Pricing Mechanisms
For Handling Uncertainty:
a CASMI working paper

A working paper on flexible pricing mechanisms in use in Europe, to manage uncertainty in decisions on cost-effectiveness.

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PRICING MECHANISMS FOR HANDLING UNCERTAINTY

Introduction

Policy initiatives in recent years have drawn attention to the challenges of making funding decisions in the presence of uncertainty. These include adaptive licencing approaches (such as the UK's Early Access to Medicines Scheme (EAMS), the Accelerated Access Review (AAR) and the reform of the Cancer Drugs Fund (CDF). In such situations, both cost effectiveness and budget impact may be difficult to evaluate.

Where there is uncertainty in the data, one policy tool to manage that uncertainty is pricing – setting a price that means an intervention is cost-effective across the probable range of effectiveness, often alongside additional data collection to resolve the uncertainty. The AAR report called for NHS England to be able to consider a range of flexible pricing models (1). [Update 2017: the AAR proposals were accepted by the Department of Health in November 2017 (2)]

There have been calls from advocacy groups (eg Breast Cancer Now and Prostate Cancer UK, (3)) and the pharmaceutical industry (eg ABPI, (4)) for increased flexibility in pricing negotiations and commercial arrangements to enable patient access to drugs.

This working paper was developed by CASMI during summer 2016, and compiles CASMI's findings from several project areas, on the topic of flexible mechanisms. We describe the findings of case studies of "Managed Entry Agreements" that have been used in the UK and Europe as part of managing uncertainty, including conditional reimbursement arrangements. In addition we also consider other budget-based and performance-based pricing approaches to limit risk, and examples of an alternative price negotiation approach based on therapeutic added value.

The Findings section provides a narrative review of the case studies – key conclusions are summarised below.

The case studies are also described in a paper co-authored by CASMI, Strategy& (PWC) and AIFA, on flexible pricing approaches in adaptive pathways (5), which incorporates work reported through the AAR by Strategy& (6).

[This work was funded by the Policy Department, Cancer Research UK (CRUK). This is a working paper, and reflects our developing thinking during scoping work in the summer of 2016. It does not necessarily reflect the current policy position of either CRUK or CASMI.]

Conclusions

1. A common challenge for conditional reimbursement schemes has been the *ability to make effective decisions at the end of a conditional coverage period*, particularly where that decision would have been to delist or reduce prices. To maintain credibility of conditional reimbursement schemes, we urgently need well-documented examples of effective decision-making. The planned re-appraisals for drugs in the reformed Cancer Drugs Fund in England will be an important weather-vane, and CASMI will be watching those decisions closely.

2. The case studies highlight the importance of *identifying the comparator data* to be used in the analysis of data collected during conditional coverage.

3. High quality data is more likely to be achieved when the data collected are in line with what would be collected for routine clinical use (rather than measures used in clinical trials) and where there is established capability in collecting such data. For the UK, improvements in completeness of SACT data have led to its use in data collection within the reformed Cancer Drugs Fund during 2017; upcoming re-appraisals within the CDF will show whether this approach has been effective.

4. Patient Access Schemes in the UK – and similar finance-based schemes elsewhere – are not always consistent with the concept of *paying more for higher value*. Improving the link to value will require schemes where the NHS pays (more) for patients who do well on the drug, but without the administrative burden of some earlier schemes; for example, avoiding data-based rebate claims, requiring only the patient tracking that would be used for clinical decisions, and crediting the relevant budget-holder directly.

5. Evaluations based on therapeutic added value incorporate a price negotiation based on the evaluation, rather than a binary evaluation based on a specific price. Whilst the UK is unlikely to move away from cross-disease cost-effectiveness assessment, there may be elements of these negotiation routes that could be incorporated in the UK, such as the expectation of negotiation as part of HTA, and the direct involvement of the payer(s) in that process. Recent organisational changes in England formalise an increased role for NHS England in this context.

