Practical Application of Outcomes Based Pricing Models in Scotland

A feasibility project design:

Can Scottish NHS data support Outcome Based Pricing?

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This report was produced following round table discussion by the expert advisory group and subsequent review of a draft report. Pre-read material was made available to members prior to the round table that included the findings of a literature review, desk analysis and stakeholder consultation.

Executive Summary

Based on consultation with the expert advisory group, the objective of this report is to make recommendations on the next steps necessary to understand the practical application of an Outcomes Based Pricing (OBP) scheme in Scotland.

Current situation

In recent years in Scotland, the UK, and internationally, there has been a regulatory move to more rapidly approve new medicines that address unmet need based on less complete evidence to facilitate reimbursement. OBP, when pricing is linked to outcomes, is one mechanism to manage uncertainty in the evidence. Early experience of OBP schemes in Scotland was associated with high administrative burden to manually collect data on patient outcomes. The oncology data landscape has continued to evolve, and the time is now right to re-consider the feasibility of a data-driven approach.

In 2019 Cancer Research UK (CRUK) commissioned a report that summarised the current options for a generic OBP framework. Many of the proposed outcome measures were aspirational, but some may now be measurable using routine data available in Scotland at a National or Health Board level.

The introduction of routes of medicine licensing that supports accelerated access to new and innovative medicines, such as Project ORBIS and the Innovative Licensing and Access Pathway (ILAP) could create demand for viable ongoing data collection to help to manage the uncertainty of early phase trial data / small patient populations in the health technology appraisal process which determines whether a medicine should be routinely available. And ultimately to maintain acceleration to patient access.

The examples of Acute and Chronic Leukaemia were selected by the expert group, who noted a number of surrogate and clinical outcomes that can now be measured relatively easily in Scotland. These examples were selected due to the contrasting disease trajectories and treatment intensities where the value medicines for improving patient outcomes may differ in nature and timescale. Outcomes may include cancer progression and relapse events, survival and laboratory-based measures. There is also a wealth of further information about clinical endpoints in free text of health records. Currently, there is no routine collection of Patient Reported Outcome Measures (PROMS) in Scotland, although there may be the opportunity to include these in the future.

The expert group was informed of the data potential from the Edinburgh Cancer Centre, which provides comprehensive cancer services for the four Health Boards comprising the South East Scotland Cancer Network. Hosted by NHS Lothian, the Centre's informatics programme and the 'DataLoch' initiative provide a world leading testbed for data and informatics development.

Challenges

The expert group identified issues concerning data collection and quality, clinical pathways, selection of outcomes, and scalability to the national setting in Scotland. OBP schemes must be practical and simple procedures, administratively manageable if they are going to work in practice, and potentially scalable across NHS Health Boards and Cancer Centres. Data quality needs to be robust, data provision needs to be timely, and relevant outcomes need to be measurable. Where intermediate outcomes are used, these need to be valid predictors of clinical outcomes of recognised patient benefit with the treatment. A mechanism for

sustainable PROMS data collection needs to be developed if such measures are used to inform OBP schemes.

Any scheme would need to be adaptable to a rapidly changing policy environment and selecting a suitable time frame for a prospective pilot would be difficult. Ultimately, national scalability is essential, but logistically complex to set up, whereas a local feasibility project would be achievable and could focus either on the full breadth of granular local NHS data to demonstrate the aspiration of what is possible; or could take a restricted look at local data which is replicable using national data opportunities.

Feasibility

The expert group considered the feasibility of three options for a proof-of-concept project design:

1. **A prospective pilot study using an Acute Leukaemia example** – enrolling future patients in a demonstration scheme, recording/measuring real-world outcomes such as event-free survival and remission.
2. **A retrospective feasibility project using a Chronic Leukaemia example** – simulating implementation of an OBP scheme, assessing the measurability of pertinent outcomes including haematological response, event-free survival, time on treatment discontinuation and using existing data collection methods to identify gaps/future needs
3. **A PROMs pilot** could take one of two designs:
    a. Test a sustainable implementation of a PROMs capture mechanism making use of recent digital innovation (e.g. HM-PRO http://hmpro.co.uk/).
    b. Undertake retrospective curation of patient-relevant and reported outcomes to understand what is obtainable from routine clinical records, with the concern that these are not true patient-reported outcomes but rather surrogates recorded by the Healthcare Professional (HCP) based on consultation with the patient.

Any feasibility project should focus on a single medicine indication within a single disease pathway and should align with a recent or future NICE and SMC appraisal. Good options would be a first- or second-line treatment to allow sufficient patient numbers and a relatively homogeneous population. If there is capacity and data quality, the project could assess one or more medicines for a given indication in parallel.

A clear mechanism exists for managing information governance of a retrospective feasibility project. Further consultation would be required to understand if a prospective pilot project would require research ethics approval and individual patient consent.

