience, as well as the results of each stage of the sifting process. Note that all the documents retrieved were systematic literature reviews

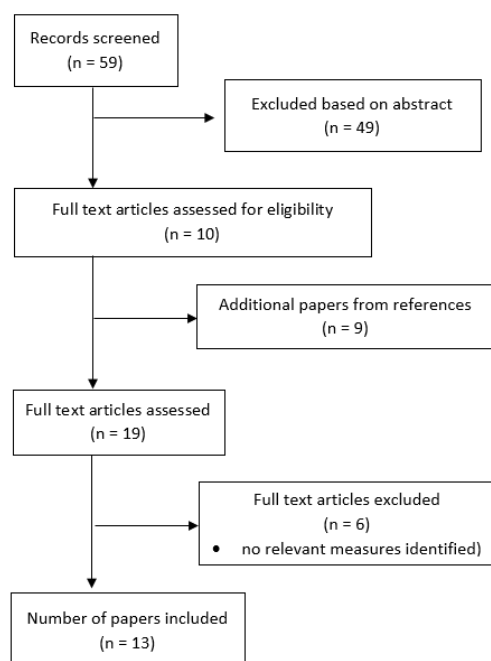


Figure 2: PRISMA Flow Diagram for return to normal activities (RN)

A total of 46 different instruments were identified in the search. (Only measures reported in more than one extracted paper are listed in Table 2, p.6<sup>v</sup>) The instruments were classified into three overall groups:

- Generic or cancer-specific (but not cancer site-specific) instruments which can be used across areas. For example: *EQ-5D*, *SF-6D*, *EORTC QLQ-C30*, or *FACT-G*.
- Cancer site-specific measures which consist of the adaptation of a cancer-specific instrument to a particular type of cancer. These measures include domains that are tailored to cancer site, but they still share core domains among them (examples: *PSS-H&N*, *FACT-L*, *FACT-F*, or *FACT-H&N*).
- Cancer site-specific instruments which are not derived from a broader instrument (examples: Eating Assessment Tool (*EAT-10*) or Head and Neck Quality of Life (*HNQOL*) for head and neck cancer). These instruments will not be considered here, since they may add sensitivity but in detriment of the practicality of using broader measures.

Normal activities of daily life were usually captured as part of patient questionnaires that

<sup>v</sup> A detailed list of the retrieved measures and references is available upon research

covered a number of domains. For example, physical functioning levels was introduced in questionnaires in different items as *level of fatigue*, *impact of fatigue on daily work*, and *physical and social activities*.<sup>9</sup>

Some measures focused on limitations of daily life (for example, *Katz Index of Independence in activities of daily living*, and *Lawton instrument Activities of Daily Living scale*)<sup>10,11</sup> and associated impairments, such as those relating to basic functions (as bathing or feeding) to more complicated actions (for example, food preparation or handling finances). Most frequently, the identified measures focused on functions that are specific to the location of disease or type of treatment. For example, measures following treatment for oropharyngeal cancer focus on *ability to speak, swallow and related pain*.<sup>12</sup> Others may be more generalised to cover aspects such as *ability to function*<sup>7</sup> or *independence*.<sup>11,13</sup>

**Table 2: Summary of the main outcome measures identified in the review, by core outcome**

<b>Survival</b> Overall survival All-cause mortality Disease-specific mortality	<b>Return to normal activities of daily life</b> Brief fatigue inventory (BFI) Eastern Cooperative Oncology Group Performance Status (ECOG) European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) EQ-5D Functional Assessment Measure (FAM) Functional assessment of cancer therapy-General (FACT-G) Illness intrusiveness ratings scale (IIRS) International classification of functioning, disability and health (ICF) Karnofsky Performance Status Scaler (PSS) Katz Index of Independence in Activities of Daily Living (ADL) Medical outcomes study 12-item short form survey (SF-12) Medical outcomes study 36-item short form survey (SF-36) Nottingham extended activities of daily living (NEADL) Nottingham health profile (NHP)
<b>Disease progression, relapse or recurrence</b> Response Evaluation Criteria in Solid Tumours Objective Response Rate Time to Progression Progression-Free Survival Time to Treatment Failure Time to next treatment	
<b>Long-term treatment side-effects</b> Fatigue Increased risk of other cancers Difficulty with focused thinking Infertility Early menopause Lymphedema Long-term pain	

## B. Research and clinical data

A summary of the main findings can be found in Table 3 (clinical and research datasets), Table 4 (platforms for data collection), and Table 5 (platforms/software with/for data linkage).

**Table 3: Electronic Health Record (EHR) datasets**

Name	Details
<b>HES</b>	Hospital Episode Statistics show all patient episodes at English NHS hospitals (admissions, outpatient appointments and emergency attendances)
<b>OPCRD</b>	Optimum Patient Care Research Database Mostly for Asthma and COPD, GP level

Name	Details
<b>SACT</b>	The Systemic Anti-Cancer Therapy database has been collecting longitudinal data relevant to all systemic anti-cancer therapies in England from 2012. Submitting data to SACT is mandatory for all hospital trusts. Recent publications suggest that the SACT dataset in isolation is largely unfit for enabling OBR in oncology, whether through clinical, economic or humanistic outcomes
<b>COSD</b>	Cancer Outcomes and Services Dataset provides information. on pathology and patient pathway
<b>NRD</b>	National Radiotherapy Dataset has been collected since 2009 in England for all cancers. Among the outcomes collected we highlight the intended outcome of treatment (palliative and radical treatment)
<b>NCPES</b>	The National Cancer Patient Experience Survey is addressed to all adult patients in England with a primary diagnosis of cancer, who have been admitted to hospital or seen as day case patients for cancer related treatment. The NCPES questionnaire includes 69 multiple choice and one free text questions which are organised under twelve sub-headings (such as access to GP, diagnostic services, shared decision-making with patients, holistic care or communication) and a last section ("About you") with information on age, gender, ethnicity, and any long-standing condition besides cancer.
<b>NCWTMDS</b>	Cancer waiting times
<b>CPRD</b>	Clinical Practice Research Datalink is collected since 2012. Its scope is primary care, and it mainly provides the information on referrals to secondary care
<b>RCGP RSC</b>	Royal College of General Practitioners Research and Surveillance Centre
<b>ONS</b>	Mortality data provided by the Office for National Statistics
<b>Cancer QoL</b>	PHE and NHS England are developing a new quality of life metric, which will combine some dimensions from the EQ-5D-5L and EORTC QLQ-C30 questionnaires. A first stage will collect data from <i>all</i> breast, lung and colorectal patients who are alive 18 months post diagnosis. From Summer 2021 onwards, the collection is planned to be extended to all cancer sites
<b>ePROMs</b>	A survey collected at The Christie which includes a list of the most common/important symptoms, with questions adapted from the EORTC-QLQ-LC13 instrument, as well as EQ-5D-5L. Currently piloted for all patients (16+ years of age) receiving proton therapy, and with all breast, lung and colorectal patients being treated with proton other treatment modalities

**Table 4: Relevant applications or platforms for data collection**

Name	Details
<b>DrDoctor</b>	Data Platform that includes a tool for effective patient follow-up management through real time outcome data collection. The Christie is currently piloting the use of this platform for PROM collection from patients in lung and head & neck clinics since January 2019.
<b>Blueteq</b>	<p>This electronic system allows to collect data on drug prescription and use at patient level. For nationally commissioned drugs (e.g. CDF), submitting the drug use via the Blueteq system is essential for having a refund. NHS England specifies the details to be collected at prescribing, and at follow-up/outcome (e.g. NHS number, hospital, drug, indication, line, meet success criteria, or meet criteria for continuing). Data collected will therefore vary with every drug and will be determined by approval status. Note that for locally commissioned drugs, forms for data entry are designed by the CCG (i.e. not standardised).</p> <p>Data may be entered into Blueteq by clinician, nurse, pharmacist at prescribing and follow-up. We could not find references of Blueteq data linked with other datasets.</p>

Note: There are also further clinical tools that are primarily used to manage electronic prescriptions, such as ChemoCare.

Table 5: Platforms/software with/for data linkage

Name	Details
<b>NCRAS</b>	The National Cancer Registration and Analysis Service is run by Public Health England. It provides the linkage between clinical outcomes and services datasets (PAS, MDT, pathology reports, imaging, and SACT), NHS Digital (CWT, HES, and DID), and population and mortality figures from the ONS registries. It has records of every cancer patient diagnosed in England.
<b>Graphnet CareCentric</b>	This integration service works by connecting different systems and sharing information between them. The Christie has recently purchased this software, which will allow them to link primary and secondary care data <a href="#">Link</a>
<b>LHCRE</b>	NHS England Local Health Care Record Exemplars will be recording individual's integrated care. Unclear which outcomes. Aimed to enable the safe and secure sharing of an individual's health and care information as they move between different parts of the NHS and social care. GM is one of the five "Exemplars", and it is adopting Graphnet CareCentric for integration of health and care records.
<b>DATA-CAN</b>	The Health Data Research Hub for Cancer – will work with patients across the UK to bring their clinical data together. The Hub will be supported by patients, charities, clinicians, academic and industry-based researchers and innovators, and will involve cancer hospitals across the UK. Cancer Research UK and The Christie NHS are two of the large group of organisations involved in DATA-CAN <a href="#">Link</a>
<b>Datalab</b>	Datalab is a project under the GM partnership, which will explore how routinely collected information - including anonymised data derived from patient records - might be used to evaluate the effectiveness of medicines, new technologies and interventions in the development of NICE guidance
<b>HIC</b>	The NIHR Health Informatics Collaborative (HIC) brings together all NHS trusts with NIHR Biomedical Research Centres (BRCs) and their partner trust to make NHS clinical data more readily available to NHS trusts, researchers, industry and the wider NHS community.

## C. Selection criteria

Factors 'feasibility' and 'pragmatism' were constantly addressed by all the expert opinions consulted. There was a general agreement on the main criteria to select the most appropriate outcome measures, based on data availability and quality, as well as validity, objectivity, and comparability of the responses. Additional criteria were also discussed in relation to each core outcome. There was also a broad agreement that the best outcome measures should not be considered on a one-fits-all basis: factors as cancer site, disease stage, line of therapy, and treatment type, all those should also play a significant role on the selection of the most suitable outcome measure. A summary of the preferred measures by core outcome, together with the criteria applied for their selection as well as additional factors to be accounted for, can be found in Table 6.

Table 6: Summary of preferred outcome measures, selection criteria and relevant factors, by core outcome

Outcome	'Best' Measures	Criteria	Factors
Survival	Overall survival All-cause mortality Disease-specific mortality	Data availability Time delays on data retrieval and subsequently delays on payment Validity (robust to diagnosis errors, quality of data collection) Missing data	Prognosis (Long/Short survival) Cancer site/type Disease stage

Outcome	'Best' Measures	Criteria	Factors
Disease progression, relapse or recurrence	Time to next treatment Treatment duration Time to treatment failure Progression-free survival Relapse-free survival	Existence of data sources Data quality and completeness Consistency in the terminology and comparability Objectivity	Curative/Non-curative Cancer site/type Line of therapy Disease stage Age
Long-term treatment side-effects	Toxicity or adverse effects	Data availability and quality Completeness incl. follow-up Objectivity Comparability	Cancer site/type Disease stage Treatment type
Return to normal activities	EQ-5D ("Usual activities") SF-6D (specific items), EORTC-QLQ30 (specific items) FACT-G (specific items) ADL	Data availability and quality Completeness incl. follow-up Used in RCTs Objectivity Comparability, robustness, validity, responsiveness	Treatment type Disease stage

Preferences over measures of survival depended on whether the target population concerns patients with late stage cancer (where overall survival and disease-specific survival largely overlap) versus early stage disease where disease-specific survival would be preferred because overall survival would be influenced by many other factors beyond any anti-cancer treatment provided. In situations where overall survival was preferred, respondents suggested measuring overall survival from start of treatment (initiation) for a limited time-period, say 1 year.

There was a general consensus that existing data sources are not sufficiently adept for capturing progression, recurrence or relapse. Suggested proxies for progression included time to next treatment, treatment duration, or time to treatment failure.