Findings

1. Managed Entry Agreements: definitions and taxonomy

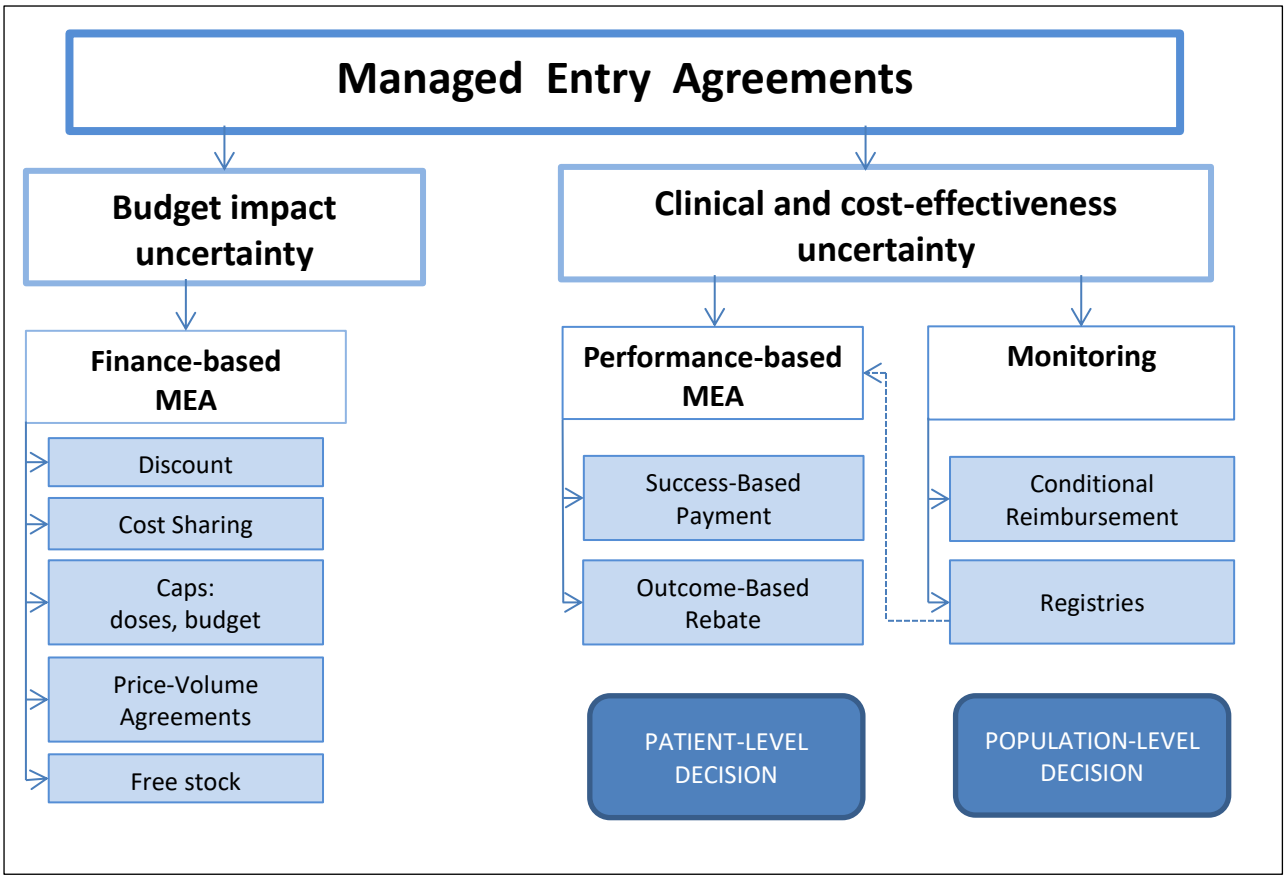
Managed Entry Agreements (MEAs) have been defined as: "*an agreement between a pharmaceutical company and payer/provider that enables access to (coverage/reimbursement of) a health technology subject to specified conditions. These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize effective[-ness of] their use, or limit their budget impact*" (7).

Various taxonomies have been proposed. Essentially MEAs can be classified as finance-based aiming to manage budget uncertainty and impact (eg discounts, caps, and price-volume agreements) or performance-based (outcome-based payments). A typical taxonomy is shown in Figure 1, largely based on the experience of AIFA in Italy, with the addition of mechanisms seen in other countries. MEAs aiming to improve cost effectiveness and manage budget impact and uncertainty are also known as Patient Access Schemes in the UK.

In the terminology used by AIFA in describing their range of schemes, a cost-sharing scheme applies a discount to initial treatment costs for all patients; only those who respond will continue treatment, with non-responders stopping treatment (8). Some free stock schemes are an extension of this concept, with drug provided free for the initial cycles. Performance-based schemes are termed 'success-based' if the payer only pays for drug for patients who meet pre-specified outcome criteria; with an outcome-based rebate, the payer funds all patients, but claims back a rebate of all or part of the cost for patients who do not meet the outcome criteria. Note that these performance-based schemes can be used within registries, shown by the dotted arrow, and exemplified by AIFA (8).

Conditional reimbursement can be considered as an extension of the performance type; a typical outcome-based scheme will use outcome data to determine reimbursement at the individual patient level, whereas conditional reimbursement pays for treatment conditional on data collection, to allow a future coverage decision at the population level. Hence conditional reimbursement aims to systematically provide data to reduce the uncertainty in the funding decision.