Recommendations

- **A retrospective feasibility study is the most worthwhile next step. Such a project would provide proof of concept that data are now sufficient to support a prospective scheme. It could be conducted rapidly without any dependency on clinical services which are under significant pressure due to the COVID-19 pandemic.**
- **Following demonstration of proof of concept, a prospective pilot could be considered. Further scoping is needed to understand how best to capture PROMs as part of an OBP scheme before a pilot or feasibility project could be undertaken.**

Current situation

Experience of Outcomes Based Pricing (OBP) in Scotland, data requirements, frameworks, data assets and opportunities in NHS Lothian and Scotland

Innovative treatments for cancer address unmet need and therefore increasingly come to market following expedited regulatory approval pathways which can be based on early clinical trial data which creates uncertainty around the evidence of clinical benefit in the key clinical outcome of interest. This can leave major uncertainties about the added value of treatments to NHS patients, and questions about the real-world effectiveness of the treatments outside a clinical trial setting.

For promising treatments, where there is high unmet need, it may be possible for the SMC to recommend a new treatment for use, whilst collecting additional data (on outcomes). This enables patient access in a controlled manner. These Complex Patient Access Schemes (PAS) come in two forms:

(1) *Population-based*, collecting a range of outcomes to enable analysis across all treated patients after several years (coverage with evidence development). After a defined period, data is used to re-appraise the treatment with the potential for a block rebate to the NHS or manufacturer.

(2) *Patient-based*, identifying whether each individual patient has achieved a pre-specified outcome. Payment for the treatment is based on that outcome. For example, not paying for, only partially paying for, or getting a refund for a partial or no response; or paying in full for complete response.

Both of these types of PAS rely on the collection of high quality, reliable and affordable data which can inform the appraisal of outcomes. Historically the difficulty in collecting the required data in a timely and accurate manner has limited implementation of OPB.

This report uses the illustrative examples of chronic and acute leukaemia to explore the feasibility of an OBP initiative in Scotland. The expert group agreed that these disease areas reflect well in the scope and focus of the CRUK OBP framework. It focusses on the data aspects of feasibility, to understand if recent advances in cancer data capture could enable OBP data collection in support of a scheme.

The report has been developed using methods that included a desk analysis of relevant published materials and studies and a round table event with expert advisory board members. Membership included a patient, clinicians and experts in medicines reimbursement. The round table event consisted of a structured 2-hour discussion and subsequent one-to-one engagement with the relevant subject matter experts on the group. The scope of this project covers only the diseases AML and CLL but may offer learnings for other tumour types.

Experience of OBP in Scotland

Few OBP schemes have operated in NHS Scotland to date. The most notable is a complex PAS introduced to support HTA approval of a proteasome inhibitor used as monotherapy in multiple myeloma in 2009[1,2]. Key concerns with this type of scheme from the NHS perspective have largely been operational issues, including high administrative burden on clinical staff to collect patient level data manually and handle complex claim procedures at a local level, and the impact this has on the ability of the NHS to realise perceived financial benefits (i.e. financial risk). Clinical concerns, also relevant to HTA assessment, have focussed on the robustness of the chosen scheme outcome to predict longer-term clinical outcomes. However, given the very high cost of some new treatments and improvements in electronic health records, there is renewed interest in OBP. The capability of the NHS in Scotland to collect outcome data is seen as a real opportunity to progress novel pricing approaches such as OBP[3].

Outcome options for OBP

Acknowledging that an OBP scheme is specific to the treatment and designed to address the key uncertainty in the evidence available for appraisal, a major report in 2019 by Cancer Research UK[4] reviewed common uncertainties for cancer treatments. A core set of four broad outcomes were recommended that could form the basis of an outcomes framework for an OBP scheme in the NHS:

- Survival;
- Progression, relapse or recurrence of the cancer;
- Long-term side effects; and
- Return to normal activities of daily life.

The CRUK report is the most in depth and contemporary review of OBP in the UK in recent years and the expert group considered it to be the most relevant to the current project, providing a robust foundation for applied feasibility work.

More specific examples put forward by the expert group considered that potential outcomes might focus on intermediate or surrogate outcomes specific to the tumour type or indication. It also made clear that there needs to be a realistic chance of outcomes being measurable with current data that are routinely collected and available in clinical practice. Examples proposed that are of relevance to cancer examples included:

- Response according to biomarker threshold
- Radiological response
- Time on treatment (a proxy for progression free survival or excess toxicity)

It is very clear that outcomes chosen should be objective and clearly defined. Intermediate or surrogate outcomes should reliably predict longer-term clinical outcomes.

Example of treatment pathways in Acute and Chronic Leukaemia

Acute leukaemia is classified into two main types according to the type of white blood cells affected – lymphocytes which fight viral infections (ALL) or myeloid cells (AML) which fight for example, bacterial infections defending the body against parasites and preventing tissue damage spreading. The acute nature means both types progress quickly and aggressively, and so usually will need immediate treatment. AML is most common in elderly adults (aged over 75 years) with around 3,100 people diagnosed annually in the UK. In Scotland (2017 figures) around 169 people are diagnosed annually with AML with 22 registrations in the NHS Lothian health board region[5]. In terms of survival, five-year relative survival for AML in men in Scotland is 13% and for women 18%[6].