Fatigue, pain, and difficulties with focused thinking were reported to be the most common side effects of anti-cancer treatments. However, there was a general agreement that a 'one size fits all' approach does not apply specially in relation to this outcome, as side effects from cancer treatment vary by type and stage of cancer, treatment modality used, plus patient to patient variation.

Respondents were unanimous in that there were currently no national databases to collect data on ability to return to normal daily activities from patients treated for cancer. For the purpose of OBC-schemes, respondents generally preferred generic quality of life measures over condition-specific ones, mainly for practical reasons.

The research team took a closer examination of the outcome measures categorised as most appropriate (see Table 6), with the aim of discern additional practicalities related to their potential implementation in a OBP scheme. The following factors were examined: burden of completion and data retrieval; inconvenience of the response; quality, completeness, and linkability of existing NHS data on the measure; and difficulty to introduce at scale. Review of the relevant literature, as well as expert opinion, were the main consulted sources. Results can be found in Table 7.



Table 7: Characteristics of the core outcome ‘best’ metrics/instruments (in red: more negative factors; in green: positive factors)

Core Outcome	Burden (completion)	Burden (data retrieval)	Inconvenience (Elapsed time)	Quality of existing NHS data	Completeness of existing NHS data	Linkability of existing NHS data	Difficulty to introduce at scale
Outcome metric/instrument							
<b>Survival</b>							
All-cause mortality	Low	Low	High	High	High	High	Low
<b>Progression/relapse</b>							
Treatment duration	Low	Medium	Low	Medium	High	High	Low
Time to next treatment	Low	Medium	Medium	Medium	High	High	Low
Time to treatment failure	Low	Medium	Low	Medium	Medium	High	Low
Relapse-free survival	Medium	High	High	n/a	n/a	n/a	n/a
Progression-free survival	Medium	High	High	n/a	n/a	n/a	n/a
<b>Post-treatment consequences</b>							
AE questionnaire (ePROMs)	Medium	Low	Medium	n/a	High	High	High
<b>Return to normal activities</b>							
Activities of Daily Living questionnaires	Medium	Low	Medium	n/a	n/a	Low	High
EQ-5D-3L/5L (ePROMs)	Medium	Low	Medium	n/a	High	High	High
EQ-5D-5L *	High	Medium	Medium	n/a	n/a	Low	Low
EORTC QLQ-C30 *	High	Medium	Medium	n/a	n/a	Low	Low
EORTC QLQ-C30 (CTs)	High	Medium	Medium	High	High	High	Low
FACT-G (CTs)	High	Medium	Medium	High	High	High	Low

AE: adverse effects; \* Instruments collected as part of NHSE/PHE national quality of life metric, due to be at national scale from summer 2021; CT: Clinical Trials

## A pragmatic example

A realistic – though hypothetical- example was constructed, based on the main findings in the previous sections of the Appendix. We first suggested the ranking of measures to be used for each core outcome. This categorization of measures was mainly based on the results summarised in Table 6 and Table 7. Then we illustrated how the selected measures could be used in a hypothetical OBP scheme, including which dataset could be used to retrieve the measure, and which outcome thresholds could be considered as reasonable to implement. We present two scenarios: OBP at patient level, and scheme at population level.

The drug chosen for this example was panobinostat, which was recommended by NICE in early 2016 as a 3<sup>rd</sup> line treatment (administered in combination with bortezomib and dexamethasone) for multiple myeloma.<sup>14</sup>

All figures are approximate and included for illustrative purposes only.

## Survival

We propose that for cancers with a median patient prognosis of less than one year of survival, all-cause mortality would be the preferred measure. For patients / populations with a longer survival prognosis, disease-specific mortality could be the preferred measure. However, the accuracy of disease-specific mortality has been questioned by a number of the experts interviewed, since identifying the cause of death requires additional interpretation and validation of data, which may introduce bias. Therefore, the use of disease-specific mortality would potentially need a bespoke data collection based on patient records, which will incur an additional expense and suffer from a lack of scalability.

We recommend the use of disease-specific mortality for treatments with survival prognosis of more than one year, but advise careful planning of extra resources and clarification of the terms



of reference needed for that purpose. The ranking of preferred outcome measures for survival are shown in Table 8.

**Table 8: Measures for core outcome survival**

Survival prognosis	Ranking of outcome measures
<1y	1. All-cause mortality 2. Disease-specific mortality
>1y	1. Disease-specific mortality 2. All-cause mortality

Regarding datasets available for tracking overall or disease-specific survival, mortality figures from ONS registers and Systemic Anti-Cancer Therapy (SACT) dataset are both part of the National Cancer Registration and Analysis Service (NCRAS); therefore, linking the two is relatively straightforward.

With respect to time horizons, respondents suggested measuring overall survival from start of treatment, for a limited time-period that may vary by cancer type, line of therapy, or prognosis. For piloting the outcome-based payment (OBP) scheme with a specific drug, the median overall survival as estimated in the main trial informing NICE's assessment of the drug could be used to inform the most appropriate time horizon of the outcome measure. However, note that many of the newer drugs coming on the market may not have reached median overall survival (OS) in the trial, meaning this cannot always be used to estimate time horizons.

Table 9 illustrates how the approach described above could be used in a hypothetical OBP scheme for panobinostat. Patients in the RCT have a median age of 63 years, making the trial population younger than most patients in the UK (Evidence Review Group (ERG) critique). Median survival prognosis of multiple myeloma patients is as follows: Stage I – endpoint not reached; Stage II - 83 months; Stage III - 43 months<sup>15</sup>. Five-year survival rate is about 50%. For the 5% of people who are diagnosed at an early stage, the 5-year survival rate is 71%. If the cancer has spread to a distant part of the body, the 5-year survival rate is 48%<sup>16</sup>. No data on survival rates by line of therapy was found.

Table 9 and Table 10 show the relevant information for the measurement of survival required (adapted from Fayanju et al.<sup>1</sup>). Note that the illustrations in Table 9 and Table 10 assume the OBP scheme would operate at the patient and at the population level, respectively.

**Table 9: Measurement of core outcome survival – OBP scheme at patient level**

Overall survival (all-cause mortality)	
<b>Description</b>	Overall survival of the patient after treatment initiation
<b>Patient population</b>	All patients who receive panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Targets</b>	Patient alive at T months after treatment initiation
<b>Data stratification</b>	T will be set as a function of: Stage of disease at treatment initiation; Age
<b>Data sources</b>	NCRAS (ONS + SACT)

Table 10: Measurement of core outcome survival – OBP scheme at population level

Overall survival (all-cause mortality)	
<b>Description</b>	Percentage of patients who are alive 1 and 3 years after treatment initiation
<b>Time frame</b>	1 and 3 years after treatment initiation
<b>Patient population</b>	All patients who receive panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Numerator</b>	Patients alive at 1 and 3 years after treatment (panobinostat in combination with bortezomib and dexamethasone) initiation (year x+1 and year x+3)
<b>Denominator</b>	All patients who receive panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Targets</b>	1-year Target $\geq 95\%$ 3-year Target $\geq 70\%$
<b>Data stratification</b>	Stage of disease at treatment initiation; Age
<b>Data sources</b>	NCRAS (ONS + SACT)

## Disease progression, relapse, or recurrence

For the purpose of an OBP-scheme disease progression, relapse or recurrence would ideally be collected prospectively using real-world data. However, our findings did not identify data sources sufficiently adept for capturing these items, as (parts of) the information needed to assess this is captured in free text or non-standardised data fields. Suggested proxies for progression include time to next treatment (when applicable), treatment duration, or time to treatment failure. These proxies provide figures which are relatively consistent with progression-free survival. Most of the interviewed experts flagged that of ‘recurrence’ is not consistently defined in routine practice. Hence, if a direct measure for recurrence is required, there will be a need to clearly define the concept upfront in any OBP scheme.

While there is little research to support the best approach for ranking outcomes (and hence this is very much open to discussion), one proposed approach is shown in Table 11.

Table 11: Measures for core outcome disease progression, relapse/recurrence

Line of treatment		
		1, 2
		3 +
Prognosis (survival)	>1y	1. Progression-free survival 2. Relapse-free survival 3. Time in remission 4. Time to next treatment 5. Treatment duration 6. Time to treatment failure
		1. Relapse-free survival 2. Progression-free survival 3. Time in remission 4. Treatment duration 5. Time to treatment failure 6. Time to next treatment
	<1y	1. Time to next treatment 2. Treatment duration 3. Time to treatment failure 4. Progression-free survival 5. Relapse-free survival 6. Time in remission
		1. Treatment duration 2. Time to treatment failure 3. Time to next treatment 4. Relapse-free survival 5. Progression-free survival 6. Time in remission

Data collection for this outcome is challenging. No data fields related to remission, or scan or text results, are provided in the SACT database. At present, it also does not seem possible to track progression-free survival through SACT. The survey includes the field 'Regimen outcome summary', which allows users to indicate whether the treatment regimen was stopped due to 'Progressive/recurrent cancer'. However, this entry does not specify the date of remission. In addition, the percentage of completeness of the field 'Regimen outcome summary' was about 12% in 2017-18 when measured against all regimens.<sup>17</sup>

Interviewees have observed that collecting data on 'Treatment duration' seems more realistic. One potential method for measuring this is through using the same methodology as that for drugs funded by the CDF source of funding, where the earliest date out of 'Start date of regimen', 'Start date of cycle' and 'Administration date' is used as treatment start date, and the latest date of the same three items is used as the patient's final treatment date. The treatment duration is then calculated as the difference between these two dates, plus any administration interval (measured in days). Note that all three items are mandatory.

Again, we illustrate an application of this approach (in Table 12 and Table 13 below) using the example of panobinostat.<sup>14</sup> The outcome measure illustrated here is 'Treatment duration'. In the ERG's critique and exploratory analyses, it was noted that the RCT "considered that people in the trial had bortezomib up to cycle 16, but in UK clinical practice patients do not have bortezomib beyond cycle 8, with a stopping rule at 4 cycles if no response is seen."

Note that the illustrations in Table 12 and Table 13 assume the OBP scheme would operate at the patient and at the population level, respectively.

Table 12: Measurement of core outcome disease progression, relapse/recurrence – OBP scheme at patient level

Disease Progression, Relapse of Recurrence	
<b>Description</b>	Number of cycles of treatment (21-day cycle) completed by the patient
<b>Patient population</b>	All patients who receive panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Targets</b>	Patient completes C cycles
<b>Data stratification</b>	C will be set as a function of stage of disease at treatment initiation
<b>Data sources</b>	NCRAS (SACT) as potential

Table 13: Measurement of core outcome disease progression, relapse/recurrence – OBP scheme at population level

Disease Progression, Relapse of Recurrence	
<b>Description</b>	Percentage of patients who complete 8 cycles of treatment (21-day cycle)
<b>Time frame</b>	Six months after treatment initiation
<b>Patient population</b>	All patients who receive panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Numerator</b>	Patients who have completed 8 cycles of treatment (year x + 6 months)
<b>Denominator</b>	All patients who receive panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Targets</b>	Target $\geq 80\%$
<b>Data stratification</b>	Stage of disease at treatment initiation
<b>Data sources</b>	NCRAS (SACT) as potential

## Long-term treatment side effects

Side-effects from cancer treatment can vary significantly by type and stage of cancer, treatment modality used, and between-patient variation. We also identified a number of side-effects (e.g. related to checkpoint inhibitor treatment) that typically appear within a few weeks or months of starting treatment, but they can arise at any time during or after treatment – sometimes as early as days after the first infusion, but sometimes more than a year after treatment has finished. A proposed approach is shown in Table 14.

Table 14: Measures for core outcome long-term treatment side-effects

Long-term treatment side-effects	
Common symptoms include:	Other specific symptoms vary by:
<ul style="list-style-type: none"> <li>- Fatigue</li> <li>- Diarrhoea</li> <li>- Nausea</li> <li>- Pain</li> <li>- Cognitive impairment</li> </ul>	<ul style="list-style-type: none"> <li>- Cancer site/type</li> <li>- Disease stage</li> <li>- Treatment modality</li> </ul>

We have not identified a national-level dataset that fully captures long-term treatment side-effects. While the SACT database captures ‘toxicity’ in the list of reasons for discontinuing a treatment, it does not include a more specific field regarding side effects or toxicity which may

not have led to treatment discontinuation. To some extent, it should be possible to determine long-term treatment side-effects through the Clinical Practice Research Datalink (CPRD), which is linked with relevant, nation-wide dataset as Hospital Episode Statistics (HES) and NCRAS. However, this dataset would impose the restriction that only toxicity or adverse events reported to primary or secondary care clinicians would be recorded (for example, we would know about a patient's thyroid function problems only if that information is available on GP or hospital records).