Figure 1: taxonomy of MEAs, adapted from AIFA, Italy (8)



2. UK: the Multiple Sclerosis Risk-Sharing Scheme (RSS)

The Multiple Sclerosis RSS is one of the earliest conditional reimbursement schemes, created in 2002 to resolve uncertainty in the long-term cost-effectiveness of disease-modifying treatments, which NICE had determined not to be cost-effective in the short term. The scheme aimed to monitor effectiveness and long-term cost effectiveness over a 10-year period, relative to a historical comparator data set from Canada, with the intention of reducing prices if the results indicated that the drugs would not hit a cost-per-QALY target of £36000. Drug prices were negotiated at the start of the scheme to ensure cost effectiveness through the evaluation period.

The scheme provided patient access, with over 5000 patients enrolled onto the scheme by mid-2005 (9). It also stimulated investment in MS services. The initial analysis at 2 years suggested patient outcomes were worse than expected; however it was deemed too early to adjust prices, and issues were identified in the comparator data and the modelling approach (10). These were then adjusted for subsequent analyses (11), and the 6-year data published in 2015 suggest that the drugs are cost effective over a 20 year horizon (9).

The early results and the subsequent absence of a price adjustment led the scheme to be described as "a costly failure" by critics (12); further criticisms were made concerning the independence of governance of the scheme, with both manufacturers and charities having significant influence (13).

[Note added June 2018: the RSS has now come to an end and NICE have reappraised the drugs involved, including data collected via the RSS, and recommended 3 drugs for routine use, with patient access schemes (NICE TA527, published June 2018).]

More recently, the UK (England) has given conditional reimbursement to drugs for very rare metabolic conditions: for example elosulfase alfa for mucopolysaccharidosis type IVa, and ataluren for nonsense-mutation Duchenne muscular dystrophy. Both of these were evaluated by NICE through the Highly Specialised Technologies (HST) process. The agreements provide funding (through discount schemes) for 5 years, with data collection for 4 years in preparation for a re-evaluation. The agreements also contain tightly defined start/stop criteria, intended to maximise the value of the treatments by restricting to those patients most likely to benefit. The ataluren agreement also contains prospective details of the analyses and criteria for re-evaluation, including specification of comparator datasets.

Neither drug was accepted in Scotland, despite consideration under the ultra-orphan process with use of a PACE meeting to collect additional information on the value of the technologies to patients.

3. Netherlands: conditional reimbursement agreements

Conditional reimbursement was introduced in 2006 to facilitate access to orphan drugs following public pressure; drugs were temporarily approved, with additional data collection and re-evaluation in 4 years.

As of May 2013, 14 orphan drugs had received conditional reimbursement. Of these only 4 had been re-evaluated, with 3 receiving negative advice on cost effectiveness. These reports were leaked to the press prior to a final decision, resulting in significant public pressure, and to date none have been delisted (14).

Observers of the schemes have also commented on the multiple management models for data collection, with a model led by an expert clinical centre appearing to be the most efficient, with pre-existing links between clinicians and patient groups, and some level of data collection capability; an alternative model with the pharmaceutical company as co-ordinator was used in cases where sub-contracting to multiple centres was needed (14).

An evaluation of the data collected on bortezomib in multiple myeloma concluded that while the observational data provided useful information on how the drug was being used, but the effectiveness data and safety signal were not considered as robust, suffering from missing data, and challenges in methods for establishing key endpoints such as time-to-progression in a clinical context rather than in a trial (15).

4. Italy: managed access and monitoring registries

Italy is actively using a range of MEA approaches, alongside an established system of monitoring registries set up by AIFA, the Italian medicines agency. The registries have been operating since 2005, with an improved web-based information system implemented in 2013. The range of schemes in use is illustrated in Figure 1.

At the end of 2015, 76 medicines were being monitored through registries, for use in more than 55 different diseases, and covering a population of about 714,000 patients (8). Data from the registries can be used for re-evaluation of cost effectiveness, after a pre-specified period, of typically 2 years, leading to re-negotiation of pricing and reimbursement status with the licence holder (6, 8).

Finance-based MEAs include volume agreements, budget cap, and cost-sharing schemes where initial cycles are provided free of charge. Performance-based schemes include rebates (partial or complete) for non-responders, or more recently, success fees where the health service only funds patients who show a response. A snapshot of the active MEAs in September 2016 shows that of 126 active monitoring programmes, around 40% are concerned with appropriate ustilisation, and of the remaining schemes around two-thirds are outcomes based. Cancer drugs account for a large proportion of these schemes, particularly the outcomes-based type (Table 1, CASMI unpublished analysis).