Chronic lymphocytic leukaemia (CLL) affects the white blood cells and tends to progress slowly over many years. Specifically, the bone marrow produces too many white blood cells (lymphocytes) which are neither fully developed nor work properly. CLL affects all ages, but is most common in older adults (aged over 60 years). In Scotland (2017 figures) around 141 people are diagnosed annually with CLL with 18 registrations in NHS Lothian health board region[7]. Five-year relative survival for CLL in men in Scotland is 72% and for women 81%[8].

Due to its chronic nature, CLL can lead to problems including an increased risk of picking up infections, persistent tiredness, swollen glands in the neck, armpits or groin, and unusual bleeding or bruising.

Outcomes options in Acute and Chronic Leukaemia

The range of potentially relevant outcomes in the two tumour types, consistent with the overarching CRUK framework, are presented in Table 1.

Table 1. Potential outcomes in AML and CLL

Core Outcome Category	OBP measurable event for Acute and Chronic Leukaemia	Comments
Death/survival	Death (cause specific)	Comprehensively collected within 1 week
Disease progression	Progression	Not routinely coded but time to next treatment is available as a surrogate
Response/relapse	Disease clearance or complete response followed by a relapse event Biomarker thresholds (e.g. Minimal Residual Disease - MRD)	Less detail in RWE than in trials – other than biochemical or haematological values will require manual case-note review.
Long term side effects	Treatment or disease related diagnoses with severity indicator	Patient reported would require PROMs – not currently routinely collected. Possible to extract coded data from inpatient coding or surrogates from e.g. prescribing patterns

Return to normal activity	Morbidity or quality of life (clinician or patient reported)	Would require PROMs or bespoke clinical assessment.

Current data assets in NHS Lothian and Scotland

Datasets currently available in NHS Lothian are presented in Figure 1 and more information can be found at https://edin.ac/cancer-data-wiki. The key datasets for haematological malignancies include the TRAK MDM module, SCAN Audit, ChemoCare, SES Cancer Database and Scottish Cancer Registry. The system used for the prescription of Systemic Anti-Cancer Therapy (SACT) is ChemoCare. This system is live, and its associated reporting database is refreshed every 24 hours. Treatment discontinuation and next therapy are recorded in the system. Death dates are refreshed from National Records Scotland (NRS) weekly with all-Scotland ascertainment accessible to Edinburgh Cancer Care team via the Public Health Scotland ACaDMe datamart. Death dates are also manually entered into SESCD by the Edinburgh Cancer Centre (ECC) coding team until they are superseded by the NRS feed. Work is underway by Public Health Scotland to implement a national set of ChemoCare-derived dataset for all-Scotland.

The expert group stressed that pertinent outcomes need to be measured easily in routine care. They held the view that death dates and cause of death are accurate. Data on treatment discontinuation or information about commencing next lines of treatment were also generally agreed as obtainable in near-real time from ChemoCare. Endpoints that rely on healthcare utilisation such as inpatient and outpatient activity, with associated procedure and diagnostic coding, were expected to be available with only a short delay.

