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ORIGINAL RESEARCH ARTICLE

Value-Based Healthcare in Practice: IDEATE, a Collaboration to Design and Test an Outcomes-Based Agreement for a Medicine in Wales

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Abstract

Objective To develop a sustainable, scalable methodology for the design of outcome-based agreements (OBAs) that works on the ground and dynamically overcomes historical challenges.

Methods Project IDEATE co-created solutions to known (and emergent) challenges via iterative workshops and real-world data analysis to develop and refine a hypothetical model for an OBA in a trusted research environment. A cross-disciplinary collaboration between National Health Service (NHS) Wales, industry and academia was developed. Data were collected from Welsh national datasets and used to construct a novel linked dataset. OBA scenarios, with different contract parameters, were analysed to assess impact on the proportion of contract payment due and the volatility of payments.

Results An approved, in market, locally advanced and metastatic breast cancer treatment was selected as the test case. The total number of patients in the treatment cohort (2017–2020) was $n = 99$, and 286 in the control cohort (2014–2016). The final outcome variables selected were: (1) 1-year survival,(2) intolerance to treatment (deferral), and (3) the total days disrupted by care. The primary scenario included all three outcomes measured at the population level and used a linear payment model. Volatility analyses demonstrated contract parameters can dramatically alter the contract output with greatest risk from a single, binary outcome contract design.

Conclusions The design of an OBA is a complex process that requires a multi-disciplinary approach. By assessing solutions to data, outcomes and contracting challenges, IDEATE provides a strong foundation for future success of OBAs in the UK.

Plain Language Summary Outcome-based agreements (OBAs) are a way to pay for medicines if they help patient health in a specific way over time. These agreements can make it faster for people to get new medicines, but they also have challenges, like needing a lot of time and effort to manage them. A team from the NHS Wales, life sciences, and Swansea University created Project IDEATE to find a better way to design OBAs and solve some of these problems. Welsh datasets were used to create a new breast cancer dataset to test different OBAs and see how payments would change. A breast cancer treatment was used for the project. The project had 99 patients who got the medicine (2017–2020) and 286 patients who had breast cancer but did not get the medicine (2014–2016). Three health outcomes were measured: (1) living for one year after treatment, (2) patients needing to stop the medicine, and (3) days spent in care. The main OBA option we tested used all three health outcomes; the more the outcomes improved, the more the payments could go up until they hit the highest amount agreed. The analysis showed that the way an OBA is designed can make a big difference in how stable or risky it is, especially if one of the health outcomes has only two options. Project IDEATE showed that making an OBA can be hard, but when people from different fields work together, they can overcome many challenges and succeed.

1 Introduction

Health care systems are facing unprecedented pressure from increasing complexity of patient care and higher costs, while contending with constrained resources and budget deficits following a global pandemic, inflation, and cost-of-living crisis [1–5]. At the same time, new medicines and therapies, expected to improve patient outcomes significantly, are being made available with higher prices, creating patient access challenges which can be difficult to resolve and which threaten NHS economic sustainability [6, 7].

Addressing the affordability challenge requires rethinking value. Value-based healthcare (VBHC) [8] is the equitable, sustainable and transparent use of available resources

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Key Points for Decision Makers

It is possible to design a feasible outcome-based agreement in Wales with low-burden to the system using linked national datasets in a secure data environment.

Cross-organizational collaboration with a commitment to improving patient health outcomes is critical for success.

The definition of the patients included in an OBA, the outcome variables selected and the choice of contracting parameters can all have a significant impact on the outcome of a contract.

Investment in data and data infrastructure can better enable the evolution of health care systems to deliver optimised patient care.

to achieve better outcomes and experiences for every person [9], allowing organisations to align on the shared goal of improving patient health outcomes. A shift to strategic allocation of resource, where there is demonstrable benefit and value, reorients payment of medicines to focus on the achievement of clinically meaningful and patient-centred health outcomes, thus offering a higher probability for return on investment by health services. This includes the use of biosimilars where they do not compromise outcomes and outcome-based pricing agreements for originator and patented medicines [10]. Wales has spearheaded the drive towards VBHC in the UK since 2016, when the principles of Prudent Healthcare [11] were adopted and a Policy Strategy grounded in addressing the health and social care needs of the Welsh population was published in 2018 (and updated in 2022) [12], followed by the launch in 2019 of the National Action Plan for VBHC in Wales [13].

VBHC is the paradigm that underpins outcomes-based agreements (OBAs), a commercial arrangement where reimbursement for a medicine is dependent on achieving predefined metrics for a health outcome(s) in a performance-based contract, over time. There are numerous examples of implementation of OBAs across the world. In the USA, 99 OBAs were executed or publicly announced between 2009 and 2021 [14] while 35% of all public OBAs are in Italy [15]. Over the last approximately 20 years, at least five OBAs have occurred in the UK; whilst the details of these agreements are confidential, most involved pricing discounts and few, if any, used comprehensive patient-centred data, rather depending on financial performance to determine payment [16, 17].

There are multiple definitions of OBAs (or outcomes-based contracts) and some would use this as an umbrella term for any form of reimbursement agreement that involves pay-for-performance, which could include managed entry agreements (MEAs) [18]. To address uncertainty and risk, the existing framework in the UK allows for managed access agreements (MAAs), a form of coverage with evidence generation, e.g. via the Cancer Drugs Fund and the Innovative Medicines Fund in England. MAAs in their current form are not equipped to incorporate multidimensional performance metrics (from clinical, patient-reported and health economic outcomes) [14, 19], nor is there well-established infrastructure and governance to facilitate the operational processes, including health technology assessment (HTA) re-review and performance data availability to be used in optimising patient care [20]. Multi-dimensional OBAs, that encompass both key clinical outcomes measures and those that better reflect the impact of the disease and treatment on the patient's daily life, may bridge these gaps.

There are several potential advantages to multi-dimensional OBAs: (1) accelerating patient access to innovative medicines that could maximise improvements in health outcomes, particularly in instances where there is high uncertainty at the point of HTA evaluation or low understanding of real-world outcomes, (2) reducing medical costs incurred by poorly controlled disease (e.g., emergency visits or hospitalisations) and (3) promoting value for money and effective allocation of resources in healthcare systems [18, 21]. However, there are also numerous challenges involved in the design and implementation of OBAs [19], including: difficulty in translating clinical outcomes into financial parameters for reimbursement (i.e. adjustments of a value-based price over time), outcome selection (with outcomes that are relevant for patients, clinicians and payers), payment volatility, dataset linkage, payer and supplier commitments to OBAs, increased administrative burden, and the multidisciplinary skillset required for design and implementation. Decisions to withdraw medicines when outcome thresholds are not met may also be difficult [22]. While healthcare systems globally are interested in moving to VBHC, the volatility of payments can be a barrier to implementation, as uncertainty of price or reimbursement creates risk that disincentivises OBAs for some stakeholders.

Successful implementation of OBAs in the UK requires a new commitment of cross-organisational partnership to resolve historical challenges around OBAs [16, 21]. Project IDEATE (Innovation in Data to Evolve Agreements That Enhance patient health outcomes) was developed to test whether it is possible to overcome the challenges of OBAs, use currently available real-world data to design and evaluate an OBA to prevent additional administrative burden to clinicians, and demonstrate the variations in payment volatility through contract design.