At the local level, the ePROMs Team at The Christie is collecting data directly from patients through a survey which includes a list of the most common/important symptoms (see table 3). Patients are contacted by the ePROMS team at The Christie during their first visit and prompted to respond to the questionnaires via text or email after every appointment during treatment, and during follow-up until patients are discharged. The time between end of treatment and discharge is quite variable, from 4-6 weeks to 5 years. About 40% of patients complete the surveys in the last wave (before discharge). All PROMs are collected through the 'DrDoctor' data platform. Data can be linked with electronic health records at The Christie using the patient's NHS number as a unique identifier.

Table 15 and Table 16 below illustrate an application of this approach for panobinostat. In the final appraisal document<sup>14</sup> we identified the following relevant symptoms for toxicity and adverse effects: diarrhoea and fatigue are reported as the most frequent ones ( $\geq 2\%$ ), together with asthenia peripheral neuropathy, pneumonia thrombocytopenia, anaemia, and nausea. The report also shows that incidence of adverse events was much lower during phase 2 of treatment (starting on day 1 of cycle 8 for those who experienced clinical benefit) when bortezomib and dexamethasone were administered less frequently. Note that the illustrations in Table 15 and

Table 16 assume the OBP scheme would operate at the patient and at the population level, respectively.

**Table 15: Measurement of core outcome long-term treatment side-effects – OBP scheme at patient level**

Long-term treatment side-effects	
<b>Description</b>	Number of adverse events reported among the following adverse events: diarrhoea and fatigue (most frequent); asthenia peripheral neuropathy, pneumonia thrombocytopenia, anaemia, and nausea (less frequent), two and six months after the therapy ends
<b>Patient population</b>	All patients who received panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Targets</b>	Patient reporting less than M adverse events among the most frequent adverse events (diarrhoea and fatigue) Patient reporting less than L adverse events among the less frequent adverse events (asthenia peripheral neuropathy, pneumonia thrombocytopenia, anaemia, and nausea)
<b>Data stratification</b>	M and L will be set as a function of: Number of treatment cycles covered (e.g. <4, 5-8, 8+); Stage of disease at the end of the treatment; Sex; Age
<b>Data sources</b>	ePROMs ('Adverse-effects' module of the collected questionnaire)

Table 16: Measurement of core outcome long-term treatment side-effects – OBP scheme at population level

Long-term treatment side-effects	
<b>Description</b>	Percentage of patients that report each of the following adverse events: diarrhoea, fatigue, asthenia peripheral neuropathy, pneumonia thrombocytopenia, anaemia, and nausea, two and six months after the therapy ends
<b>Time frame</b>	Two and six months after the therapy ends
<b>Patient population</b>	All patients who received panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Numerator</b>	Percentage of patients that report each of the following adverse events: diarrhoea, fatigue, asthenia peripheral neuropathy, pneumonia thrombocytopenia, anaemia, and nausea, two and six months after the therapy ends (year x + 2 months, year x + 6 months)
<b>Denominator</b>	All patients who have terminated the treatment with panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x + 2 months, year x + 6 months) , at The Christie
<b>Targets</b>	Target $\leq 5\%$ for diarrhoea and fatigue Target $\leq 2\%$ for asthenia peripheral neuropathy, pneumonia thrombocytopenia, anaemia, and nausea.
<b>Data stratification</b>	Number of treatment cycles covered (e.g. <4, 5-8, 8+); Stage of disease at the end of the treatment; Sex; Age
<b>Data sources</b>	ePROMs ('Adverse-effects' module of the collected questionnaire)

## Return to normal activities

For the purpose of OBP schemes, respondents generally prefer generic health-related quality-of-life (HRQoL) measures over condition-specific ones. The rationale provided was based on practical issues (including data availability) as well as additional concerns regarding limitations in comparability across OBP schemes if condition-specific measures were used. There was also concern regarding the general difficulty of defining what a “normal activity” means for patients at different cancer stages. The recommendation of using generic quality-of-life measures is supported by literature on PROMs: there is evidence that generic measures EQ-5D, SF-6D, and HUI-3 (all of which include at least one question related to usual activities as work, study, housework, family or leisure) perform well in capturing health-related quality-of-life for cancer patients, in terms of validity and responsiveness of the measure, for most cancers. A high-quality review on psychometric properties of these measures at cancer site level has been published.<sup>18</sup>

The EQ-5D might be a good choice as preferred HRQoL measure. First, it is arguably the most widely used HRQoL measure in England, since it plays a key role in health technology appraisals and is also collected by some primary care centres. Also, the EQ-5D-5L is systematically collected by the ePROMs Team at The Christie.

Table 17 shows the suggested measures to capture the degree of return of patients to normal activities.

**Table 17: Measures for core outcome return to normal activities of daily living**

Return to normal activities of daily living	
<u>EQ-5D-5D questionnaire:</u>	
Dimension “USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)”	
[1] I have no problems doing my usual activities	
[2] I have slight problems doing my usual activities	
[3] I have moderate problems doing my usual activities	
[4] I have severe problems doing my usual activities	
[5] I am unable to do my usual activities	
<u>EORTC-QLQ-C30 questionnaire:</u>	
Modules related to usual activities during the past week:	
- “Were you limited in doing either your work or other daily activities?”	
- “Were you limited in pursuing your hobbies or other leisure time activities?”	

Table 18 and Table 19 illustrate an application of this approach for panobinostat.<sup>14</sup> Note that the illustrations assume the OBP scheme would operate at the patient and at the population level, respectively. EQ-5D is shown to be valid for multiple myeloma.<sup>19,20</sup> In addition, there is a significant mean change for EQ-5D (and some EORTC QLQ-C30 dimensions) at selected follow-up time points for people with multiple myeloma, which indicates that EQ-5D also performs well in relation to responsiveness.<sup>21</sup> As a caveat, note that using only part of the instrument (i.e. the ‘usual activities’ dimension of the EQ-5D-5L) for the purpose of capturing the relevant outcome raises questions about its validity.

**Table 18: Measurement of core outcome return to normal activities of daily living – OBP scheme at patient level**

Return to normal activities of daily living	
<b>Description</b>	Level reported by the patient in the dimension of ‘usual activities (e.g. work, study, housework, family or leisure activities)’ included in the EQ-5D-5L questionnaire, two and six months after the therapy ends
<b>Patient population</b>	All patients who received panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Targets</b>	Patient reports level N or lower on doing usual activities (e.g. work, study, housework, family or leisure activities), two and six months after the therapy ends.
<b>Data stratification</b>	N will be set as a function of: Stage of disease at the end of the treatment; Age
<b>Data sources</b>	EQ-5D-5L questionnaire, dimension on ‘Usual activities’, through ePROMs (‘Quality of life’ module of the collected questionnaire)

Table 19: Measurement of core outcome return to normal activities of daily living – OBP scheme at population level

Return to normal activities of daily living	
<b>Description</b>	Percentage of patients that report having no problem or slight problems on doing their usual activities (e.g. work, study, housework, family or leisure activities)
<b>Time frame</b>	Two and six months after the therapy ends
<b>Patient population</b>	All patients who received panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x), at The Christie
<b>Numerator</b>	Percentage of patients that report no problem or slight problems on doing their usual activities (e.g. work, study, housework, family or leisure activities), two and six months after the therapy ends (year x +2 months, year x + 6 months)
<b>Denominator</b>	All patients who have terminated the treatment with Panobinostat (in combination with bortezomib and dexamethasone) for treating multiple myeloma after at least 2 previous treatments, with Stage I, II, or III. (year x + 2 months, year x + 6 months) at The Christie
<b>Targets</b>	Target $\geq 70\%$
<b>Data stratification</b>	Stage of disease at the end of the treatment; age
<b>Data sources</b>	EQ-5D-5L questionnaire, dimension on 'Usual activities', through ePROMs ('Quality of life' module of the collected questionnaire)

## Summary

Our findings on objectives A, B, and C, highlighted that there is not a 'one-size-fits-all' set of measures and datasets that can currently be recommended, yet the findings shed light on which outcome measures and data sources would be the most appropriate under the assumption of a realistic, pragmatic scenario. A suggested ranking of measures was derived for each core outcome, though by no means the authors pretend this to be the one and only reasonable characterisation of outcome measures. Similarly, a detailed illustration of a hypothetical OBP scheme was provided, in order to exemplify the feasibility of such a scheme – with all the caveats related to the simplicity of the suggested scheme as well as the latent assumptions in the model.



# Appendix 2 – Workshop participants

The following table indicates the Steering Group members who participated in, respectively, the consensus workshop in February 2020 and the ‘principles’ workshop in June 2020. Both workshops were facilitated by members of the research team.

Table 20 Participants at Steering Group workshops

Name	Organisation	February 2020	June 2020
<b>Cath Barrow</b>	Health Innovation Manchester	✓	
<b>Paul Blakeley</b>	Office for Life Sciences	✓	
<b>Alexandra Feast</b>	Cancer Research UK	✓	
<b>Brad Groves</b>	National Institute for Health and Care Excellence	✓	
<b>Rosie Hinchliffe</b>	Cancer Research UK	✓	
<b>Sophie Kay</b>	Cancer Research UK	✓	
<b>Tom Lawrence</b>	National Institute for Health and Care Excellence		✓
<b>Andrew Miniuks</b>	Association of the British Pharmaceutical Industry	✓	
<b>William Olivier</b>	Department of Health and Social Care	✓	
<b>Stephen Palmer</b>	University of York		✓
<b>Nina Pinwill</b>	NHS England	✓	✓
<b>Richard Preece</b>	School of Health Sciences, University of Manchester	✓	✓
<b>Emma Robertson</b>	Service user	✓	✓
<b>Emlyn Samuel</b>	Cancer Research UK	✓	✓
<b>Mark Saunders</b>	The Christie NHS Foundation Trust		✓
<b>Duncan Sim</b>	Cancer Research UK	✓	✓
<b>Yvonne Summers</b>	The Christie NHS Foundation Trust	✓	
<b>Mike Thorpe</b>	Service user	✓	✓
<b>Alice Turnbull</b>	Public Health England	✓	
<b>Jyotsna Vohra</b>	Cancer Research UK	✓	✓
<b>Andrew Wardley</b>	The Christie NHS Foundation Trust	✓	

# Appendix 3 – Interviews

## Objective

The purpose of the interviews was to gain a greater understanding of the current collection of data relating to cancer outcomes in the NHS and what is required to implement an OBP scheme (e.g. staff, data infrastructure). Interviews were conducted with three different groups to explore these points from different perspectives: operational NHS staff, national system stakeholders and pharmaceutical industry representatives. Separate discussions with patients were held in a focus group which is described in Appendix 4.

The aim of the operational staff interviews was to explore how data on the outcomes of interest for the proposed OBP scheme (survival, disease progression, relapse and recurrence, long-term treatment side-effects and return to normal daily activities) are currently collected in the NHS and how it could be collected and brought together for an OBP scheme. The overall feasibility and burden of the proposed OBP scheme were also explored.

For the national system and industry stakeholders, the aim was to explore the feasibility and potential burden of the proposed OBP scheme at a system level. Specifically, the commissioning, financial, governance and data management aspects of an OBP scheme were discussed, as well as the interactions of an OBP scheme with other processes and initiatives, such as HTA and the CDF. In addition, with the industry representatives there was an exploration of what negotiations might look like between industry and the NHS.