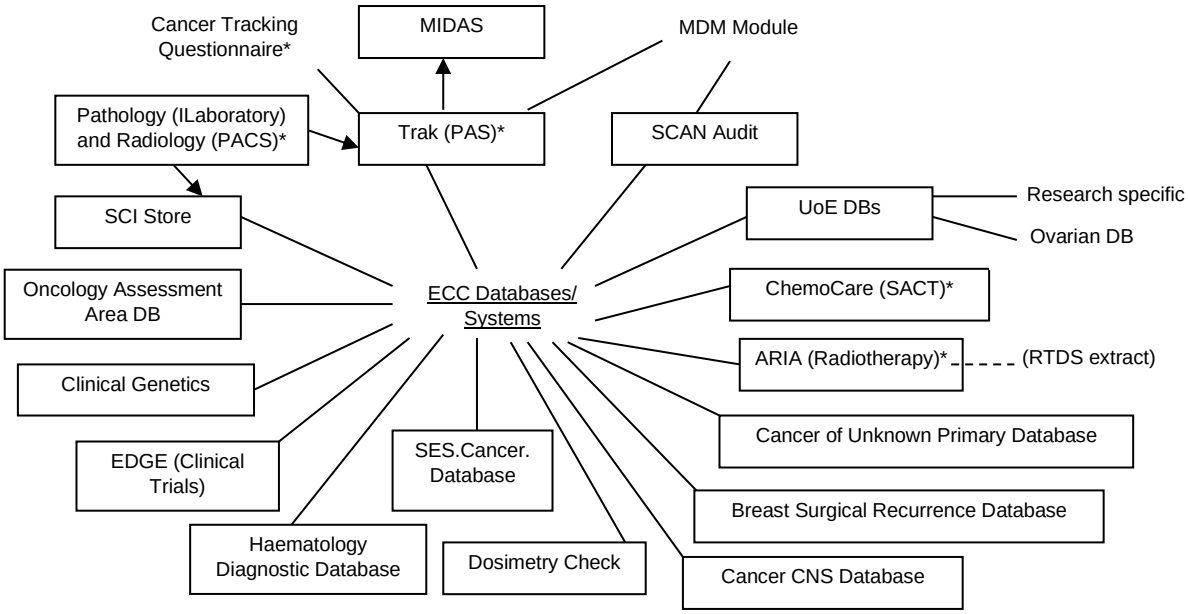
Other endpoints that the experts discussed in referring to AML/CLL outcomes in particular included progression, relapse, and response. It was highlighted that such clinical endpoint data usually exist as free text, for example, radiology reports describing a progression event. There is an opportunity to explore if progression and relapse events can be defined from haematology and biochemistry coded labs data which is a particular opportunity for haematological malignancies. Routine patient reported outcome measure collection in Lothian is not currently performed. A PROMS pilot carried out by the Edinburgh Cancer Centre in 2019[i] demonstrated that patients will complete PROMs via an electronic platform, but that missing data is a real issue unless patients see personal value in entering the data, e.g. where the results directly influence their care, symptom or side effects management. Missing data is likely to be a significant barrier to a patient level OBP scheme that relied on PROMs collection without significant monetary and staff time investment to support implementation.

An element of manual coding will continue to be essential to generate high quality coded data. NHS Lothian currently has several manual coding and database management teams whose roles could be expanded to meet the needs of OBP schemes. These include the routine hospital coding team, a dedicated cancer audit team supporting national reporting against

[i] For more information about the Edinburgh Cancer Centre PROMs Innovation pilot see https://cancer-data.ecrc.ed.ac.uk/2020/01/08/cancer-proms-pilot-project-with-my-clinical-outcomes/

quality performance indicators, and the Edinburgh Cancer Centre with its regional audit database which is maintained by the Cancer Information Team. These teams would be capable of either collecting specific additional data or perform quality control (validation) of outcomes-related data that is automatically extracted from electronic systems.

Figure 1. NHS Lothian and South East Scotland Regional Databases



*live systems with inherent real-time data, other databases rely on data entry with variable time lags.

In addition to these core datasets, there are several new regional data opportunities via the DataLoch™ (https://dataloch.org), including Primary Care data from GP systems, Social Care data – from the social care survey, COVID-19 – including test results and vaccination events, Laboratory values (Biochemistry, haematology).

Many of the NHS Lothian and South/East Scotland databases and systems exist in all Scottish Health Boards. South/East Scotland has the additional asset of the South/East Scotland Cancer Database that includes data on all patients in South East Scotland seen by an oncologist (e.g. treated with chemotherapy or radiotherapy). Uniquely this includes coded data on cancer recurrence events and could be a vehicle for additional coded outcome data, subject to further development. Transplant and bone marrow biopsy databases also exist and can provide a flag to identify relevant events – these are Health Board specific.

Current national datasets are made available as local extracts but may be subject to a time lag. These include the Scottish Cancer Registry (1 year lag), Scottish Morbidity Record (Inpatient, Outpatient, Mental Health, Maternity) (3 months lag), Unscheduled care datamart (A&E, Ambulance, GP OOH, NHS 24), Prescribing Information System (Community prescribing), National Records Scotland (Death registrations), National Screening data, Cancer waiting times data.

Table 2. Local, Regional and National Datasets

NHS Lothian datasets	South/East Region datasets	Scotland National datasets
Trak (PAS/EPR)	South East Scotland Cancer Database (SESCD)	SACT (SCRIS)
Clinical Genetics	SACT (Chemocare)	Radiotherapy (RTDS)
Primary Care data from GP systems (DataLoch)	Radiotherapy (ARIA)	QPI/Audit
Cancer CNS Databases		Cancer Registry
Social Care data – from social care survey (DataLoch)		EDGE (Clinical Trials)
Laboratory values (Biochemistry, haematology)		Radiology Imaging (PACS)*
Disease-specific audit databases		Scottish Morbidity Record (Inpatient, Outpatient, Mental Health, Maternity) (3 months)
		Unscheduled care datamart (A&E, Ambulance, GP OOH, NHS 24)
		Prescribing Information System (Community prescribing)
		National Records Scotland (Death registrations)
		National Screening data
		Cancer waiting times data
		COVID-19 testing and vaccination

Challenges to data provision for OBP

In considering a list of 'success criteria to be met' for the implementation of flexible OBP, the expert group identified several challenges that need to be resolved, as well as potential solutions that could be worked up in an OBP feasibility project.