2 Methods

Project IDEATE sought to understand the challenges of developing, implementing and transacting an OBA in practice and by co-creating solutions (and mitigations) in a co-operative and low-risk environment.

A hypothetical OBA was designed, and retrospective real-world data were run through the model in a secure research environment, with hypothetical payments, under a range of scenarios, forming the outputs of the project [23]. An approved, in market, locally advanced and metastatic breast cancer (mBC) treatment was selected as the test case for this collaboration. No live contract negotiations were tied to the outputs of the project and existing agreements were not modified based on IDEATE. A range of stakeholders were involved to ensure the project and its findings would have relevance and applicability for future utilisation.

The project was developed across five phases:

- *Feasibility*: Identified parameters to determine suitability of a medicine for an OBA [24].
- *Patient population*: Defined inclusion/exclusion criteria, patient baselines, and better understood expected health outcomes by exploratory sub-group(s) analysis [25].
- *Outcomes*: Identified feasible, measurable patient-centred outcomes that describe value for the mBC population; determined which outcomes would be included in the OBA [24, 25].
- *Data*: Identified a compliant process for accessing the data; identified and linked appropriate datasets [26].
- *Contract design, modelling and implementation*: Analysed three different OBA scenarios (combinations of outcomes) and different contract parameters to assess impact on proportion of contract payment due and the volatility of payments [27]; considered the challenges of operationalising OBA contracts and modelling their output.

2.1 Cross-Organisational Collaboration

Although not specified as a project phase, the most important factor in the success of IDEATE was effective cross-organisational and cross-functional collaboration. Multidisciplinary stakeholder input was achieved through a series of workstream-aligned workshops, and regular cross-organisational meetings. A consensus was sought for major contract design and scenario decisions primarily through group ideation and voting. However, since an aim was to explore challenges in real-world implementation, dynamic problem-solving was found to be more effective than a systematic process. As such, weekly cross-organisational sessions offered dedicated space to rapidly raise and resolve emergent challenges and barriers. Additionally, continuously orienting the team back to the shared goal of improving patient health outcomes helped remove the adversarial component many expected in the process.

2.2 Feasibility

The initial step was to identify a medicine suitable for an OBA to be used as the test case in Project IDEATE. This medicine is referenced as the "study treatment". Typically, three areas would need to be considered: (i) uncertainties at the point of HTA and impact on reimbursement, (ii) commercial viability of the agreement and (iii) feasibility and cost of implementation, including associated administrative burden [24]. Areas (i) and (ii) were out of scope of project IDEATE due to its retrospective nature. IDEATE instead focused on partnering with a healthcare system that is open to implementing OBAs and selecting a therapy area with sufficient potential eligible patients to confer statistically significant results. To address area (iii) and reduce the administrative burden of a potential OBA, IDEATE assessed the routinely collected data in each potential therapy area to determine whether it would support easy transaction of data within the agreement.

2.3 Patient Population

IDEATE defined two patient populations: (i) a treatment cohort, those patients receiving the study treatment, and (ii) a control cohort, a cohort with similar characteristics to the treatment cohort, not receiving the study treatment. The control cohort was used to establish a baseline against which outcomes could be compared after treatment.

Initial inclusion/exclusion criteria were developed by study clinicians to ensure homogeneity within and between the study populations and assessed to ensure all necessary data variables feasibly could be populated from routinely available datasets. This was achieved by a review of data dictionaries, speaking with data owners and running a feasibility check using the Cancer Network Information System Cymru (CaNISC) dataset [28], ChemoCare™ (CIS Oncology) [29], and other national datasets. Study entry was determined by diagnosis date for both the control and treatment cohorts, or the date patients met staging criteria/started treatment (within 6 months of diagnosis). Study exit was determined by death or discontinuation of study treatment.

2.4 Outcomes

A structured process was used to determine a shortlist of measurable outcomes across multiple workshops with four clinicians (three medical oncologists working in each of the three cancer centres in Wales and one practicing oncologist working in life sciences) from the community, academia and life sciences:

- A literature review was conducted to identify sources of outcomes for people with any cancer, any stage of breast cancer and advanced breast cancer.
- The four clinicians then participated in an offline voting process to select the top outcomes of importance, focussing on those clinical and patient-reported outcomes (PROs) that drive the biggest impact on patient long-term health and health-related quality of life. Any outcome that received at least two votes was short-listed, and any outcomes that measured the same domain were reduced to a single outcome through discussion with all stakeholders.
- A feasibility exercise was conducted to assess whether data were available for each outcome within the Welsh national datasets in the time period of the study. PROs were not feasible for inclusion at the time as they were not yet routinely collected. For several key outcomes deemed to be a priority, but not routinely collected or easily extractable from Welsh national datasets, proxy variables were constructed with clinical feedback, e.g. intolerance to treatment. Other outcomes were excluded due to no standard clinical data collection (e.g. return to work, dying in preferred place of death, role functioning).

2.5 Data

DHCW created a novel, oncology linked-data environment, consisting of data from the Welsh Breast Cancer Audit (WBCA), Cancer Network Information System Cymru (CaNISC) [28], ChemoCare™ (CIS Oncology) [29], Patient Episode Database for Wales (PEDW) [30], Admitted Patient Care (APC) [31], Outpatient Appointments (OPA; from the Outpatient Activity Minimum Dataset) [32], Emergency Department Dataset (EDDS) [33], and Office for National Statistics (ONS) mortality datasets [34].

The data were collated within a Trusted Research Environment (TRE): The Secure e-Research Platform (SeRP) (Supplementary Fig. 1) [35]. SeRP provides a mechanism to analyse data whilst ensuring patient data are safeguarded. Access to the data is strictly controlled by the data custodians. Prior to entering the secure environment, data were de-identified and pseudonymised and then linked across datasets by DHCW [36]. Project data scientists worked with Welsh oncologists and data owners to develop a protocol for analysis of the data, including algorithms for each outcome of interest.

2.6 Contract Design, Modelling and Implementation

The contracting workstream aimed to design and model different OBA scenarios to assess the optimal OBA design for value across all organisations. Two workshops were conducted with cross-organizational stakeholders (including clinicians, data experts, commissioners and members of procurement and finance within NHSW) to make decisions on the design of the OBA to be modelled. Anticipated challenges with implementation were also broadly considered.

The contract design workshops made initial decisions about key contract elements that were further refined by IDEATE data scientists:

1. Scenarios to be modelled (combination of outcomes).
2. Contract parameters.
    a. Patient population (inclusion criteria, segment or sub-groups included).
    b. Outcome measurement level (population or patient level).
    c. Years modelled (time range).
    d. Contract duration (number of years).
    e. Outcomes weighting (percentage of total possible contract payment).
    f. Benchmarks and targets (lower and upper limits of outcome performance, relating to payment trigger).
    g. Caps (presence/absence of a ceiling on payment).
    h. Performance measurement and payment model (linear or threshold model).
3. Contract payment (actual financial output from OBA if implemented).
4. Volatility analyses.

2.6.1 Scenarios

The combination of outcomes within each contract scenario were discussed by the workshop participants, with the aim of exploring the impact of single versus multiple outcomes and different types of variables (binary, continuous) in driving contract volume output and volatility. One outcome scenario was agreed as the primary scenario to be modelled and is presented in the main results section. Two additional scenarios were agreed for comparison purposes.