TABLE 1: AIFA Registries and Therapeutic plans, active schemes September 2016

Type	No. of MEAs	Disease area		
		Blood cancers	Solid tumours	Other key categories
Outcome-based	47	6	33	Opthalmics 4
Outcome and financial	2		1	Multiple sclerosis 1
Finance-based	25	11	8	Hepatitis 5
Optimised utilisation	52	7	11	Musculoskeletal 10
	126	24	53	

Note that each drug-indication is monitored separately, and can have different arrangements within the MEA. There are therefore *de facto* different net prices by indication, despite a single list price, ie indication-specific pricing.

Data entry into the AIFA registries is mandatory in order to access the drug. An analysis of the patient report forms indicated that the data requested are typically in line with the indication (ie data needed for clinical decisions) rather than extending the clinical assessment (16). The data are owned by AIFA, and the costs of maintenance of the registries are shared between AIFA and the licence holder. Until 2012 the registries were managed by a consortium of universities, costing companies a fee of 30,000 to 60,000 Euros in the first year of a registry, then reducing. Since 2012, however, AIFA has offered a tender to a commercial provider, as a cost of 8.7 million euros over 3 years. (16)

AIFA acknowledges that the schemes create administrative complexity, and there is work ongoing to simplify the processes (6, 8). There have also been difficulties in negotiating unambiguous data collection specifications and endpoints between the health service and industry, which have led to disputes and delayed rebates. An analysis of rebates over the first 6 years of operation of MEAs (2006-2012) found a total rebate of 121 million Euros out of a total spend of 37 billion Euros on the 22 performance-based schemes (17). Considering 2012 data, the same study found that only 5.6% of eligible drug spend went through the rebate procedure (46.3 million euros of a total of 823 million), and only 2/3rds of that was actually rebated. This led to introduction of Success Fee schemes where instead of claiming a rebate, the health service only pays for responders (17); however we have to date found no published data showing the extent of implementation of this type of scheme.

5: UK patient access schemes (PAS)

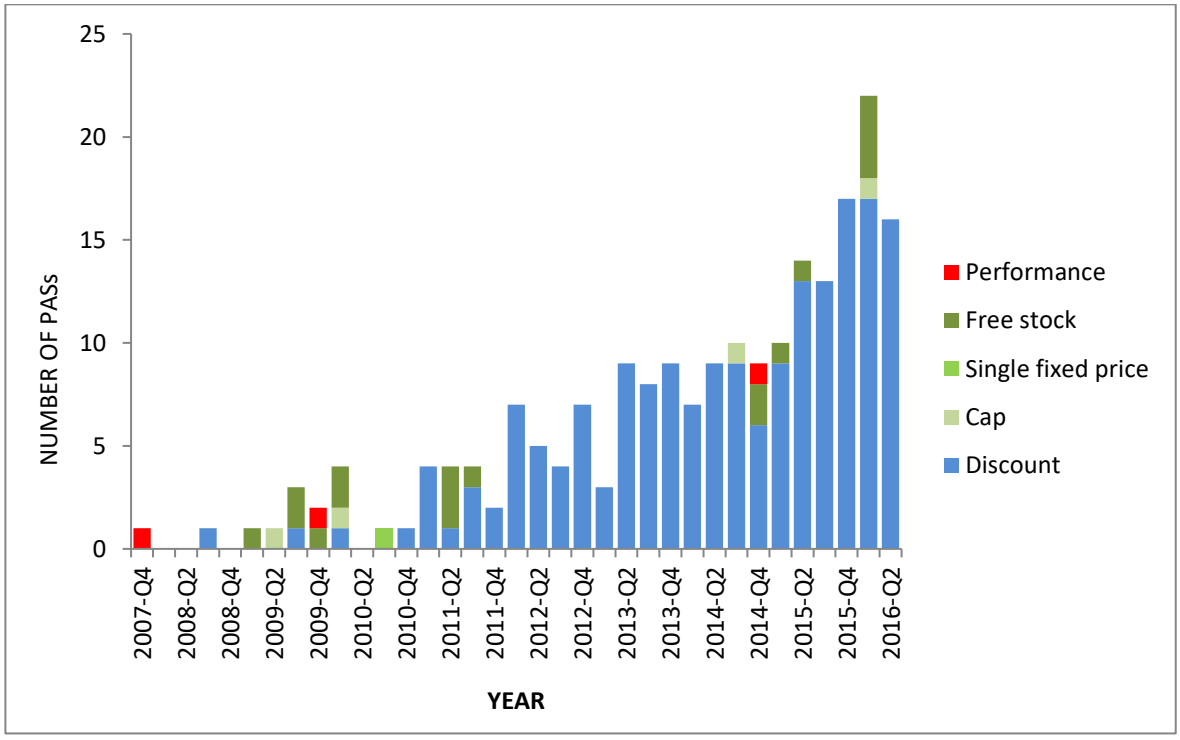
PAS are an established part of the access landscape in the UK for high-cost drugs, and can be used as an enabler of coverage in conditions of uncertainty, by managing either budget uncertainty (financial schemes), or reducing clinical uncertainty (performance-based).