Healthcare and IT systems

The administrative burden and the complexity of schemes is repeatedly highlighted as a barrier for delivery within a stretched NHS. Adding schemes that don't rely on existing systems and infrastructure will be likely to lead to an unsustainable cumulative administrative burden. The prediction that schemes will pay for their own administration is insufficient in the face of staff recruitment challenges. A feasibility project should therefore focus on demonstrating the potential of using selected existing local datasets, or focus on demonstrating the feasibility of adoption at scale using national datasets.

Data collection and data quality

NHS capability to collect outcome data with sufficient completeness and accuracy is critical to the OBP approach. The data must be available, sufficiently high quality, and reliably collected across the population. If the OBP data for a future scheme must be collected manually, each NHS Board and Cancer Centre would need funding and available staff to collect the data or the financial benefits of the scheme would not be realised.

Selection of outcomes

Outcomes must meet the following criteria:

- Pertinent to a key area of uncertainty in the appraisal of a medicine
- Measurable within a reasonable timeframe
- Adheres to a standard definition
- Causally related to the drug.

Target population and patient numbers

An OBP feasibility scheme would be expected to include a reasonable number of patients to avoid exceptional responders skewing the conclusions. A review of the South/East Scotland region for 2019-2020 identified 70 new cases of AML or CML including 50 new cases within NHS Lothian.

Evidence generalisation

Population characteristics will often differ in real world settings compared with patients recruited into clinical trials with selective eligibility criteria. For this reason any method to capture outcomes should be sensitive to the fact that outcomes may well differ from those observed in the clinical trials that provided the evidence basis for Health Technology Assessment. It will be important to fully capture patient characteristics in a manner that allows comparison with the trial patients.

Time period of interest

There are unique challenges facing cancer patients due to the COVID-19 pandemic which has led to population behaviour change, health system changes, and temporary pathway suspensions and alterations. These complicate any OBP work based on real world data during the pandemic period and this needs to be taken into account. On a more positive note, the data environment is rapidly improving as part of the response to the pandemic, lending optimism to our ability to conduct OBP in the near future. The choice of a start date of an OBP pilot would need to be sensitive to these factors and may impact how it might be subsequently rolled out, particularly as national datasets and data quality improve.

Challenges specific to AML and CML as two potential example diseases for OBP

Over the last couple of years, several new treatment options for AML have been approved, but there has been no standardised approach across the UK or Scotland on how these should be used. This has led to variation in care pathways with the consequence that an OBP scheme may face challenges in defining therapeutic sequencing within a pathway precisely in advance.

An outcome for an OBP scheme needs to be measurable within a timeframe that fits a time-limited scheme. Progression-free survival in CLL may be several years, creating a challenge in the delivery of a prospective OBP pilot project that relied on this endpoint.

Minimal Residual Disease (MRD) is becoming more important in CLL trials and may be a more rapidly achieved measurable for an OBP pilot. It has, however, not yet been seen in HTA models in CLL as an endpoint, possibly because most trials have sufficient data to use PFS. MRD is, however, being used more frequently in determining research design and treatment decisions so may be pertinent. An interesting example of MRD being used as an endpoint is in FLAIR, an adaptive trial and one of the largest UK CLL trials. MRD is driving the design of the trial and it includes a stopping rule based on MRD negativity.

Assuming that MRD or other more rapid surrogate endpoints are not suitable ways to overcome the timeline challenge, the expert group considered that AML may be a more suitable basis for a prospective pilot OBP scheme due to more rapid outcome ascertainment. CLL may well be suitable for a retrospective feasibility study of a hypothetical OBP scheme where the timeline challenge becomes hypothetical only.

Feasibility pilot options

The expert group agreed that an OBP pilot should meet recent CRUK report's recommended requirements for an OBP scheme. Specifically, a chosen scheme should have potentially large benefits, there should be uncertainty in the evidence base (often due to immature clinical drug trial data) and any clinical improvements from the treatment should be seen as valuable. They agreed that these criteria are met with the disease examples of AML and CLL for several recently adopted drugs.

There was disagreement on the CRUK report's recommendation that OBP should focus on contexts where numbers of patients are small, assuming that the administrative burden of the scheme can be reduced by efficient data collection.

The concept of conducting a feasibility OBP pilot in Scotland, initially within NHS Lothian, was strongly supported. The main objective of a feasibility project should be to inform the design of an applied prospective pilot OBP scheme. It should inform the choice of type of scheme, choice of endpoints, reliance on routine data and scalability beyond a single Health Board.

It was felt that an individual patient reimbursement scheme was the preferred option, in preference to a population-level scheme. This was mainly on grounds of practicalities of implementation.

The expert group noted that demonstrating the feasibility of data collection should be the core aim of a feasibility project. Specifically, it should focus on the ability to collect data on a relevant outcome in AML or CLL to demonstrate proof of concept.