2.6.2 Contract Parameters

Most contract parameters were agreed in the workshop, including linear payment model (percentage outcome performance achieved is related to a percent of payment made) versus a threshold payment model (outcome achieved/not achieved is related to payment made or not made) (Supplementary Fig. 2).

The benchmarks and targets (the minimum and maximum outcome performance metrics that trigger payment) were defined by comparing the treatment and control cohort outputs for each outcome between 2014 and 2020; where insufficient due to high levels of prescription data missingness and heterogeneity, literature on the study treatment was consulted and clinician feedback was obtained.

2.6.3 Contract Payment

The output of the OBA was calculated as the (median) proportion of total payment possible; contract volume and percentage of payment (for each of the outcomes in the model) were used to calculate the total output (and therefore value) of the OBA in the primary scenario. No price was identified as part of the IDEATE workshops to use in modelling the financial output of each scenario to keep focus on the relative impact of different parameters versus on the absolute price differences.

2.6.4 Volatility Analyses

Volatility analyses were conducted to understand the sensitivity of benchmarks and targets and the impact of different design decisions including type of outcome (binary versus continuous), outcome measurement level (patient versus population) and payment model (linear versus threshold) on the performance of the primary scenario. The Monte Carlo method was used to perform the volatility analyses. Bootstrapping (with replacement) was used in Microsoft Excel to create randomly drawn, similar sized ($n = 91$) cohorts to perform the OBA calculation with 500 iterative simulations. The analyses also contextualized the potential financial risk associated with the defined primary scenario and each of its constituent outcomes. The greater the volatility, the greater the financial risk.

3 Results

3.1 Feasibility

An approved, already in market locally advanced and mBC treatment was selected as the study treatment test case for this collaboration, because there were sufficient follow-up data, an established electronic health registry, meaningful outcomes in the timescale available and a large enough patient population in Wales to avoid deductive disclosure of patient identities.

3.2 Patient Population

The inclusion criteria were defined through an iterative process that considered clinical input and data feasibility: human epidermal growth factor receptor 2 negative (HER2−), oestrogen receptor (ER+), aged 18 or older, locally advanced or metastatic breast cancer (including T3+ or N1+ or M0/M1 from the Tumour, Node, Metastasis staging system [37]) and non-operable breast cancer (when surgery was not completed prior to treatment). There were no exclusions based on sex.

This inclusion criteria resulted in a patient sample size of $n = 99$ for the total population in the treatment cohort (2017–2020) and $n = 286$ in the control cohort (2014–2016) (Fig. 1). A sizable sample of patients met the inclusion/exclusion criteria from 2017 to 2020 but were excluded from the analysis, because they were not prescribed the study treatment ($n = 311$). Additional demographic details of the treatment and control cohorts are available in Table 1.

The number of patients with metastases (M1) versus locally advanced disease (M0) differed considerably between the treatment cohort (92% metastatic disease) and control cohort (31% metastatic disease). This suggested a higher severity of the disease in the study treatment population. As 92% of the study population had M1 at inclusion, this subgroup was used for modelling of the primary scenario to improve comparability of results across the two cohorts (i.e. M0 patients were not included in the primary volatility analysis). Staging of patients was determined by the staging tables within ChemoCare™ or CaNISC at diagnosis and not split into histopathologic or clinical assessment.

3.3 Outcomes

A pragmatic literature review identified 47 sources of outcomes for mBC [e.g. International Consortium for Health Outcomes Measurement (ICHOM), the Welsh Cancer Network]. Within these sources, a long list of 219 health outcomes relevant to metastatic breast cancer were identified. Following two workshops and a voting exercise, clinicians selected a short-list of the top 57 outcomes of importance for patient long-term health and health-related quality of life. The feasibility of inclusion of these variables for use in an OBA was considered in two ways: (i) multiple outcomes that measured the same domain were reduced to a single variable via clinician input and (ii) variables were

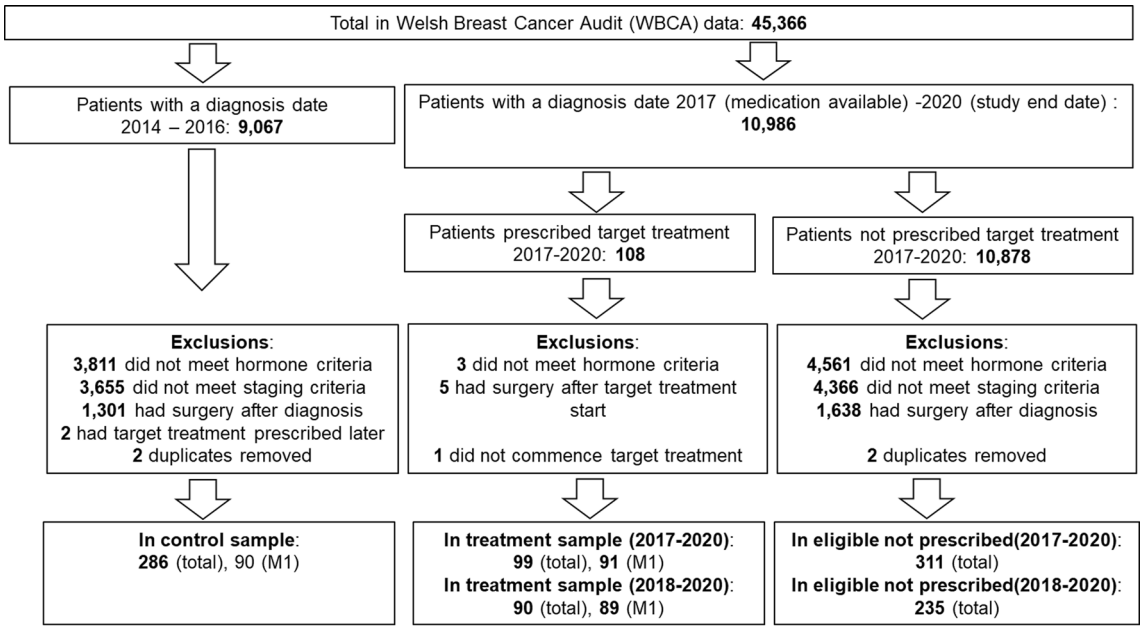

Fig. 1 Patient sample by inclusion/exclusion, identifying the final cohorts (control, treatment, and eligible population not prescribed the medication). *M*1 = metastatic disease at inclusion

assessed to determine their likely availability in the Welsh data environment. The ten outcomes that were considered to be feasible for inclusion were (1) days disrupted by care, (2) intolerance to treatment (deferral and discontinuance), (3) 30 day mortality, (4) 1 year survival, (5) progression free survival (PFS), (6) spinal cord compression (SCC) incidence, (7) severe bowel symptoms, (8) symptom control in palliative care, (9) pain management, and (10) treatment response (Table 2, definitions provided). The variable "intolerance to treatment" was considered in two ways: discontinuance and deferral.

Once the linked datasets became available in UK SeRP, outcomes were reviewed for data availability during the study period, missingness, type of data (e.g. free text) and low incidence (risk of deductive disclosure of patients). In total, seven of the remaining variables were excluded (as well as intolerance to treatment: discontinuance) (Table 2).