CASMI recently carried out an analysis of PAS in the UK. Key findings were perhaps unsurprising, and include:

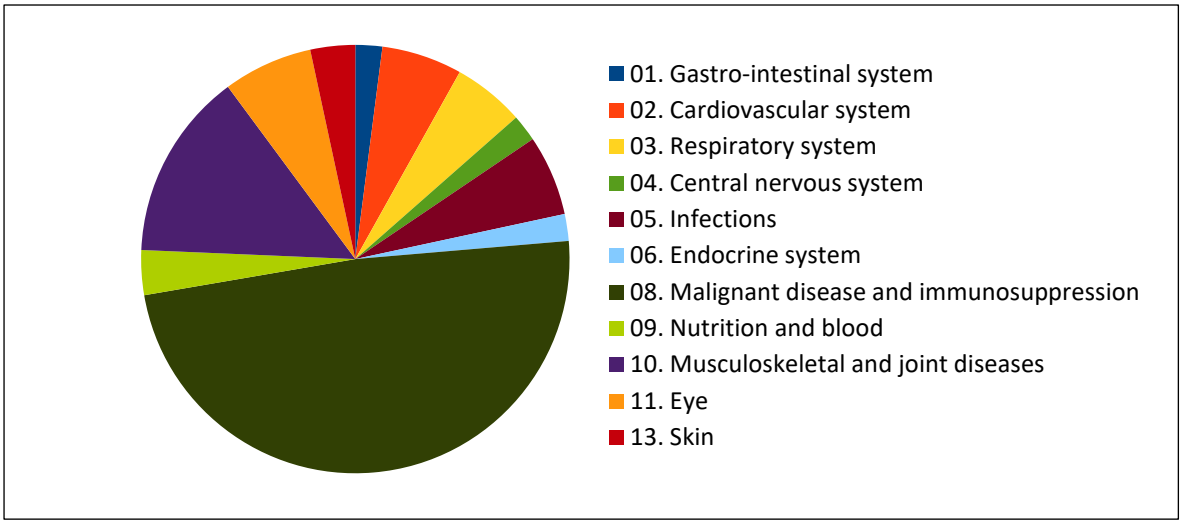
- Since the first PAS submissions to NICE in 2007, the number of schemes has risen over time. In total, there are now 148 unique drug-indications approved with a PAS across England, Scotland and Wales.
- Approximately 70% of the PAS are simple discount schemes. From 2011 there is a shift towards discount schemes and away from other types.
- The main disease areas are malignant disease and immunosuppression (47%) and musculoskeletal and joint diseases (14%)
- Companies appear mostly to be offering the same type of PAS to all three nations for a given drug.

Figure 2: UK Patient Access Schemes.

a) by type, over time



b) by therapeutic category



Performance-based PAS's are becoming increasingly rare in the UK NHS. Velcade (bortezomib: multiple myeloma) is the only purely performance-based scheme, dating from 2007 in England. Some of the early performance-based schemes were criticised for (18):

- heavy administrative load
- difficulties for finance systems handling rebates, free stock and credits
- crediting the rebate to the funding organisation
- strict time and data requirements that could lead to trusts failing to claim rebates

As a result, finance-based schemes and discounts tend to be preferred, particularly by the NHS (6). These schemes enable budget management and reduce financial uncertainty, but do not provide learning to reduce uncertainty in clinical and cost effectiveness outcomes, and may not incentivise the pharmaceutical industry to develop technologies with high added value.

Some non-discount schemes do have a weak link to performance, such as free initial stock, and free top-up dose for patients who do not respond fully to the standard dose. Free stock has the advantage of not requiring a rebate claim, and the initial free stock approach could require minimal additional patient tracking. This approach improves cost-effectiveness and utilisation for the NHS by only paying for the patients who respond well, providing response can be evaluated within the free period. It also presents a relatively low risk to industry provided that the marginal cost of production (ie actual product cost) is low relative to price.

In contrast, the cap schemes in this dataset (dose, cost, or time caps) work counter to rewarding performance: in all these cases the drugs are used for ongoing maintenance, taken until the disease progresses, so the patients funded by industry post-cap are those gaining the most value for the NHS.