Specific recommendations by the expert group included:

- Treatment outcomes like overall survival would likely take too long to measure for the purposes of a feasibility project. Time to treatment discontinuation or progression may be more suitable.

- There was a preference for a simple clinical context looking at a single pathway, for example, focusing on either first line or second line treatments.

- A feasibility project does not need to be limited to any one specific medicine, it could include a group of medicines used for a specific indication; acknowledging that a prospective OBP pilot scheme would need to choose a single medicine and single indication.

- A feasibility project does not need to be dependent on a specific sample size – numbers only need to be sufficient to demonstrate proof of data acquisition.

- A project should be based on those outcomes for which uncertainty is common in the appraisal of new medicines (for the specific disease chosen) – for instance due to immature data, but where large health benefits/improvements are reflected in that endpoint. Progression free survival, event free survival and time to treatment discontinuation were suggested as good options.

- Data on patient perspectives, QoL, PROMs are also important outcomes to consider, but given that data collection is currently lacking and is challenging in a routine care context, it would only be possible to look at these outcomes in a prospective pilot.

- A feasibility project should take account of the MHRA involvement in Project Orbis[ii] and the Innovative Licensing and Access Pathway (ILAP)[iii] in which the SMC is a partner.

- General preference emerged from the expert group for a retrospective feasibility study due to several factors including:
    - It could look at surrogates for quality of life, symptoms and side effects in the routinely collected data in the absence of PROMS
    - It could allow comparison of data extracted from EHRs with manually curated data to confirm accuracy
    - It would have a low administrator burden compared with a prospective project.
    - It would allow sufficient patient numbers for a rapid and informative feasibility project – a prospective project, particularly in AML or CLL, would take a significant amount of time to complete with meaningful numbers.

From the expert group discussion, three potential options for a feasibility project emerged.

1. Prospective pilot study

- Based on an AML indication a prospective study would enable a pilot implementation of an illustrative OBP scheme to run, potentially taking event free survival or maintenance of remission as outcomes. Prospective patient recruitment would be required, with a dependency on full participation.

2. Retrospective feasibility project

- A CLL retrospective analysis – simulating *implementation* of an OBP scheme, assessing the measurability of pertinent outcomes which might include haematological response, time to treatment discontinuation as a proxy for progression.

3. A patient reported outcomes (PROMs) methodology study

[ii] Project Orbis https://www.gov.uk/guidance/guidance-on-project-orbis
[iii] Innovative Licensing and Access Pathway (ILAP) https://www.gov.uk/guidance/innovative-licensing-and-access-pathway

Option A - Prospective, could involve direct collection of PROMs from patients e.g. using novel technology-based approaches as the measurement tool, such as using a smartphone app. Objective to test the ability to collect PROMs in a prospective OBP scheme, linked to routine Electronic Patient Records (EPR) data.

Option B - Retrospective, extracting surrogate variables from existing clinical records and assessing their wider ability to reflect patient-centred outcomes such as symptoms, toxicity and quality of life.

Options appraisal on potential feasibility study designs

1 - Prospective pilot study

AML is recommended given the more timely acquisition of meaningful clinical outcomes compared with CLL. Treatments for AML are largely unchanged since 2018, providing a stable medicines landscape for study. It was, however, noted that patient numbers will be fewer with AML compared to CLL. The measurement of AML outcomes may be obtainable within a short time frame that would enable demonstration of feasibility in a timely manner.

Table 3. Summary of data needs for a prospective pilot study in AML

Possible outcomes to use in OBP	**Expert recommendation**
Overall survival	Takes too long
Progression free survival Event free survival (failure of treatment strategy)	Progression events not routinely coded. Treatment discontinuation or start of alternative treatment could be a surrogate.
Remission (3 categories: morpho/cyto/molecular)	Time-point: after 1st cycle (intensive, >85%), non-intensive less consistent
Minimal Residual Disease (still in development as an outcome measure)	Universal approach required, this standardisation is underway, so may be more suitable as an outcome for AML in 12-18 months' time. NPM or core binding factor is standard
PROMS	Crucial to include, but requires significant development and testing for implementation

2 Retrospective feasibility project

A CLL retrospective analysis – simulating implementation of an OBP scheme on existing data A 'look back' at past patients and their outcomes would help us to understand what is possible using existing data capture.

The expert group considered that a project of this design would have several advantages:

- Feasible without needing a system change
- Quick to conduct
- No requirement for prospective recruitment or individual consent
- Multiple endpoints could be assessed, including surrogates for PROMs
- Manageable for a CLL example with long follow up which – the relatively simpler patient pathway and larger patient numbers has some advantage over AML.

- Alternative OBP scheme designs could be simulated

Table 4. Summary of data needs for a retrospective feasibility study in CLL

Possible outcomes to use in OBP	Expert recommendation
Overall survival	Long follow-up requirement is not a barrier in a retrospective design
Progression free survival Event free survival (failure of treatment strategy)	Progression events not routinely coded but surrogates or algorithms for capture could be explored. Treatment discontinuation or start of alternative treatment could be a surrogate.
Minimal Residual Disease (still in development as an outcome measure)	Remains in development as an endpoint so unknown if will be suitable – requires exploration
PROMS	Not possible in a retrospective analysis, but surrogates could be explored.