The final set of three outcome variables for use in the contracting exercise was identified: (i) 1-year survival, (ii) days disrupted by care and (iii) intolerance to treatment-deferral. "One-year survival" measured the number of patients who survived one year after diagnosis. "Days disrupted by care" used inpatient, outpatient and accident and emergency (A and E) data to identify planned and unplanned admissions to secondary care. "Intolerance to treatment-deferral" calculated the percent of treatment cycles delayed or stopped due to intolerance of treatment. The outcome selection process was carried out iteratively and refined over a few months.

Outcome data are reported for both treatment and control cohorts, including exploratory sub-group analysis by metastases (Table 3). The survival rate at 1 year was higher in the treatment cohort (total: 91.9%, M0: 100%, M1: 91.3%) than in the control cohort (total: 83.8%, M0: 92%, M1: 64.7%). The intolerance to treatment was lower in the treatment cohort (total: 5%, M0: 2%, M1: 5%) than the control cohort (total: 8%, M0: 11%, M1: 7%), and the total days disrupted by care per year was lower in the treatment cohort (total: 19.97, M0: 15.2, M1: 20.5) than the control cohort (total: 21.9, M0: 17.4, M1: 30.2).

3.4 Contract Design, Modelling and Implementation

3.4.1 Contract Scenarios

During the interdisciplinary workshops, three contracting scenarios were agreed: (1) one scenario including all three outcomes (1-year survival, days disrupted by care and intolerance to treatment), (2) a second scenario including mortality and morbidity (1-year survival and days disrupted by care), and (3) a third scenario with mortality alone (1-year survival). Scenario 1 was deemed the primary OBA scenario (Fig. 2e) and is presented in the results; the other two scenario outputs are reported in Supplementary Fig. 3.

Table 1 Demographic characteristics of treatment and control cohorts at baseline, 2014–2020

Demographics	Control cohort	Treatment cohort
Number of Patients (with new diagnosis)	286	99
2014	97	
2015	89	
2016	100	
2017		9
2018		43
2019		29
2020		18
Age at inclusion		
20–29	1 (0%)	0 (0%)
30–39	3 (1%)	4 (4%)
40–49	27 (9%)	12 (12%)
50–59	40 (14%)	19 (19%)
60–69	60 (21%)	22 (22%)
70–79	72 (25%)	30 (31%)
80–89	63 (22%)	12 (12%)
90+	20 (7%)	0 (0%)
WIMD quintile		
1 (Most deprived)	43 (15%)	13 (13%)
2	72 (25%)	15 (15%)
3	74 (26%)	27 (27%)
4	54 (19%)	25 (26%)
5 (Least deprived)	43 (15%)	19 (19%)
Patients with TNM staging that met inclusion		
T3+	149 (52%)	38 (38%)
N1+	203 (71%)	54 (55%)
M1 (Metastases present)	90 (31%)	91 (92%)
M0 (Locally advanced, no metastases present)	196 (69%)	8 (8%)

No male patients were prescribed the medication (2017–2020) and there were < 5 male patients in the control cohort

WIMD Welsh Index of Multiple Deprivation, *TNM* Tumour, Node, Metastases staging system, *T3+* tumour is more than 5 cm and/or has spread into the chest wall and/or the skin [37], *N1+* cancer cells present in one or more lymph nodes, *M0* no metastatic disease at inclusion, *M1* metastatic disease at inclusion

3.4.2 Contract Parameters

Contract design parameters for the primary OBA scenario are reported in Table 4. Per patient limits were included despite the overall contract being measured on a population basis to prevent distortion in averages due to outliers in the cohorts. A payment cap was incorporated for the 1-year survival outcome to ensure performance could not result in greater than 100% payment contribution. The other outcomes in the primary OBA scenario (days disrupted by care and intolerance to treatment) were not capped. This meant that if the performance measure was higher than the target—for example, in such cases where outcomes are better than expected—the payment is calculated using linear interpolation allowing bonus payments beyond the base 100% agreed payment.

We defined the minimum outcome level for the 1-year survival outcome as the 1-year survival rate of the placebo population used in the HTA cost effectiveness model [38] with a 5% marginal reduction. We defined the maximum outcome level for the 1-year survival outcome as the 1-year survival rate observed for the mBC study population plus a 5% margin. The 5% margin is required to allow variation between the minimum and maximum outcome levels due to variation in the confidence intervals, as a narrower margin would increase payment volatility. We defined the benchmark for days disrupted by care as the adjusted days disrupted of the comparator cohort in the first 4 years since diagnosis and weighted by the time since diagnosis of the

Table 2 Shortlisted outcomes, definitions, and reason for exclusion

		Outcome definitions	Reason for exclusion
Included	1-year survival	Proportion of patients who survive for 12 months within the contract period. Patients in the study population were only eligible for this outcome if they were prescribed the target treatment within six months of diagnosis (Binary variable)	Not applicable
	Days disrupted by care	Annualised number of days in secondary care (inpatient or outpatient) over the contract period (Proxy by design, continuous variable)	Not applicable
	Intolerance to treatment (deferral)	The percentage of cycles (from cycle 4 onwards) delayed by more than 7 days to a maximum of 6 weeks due to intolerance of treatment (Proxy by design, continuous variable)	Not applicable
Excluded	Intolerance to treatment (discontinuance)	Shortlisted outcomes	Less detailed prescription data than expected; too heterogenous for significant interpretation of results comparing treatment and control cohorts; additionally, clinicians indicated early exits are less relevant to patient outcomes than ongoing side effects
	30-day mortality	Measurement of either time between start of last cycle and death or mortality 30 days from the start of the target treatment, or end of study period	Stakeholders felt this is a safety outcome rather than a measure of performance and therefore not relevant for an OBA
	Symptom control in palliative care	Determine level of symptom control during palliative care using symptom scores held in PalCare	Data on symptom control is only available as free text, which was not feasible for analysis within project IDEATE
	Severe bowel symptoms	Number of occurrences using ICD-10 codes of both confirmed or suspected severe bowel symptoms such as constipation of diarrhoea	This was not deemed specific enough to provide targeted results and therefore not feasible for inclusion within an OBA
	Pain control	Identification of any new diagnosis of pain	Prescription data was not available for project IDEATE and could not be used to capture pain prescriptions
	Treatment response	Identification of any tumour shrinkage following treatment	Radiology data is only available in free text which was not feasible for analysis within project IDEATE
	Progression-free survival	Measurement of either time between start of last cycle and progression, or progression from the start of the target treatment, or end of study period	There was high missingness of the reporting of subsequent staging following diagnosis. Stakeholders report this might be better captured in free text fields which were not feasible for this analysis
	Spinal cord compression	Number of occurrences using ICD-10 codes of both confirmed and suspected spinal cord compression plus radiotherapy	Less than 5% of patients were observed to have spinal cord compression, limiting reporting of this metric

OBA outcome-based agreement, *IDEATE* Innovation in Data to Evolve Agreements That Enhance patient health outcomes, *ICD-10* 10th revision of the International Classification of Diseases and Related Health Problems

Table 3 Outcome data by control and treatment cohort (2018–2020), including M0 and M1 sub-groups