## Method

In total, 21 interviews were conducted across the three key groups. The targets of the operational interviews were cancer clinicians, oncology nurses, data custodians, finance staff, pharmacists and other roles that may be relevant to the topics we explored in the interviews. Unfortunately, we were unable to obtain interviews with any finance staff members, however we did consult at least one individual in the other roles. These staff were based at one of four NHS Trusts or hospitals across England (Christie NHS Foundation Trust, Manchester Royal Infirmary, Essex Partnership University NHS Foundation Trust and Leeds Teaching Hospitals NHS Trust). These were selected based on consultation with the project steering group and the research teams experience and networks. In total, 12 interviews were held with operational staff. Interviews were also held with national-level stakeholders, which included representation from NHS England, NHS X, NICE, NHS Digital and Public Health England. In total, six national stakeholders were interviewed. In addition, three interviews were conducted with industry representatives (these were the same individuals consulted for Phase 1 of this project).

It should be noted that these interviews took place during the escalation of the COVID-19 pandemic (May-August 2020). This posed challenges in recruiting interviewees, particularly frontline clinical staff, many of whom had been redeployed to support the pandemic response. Recruitment of frontline staff was paused for some time to adhere to NIHR research guidance and started again when NIHR recommended. However, many staff members were still very busy in dealing with COVID-19 and this has resulted in the research team consulting fewer clinical staff that was originally planned.

Due to these challenges in recruiting frontline NHS staff to participate in an interview during the escalation of the Covid-19 pandemic, the research team do not think saturation was reached with this set of interviews. It would have been beneficial to conduct a higher number of interviews, as was originally anticipated, across both the different job roles (particularly finance roles in which we were unable to conduct any interviews) and the 4 hospitals we engaged with. However, across the frontline staff we did interview, there were not widely different views held and we did speak with individuals from a range of background and experiences. The research team considers that the most important insights and perspectives relating to OBP have been identified. The interviews and the roles covered are summarised in Table 21.

**Table 21 Summary of interviewee stakeholder groups and numbers**

Stakeholder groups	N/A	Cancer clinician	Oncology nurse	Data custodian	Finance staff	Pharmacist	Other	Total
National system stakeholders	6*							6
Industry representatives	3							3
Christie NHS FT		2	1	1				4
Manchester Royal Infirmary			1			2		3
Leeds Teaching Hospitals NHS Trust		1						1
Essex Partnership University NHS FT		2	1				1	4
<b>Total</b>	<b>9</b>	<b>5</b>	<b>3</b>	<b>1</b>	<b>0</b>	<b>2</b>	<b>1</b>	<b>21</b>

\* One national stakeholder interview was held with three individuals (NICE representatives)

Interviewees were identified through steering group and research team networks, as well as snowballing from other interviewees. They took place between May and August 2020 and lasted between 30-60 minutes. Individuals were invited to interview via email. All interviews were conducted in a semi-structured format, following a set of questions to allow comparability of findings across interviews while allowing some freedom to allow interviewees to raise and develop themes of particular interest. Some questions were the same across all stakeholder groups whereas others were tailored to specific groups based on their expertise. The interview topic guides are provided in the Annexes to this Appendix. Each interview was conducted by one or two members of the research team (AC, JS, KZ, LH). Explicit consent was obtained from interviewees and, if the interviewee agreed, the consultation was audio-recorded. Interviews were held either by phone or MS Teams and the interviewer took notes to summarise each interview.

The interviews were thematically analysed using Nvivo 11. Two members of the study team initially iteratively developed a set of coding nodes in Nvivo based on the interview protocols

and other themes arising from the interviews. In the first step, one member of the research team developed a draft coding template which was reviewed and refined by a different member of the team. All interviews were then coded against this framework, in addition to stakeholder-specific analysis to identify specific themes arising from the operational, national and industry interviews. After this initial coding, a draft flow diagram based on the analysis outlining what an OBP scheme may look like within a patient's journey (from diagnosis to decision about whether a treatment had been successful) was developed. Additionally, short summaries of the operational interviews (focusing on the potential burdens of an OBP scheme and the changes needed to introduce OBP), national and industry interviews were drafted. These different analyses were discussed and refined in a workshop held with the research team as well as a steering group meeting. The themes identified from these analyses are described in the following pages.

The interview stage was reviewed and received ethical approval from the University College London (UCL) Research Ethics Committee (project ID number: 17229/001).

## Findings

The qualitative analysis of the interviews has been grouped into five key themes relating to the objectives outlined above:

1. Current collection of cancer outcomes data
2. Potential burdens of an OBP scheme
3. The circumstances that would permit OBP to be used
4. Outline of what an OBP scheme could look like
5. What is needed going forward to support the implementation of OBP

The remainder of this section considers each of these five themes in turn. This is then followed by a summary section which draws together what was learnt from across the 21 interviews in relation to these key themes.

### Current collection of cancer outcomes data

It became clear during the interviews that the type and extent of cancer outcomes data collection varied across the four hospitals we consulted. It ranged from little data collection, focusing on data that is required for SACT (e.g. mortality) and/or data collection in primarily unstructured, qualitative forms, such as clinician notes, to a wider range of outcome data collection in more structured forms, such as e-prescribing systems.

Data that is collected universally from cancer patients appears to be treatment information<sup>vi</sup> (e.g. type of treatment, dosage), mortality and – to varying extents – morbidity. It was also noted by interviewees that outcomes data collection on medication taken at home by patients (primarily oral medication) is most likely patchier than medication administered in hospital. This is because it cannot be assured that the patient has taken the treatment at home and it is more difficult to follow-up with patients once they leave the hospital.

*"I am constantly nagging everybody to make sure that they prescribe all systemic anti-cancer therapy treatment through our e-prescribing system. The second it is in an e-prescribing system, then you have a tight ability to review and audit that data. There are many clinicians who will say it is so much quicker for this oral treatment*

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<sup>vi</sup> While treatment information is not an outcome, it is important to know for an OBP scheme.

*to write a prescription and give it to the patient. And at that moment we tend to lose that information. So within our trust, I can guarantee that we have perfect data on intravenous therapy... for oral chemotherapy drugs or expensive cancer therapy drugs, we have perfect data. When you start getting into hormone therapy for certain cancers, then I can't tell you it is perfect data from our prescribing system because I'll come across lots of examples of clinicians who say in their letters I've given a patient a prescription for hormones, but actually it is nowhere in the prescribing system. And therefore... if it isn't in the prescribing system...you've missed a progression event."* (Cancer clinician, Leeds)

Although these variations in data collection existed across the hospitals we consulted, all operational staff noted that data on quality of life (which relate to two of the outcomes of interest for this study; long-term treatment side-effects and return to normal daily activities) was poor or non-existent. While consultants and other staff ask how patients are feeling in their regular follow-up appointments, the responses are not formally recorded anywhere. However, a number of interviewees noted ongoing initiatives to create more formal and systematic approaches to collect quality of life data.

*"Patients are asked informally about these three outcomes in their regular consultations (e.g. how are you feeling) but this is not formally recorded or collected in a standardised way or in much detail (e.g. patient notes might say "not feeling too well")."* (Cancer clinician, Essex)

The outcomes data that is collected formally, and could be used for an OBP scheme, is recorded primarily through electronic health records (EHR) and e-prescribing systems. While some data is still collected manually on paper, there is a move across the hospitals we engaged with to collect all data electronically and in more a more automated fashion. However, this is still an ongoing initiative in all hospitals and is a slow process for some. It is also relevant to note that even for the data collected in a format that could be used for an OBP scheme, the data collected is rarely checked for quality and accuracy unless it is sent to another organisation (e.g. SACT) or is for a clinical trial.

Multiple interviews noted that lack of motivation and incentives for clinical staff to record outcomes data as they are not aware of the value of the data and what it is used for. This can result in patchy and poorer quality data.

*"Pretty much everywhere has gone over to e-prescribing for most cancer drugs. All of the electronic prescribing systems that I've ever used... include the ability to record toxicity and have an end of treatment or end of regimen outcome. But because entering that data isn't mandated at most trusts... it's the usual story of if you don't have to do it, you're not going to do it. If there's 10 seconds less that I can spend for each patient, then I won't spend that 10 seconds. I think that's human nature. If it was mandated in the programme, and if at the end of somebody's chemotherapy cycle you were locked out of the system until you had completed your outcomes, then we would all do it because we would have to do it."* (Cancer clinician, Essex).

## Potential burden of an OBP scheme

Before an OBP scheme is to be implemented, it is important to understand the potential burdens it may place on NHS trusts. Three key themes of burden were identified by the participants: staffing requirements, financial costs and time pressures. While the research team tried to explore the quantification of these burdens (e.g. x number of staff would need to be hired or the additional financial costs would be £Y), interviewees struggled to provide a

response to this given the forward-looking nature of the question and the uncertainties that remain regarding what exactly an OBP scheme would look like and what would be required of them and their trust. However, where interviewees did comment on the scale of burdens, these have been provided in this section.

With regards to staffing, it was noted that either extra staff would need to be hired to deal with the additional data collection, collation and analysis, or existing roles could be expanded to include overseeing the OBP scheme for the hospital. For example, additional pharmacists could be hired to deal with additional data and systems, or dedicated data teams could be established (or teams/roles expanded if these are already in place) to run the OBP scheme. The scale of additional staffing required would depend on the size of the hospital the OBP is to be implemented in, the number of patients included in the OBP scheme and the extent to which these roles already exist in the hospital. This could vary from not hiring any new staff (and just expanding existing roles) to hiring new teams of dozens of people.

*“Largely for cancer patients, a lot of it [outcomes data] is collected through the MDT process that discusses and decides management plans for patients. A key element of those meetings is to make sure that we have the right tumour site, date of diagnosis, the stage, the grade, the morphology and a clear treatment plan... One of my bugbears is the overhead that this process creates for clinical care. A centre the size of Leeds employs 40 people who support the cancer teams to collect the national datasets. 40 people is best part of £1 million probably...”* (Cancer clinician, Leeds)

There a number of financial costs that are likely to come with implementation of an OBP scheme. These include the potential need to hire new staff (outlined above) as well as costs associated with additional data collection and cleaning, data linkage and data storage (e.g. server costs).

*“There is the cost of the IT infrastructure involved, both in terms of capital purchase of equipment and there is the cost of the licencing and continuing upgrades of those systems. Those systems would then need to be kept up to date and maintained which can run to a significant cost.”* (Pharmacist, Manchester Royal Infirmary)

The additional time pressures an OBP scheme may bring was mentioned frequently, including by patients. Some interviewees mentioned that any tasks on top of existing workloads would be too much of a burden, particularly for clinical staff. While dedicated data roles or teams could spend some of their time on running an OBP scheme, which may reduce pressures on clinical staff, it was noted that clinical staff will need to play a role in data collection and cleaning but were unsure how they would find time for this. With regards to quantifying the time taken to clean the data required for an OBP scheme, one interviewee estimated this to be roughly a few hours per week, per drug.

*“It’s not really something that can be done by groups of people like coders, you tend to have to have a reasonably detailed knowledge of the clinical context and associated clinical management of the patient in order to accurately collect that data and make sure it corresponds to what is clinically relevant to that patient.”* (Pharmacist, Manchester Royal Infirmary)

In addition to pressures on clinical staff time, some interviewees commented on the lack of capacity within the hospital team to complete the rebate process, should a treatment be deemed to have been unsuccessful. This may mean trusts do not receive the rebate money they are entitled to.

*“The red flag that I would feel is you said that if the outcome wasn’t good, that it would be going back to the pharmaceutical company to get some of that payment back. The red flag is work... we have to find someone to go back to the company to [get] that money out. And it’s always harder to get money back, and I just know with finance in the NHS that things get lost quite a lot. You want it as simple as possible, either in or not in.... If someone has to check if request has gone to someone, and I would worry that we would need to make sure that the next bit happens. You could just get into a situation where nobody bothers to bring the money back in because it’s too much work.”* (Oncology nurse, Essex)

Finally, with regards to time, it was noted that the proposed OBP scheme criteria of following up with individual patients is a more time-consuming approach to collect data. However, all interviewees felt that this was the preferred approach than measuring outcomes across a patient population.

*“The only area that increases burden with regards to data collection for the scheme is the focus on individual patient, especially when reaching target population is hard. Tracing and analysing data may be more burdensome in this regard. It is fairer to evaluate based on individual patients, but the burden would be higher.”* (Industry)

## **The circumstances that would permit OBP to be used**

An OBP scheme is not possible to use for all cancer treatments due to the intensive data collection requirements. All interviewees agreed with the proposed suggestion that OBP schemes should only be used for those treatments where there is limited evidence on clinical efficacy. In addition, given that some outcome data is more thoroughly collected on hospital-administered treatments compared to those taken at home, it may be preferable to focus OBP schemes (at least initially) on treatments given in hospital.