6: France and Germany: therapeutic added value

An alternative mechanism to link pricing and coverage decisions to the value provided by a drug, is based on therapeutic added value, or relative effectiveness. Drugs are compared to established drugs of the same class, in terms of clinical efficacy and other parameters considered relevant, and higher prices can be negotiated for drugs that can be demonstrated to be superior (19).

Both France and Germany use versions of therapeutic added value to negotiate prices and reimbursement. Common features of the two processes include valuation of added benefit on an *ordinal* scale (ie in categories, rather than a numerical value), and the expectation of a price negotiation based on the outcome of the evaluation.

In **France**, there are two evaluations: the SMR (absolute clinical benefit) which determines the level of reimbursement, and the ASMR (relative value) which is used to negotiate pricing. ASMR classes I-III can claim a price in line with European benchmarks, which can be higher than the comparator; class IV can have a higher price if it is a cost saving, and class V must have a lower price. Pricing is thus negotiated by indication, and a single list price is determined as a weighted average.

Figure 3: assessment of therapeutic added value in France

FRANCE	**SMR (clinical benefit)**				
	Important	Moderate	Mild	Insufficient	
reimbursement	65%	30%	15%	none	
	ASMR (improvement)				
	I: Major	II: Important	III: Moderate	IV: Minor	V: No clinical improvement
pricing	European reference price				
	Can price above comparator				Lower price

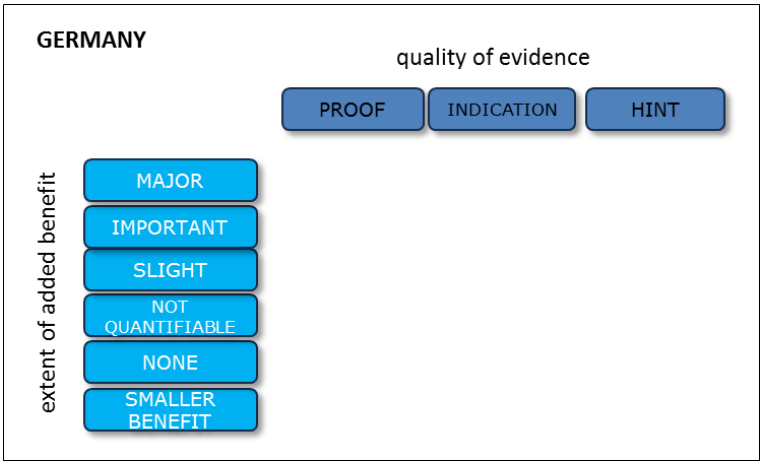
ASMR is determined predominantly by improvements in mortality, morbidity and quality of life. Secondary parameters which may be considered include severity, prevalence, target population, unmet need, and the impact on health service delivery. A comparison of French and English evaluations of cancer drugs to 2012 found correlation between the ASMR designation and QALYs gained, ie the assessment of value was similar in the two countries (20)

Note that the level of reimbursement is determined independently of the price in the French approach; there is an additional class of medicines for severe and chronic diseases (ALD) which are 100% reimbursed, and cancer drugs fall into this group.

Since 2012, France also requires economic evaluation on innovative drugs (ASMR classes I-III) with high budget impact; the evaluation will be used to inform the price negotiation.

In **Germany**, a similar scale of added benefit relative to comparator is used to negotiate price, combined with an assessment of the strength of the evidence (Figure 4). Drugs have free pricing during the first 12 months post-launch, during which it undergoes benefit assessment by G-BA and IQWiG. If no added benefit is found, the drug receives a reference price; if added benefit is shown, there is a price negotiation with the social health insurance providers, and a rebate agreed if the price is reduced.

Figure 4: assessment of therapeutic added value in Germany



Comparison: cost effectiveness analysis vs therapeutic added value

Therapeutic added value has the benefit of being perhaps intuitively easy to understand, for the public as well as professionals – in contrast to the complexities of cost effectiveness analysis. However it can be criticised for the lack of transparency of the balance of factors being considered in the categorisation, and in the price negotiation, as these are not explicitly quantified (20). It is also not clear how uncertainty is handled, although it is categorised as part of the German assessment.

Both the French and German processes as currently described, rely on within-disease comparisons. This can allow for societal preferences in funding certain diseases more generously than others, but has the risk of entrenching historical inequalities in spending between therapeutic categories. This contrasts with the UK, where comparisons of cost-effectiveness are made across disease areas, using generic measure of health and a cost-effectiveness threshold; this stems from an equity position that aims to allocate funds efficiently for all patients regardless of condition. For the UK to move away from cross-disease comparability would require a significant change in philosophy, which seems unlikely.