		Control cohort			Treatment cohort		
		Included in outcome	No. survived (1-year)	1-year survival rate	Included in outcome	No. survived (1-year)	1-year survival rate
1-year survival	Total (M0+M1)	284	238	83.8% (79–88%)	62	57	91.9% (83–97%)
	Metastases (M1)	88	57	64.7% (54–74%)	58	53	91.3% (82–97%)
	Locally advanced (M0)	196	181	92.0% (88–95%)	4	4	100% (51–100%)
		Total days exposed	Days disrupted	Days disrupted by care per year	Total days exposed	Days disrupted	Days disrupted by care per year
Total days disrupted by care	Total (M0+M1)	293,746	17,585	21.85 (21.5–22.2)	47,689	2609	19.97 (19.2–20.7)
	Metastases (M1)	62,468	5169	30.2 (29.4–31.0)	43,001	2414	20.49 (19.7–21.3)
	Locally advanced (M0)	231,278	11,019	17.39 (17.08–17.71)	4688	195	15.18 (13.23–17.41)
		Total cycles included in outcome	Total cycles deferred	Intolerance to treatment	Total cycles included in outcome	Total cycles deferred	Intolerance to treatment
Intolerance to treatment	Total (M0+M1)	663	55	8.0% (6–11%)	1131	56	5.0% (4–6%)
	Metastases (M1)	483	35	7.0% (5–10%)	1004	53	5.0% (4–7%)
	Locally advanced (M0)	180	20	11.0% (7–17%)	127	3	2.0% (1–7%)

M0 no metastatic disease at inclusion, *M1* metastatic disease at inclusion

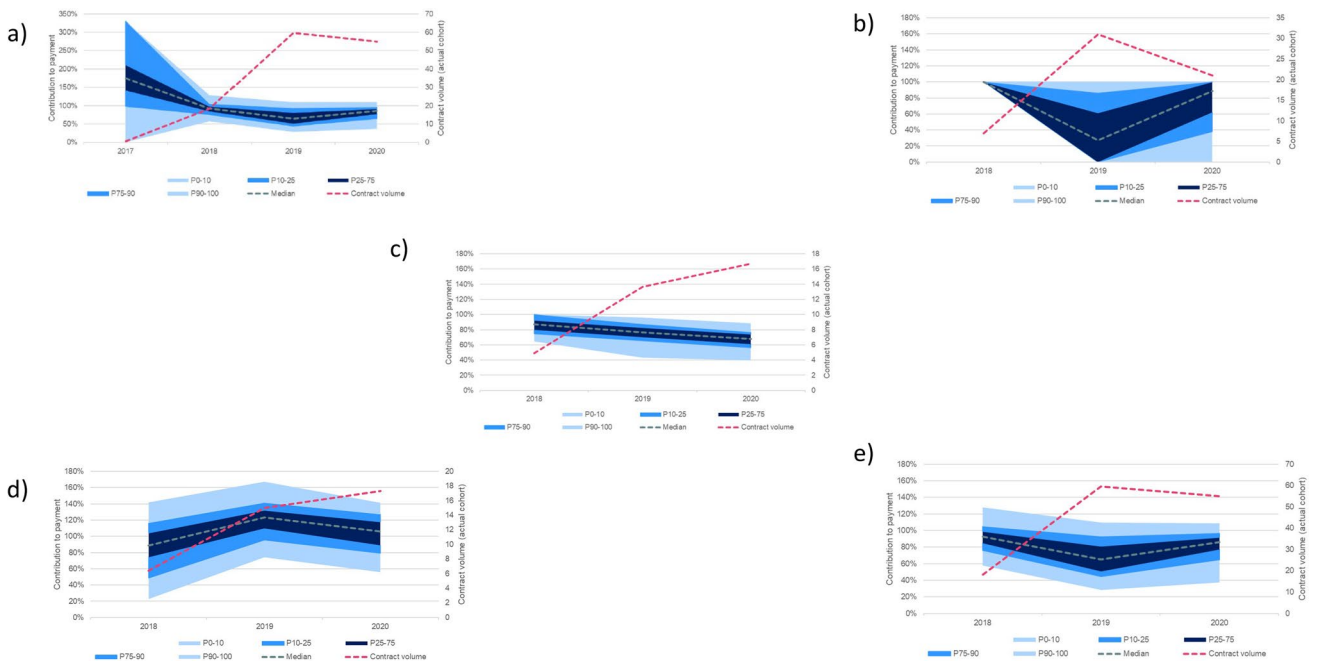

Fig. 2 OBA payment by outcome using a population-based, linear payment model with M1 treatment cohort, including volatility analysis. (**a**) All outcomes (2017–2020), (**b**) 1-year survival (2018–2020), (**c**) intolerance to treatment (2018–2020), (**d**) days disrupted by care (2018–2020), (**e**) all outcomes = primary scenario (2018–2020). *OBA* outcome-based agreement, *M1* metastatic disease at inclusion, *P* Percentile

Table 4 Contract design parameters for primary OBA scenario (2018–2020)

Contract Parameter			Results
Patient population included			M1
Outcome measurement			Per population (aggregated)
Years modelled			2017–2020 (outcome measurement) 2017 had too small of *n* to be included in volatility analyses, so these included 2018-2020
Contract duration			3 years Outcomes measured yearly Payments based on outcomes achieved in the previous year (a 'prospective ratchet') Forecasting review for payments preferred at least bi-annually by NHS and life sciences
OBA core scenario	Outcome weight	1 year survival	33% of total contract
		Days disrupted by care	33% of total contract
		Intolerance to treatment	33% of total contract
	Benchmark (min required performance for payment)	1 year survival	84%
		Days disrupted by care	30 days per year
		Intolerance to treatment	15% of cycles per year
	Target (max outcome level)	1 year survival	97%
		Days disrupted by care	20 days per year
		Intolerance to treatment	0% of cycles per year
	Payment Cap	1 year survival	100%
		Days disrupted by care	Nil
		Intolerance to treatment	Nil (although the target enforces a max cap)
	Per patient limit (prevent distortion of the population average due to outliers)	1 year survival	Nil
		Days disrupted by care	40 days in hospital per year (est. 1 standard deviation of treatment cohort)
		Intolerance to treatment	3 cycles deferred in a year (est. 1 standard deviation of treatment cohort)
Performance measurement and payment model	Linear (if the performance measure is between the benchmark and target, the payment is calculated using linear interpolation)		
Volatility analysis simulations	500, Monte Carlo method		

OBA outcome-based agreement, *M1* metastatic disease present at inclusion, *NHS* National Health Service

study population. The target was defined as 10 days less than the benchmark (i.e. the difference between the study and comparator population in 2014–2020). The intolerance to treatment benchmark was 15% while the target was set to the minimum possible (0%) based on discussions with clinicians. Exploratory sensitivity analyses of the benchmarks and targets for each outcome showed that narrowing the benchmark to target gap made the target more difficult to achieve, adversely affecting total contract value.

3.4.3 Contract Payment

3.4.3.1 Median Percent Contribution Since medicine pricing was not included in the OBA parameters, total contract value was modelled to understand the proportion of total payment that would be made for the primary scenario based on performance of the outcomes (Table 5). Each outcome's performance translates to a percent contribution relative to the total contract value (i.e. each of the three outcomes could contribute a maximum of 33% to the total contract over three years; contract parameters in Table 4). Therefore, the sum of the "1-year survival", "intolerance to treatment" and "days disrupted by care" contributions equal the percent of the maximum contract value that could be paid (when considered in relation to the total possible OBA payment if all outcomes performed at 100%).