Given that outcomes data will be collected on individual patients, rather than patient populations, it is important to consider the types of patient populations that would be best placed to be involved in an OBP scheme. Treatments prescribed to a large patient group are unlikely to be feasible for an OBP scheme due to the resources needed to follow-up with each patient. On the other hand, patient groups that are too small may also be less feasible as the resources needed to set up an OBP scheme may outweigh the costs saved for the NHS. If the infrastructure required for an OBP scheme became more mainstream (e.g. more rigorous and electronic collection of outcomes data) then smaller patient groups could be used for OBP.

An additional aspect to consider in terms of the patient population is the ease of following-up with the patient during and after treatment to collect the outcome data. It is important that the patient has hospital consultations within the timeframe that outcomes are to be collected (e.g. 1 year, 5 years). It may be most appropriate to focus on a drug which will have measurable impacts in the short-term (e.g. within one year) as some outcomes can take many years to appear. If patients are to self-report their quality of life outcomes (covering long-term treatment side-effects and return to normal daily activities outcomes), it is important that they are both physically and mentally able to do so.

*“Data collection should occur close to treatment. Payments cannot be processed for more than one year after end of treatment as there is a limit to how long afterwards this can be traced. Timeframes longer than one year is not realistic...Consider dropping ‘return to normal activities’ and ‘long term consequences’ if timeframe is one year”. (NICE)*



*"[The time at which to measure outcomes is] dependent on the drug. In acute leukaemia, we would want to see 2 cycles of a drug at least, and do bone marrow tests to see what it looks like to see the impact on the marrow from the drug. It depends on disease group and drug. Some drugs you can see effects early on. We would want to get an initial response (2-3 courses) and then longer term (6 courses)." (Oncology nurse, Manchester Royal Infirmary)*

It is also important to be able to attribute a particular side-effect to the drug covered by the OBP scheme and consider whether these effects could be due to other treatments (that the patient is on at the time, or took previously that are still having consequences), the cancer or other co-morbidities. Because of this issue, it may be useful to collect relevant data from patients before they are prescribed the treatment on the OBP scheme.

With regards to the data collection, mechanisms need to be put in place to be able to collect data on each of the four outcomes of focus (if they are not in place already). For example, effective e-prescribing systems need to be in place, and it needs to be ensured that clinical staff input the required data into these systems.

*"Need financial investment, IT platform and the ability to link data from three trusts that have recently merged. We currently use three IT systems which are difficult to communicate across." (Oncology nurse, Essex)*

*"Fundamentally, there needs to be some sort of digital platform. Without a really slick IT system, even with resource and with people, there is no way that it would work... Once you've got that, it should become quite light touch." (Other operational role, Essex)*

## **Outline of what an OBP scheme might look like**

The interview data covering the current data collection, additional data to be collected and other OBP requirements were analysed. These findings were detailed in a flow diagram outlining the different OBP stages and associated requirements (as well as staff roles and additional aspects to consider). This was further refined in the interview analysis workshop with the project team. This diagram is presented in Figure 3.



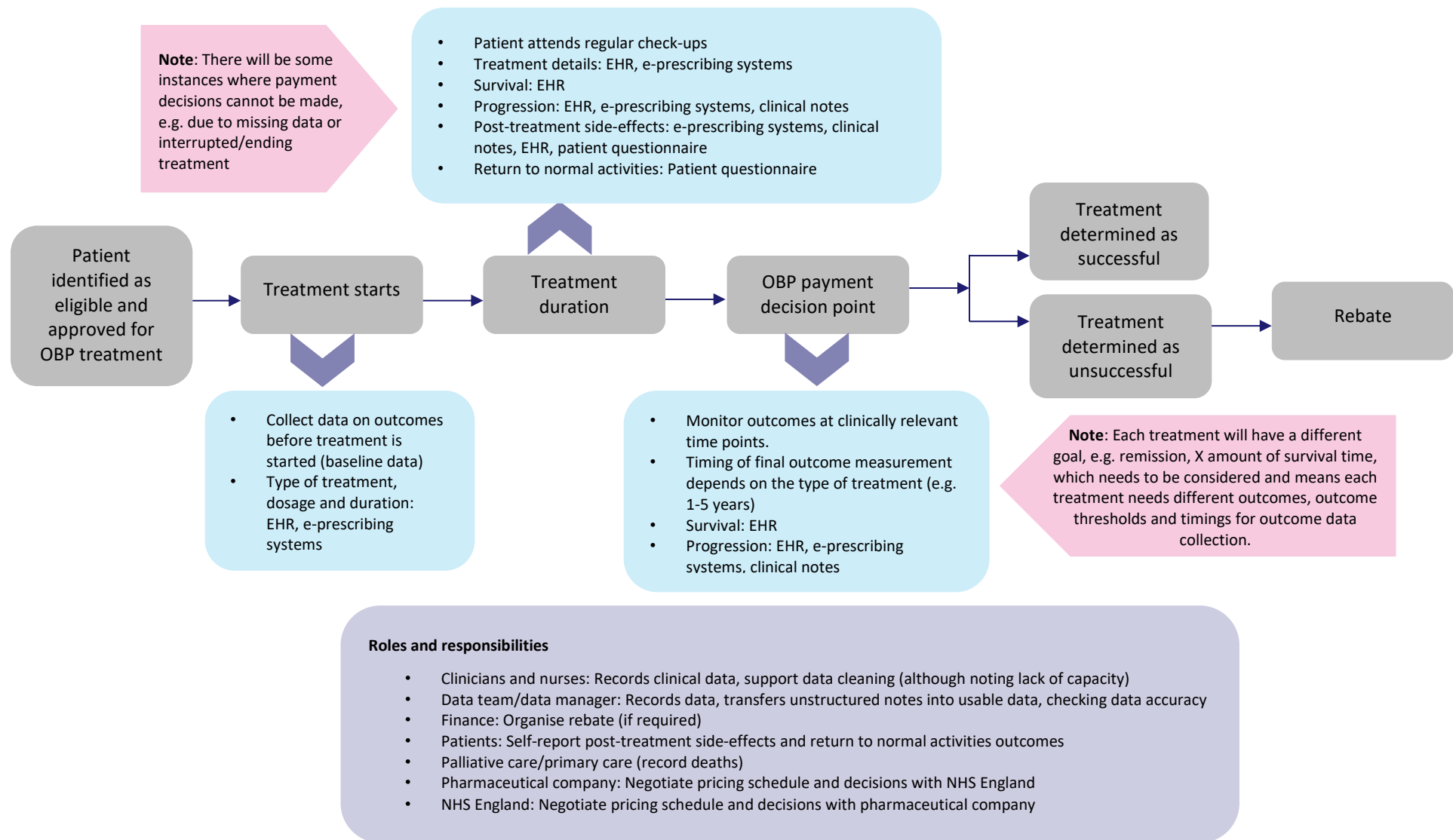


Figure 3: Flow diagram of the proposed OBP scheme and the requirements at each stage

Key: Grey box = Key points in the OBP pathway; Blue box = What types of data need to be collected and how; Pink box = Points to consider for data collection; Purple box = Roles and responsibilities

## What is needed going forward to support the implementation of an OBP scheme

A number of key areas were noted in terms of what needs to be considered or improved to be able to implement an OBP scheme. These are IT and data systems/infrastructure, buy-in, the rebate process and staffing. Each of these will be discussed in turn here.

### IT and data systems/infrastructure

As has been mentioned, it is important for an OBP scheme that hospitals have systems in place that allow the systematic collection of outcome data across the four key outcomes of focus. This data can come from a variety of sources, such as EHR, e-prescribing systems and patient self-reported data. However, these systems are not always established and/or used effectively, particularly for e-prescribing.

Consideration also needs to be paid to the structure of the data that is collected. Extracting and analysing clinical notes is time and resource intensive. In general, there is a need to collect structured data in real-time that can be easily analysed. Additionally, investment is required to link datasets and collate data collected for all four patient outcomes, including patient reported outcomes. The challenges of different datasets and systems used across hospitals and hospital departments was noted here. Resources also need to be invested in cleaning data to ensure it is of high-quality and accurate. This can be a highly resource-intensive process, as was noted by interviewees familiar with the processes required to produce very high-quality data for the CDF.

*“At the moment, it is difficult to say who acts on data at the moment. Everyone interprets data differently so would need to be careful of that. The people would need to be well trained and entering standardised data in a clean way.”* (Cancer clinician, Essex)

New, standardised and simple approaches to data collection could be set up to aid data collection for an OBP scheme. Standardised templates could be created for clinical staff collecting data and some or all of these data fields could be made mandatory to complete. This would reduce the risk of missing data. For example, if long-term treatment side-effects and return to normal activities outcomes are to be self-reported by patients, it may be useful to create an online patient portal to collect this data which will allow patients to complete this at a time convenient to them (either at home or during their regular appointments). This would also mean that patient reported data is already in a standardised and electronic form, reducing the resources required to clean and process it. It is important that any method of collecting patient data is accessible to all patients, e.g. use of lay language, ability to provide data through non-digital means and offered in multiple languages. However, patients participating in the focus group noted that some patients may prefer not to be involved in providing additional data.

*“Currently, new patients at the Christie fill in a new patient form which captures some data in a structured way. It should be possible to expand this to include more information, i.e. ask people to fill in electronic capture forms as part of routine care.”* (Cancer clinician, Christie)

*“You are dealing with quite a diverse population. Illness doesn’t respect your intellect or your social class so there will be some people who aren’t interested and don’t have the capacity to understand very technical language and may, emotionally, want to block off the whole thing of their health. There are other people... who are taking*

*a very active part in their management. The only person who can really manage my treatment is me.” (patient focus group)*

## **Buy-in**

Incentives and buy-in for implementing OBP need to be established across a number of stakeholders. Firstly, as mentioned previously, clinical staff need to understand the value of “clean” data and how it will be used (emphasising the benefit to their patients). Emphasising how accurate data collection can improve patient care may incentivise the production of high-quality data.

*“Having such a scheme in place may give incentive to oncologists and other clinicians to collect data. If they understand that this data will be used to inform decisions, and can see how it will be helpful, they are more likely to submit better data.”*  
(Cancer clinician, Christie)

There is also a need to generate buy-in from system stakeholders, such as NHS trust chief executives, NHS England and relevant government departments. As with creating incentives for clinical staff, system stakeholders need to understand the benefit to patients, such as quicker access to treatments, but also financial benefits to implementing an OBP scheme. In addition, system stakeholders need to have demonstrated that patient-reported outcome measures used (which can often be seen as subjective) are robust, standardised and objective.

*“A lot of challenges with quality of life data - many don’t think EQ-5D data is usable for certain populations, for example. So there would be debate on the best quality of life instrument to use. This would attract more discussion and debate than a more concrete outcome. But this would be healthy debate and patient reported outcomes are important to include.”* (Industry)

## **Considerations for the rebate process**

Some interviewees raised concerns over the proposed rebate approach for two main reasons. The first, which has been mentioned before, is the perceived lack of capacity for hospitals to process rebate requests which would result in hospitals not receiving payments they may be entitled to.<sup>7</sup>

*“It would be a lot of work for the trust to have to monitor outcomes from patients and then manually claim the drug back. We have managed those sorts of patient access schemes before and they have fallen onto pharmacy to claim it back and it’s just so labour intensive. It would have to be done by the finance team, and it will end up costing the trust money because they have got to have the manpower to do it. So if this sort of system were introduced, someone would have to fund staff within each organisation to be able to do that... It would be less labour intensive for the trust if you didn’t pay for the drug until you had an outcome and then the outcome triggered the payment of the invoice, rather than automatically paying it and then having to claim it back.”* (Pharmacist, Manchester Royal Infirmary)

An additional challenge is the uncertainty around who is responsible for requesting the rebate and which organisation the rebate money is directed to as cancer drugs are paid, ultimately, by commissioners rather than NHS trusts. Some interviewees felt it would be preferable if the cost of the drug was paid after the outcomes were measured which would help to reduce time and resource burden.