3. A patient reported outcomes (PROMs) methodology study

PROMs either retrospective or prospective

  - Prospective – use of a cancer specific PROM
  - Retrospective – do patient records contain any information that enable determination of quality of life? This would involve extracting patient relevant variables that are not the strict outcomes from the trial.

- Doing a pilot that focused on PROMs is central to developing an OBP scheme, but will require a significant system change. There are many and various initiatives looking at the comprehensive use and collection of PROMs in cancer patients. Any OBP scheme seeking to collect PROMs would need to integrate with and build on these other initiatives. Significant further fact-finding and scoping work would be needed prior to designing a PROMs pilot project.

Recommendations of the expert group

A retrospective feasibility study is the most worthwhile next step. Such a project would provide proof of concept that data are now sufficient to support a prospective scheme. It could be conducted rapidly without any dependency on clinical services which are under significant pressure due to the COVID-19 pandemic.

Following demonstration of proof of concept, a prospective pilot could be considered. Further scoping is needed to understand how best to capture PROMs as part of an OBP scheme before a pilot or feasibility project could be undertaken.

Planning and costs

A key challenge faced by previous OBP schemes was generating the outcomes data of sufficient standard with a manageable workload on the NHS clinical, data and administrative teams. The team considered the feasibility and cost of each three options discussed by the advisory group, and subsequent research which brought up additional details on potential timelines and costs, as follows. This subsidiary section is intended to be separable from the main paper so that the previous sections remains at an overall policy level, and can be made available to illustrate specific options mentioned in the full report.

1 - Prospective option

A prospective data capture pilot was not currently recommended, as the resources required and time to a result are similar to setting up an actual OBP scheme. It would be easier to justify and better to allocate the required investment and effort for measuring outcomes in an actual HTA recommendation. This is likely to be in an acute disease or one where reliable outcomes (e.g. PFS, CR, treatment discontinuation) are available in the short term, meaning outcomes could be measured reasonably quickly. The project would be related to an outcome that was deemed by SMC as driving the uncertainty in the determination of clinical or cost effectiveness.

The economic model in the company submission would need to assess the feasibility of data capture using retrospective data and highlight historic outcome levels and correlations. This information then informs a clinical and cost-effectiveness assessment of the value of the specific data-point for assessing success or failure of the drug, and subsequent negotiation around this. The costs of the project will depend on the quality of the outcome capture in routine care, with significantly higher costs for adding new procedures into the clinical path for the collection of the outcome, for example additional MRD testing. The four steps in the process are therefore:

1. Uncertainty identified by the company and included in economic modelling
2. Retrospective feasibility of data capture and outcome benchmarking
3. Clinical assessment of value of data in context and negotiation on outcome level and quality
4. If cost-effective and agreed, OBP scheme, initially as a prospective pilot.

2 – Retrospective option

A retrospective data capture pilot was recommended as cost-effective and feasible in existing systems. This would reassure the payer and the industry that the data collection issues raised in previous OBP schemes have decreased and that OBP from routine clinical data is technically feasible. The retrospective pilot can be done standalone, or form a natural first step in the process for actual OBP described above as “feasibility”. If standalone, the retrospective pilot could be delivered as a service evaluation by NHS Lothian.

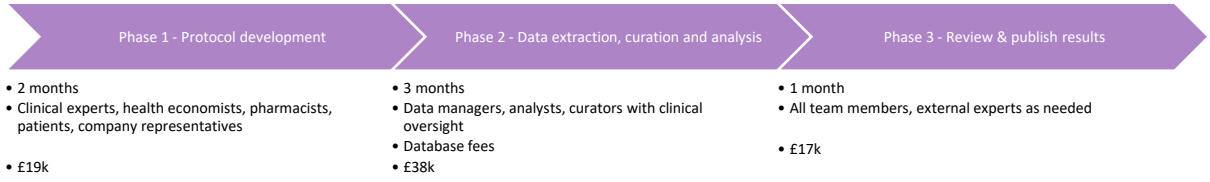
One advantage is the speed to deliver the project as the outcomes have already been reached, meaning this pilot could be done in a chronic disease over many years to assess the impact of an outcome on reducing uncertainty, combining both clinical value and data availability. The

expert group discussed a specific CLL indication which would be appropriate and the costs and timelines for this are shown below: the actual choice of medicine(s) should be from an independent scientific panel. The outcome of this drug could be assessed defining response in relation to full blood count (FBC), which is routinely collected for CLL patients. CLL has had relatively stable treatment pathways, meaning that the outcomes should be reliably linked to the use and success of the medicine.