While target population data from 2017 to 2020 and comparator data from 2014 to 2020 were used to inform benchmarks and targets, significant variability was observed in the contribution to payment when including 2017 within the contract period. This was due to low contract volumes (nine actual patients within the contract but

Table 5 Outcome measurement translated to financial performance (median contribution to total OBA payment by outcome per year), 2017–2020

Outcome (observed cohort outputs)	Median contribution to payment per year			
	2017	2018	2019	2020
One year survival	–*	100%	24%	87%
Days disrupted by care	203%	87%	123%	103%
Intolerance to treatment (deferral)	100%	86%	75%	69%

*A minimum of 12 months is required to calculate one year survival, so this was not possible in the first year of the contract

OBA outcome-based agreement

not all were eligible for outcomes) (Fig. 2a). Additionally, no patients were eligible for the 1-year survival outcome until 2018, so it was determined most appropriate to only consider 2018–2020 data for payment and volatility analysis.

"One year survival" demonstrated the volatility of a binary outcome with narrow benchmark and target ranges. In 2019 the observed performance was 24%, despite 100% and 87% contributions in 2018 and 2020 respectively due to high expected survival for patients with the disease, irrespective of receiving the study treatment, and small patient numbers. "Intolerance to treatment" showed the most consistent performance across 2018–2020 ranging from 69–85% median contribution to payment per year. The contract design did not include a patient cap for "days disrupted by care" which is relevant as the treatment cohort did outperform in all years except 2018 (Table 5; over 100% 2017 to 2020, except 87% in 2018).

When measuring the performance of all outcomes together, the overall payment due remains less than 100% for all years (92% in 2018, 61% in 2019 and 87% in 2020) (Fig. 2e, M1 population). When comparing the OBA model with the total population (M0 and M1), not only does the overall contract perform less well, but there is also greater volatility (Fig. 3c).

3.4.3.2 Type of Outcome and Volatility Analysis To understand the impact of each individual outcome on the total OBA contract output (payment) between 2018 and 2020 and how different types of outcomes behave (binary or continuous), each of the contract outcomes was assessed separately before being considered in the same model (Fig. 2).

The binary outcome, 1-year survival, showed payment contributions with a dramatic range, which resulted in very high volatility and higher financial risk (Fig. 2b). In 2018, the performance of the outcome is high but there was small contract volume. This compared well with 2019 when there was a decrease in outcome performance (due to the lower survival rate observed) and a peak in contract

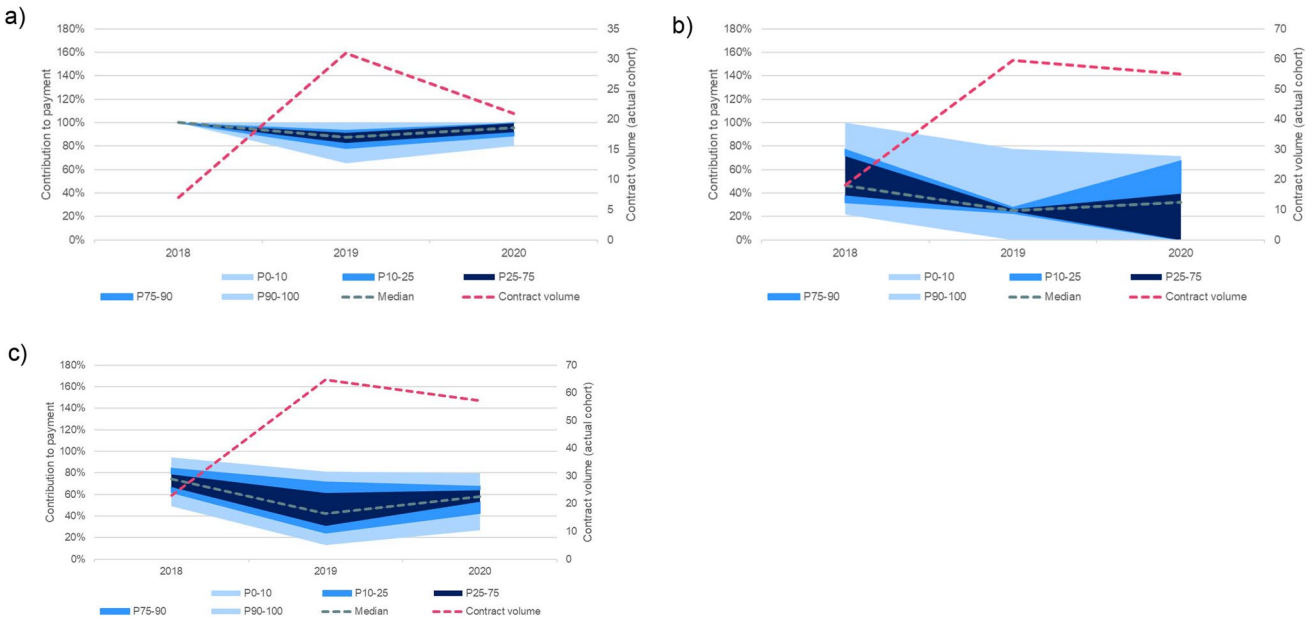

Fig. 3 Exploratory analyses of OBA payment (2018–2020), including volatility analysis. **a** Using a per-patient, threshold payment model for 1-year survival only with M1 treatment cohort, **b** using a population-based, threshold payment model with M1 treatment cohort, **c** using a population-based, linear payment model with the total (M0 + M1) treatment cohort. *OBA* outcome-based agreement, *M0* no metastatic disease at inclusion, *M1* metastatic disease at inclusion, *P* Percentile

volume. In 2020, performance improves and although contract volume decreases it remains sizeable.

In comparison, the continuous variables, i.e. days disrupted by care and intolerance to treatment, showed a tighter range around the median payment contribution and, as such, lower volatility (Fig. 2c, d) and lower financial risk. Of the three outcomes included in this primary scenario, intolerance to treatment (Fig. 2c) has the narrowest overall payment band around the median proportion of payment, and days disrupted by care (Fig. 2d) shows a moderate payment band widened by overperformance in most years. These outcomes thus demonstrated less volatility than one year survival, with intolerance to treatment showing the most stable performance of the three in the scenario. Combined in the same model (Fig. 2e) the outcomes demonstrate the impact of the binary variable's volatility offset by the less volatile continuous variables.

3.4.3.3 Outcome Measurement Level and Volatility Analysis Both population and per patient calculations for the intolerance to treatment and days disrupted by care outcome should result in similar payment contributions. As 1-year survival on a per patient basis becomes a threshold payment model rather than linear, payment contributions would be made at 100% if a patient survives and 0% if they die. This results in a much narrower band across 2019 and 2020 (2018 will still remain at 100%) (Fig. 3a).

3.4.3.4 Payment Model and Volatility Analysis While a linear payment model was used to calculate the output of the primary OBA scenario and investigate the impact of each outcome on the overall proportion of payment (Fig. 2e), a threshold payment model was developed for comparison (see Fig. 3b). The threshold model resulted in sharp contraction of the total contract payment based on lower outcome performance and contribution by year; this is paired with considerably higher volatility than the linear model for the primary scenario.