*“There is the issue that the cost of chemotherapy drugs are paid for by the*

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<sup>7</sup> Note that we were unable to obtain an interview with an individual involved in finance or procurement at any of the four hospitals we engaged with. We were therefore unable to confirm these concerns with an individual who would be responsible for processing the rebates.

*commissioners... the hospital buys the drug and the recharge the costs back to the commissioners at the cost that the hospital has paid. So it's whether those rebates go back to the commissioners rather than the hospital because the commissioners would expect any rebate that the hospital gets to potentially be passed back through to the commissioners. So it may be that the commissioners have a role in that process and that would need to be discussed with the commissioners who ultimately pay for the drugs."* (Pharmacist, Manchester Royal Infirmary)

## Staffing required

The staffing requirements to implement and run an OBP scheme have been outlined earlier in this appendix. However, it is an important consideration when designing future OBP studies as to whether new staff need to be hired to deal with additional data collection and cleaning. While existing clinical roles could be expanded to include data collection and cleaning for an OBP scheme (e.g. nurses), there are challenges of limited existing capacity.

*"In an ideal world, a clinician would collect the data but from personal experience, clinicians are overworked and would be too busy to collect and collate the data. You would need data support workers or managers to do this."* (Cancer clinician, Essex)

*"Often nurses are given extra tasks which would be difficult to do in current capacity. Some of this might fall on nurses who already lack time."* (Oncology nurse, Manchester Royal Infirmary)

## Summary

The information provided by the interviewees covered a broad range of topics and perspectives covering the current data collection situation and what a future OBP scheme might look like (and what would be needed to support this). Overall, interviewees were largely positive about the idea of OBP and felt it would be a feasible initiative to introduce (as long as the required changes and improvement to infrastructure were made). Only one interviewee felt that OBP would not be possible to implement even if the supporting infrastructure was put in place. In addition, some interviewees noted the opportunity that may have been created as a result of COVID-19 and the focus on collecting data to monitor the spread of infection. While current resources are diverted towards dealing with the outbreak, it has also demonstrated the potential uses of data and that the NHS is able to collect data on a large scale.

*"COVID shows that the NHS can move quickly if it needs to, but the go-to excuses for OBP is that it would take too long to set up... COVID could be used as a reason to get the data collection up to scratch, and then there would be no excuse to not have OBP. The NHS would just need to set up the staffing structure from the centre to do so."* (Industry)

Below, we provide a short summary of the themes discussed throughout this appendix.

*Current collection of cancer outcomes data.* The collection of cancer outcomes data varies across hospitals. Key challenges in terms of data collection for an OBP scheme are that some data are still collected on paper rather than electronically and quality of life data is poorly collected across all hospitals we engaged with. There is also variation in the extent of data collection across types of treatment, with hospital-administered treatments having more accurate and complete data on outcomes than medication taken at home. Outcome data that could be used for an OBP scheme are most often collected as EHR and in e-prescribing systems.

*Potential burdens of an OBP scheme.* The three key challenges in implementing OBP in terms

of burden are staffing, financial cost and time. Additional staff time (clinical and/or data management roles) is needed to support the running of an OBP scheme which could come from hiring additional staff or expanding existing roles. The involvement of Clinical staff is required for data collection and cleaning, so their capacity constraints represent a challenge. Additional capacity issues arise for the hospitals in requesting the rebate, if required. Financial costs are also associated with an OBP scheme, including additional staffing costs and costs relating to data (e.g. server storage, linking datasets).

*The circumstances that would permit OBP to be used.* A number of criteria have been identified in which an OBP scheme could be useful. This includes: treatments with limited evidence on clinical efficacy; treatments administered in hospital; medium sized patient population; outcomes measurable within the set timeframe to decide on drug price; patient physically and mentally able to provide outcome data; outcomes can be attributed to the treatment in the scheme; and ability to collect data on the four outcomes.

*Outline of what an OBP scheme could look like.* The flow diagram in Figure 3 provides a proposition for what an OBP scheme might look like, the data that could be collected at each stage and the staffing required.

*What is needed going forward to support the implementation of an OBP scheme.* A number of key areas were identified as needing consideration or improvement before an OBP scheme can be implemented. The first is the need to have the IT and data systems/infrastructure in place to be able to collect, clean and analyse the data needed to inform pricing decisions. Secondly, buy-in and incentives need to be established both for clinical staff and system stakeholders (e.g. NHS England) to ensure they understand the value of an OBP scheme and undertake the activities required of them to run a scheme. Thirdly, consideration needs to be paid to the best approach to organising rebates given the capacity issues in hospitals completing the rebate process and in understanding who is responsible for leading this process given that commissioners ultimately pay for cancer drugs. Finally, appropriate staffing needs to be put in place to ensure sufficient resources to collect and collate data.

## **Annex 3A – Interview Topic Guide: Operational staff**

### **Introduction to research team and scope of the study.**

Q1 Tell us more about your role in caring for cancer patients or supporting colleagues who provide that care.

Q2 What range of cancer patients do you personally work with: types of patient (e.g. age groups), types of cancers, types of treatments?

Q3 What is your role in measuring and/or recording outcomes data?

### **Overview provided of the 4 key outcomes of interest (survival, disease progression, relapse or recurrence, post-treatment consequences and return to normal daily activities).**

Q4 Do you have a view of how you might rank the importance of these outcomes?

Q5 What outcomes data/information do you collect on cancer patients? At what points during the treatment pathway (including follow-up)?

Q6 How are these data/information collected?

Q7 How are these data/information then processed and stored, by you or others?

Q8 What mechanisms / justification do you rely on for the processing of personal data in the way it is used for your purposes (consent / justification for use in absence of patient consent e.g. section 251 / provisions in GDPR: scientific research / public interest / provision of health or social care)

Q9 What, if any, checking of such data is done; by whom, when?

Q10 What, if any, validation of such data is done; by whom, when?

Q11 Do you have a view on the responsiveness of these data (e.g. how much is missing) and their reliability (e.g. how accurate it is)?

- What could be done to improve the data quality for use in an OBP scheme?

Q12 What use is made of this information once collected; by whom; how do they access it; do you/they combine it with any other data/information and if so why and how?

Q13 Thinking of the way cancer medicines are administered: either self-administered by the patient (oral medicines) or by staff in the hospital (intravenous medicines) would this affect the way in which outcomes data/information are

- collected
- processed
- checked
- or could be used?

Q14 What proportion of your time do you think you spend on

- collecting
- processing and/or
- checking
- outcomes data/information about cancer patients?

Q15 Are you aware of how much time any of your colleagues spend on the same activities for the same patients?

Q16 Over the course of a year, for approximately how many such patients are you

- collecting
- processing and/or
- checking
- such information?

Q17 Are any other costs, apart from your time, incurred to collect and process outcomes data/information about cancer patients?

Q18 *For Leeds/Essex only:* We have heard that you are part of the Oncology Data Network (ODN).

- Are you familiar with how your hospital first became a part of this network and what criteria you needed to take part?
- Were there any challenges to getting to be a part of the ODN?
- What was the data-situation like before you joined the ODN?

**Background and details provided on the proposed OBP scheme and it's key criteria (outcomes measured on individual patient basis; binary payment; Po at 'successful treatment' level; and separate thresholds for each of the 4 outcomes).**

Q19 Do you think it would be feasible to collect all, or just some, of that kind of outcome data?

- If not feasible to collect all: What could be done to enable this type of data collection?
- When and how during the diagnosis and treatment pathway could that be done?

Q20 Which staff would be involved in

- collecting
- processing and/or
- checking
- those data?

Q21 What would be the burden on your and their time to do so compared to current time spent collecting similar data?

- How could this burden be overcome/mitigated?

Q22 Would there be any additional costs involved other than your and your colleagues' time?

Q23 Would it necessitate, or be facilitated by, any changes to information systems or other infrastructure and how could this be achieved? For example: improving data quality, expanding and linking datasets or improving the data environment more generally.

Q18 Are there any other system changes you think are needed to support the implementation of an OBP scheme?

Q24 What data governance issues would have to be considered? E.g. consent, GDPR.

Overall, how realistic do you think it would be to collect outcome data to enable the price paid for a new cancer medicine to depend on its effect on patients treated in this hospital?

Q25 Is there anything else you would like to say that has not already been covered?

Thank you for your time and the valuable insights you have provided.

## **Annex 3B – Interview Topic Guide: National and regional system stakeholders**

**Introduction to research team and scope of the study.**

Q1 Tell us more about your role with respect to NHS cancer care.

Q2 What are your responsibilities with respect to the collection, management or use of data/information on outcomes for cancer patients treated in the NHS?

**Overview provided of the 4 key outcomes of interest (survival, disease progression, relapse or recurrence, post-treatment consequences and return to normal daily activities).**

Q3 What is your role with respect to the following types of outcomes data for cancer patients treated in the NHS:

- Survival
- Disease progression, relapse/recurrence, treatment duration
- Post-treatment consequences (fatigue, pain, etc.)
- Patient's ability to return to normal daily activities?

Q4 What outcomes data/information are you currently working with?

Q5 Who collects those data and how, and where, are they collated, validated, stored nationally?

Q6 How are these data used, by whom, and how do they access the data?

Q7 What mechanisms / justification do you rely on for the processing of personal data in the way it is used for your purposes (consent / justification for use in absence of patient consent e.g. section 251 / provisions in GDPR: scientific research / public interest / provision of health or social care)

Q8 Do you have a view on the completeness of these data (e.g. how much is missing?) and their reliability (e.g. how accurate it is)?

- *If data is perceived to be low quality:* What could be done to improve the data quality for use in an OBP scheme?

Q9 Is this information/data linked with any other sources of information? Which, for what purpose, and how?

- *If data linkage is poor:* What could be done to improve the ability to link and expand datasets?

Q10 What are the costs of

- collecting,
- collating,
- validating,
- storing and
- using
- cancer outcomes data currently?

**Background and details provided on the proposed OBP scheme and it's key criteria (outcomes measured on individual patient basis; binary payment; Po at 'successful treatment' level; and separate thresholds for each of the 4 outcomes).**

Q11 Do you think it would be feasible to collect all, or just some, of that kind of outcome data?



- *If some data is not feasible to collect:* What could be done to support the collection of that type of data?
- When and how during the diagnostic and treatment pathway could that be done?

Q12 How could data from different sources be linked for the purpose of OBP?

Q13 Which staff or organisations would be involved

- in collecting,
- checking and
- processing
- those data

Q14 What mechanisms / justification do you think is most appropriate for processing of personal data for the purposes of OBP (consent / justification for use in absence of patient consent e.g. section 251 / provisions in GDPR: scientific research / public interest / provision of health or social care).

- *If unsure* – who would be best to advise?

Q15 What would be the burden on your organisation and others to do so compared to current time spent collecting similar data?

- What could be done to overcome/mitigate this burden?

Q16 Would there be any additional costs involved other than your and your colleagues' time?

Q17 Would it necessitate, or be facilitated by, any changes to information systems or other infrastructure, and how could this be achieved? For example: improving data quality, expanding and linking datasets or improving the data environment more generally?

Q18 Are there any other system changes you think are needed to support the implementation of an OBP scheme?

Q19 Overall, how realistic do you think it would be to collect outcome data to enable the price paid for a new cancer medicine to depend on its effect on patients treated in this hospital?

Q20 How do you think an OBP would fit in with / complement / contrast the current CDF? Are you aware of any examples OBP in any form, and how it was facilitated?

Q21 Is there anything else you would like to say that has not already been covered?

Thank you for your time and the valuable insights you have provided.

## Annex 3C – Interview Topic Guide: Industry representatives

### Introduction to research team and scope of the study.

Q1 Tell us more about your role at [company].

Q2 What is your experience with respect to collection and use of data relating to outcomes for cancer patients treated in the NHS?

**Background and details provided on the proposed OBP scheme and its key criteria (outcomes measured on individual patient basis; binary payment; Po at 'successful treatment' level; and separate thresholds for each of the 4 outcomes).**

Q3 Does this seem like a sensible and plausible approach to OBP?

- If not, why not?