The German approach of free pricing for Year 1 pending evaluation and negotiation, has the advantage of enabling access for patients. Informal discussions with contacts in the industry are generally positive on this approach (CASMI, unpublished observations). However, once a drug is available, it can be difficult to withdraw it, and this weakens the position of the German payers in the price negotiation.

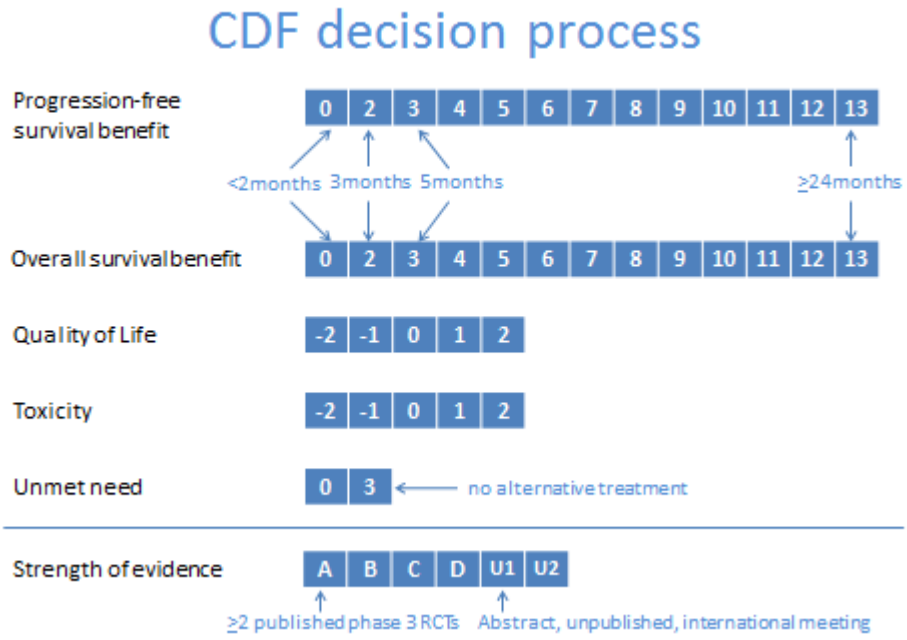
It has been suggested that the expectation of price negotiation based on the outcome of evaluation creates a more positive environment for negotiation, in contrast to a perhaps adversarial 'one shot' price (or PAS) offer in cost-effectiveness analysis. The introduction in Scotland of additional stage at which companies can offer a new PAS may facilitate flexibility in a similar way.

7. Learning from the UK original Cancer Drugs Fund (CDF)

The original CDF was not a conditional reimbursement mechanism. It therefore had no exit strategy, resulting in budget inflation; further, data collection was not mandated, and as a result was inconsistent and of poor quality (21). Nonetheless, the original CDF did have some interesting features, including an evaluation framework and direct price negotiation similar to the processes seen in France and Germany.

i. The CDF decision process was based on clinical benefit, scored on an ordinal scale, with similar evaluation of quality of life, toxicity, and unmet need (Figure 5); the scores for each parameter were summed, and drugs ranked on total score, with a confidential, budget-driven variable cut-off used to determine whether the drug offered sufficient value to be funded.

Figure 5: the CDF scoring system

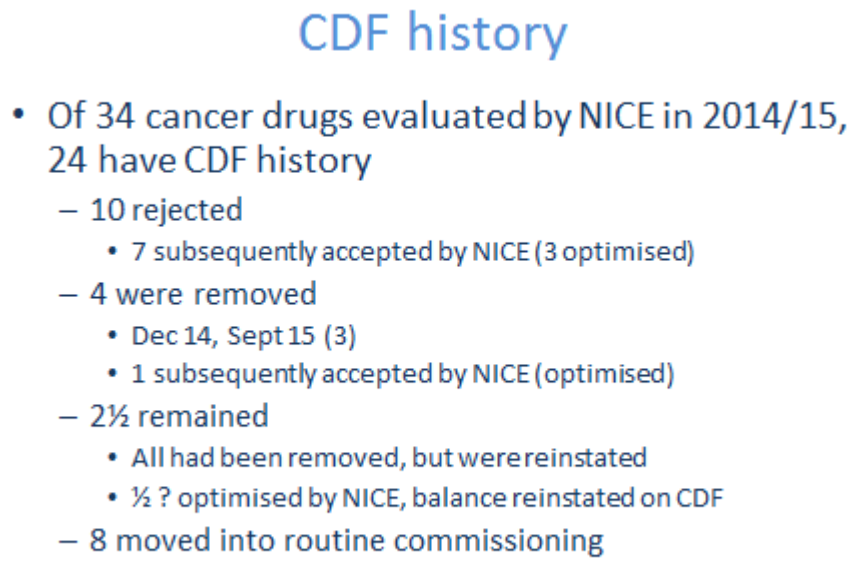


The framework was similar to those used in France and Germany in its categorical nature, focus on clinical benefit, and its incorporation of additional features. However, it has been criticised for (among others) the arbitrary implicit weightings of the parameters, and the uncertainty created by the variable cut-off (22) (L. Morrell/CASMI, unpublished observations).