4 Discussion

Project IDEATE created a hypothetical OBA for a metastatic breast cancer medicine and retrospectively assessed how a contract would have performed if it had been live. The primary OBA scenario considered by the project included three outcomes (both binary and continuous) and successfully demonstrated that a population-based, linear payment model could be used to develop an outcomes-based contract with relatively low volatility. The Welsh data environment and a co-operative approach with shared goals between all parties were crucial elements in this project.

4.1 Partnership

Project IDEATE highlights the critical importance of partnership, trust and transparency when developing an OBA. A collaboration was formed between the life sciences industry (Pfizer UK), a healthcare system (NHS Wales) and its informatics service (Digital Health and Care Wales, DHCW), a third-party finance and health analytics specialist (Lane Clark & Peacock LLP), and academia (Swansea University).

Through this successful cross-organisational, interdisciplinary collaboration, Project IDEATE developed a sustainable methodology for the design of OBAs that works on the ground and dynamically overcomes historical challenges. By uniting diverse stakeholders across the care and reimbursement pathways with a focus on improving patient health outcomes, dynamic problem-solving led to sustainable solutions for prospective use in other innovative reimbursement contexts. Local subject matter experts were instrumental in making IDEATE a success by ensuring rigor, building stakeholder trust, and creating a launchpad for sustainability and scalability of similar work in the future. OBAs can be designed during or following the HTA process. Engaging with HTA bodies early in the design of an OBA should be considered, particularly for OBAs forming part of an HTA submission.

4.2 Data

Data are the vehicle for changing how we assess performance, value and the patient benefit of a medicine. IDEATE would not have been successful without the creation of a novel linked dataset. We demonstrated how a trusted research environment, i.e. UK SeRP, within an information governance framework was a good-fit solution to allow secure, controlled access to patient data. The development of more extensive linked-data environments would aid the evolution of data infrastructure to accommodate future OBAs.

Whilst IDEATE found that OBAs can produce reasonable results based on currently available data, the project also highlighted that some of the data needed to assess the most important outcomes (as identified by clinicians) were not routinely collected in clinical practice, were spread across disparate data sources, were not easily extractable (i.e. in free-text format), or there was a high degree of data missingness. As a result, using the outcomes from clinical trial endpoints in a live OBA may not be appropriate. Progression-free survival (PFS) was identified as an important outcome for measurement in the IDEATE OBA by clinicians but due to high missingness on reporting of subsequent staging in the structured data fields (or entry in not easily extractable free-text fields), the outcome had to be excluded (Table 2). Prioritising the prospective capture of patient-reported

outcome measures (PROMs) and the entry of key data, such as disease progression, into the defined data fields within electronic patient records would transform how these data could be used to improve patient care, as well as inform outcomes-based reimbursement.

4.3 Outcomes/Variables

To ensure each organisation's confidence that the final contract for the medicine would achieve value for patients and the health care system, it was not only vital that the outcomes were selected and agreed jointly, but also that they could be measured within a viable timeframe for a commercial contract. In practice, this was generally considered no more than three years. The number and type of outcomes in an OBA need to address clinical uncertainty while minimising data collection burden. Despite a tendency to believe that single binary outcomes will minimise this burden, IDEATE demonstrates that binary outcomes can lead to significant financial risk for both parties entering an OBA due to high volatility. Determining statistical significance within a volatile outcome, particularly when the sample size is small and the time duration short, is very difficult. If a binary outcome(s) is included, additional continuous outcomes may be added to the performance assessment to reduce volatility and mitigate unpredictability. While the outcome selection process took longer than a standard contract, the process could be expedited through use of internationally validated standard outcome measures for disease types with patients directly, such as those developed by the International Consortium for Health Outcomes Measurement (ICHOM) [39].

4.4 Contract Modelling, Analysis and Implementation

In the context of OBA design, one of the greatest challenges for this project was analysing a large enough cohort with sufficient homogeneity to show a statistically significant, clinically meaningful difference in health outcomes while still being representative of a generalisable (real-world) population. Although our cohorts were defined in advance of data exploration to include any patients with relevant cancer staging, when the real-world dataset was interrogated, M1 patients on the study treatment demonstrated significantly better outcomes than the other staged patients (including the M0 segment) (Table 3). The strong performance of the M1 sub-group is diminished by the weaker performance of M0 patients when combined, as seen with the total population (M1 + M0) model for the primary scenario (Fig. 3c). This results in higher volatility when compared with the M1 sub-group alone (Fig. 2e).

In IDEATE, sub-group analysis was performed and resulted in an adjusted focus on M1 patients in the final OBA scenario (Fig. 2e) after discovering these patients represented the majority of treated patients and allowed for more comparability between the comparator and treatment cohorts. In a prospective OBA, having sub-groups performing very differently within a single cohort would have been much more challenging to manage and may have led to unintended contractual outcomes (higher volatility, greater financial risk, negative impact to total contract payment and/or value). It is therefore critical that during development and negotiation of a live OBA, the definition of the patient population(s) and outcomes measured take homogeneity into careful consideration. Where a scenario had more than one outcome, each outcome was set to contribute equally to the payment for this model. In practice, the outcome weighting could be varied.

IDEATE was able to identify several additional key considerations to support decision-making for contract parameters:

- In practical terms in the UK, it is easier to transact OBAs on a per-population basis rather than a per-patient basis, given the additional requirements (information governance and ethics) that collecting data on a per-patient basis entail.
- When using a threshold payment model instead of a linear payment model, the volatility increases considerably and impacts total contract payment. Linear payment models are a better solution if both parties want more predictable cashflows. However, threshold payments, even if riskier financially, are appropriate when an OBA incorporates a single binary outcome alone, e.g. 1-year survival.
- Payment caps shift total contract value and impact cashflows. Removing payment caps could incentivise medicines that over-perform, but establishing these caps should be part of the wider negotiations with the healthcare system (or payer). In addition, the presence or absence of a payment cap is influenced by other factors: e.g. the price of the medicine at which it can reach a plausible cost-effectiveness ratio and the budget impact over contract duration [40, 41], as well as the additional financial implications.

4.5 Implementation

A key challenge raised during the contracting workshops was the need for finance and procurement teams to manage cash flow predictably. Transacting an OBA requires the ability to transact payment over multiple years and adjust these based on the performance achieved in each year, either through a prospective top-up payment (in well performing years), or a rebate (when performance drops). The first year

of medicine introduction should include contingency planning as inclusion in routine clinical use can take time and patient data may be limited; outcome measurement and OBA payment must account for this start-up year differently than in subsequent years.

Time to achieve outcomes in an OBA is an important factor to consider when managing multi-year cashflows. Though a 3-year time horizon (2018–2020) for the IDEATE contract was assumed, some outcomes could only be achieved in certain years, e.g. "1-year survival" was only realised in year 2 and payment was only possible in years 2 and 3. Payments for "days disrupted by care" and "intolerance to treatment" are spread across all 3 years. This resulted in most payments being due in 2018 and 2020. During the contracting discussions, it was agreed that in a value-based healthcare context, prospective payments and a ratchet mechanism (whereby a contract cannot be reduced beyond a base price, in this case the cost-effective price determined by the HTA) would be more relevant, but the procurement and financial systems would need to adapt to this new form of payment.