Q4 Do you think it would be feasible to collect all, or just some, of that kind of outcome data?

Q5 What are your thoughts on the practicalities of collecting outcome data in the NHS, and then using it for an OBP scheme?

Q6 When and how during the diagnostic and treatment pathway could data be collected?

Q7 How could data from different sources be linked for the purpose of OBP?

Q8 Which staff from the NHS would be involved in collecting, checking and processing the data?

Q9 Would there be any additional costs involved other than time?

Q10 Would it necessitate, or be facilitated by, any changes to information systems or other infrastructure?

Q11 Thinking about the process of launching a new cancer medicine using an OBP scheme, what principles should govern the negotiation between you and NHS England when launching a new drug for an OBP scheme?

- Specifically, what principles should govern how to agree on success threshold levels for the medicine?

Q12 Would launching a new drug through an OBP scheme be preferable to entering it into a Cancer Drugs Fund scheme? If not, why not?

- More generally, how do you think an OBP would fit in with / complement / contrast the current CDF?
- How much sooner would your medicine get into use if OBP were an option, compared to having to negotiate a simple price (or price minus discount), or getting it into the Cancer Drugs Fund, as now?

Q13 Is there anything else you would like to say that has not already been covered?

Thank you for your time and the valuable insights you have provided.

# Appendix 4 – Focus Group

## Objective

It is important to hear the patient voice with respect to an OBP scheme, particularly as it will likely involve them providing more data of the outcomes of their treatment. The objective of the focus group with people with experience of living with cancer was to gather a range of patient experiences and insights on the practicalities of collecting data on cancer treatment outcomes.

## Method

Focus group participants were recruited via the Cancer Research UK Patient Involvement Network. The focus group was run virtually on the 4th September (2020?) for 1.5 hours and included four participants with different cancer and data experiences. Two participants had experience of participating in a clinical trial.

The focus group interview specifically queried patients' experience of data collection in the NHS and a trial/study setting; their knowledge of routine data held; views on greater patient involvement in data collection, e.g. self-report and regularity; accessibility of data and to whom; and data governance, particularly around the issue of outcomes being used to inform reimbursement decisions.

The focus group interview was reviewed and received ethical approval from the University College London (UCL) Research Ethics Committee (project ID number: 17229/001).

## Findings

Patients expressed positive views about the use of an OBP scheme and the requirement for patients to complete additional requests for data to support a scheme like this. Participants felt that if patients knew that the data were being collected to help the NHS obtain value for money and to support other patients accessing effective treatments quicker, then patients would be happy to take part in additional data collection.

Patients' experience, views and concerns are categorised thematically below.

## Data collection

All participants reported that their quality of life was asked about in some respect during their treatment and management of their cancer (e.g. consultant asking how a patient is feeling, asking about side effects to manage them etc.), however it was not clear to the patients if these discussions are systematic and if the response are recorded anywhere. Patients were in favour of these being systematically recorded like their clinical outcomes.

They shared no concerns about additional data collection placing a burden on them as patients, although there were some concerns that this would increase the burden on healthcare staff. One participant (with professional experience in the NHS) did however reflect that expected burden is often used as a reason to not introduce something new, but on implementation the requirements were not as great as expected and health professionals adapt.

Discussions on the consent process for collecting outcomes data highlighted that it was unclear particularly with respect to the requirements in an OBP scheme. Trial patients obviously

consented, and participants reported consenting for some activities and treatments (e.g. intravenous chemotherapy), although they were not familiar with why this was necessary, pondering if it was due to great risks of side effects. Discussions of consent lead to a discussion of non-compliance: what if a patient on an OBP medicine failed to self-report their quality of life, would they still be allowed the medicine? Participants held strong views that it would be unfair to exclude them for this.

## Communication

Participants noted that improved compliance would be aided by clear communication. They agreed that it would be important when engaging with patients about OBP schemes that the language is clear, particularly as different words have different interpretations (e.g. data vs information, outcomes vs effects). Participants also raised the issue of comprehension and health literacy and requirements for any self-reported data to be simple and in multiple languages.

## Concerns on “side-effects”

Participants were interested in how a scheme would identify which treatment has caused a particular side effect or consequence. One of the participants had a long-term side effects (which now express itself as a comorbidity) which was the result of earlier treatments. He queried how that would impact understanding the side-effects of new treatments. The participants additionally noted that the patient may have other, non-cancer related comorbidities that lead to negative consequences which would need to be separated from the outcomes of the cancer treatment.

## Data access, data sharing and governance

Most of the participants stated that they faced difficulties in accessing their own data (although this varied across the participants, with some finding this process simple and obtaining medical information from all appointments, whereas others faced significant challenges in accessing their own data). All the participants welcomed the idea of being able to have access to their outcomes data that is collected as part of an OBP scheme. Although there was some scepticism as many noted the lack of data sharing between primary and secondary care providers, they thought that sharing across the health service was important not just for an OBP but for improved patient care. There were some concerns expressed by participants regarding patient data being shared with the pharmaceutical industry and some government agencies (e.g. the Home Office).

Participants raised no issues with the use of their data in decisions about reimbursement. This was further explored with members of the BHF/Cancer Research UK Patient Data Panel. In an additional consultation with the members of this panel to explicitly understand data governance issues, when asked: is the use of patient data for research purposes different from the use of patient data for reimbursement purposes? One respondent answered *“Emotionally yes; logically no. They should both drive forward patient outcomes and are mutually reinforcing. Careful mass communication would be essential to ensure a positive reception for such measures.”*

## Summary

Focus group participants were generally positive about the use of an OBP scheme and they felt that if patients knew that the data were being collected to help the NHS obtain value for money

and to support other patients accessing effective treatments quicker, then patients would be happy to take part in additional data collection.

Quality of life discussions were commonplace in consultations, with all the participants reporting that their quality of life was asked about in some respect during their consultations (e.g. consultant asking how a patient is feeling, asking about side effects to manage them etc.), but they felt these discussions weren't systematic nor were the responses recorded anywhere, but they thought they could and should be. They shared no concerns about additional data collection placing a burden on them as patients, although there were some concerns expressed that this would increase the burden on healthcare staff (as noted above).

While patients raised concerns about data sharing with pharmaceutical companies and government departments, they were keen to access their own data, and shared varying experiences of obtaining their medical records, although they all agreed that data sharing between primary and secondary care providers was poor.

The only point of contention raised by patients was the issue of non-compliance, what if a patient does not self-report their quality of life? Would these patients still be allowed the medicine? Participants thought it would be unfair to exclude them on this basis.

## Annex 4A – Focus Group Interview Topic Guide

- Warm-Up/Introductions
- Experience with cancer
- Group discussion about what patients experience of data collection. “would someone like to start with sharing their experience”

[probe on self completion of surveys]

[ask if this aligns with other participants' experience]

[check with those who have not offered a view yet - would they consider providing information, particularly on side-effects and on ability to return to activities of normal living, would they think this is burdensome (and if so how burdensome) and would they would be happy to provide that information nonetheless]

[query routine data collection] “if I was to look up your health records now (with permission) I would be able to see what treatments you have had, how often, maybe information on stage/grade of tumour – did you think there would be more data on your cancer in the system?”

[probe on what data and how it was collected – paper/electronic] “do you have a preference for the way data are collected?” “do you have any ideas of making data collection easier for patients?” “what do you think of new technological advances in data collection, i.e. wearables?” “given the different data collection approaches would any of these raise accessibility or inequality issues?”

[ask about if burdensome] “consider different scenarios, of data collection daily, monthly, quarterly, etc” “what if data collection was to continue after your treatment – would you still be engaged?” “what if it required longer hospital appointments to collect the data?” “what do think about having the additional responsibility to record

this data if it is outside of a clinic appointment, i.e. self reported?"

[probe on reason/own motivation for data collection] "was it a trial or study?" "why did you get involved?"

[probe on who has access to data - theoretical] "the following are different types of people/organisations who might be able to access your data, this is very new territory, not really explored so quite theoretical but how would you feel about

- Clinicians accessing your data OR
- Researchers accessing your data OR
- Drug company accessing your data OR
- The government (DH&DC) accessing your data"

[probe further on access] "what are your thoughts on data security" [if concern shown] "what would reassure you?" "Would you like to have access to your own data?" "what about broader data sharing? So secondary use by researchers?"

[probe on what it is used for] "often data on outcomes are collected to show how effective a drug is, in our scenario it would be used to determine the price [explain relationship between price and outcome] would you be supportive of this? Do you have any concerns?" "can you offer any suggestions as to how we might communicate the purpose of the data collection to patients?" "do you think the consent process would be different?"

- Debrief: "Is there anything else you'd like to add to the discussion?"
- Wrap-up: "Overall, how comfortable are you with the idea of contributing more data on the outcomes of your treatment?" [comfortable / maybe but not sure / would not do that]

# Appendix 5 – Case Study Analysis

## Objective

The objective of this phase of the research project was to conduct a preliminary retrospective analysis and theoretical testing of an OBP scheme. The objectives were twofold (1) to demonstrate the feasibility of an OBP scheme, highlighting any gaps between what is possible/practical now, and what an “ideal” OBP scheme would look like, and (2) to understand the potential impact of using OBP on costs and outcomes associated with a cancer drug for a defined patient cohort.

## Method

### Case study selection

In the early phases of the project, interviews were conducted with five clinical advisors and two patients from the project Steering Group, to discuss and identify which medicines may have the potential to act as a useful case study for OBP. Consensus among interviewees and patients was that OBP schemes should focus on high-cost innovative drugs and patients with advanced cancer (1-2 years life expectancy). Interviewees suggested possible candidate medicines, and the project team built a short-list based on timeline of NICE TA review, launch date, NICE decision, and approximate patient population.

Following this initial scoping activity, as well as several conversations (with the project’s key contributors, advisors, and national data custodians) around data availability and access, as well as discussions on the optimal use of available data, the project team decided to use a particular drug under consideration for the treatment of previously treated advanced or metastatic cancer as the subject of our retrospective case study. In order for this report to respect commercial sensitivities, we refer to it as ‘Drug X’ and have removed specific details of the target patient population and literature references used for the basis of our model assumptions. The selection of Drug X as the basis of our hypothetical case study was seen to have the following advantages:

- Represents a real-life case study of a drug for which there was significant clinical uncertainty at launch (was routed to CDF)
- Published real-world data are available summarising the clinical outcomes of interest in the NHS (CDF report following the period of managed access)

Using the key clinical metrics published in the relevant CDF report, supplemented by published clinical trial data for quality of life estimates for Drug X, we generated a hypothetical patient cohort and used the OHE ‘OBP-Simulator’ to analyse the potential impact of an OBP scheme on key parameters of interest, e.g. level of payment rebates for unsuccessful treatment and budget impact to the NHS.

One diversion between this case study and our proposed format of an OBP scheme is that the research indicated that an OBP would preferably be based on individual patient-level outcome data. As we did not have access to retrospective patient-level data for this case study, we mitigated this by simulating a cohort of 180 individual patients, ascribing outcomes to those hypothetical individuals based on the population-level summary statistics obtained from the CDF report or trial data, constrained by the 9-month time window of data collection in the CDF.

## Data inputs

In the table below we outline our main data inputs and assumptions that have fed into the analysis. The key clinical outcomes were obtained from summary statistics published in PHE's report for the NICE Appraisal Committee review of Drug X, which contains an analysis of data collected for the 9 month CDF period.

**Table 22 Description of key variables and base-case thresholds / assumptions**

Variable	Description	Data source
<b>Patient cohort</b>		
No. of patients receiving Drug X	Total number of patients starting treatment with Drug X: <b>180</b>	CDF review: list of treatment criteria
Patient characteristics	Median age: 70 75% male	CDF review
<b>Key outcomes &amp; baseline triggers for rebate in the OBP simulation</b>		
Death	Proportion of patients that stopped treatment because they <b>died</b> within the 9-month period of the CDF: <b>18%</b> <i>Rebate trigger: patient death</i>	CDF review
Disease progression	Proportion of patients that stopped treatment because of <b>progression of disease</b> within the 9-month period of the CDF: <b>31%</b> <i>Rebate trigger: patient stops treatment because of disease progression</i>	CDF review
Toxicity	Proportion of patients that stopped treatment because of <b>acute chemotherapy toxicity</b> within the 9-month period of the CDF: <b>4%</b> <i>Rebate trigger: patient stops treatment because of acute toxicity</i>	CDF review
Quality of life	Mean <b>change in EQ-5D utility score</b> from baseline to week 15: <b>-0.04</b> (95%CI: -0.07 to -0.01) <i>Rebate trigger: change in EQ-5D score from baseline &gt; -0.04</i>	Key clinical trial HRQoL analysis
<b>OBP assumptions</b>		
Price (no OBP)	100*	Assumption
Rebate	50%	Assumption
Price (OBP)	100 (scenario: 120)	Assumption

\*To avoid any price and discount assumptions on our part, we chose the nominal value of "100" to reflect whatever the price of Drug X is/will be to the payer.