Advice from the Edinburgh DataLoch team is that Full Blood Count (FBC) data are retrospectively available in the structured electronic health record for CLL patients in NHS Lothian, meaning that a pilot is possible based on a FBC derived outcome measure.

Subsequent planning for the project indicated three major phases: protocol development, data curation and analysis, and review and publication of results. Protocol development would include agreement on the outcome of value which is present in EHR and the standards required for OBP, and the results phase would include analysis of data quality and modelling of a possible OBP threshold and impact. This could be delivered most economically if integrated into the workload of the University of Edinburgh data science team over a six-month period, while a more intensive project could be quicker but would be challenging to deliver given the other work of the project team members.

High level costing indicates approximately £75k to fund the 6-month project, with the largest cost area being £30k on data analyst, data scientist and data management time, then £16k clinical and pharmacist advisory and leadership, and £10k database fees. Approximately half of the cost sits in the data extraction, curation and analysis phase, with a quarter each in the design and set-up, and the results and conclusions. The phases, times, core roles and costs are shown below. While PROMs cannot be collected retrospectively, this pilot could be combined with Patient and Public Involvement and Engagement (PPIE) input and advice, for example an assessment on the value of patient-selected or patient-reported measures to complement the clinical data found.



3 – Patient reported outcomes option

OBP based on PROMs was welcomed in principle by the expert group and patient representative, however it was felt that immediate initiation of a scheme that relies on PROMs would be premature. It also noted that PROMs have not been a significant source of uncertainty in recent SMC decisions which may make it less of a priority compared with other outcomes as a basis for a scheme (although lack of Quality of Life data is frequently and regularly remarked upon by the SMC committee). In addition, the most common PROMs capture method is via direct contact between the patient and the care team, which can be time consuming and inconvenient if it requires additional visits, or difficult to properly cover

in routine visits. As PROMs are not routinely collected, additional resources would be needed to add this step to the clinical pathway. It is possible to infer patient quality of life by retrospective review of free text and structured clinical data from patients, however this is not a patient reported outcome measure.

A prospective pilot could show that valuable PROMs can be collected affordably, but may also face barriers within current clinical workflow. The use of smartphone and web-based apps for successful PROMs capture has now been well validated by health technology providers such as Vinehealth, Px Healthcare and My Clinical Outcomes. Dedicated electronic PROMs technologies (e.g. HM-PRO) have the ability to produce more consistent and more structured data than manual methods, and this data can be directly incorporated into the EHR. A report from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) PRO Mixed Modes Task Force said, 'Advantages of using electronic data collection include less subject burden, avoidance of secondary data entry errors, easier implementation of skip patterns, date and time stamping, reminders/alerts, edit checks, and more accurate and complete data'.[9]

As an example, Vinehealth's technology has been deployed successfully by the Royal Marsden[10] and includes a patient-facing mobile app that optimises self-management by enabling patients to track, understand and optimise their care, integrating with smartphones, wearables and EHRs. Through this, the platform gathers rich, longitudinal, patient-generated data and can also be used to deliver bespoke patient alerts, as well as to support remote clinical decision-making and faster detection and management of deteriorations. High-level costing from Vinehealth indicates approximately £64k to fund a pilot PROMs patient app within a broader project, with the majority of costs accounted for by initial customisation and set-up of the platform, leaving room for significant economies of scale with increasing patient numbers. Approximately £39k is required for customisation, study set-up and technology delivery, £15k on project management and £10k on data review and publication.

While many PROMs pilot projects have been successful around the UK, sustainable implementation with demonstrable long term use by patients remains to be demonstrated. A project designed to achieve this would need significant further scoping, likely including dedicated clinical and project management support for front line staff implementing a PROMs capture process.

Further Reading

[1] Velcade scheme Summary of VELCADE® Response Scheme (nice.org.uk)
[2] SMC bortezomib advice 302/06 bortezomib (Velcade) (scottishmedicines.org.uk)
[3] Supply and Demand for Medicines. The Scottish Parliament Health and Sports Committee 2020
[4] Making Outcome-Based Payment a Reality in the UK. CRUK OBP report 2019.
[5] Source: Scottish Cancer Registry, ISD. Data extracted March 2019. Available at: https://www.isdscotland.org/Health-Topics/Cancer/Cancer-Statistics/Leukaemias/#myeloid
[6] Acute myeloid leukaemia (AML) survival statistics | Cancer Research UK
[7] Source: Scottish Cancer Registry, ISD. Data extracted March 2019. Available at: https://www.isdscotland.org/Health-Topics/Cancer/Cancer-Statistics/Leukaemias/#lymphocytic)
[8] Chronic lymphocytic leukaemia (CLL) survival statistics | Cancer Research UK
[9] Eremenco s et al. PRO data collection in clinical trials using mixed modes: report of the ISPOR PRO mixed modes good research practice TaskForce. Value Health 2014;17:501-6
[10] https://www.vinehealth.ai/the-royal-marsden-case-study