Finally, the transparent negotiation of an OBA is critical to agree contract parameters, mutual risk, and an acceptable contract value between the life sciences company and the healthcare system/payer. Caps, benchmarks, targets and patient population for the contract cohorts are a few of the parameters where mismanaged expectations could have serious financial consequences; this could be seen in the unexpected drop in one year survival in 2019. A mechanism to query these results would strengthen outcome measurement and lead to smoother transaction of the contract. Building in a failsafe to make a mutually agreed decision to proceed with the OBA or revert to traditional reimbursement would mitigate risk of a sub-performing OBA. Building in regular review milestones for the duration of the contract would create a more nuanced understanding of contract performance and facilitate forecasting to prospectively manage multi-year cash flows and budgets.

4.6 The "So What" for OBAs

Wales is a uniquely compelling environment to optimise OBA design and implementation with national health policy focus on VBHC, distinctly advanced data infrastructure, clear system readiness and a commitment to innovation for solving the urgent challenges of the National Health Service.

Implementing OBAs in practice requires change across the healthcare system; from how outcomes are assessed, to how these data are collected in clinic, to how the system will progress standard operating procedures for the procurement of medicines. Of note, a goal of the new 2024 voluntary scheme for branded medicines pricing, access and growth is NHS England "delivering two innovative payment model pilots to explore the practicalities of outcomes-based agreements for advanced therapy medicinal products(ATMPs)", thus expanding the opportunities for learning in the UK [42].

An obstacle often cited for OBAs is the uncertainty for stakeholders. Simulation modelling can help to reduce this uncertainty by exploring the volatility of different contract designs, which can be used throughout the design process to derisk the OBA to minimise volatility and overcome this barrier.

Further work is recommended in Wales and across the UK to ensure the IDEATE methodology can be scaled, applied to other therapeutic areas and transferred to larger, more heterogeneous populations as well.

5 Limitations

Data missingness affected the inclusion criteria, final outcomes selected and proxy variable development. With additional data, the study could have considered other demographic variables, stratification factors and sub-groups. With several variables having approximately 20% missingness or more, the size of the control and study populations were adversely affected (and resulted in an increase in the volatility of the OBA), as well as decreasing the sensitivity of outcome performance measurement. Additional dataset availability, such as prescribing and/or radiographic data, could help outcome measurement and proxy variable design in the future. An intention to capture patient reported outcomes may require PROMs to be introduced alongside the OBA. Systematic literature reviews on outcomes of interest may also assist in setting more accurate benchmarks and targets.

This work was designed around a specific medicine, in part to allow for the retrospective analysis. In practice, some medicines will be more appropriate for an OBA than others; standardising criteria for which medicines are suitable is an important piece of future research and would build on the preliminary work of the team defining broad feasibility criteria [24].

The small sample sizes in both the control and treatment cohorts meant the study was not adequately powered, and as such there was a higher probability of type II error. The aim of our study was to understand the design process for an OBA, and these data satisfied the need and context of use. However, those designing an OBA should consider the size of the potential patient population when deciding the appropriateness of an OBA approach.

A significant limitation of IDEATE was that patient views were not directly captured through the outcomes selection process or via PROs for the outcome measures in the IDEATE OBA. Clinician groups provided input on likely patient views where possible; however, engagement with patients would be of tremendous value in the development of

approaches for OBA implementation. There was clear desire from all stakeholders to include PRO measures (PROMs); however, these were not available within current datasets. In order to be patient centred without additional administrative clinical burden, the healthcare system needs to routinely collect outcomes that are important to patients (e.g. PROs to measure when a patient is unwell outside of secondary care). There also needs to be alignment in value of outcome measures across stakeholders. As reported, progression-free survival was identified as an important outcome for measurement in the IDEATE OBA by clinicians in the Outcomes workstream and this also emerged as an important outcome from the European Society of Medical Oncology (ESMO) in their new system for valuing oncologic compounds according to patients; however, though time without progression is meaningful to patients with mBC, PFS continues to be a contentious outcome measure in HTA and presents challenges for reimbursement [43]. HTA bodies were not consulted for this work but should be engaged, particularly for OBAs designed to reduce uncertainty raised during the HTA process.

Lastly, operational details pertaining to implementation and running an OBA live in the National Health Service with the Welsh Government need additional research as IDEATE did not launch a live, prospective OBA.

6 Conclusion

Project IDEATE demonstrated that by assessing and addressing barriers in situ, it is possible to design a feasible outcomes-based agreement in Wales using data currently collected routinely. Through an iterative and consultative process with key stakeholders, IDEATE was able to overcome some of the major barriers and uncertainties in OBA implementation. Project IDEATE's most inimitable contribution to the exploration of OBAs has been to demonstrate the importance of the novel cross-disciplinary partnership between NHS Wales, industry and academia. With the mindset of shared problem-solving to achieve the common goal of improving patient health outcomes, all organisations built greater capacity for innovative reimbursement.

An OBA that is well-designed on paper, but lacking true partnership, will fail quickly when going live in the healthcare system due to the implementation challenges that will assuredly occur.

By assessing solutions to data, outcomes and contracting challenges, as well as identifying priorities for focus on the next stage of implementation, IDEATE provides a strong foundation for the future of OBAs.

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Declarations

Author Contributions All authors have read and approved the final version of this manuscript. JB, KH, GSF, GJ, AW, and HL were involved with the original conceptualisation. All authors contributed to the iteration of conceptualisation, methodology, workstreams, and investigation. JB, KH, GSF, JPS, RS, TP, GJ, JS, AW, ECB, and HL were involved in the formal analysis, writing, visualisation, and supervision.

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Data Availability National datasets (including Cancer Informatics Solution - CaNISC, ChemoCare, Patient Episode Database for Wales -PEDW, NHS Wales Data Dictionary, Admitted Patient Care Data Set, Outpatient Activity Minimum Dataset, Emergency Department Data Set-EDDS, Births, Deaths and Marriages) and the trusted research environment, SeRP, are overseen by NHS Digital Health and Care Wales (DHCW). Queries should be sent directly to DHCW.

Code Availability NHS Wales Digital Health and Care Wales team currently oversees all extraction from national datasets into the linked dataset in the trusted research environment, SeRP.

Conflict of Interest The authors have disclosed the following conflicts of interest: Burton: Study conducted while employed by Pfizer, Ltd. and may have held stock or stock options. Manuscript completed while self-employed at Patient-Centred Outcomes Consulting Ltd. Halsby: Employee of Pfizer and may hold stocks or stock options. Sáinz de la Fuente: Study conducted while employed by Pfizer, Ltd. and may have held stock or stock options. Currently employed at Teva Pharmaceutical Industries Ltd. Pearson-Stuttard: Partner & Head of Health Analytics at Lane Clark & Peacock LLP, Chair of the Royal Society for Public Health and reports personal fees from Pfizer Ltd outside of the submitted work. Sloan: No conflicts of interest to declare. Porter: Partner at Lane Clark & Peacock LLP and declares no further conflicts. John: No conflicts of interest to declare. Warburton: No conflicts of interest to declare. Selby: No conflicts of interest to declare. Povey: No conflicts of interest to declare. Chowdhury: Employee of Pfizer and may hold stocks or stock options. Bale: Received a stipend for professional consulting paid by Pfizer Ltd. for this research. Davies: Received a stipend for professional consulting paid by Pfizer Ltd. for this research. Clifton-Brown: Employee of Pfizer and may hold stocks or stock options. Laing: Employed by Swansea University which has received grant funding from Pfizer Ltd.

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