Note: references have been removed to protect identity of Drug X

### Notes on retrospective case study inputs versus proposed "ideal" characteristics of an OBP scheme

For the purpose of this case study the selection of outcome metrics is driven to a degree by data availability. In absence of correlation estimates between the core outcomes metrics, the simulated data for each core outcome are independent of each other. As each simulation will give a (slightly) different result, we ran 10,000 simulations and report the average results (and 95% credible intervals) of these.

In the table below we discuss the outcomes driving this case study versus the characteristics of an OBP scheme proposed and recommended in this research.



Table 23 Outcomes: recommended versus those used in this case study

Recommended outcome to capture in an OBP	Outcome used for Drug X in the OBP-simulator	Explanatory note/ discussion
<b>Overall survival</b>	Patient still alive within the data collection period (9 months)	Overall survival could not be calculated by PHE as the CDF time window was too short. The “patient still alive” criterion used in this case study may represent a realistic outcome for capture as part of a fixed-term OBP scheme.
<b>For line 3+ treatments with &lt;1year survival prognosis: Treatment duration as proxy for disease progression</b>	Patient stopped treatment because of progression of disease within the data collection period (9 months)	Treatment duration could not be calculated by PHE as the CDF time window was too short.  The use of this treatment outcome (“patient stopped treatment because of progression of disease”) provided by the CDF may offer a more direct reflection of disease progression, if this were able to be collected routinely.
<b>Long-term treatment side-effects (adverse effects)</b>	Patient stopped treatment because of acute chemotherapy toxicity within the data collection period (9 months)	Relevant treatment side-effects should include adverse effects that may not necessarily have led to treatment discontinuation, and should also capture longer-term consequences where relevant; these data were not available for this case study
<b>Return to normal activities (e.g. “usual activities” dimension of the EQ-5D)</b>	Overall change in a patient’s utility score (as measured with the EQ-5D instrument) from baseline to week 15.	No population-level data summary from the CDF report on this outcome. Reporting of quality of life data from the clinical trial was such that scores were not broken down into the composite dimensions (of which “usual activities” is one). Therefore, broader elements of quality of life are captured in this measure including mobility, self-care, pain/discomfort and anxiety/depression.

## Analytic approach

We have used key descriptive statistics from the above data sources to create a hypothetical patient cohort with a realistic distribution of outcomes across individual patients. Each individual patient in the simulated cohort receives a specific result or value on each of the four core outcomes which is evaluated against the threshold to determine whether it triggers the rebate (as described in Table 22).

We report the results of the base case and alternative scenarios, to show the likely impact of various potential OBP schemes with specific characteristics, compared to the situation where no OBP would be in place.

For reference, if no OBP-scheme were implemented then for every patient the full nominal price of 100 would be due, regardless of treatment outcome.

### Base case analysis

In the base case we determined that all four core outcomes should be met. Hence, for every patient that 1) survives, 2) sees no disease progression, 3) has no toxicity leading to stopping treatment, and 4) returns to normal activities over the timespan of nine months, no rebate is due to the NHS and the manufacturer will retain the full price as paid upfront for the drug.

If any one individual outcome is triggered, however, then the rebate would be due by the manufacturer to the NHS, which is arbitrarily set at 50% of the price.

## Scenario analyses

We also considered various scenarios considering different outcomes to be met, as well as alternative OBP-price and rebate inputs.

- Scenario 1: OBP-scheme requiring survival (S), disease progression (DP), and toxicity (T) outcome to be met.
- Scenario 2: OBP-scheme requiring survival (s) and disease progression (DP) outcome to be met.
- Scenario 3: identical to base case except that the starting price under the OBP has a nominal value of 120 and the drug price without the OBP-scheme remains 100.

Mean results of the base case and scenarios are presented including 95% credible intervals.

## Findings

Below we report the results of the base case and scenario-analyses, to show the likely impact of various potential OBP schemes with specific characteristics, compared to the situation where no OBP would be in place.

Under the base case scenario, for 73% of patients one or more outcomes would be below the threshold, triggering the 50% rebate. The average per patient drug costs would then be 64% of full cost (or a 36% rebate to the NHS).

For scenarios 1 and 2, where gradually fewer outcome thresholds would need to be met, the results show that for fewer patients a rebate would be due, i.e. for 53% and 40% of patients respectively. As a consequence, the average per patient drug cost is higher in these scenarios (74% and 80% of the full price for scenario 1 and scenario 2 respectively) than in the base case, but lower than without the OBP-scheme (100 nominal price for every patient).

Scenario analysis 3 shows that the average per patient drug cost is higher than in the base case (i.e. 76% versus 64% in the base case), but lower than without the OBP-scheme (100 nominal price for every patient). For completeness we note that in this scenario a rebate is due for the same proportion of patients as in the base case (i.e. 73%) because the outcome requirements are the same.

Results of the base case and scenario 1-3 are presented in Table 24 and Figure 4 below.

**Table 24 Results base case and scenario analyses**

Scenario	% patients for whom a rebate is due	Average per patient drug cost under OBP versus no-OBP, as % of full price to the NHS
Base case	73 (64 – 82)	64 (59 – 68)
Scenario 1 (S, DP, T)	53 (46 – 61)	74 (70 – 77)
Scenario 2 (S, DP)	40 (32 – 48)	80 (76 – 84)
Scenario 3 (OBP price =120)	73 (64 – 82)	76 (71 – 81)



Figure 4: Results base case and scenario analyses

Finally, we show how the average drug cost per patient changes with the upfront agreed rebate percentage (50% in the base case), assuming all four core outcomes need to be met.

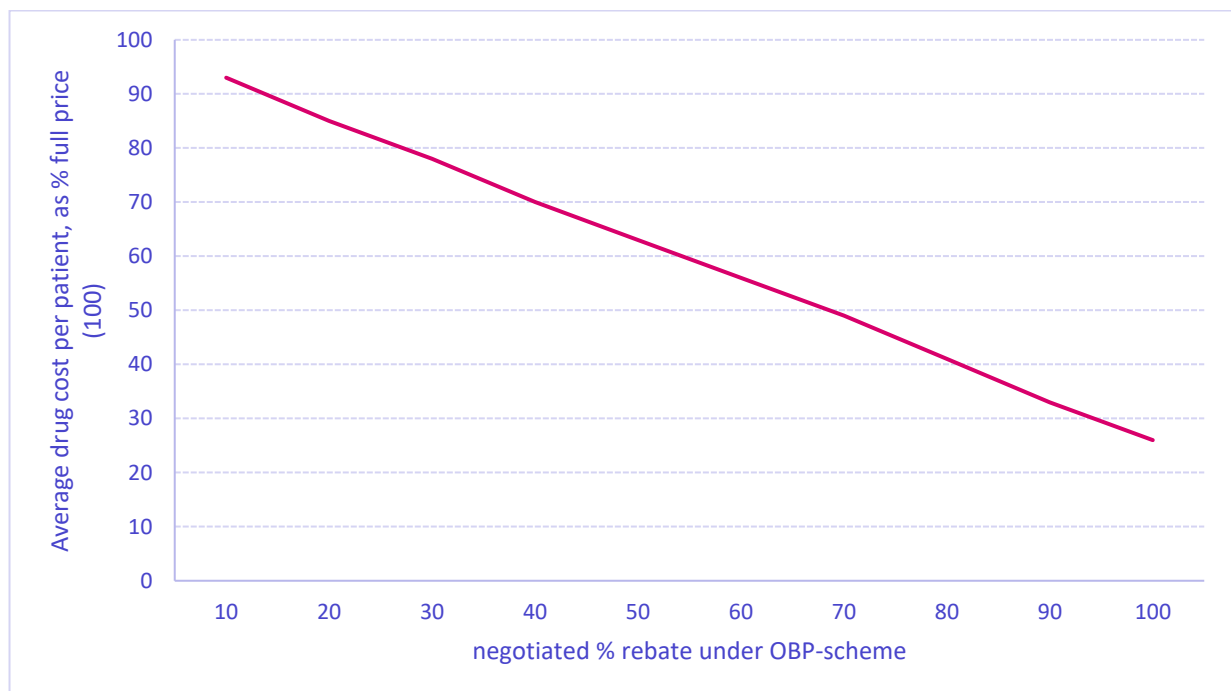


Figure 5: Average (mean) drug cost per patient as function of rebate percentage

## Summary

Through this exercise we set out to determine the feasibility of an OBP scheme; demonstrating what is possible now and what the ideal would be, and to understand the potential impact on drug costs to the NHS and manufacturer revenues from this drug in the given population.

Through the scenarios described we have demonstrated that the relative drug cost to the NHS is expected to be lower than routine commissioning (with a single price) under all scenarios but approaches non-OBP costs as % rebate reduces (and could exceed the average per patient non-OBP drug cost if the OBP price were greater than 100 and the rebate % were small). The effect of reducing the number of thresholds for 'successful' treatment is to gradually reduce the proportion of patients for whom a rebate is due, as expected, and hence gradually increase the average per patient drug cost to the NHS under such schemes.

The scenarios modelled are not exhaustive. Other scenarios could for example consider:

- 1) missing data: in section 3.2 we recommend that the way to deal with this should be part of the negotiation, yet the impact of various options can be modelled in a flexible modelling framework to help inform decisions.
- 2) outcomes thresholds: while we recommend these should in principle be based on the expected (yet uncertain) outcomes of the drug, other principles may be deemed more appropriate in other contexts for example comparing to a gold standard if that is well-defined.
- 3) relative importance of specific outcomes: if evidence exists that some outcomes are more (or less) important than others, then this could be included by weighting the outcomes.
- 4) choice of comparator for the OBP-scheme: in this study we compared the OBP scheme against the alternative of routine commissioning. Another comparator may be no (or delayed) patient access to the drug. In such case, an OBP-scheme would potentially allow earlier access to a new drug which would be a win not only for patients, but also for manufacturers as well as the NHS, enabling them to allow timely access while mitigating the financial risk caused by uncertainty around the drug's cost-effectiveness. In such case, the modelling should focus on patient outcomes, in addition to drug costs and revenues.

We have demonstrated the potential impact of an OBP scheme using a hypothetical dataset. There were some limitations to our data inputs, most notably having access to population-level estimates only. Full access to the SACT data would permit 1) individual-level analysis and linked patient-level data for each outcome, and 2) analysis according to a OBP scheme time-horizon observed at the patient-level (for the current analysis, we were limited to a 9-month window of data, with the follow-up time for some patients being shorter (minimum three months). Noting these issues serves to highlight the data requirements for a real-life prospective OBP scheme, where, as our research suggests, preferably individual-level patient data would need to be captured.

Given these were not available for this research, we mitigated this in our analysis by 'generating' individual-level data from population-level data to show 'what might have been'. In a real-world pilot, we envisage that PHE could be instrumental in providing individual-level data which are uniformly captured at the NHS level (rather than in different ways at the various local levels). This is likely to be possible for some outcomes but not for all. Patient-reported outcomes would still need to come from another source and then be linked at the individual patient level.

Finally, we note that the analyses presented considered the context of potentially cost-effective yet uncertain treatments for patients with cancer, where the expectation is that payments linked to further real-world evidence on the drug is an appropriate and feasible way

to mitigate the uncertainty. While the principles and direction of findings would likely be generalisable to other cancer and non-cancer conditions (at least for similar schemes and comparators), the exact results are not and different considerations about the most appropriate design of an OBP in other contexts will influence this.

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