There was also no mechanism to deal with *uncertainty* in the evidence base; the scores are based on statistical significance, and as a result favour drugs with mature data sets over new but promising candidates at an earlier stage of development. Analysis by CASMI identified several drugs that were rejected by the CDF but subsequently accepted by NICE following a full evaluation, including discussion of the uncertainty and its impact on the decision (Figure 6) (23); this indicates that

the NICE appraisal is not necessarily a tougher hurdle than the CDF – particularly for promising drugs seeking early market.

Figure 6: comparison of CDF and NICE decisions on cancer drugs



ii. The original CDF was able to negotiate prices directly, based on the outcome of its evaluation, with manufacturers able (even encouraged) to negotiate to ensure their product achieved or retained funding. There is evidence that this was happening on multiple occasions following a series of evaluations; CASMI analysis identified drugs that were rejected or delisted, and yet remained on the CDF list for funding. These drugs were then subsequently re-reviewed either by the CDF, or by the Rapid Reconsideration process implemented by NICE in 2016 when CDF reforms returned all cancer drug funding decisions to NICE. As there had been little change in the evidence base, we assume that these drugs retained their funding through commercial negotiations, although this is not explicit in the CDF's published documentation.

[Note added June 2018: there is evidence that such open-ness to negotiation has continued now that all cancer drug funding decisions have returned to NICE: for example, sorafenib (Nevaxar) in hepatocellular carcinoma presented revised prices on 4 separate occasions during its Rapid Reconsideration, and was recommended for routine use (26)].

Figure 7: timeline of CDF decisions on three drugs

	2013	2014				2015				2016	2017
	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4		
	CDF decisions								NICE decisions		
Pemetrexed in non-squamous NSCLC: maintenance treatment	NR					NR	NR	NR	RR	R by NICE	
Trastuzumab emtansine in advanced breast cancer		R				R		NR	RR		R by NICE
Radium-223 in prostate cancer (no prior docetaxel)	R								RR	R by NICE	

R recommended for inclusion or retention on the CDF list
NR not recommended for inclusion or retention on the CDF list
RR on the CDF list in November 2015 and transferred to NICE's Rapid Reconsideration process

This contrasts with the binary decision based on a single price proposal, as in the NICE process. [Update 2017: this year saw the transfer of the Department of Health's Commercial Medicines Unit, and responsibility for negotiating PAS's, into NHS England (2, 24). We have also seen reference in a number of Technology Appraisals to 'commercial access arrangement with NHS England'. Taken together, these suggest an increasing role for the NHS in price negotiation.]

iii. The original CDF was a single, central pot of money, so any rebate or credit arrangements were with only that single budget. This contrasts with the complexities of implementation of outcome-based schemes across the NHS as a whole, where linking credits and rebates back to the specific provider may be administratively challenging. Although the ring-fenced funding was challenged on efficiency and equity grounds (25), there may be learnings to inform funding flows for future access schemes.

REFERENCES

1. Accelerated Access Review. The Accelerated Access Review: Final Report. https://www.gov.uk/government/publications/accelerated-access-review-final-report: 2016.
2. Department of Health, Department for Business Energy and Industrial Strategy. Making a reality of the Accelerated Access Review: improving patient access to breakthrough treatments. https://www.gov.uk/government/publications/accelerated-access-review-response2017.
3. Breast Cancer Now and Prostate Cancer UK. International Comparisons of Health Technology Assessment. http://breastcancernow.org/sites/default/files/public/report_final_12_august.compressed_1.pdf: 2016.
4. ABPI. ABPI AAR response: commercial models http://www.abpi.org.uk/our-work/value-access/Documents/ABPI_response_AAR_PWC_commercial_models_assessment.pdf2015 [
5. Faulkner S, Lee M, Qin D, Morrell L, Xoxi E, Sammarco A, et al. Pricing and Reimbursement experiences and insights in the EU and US: Lessons learned to approach adaptive payer pathways. Clin Pharmacol Ther (in press). 2016.
6. Strategy&. Accelerated Access Review Proposition 2: Getting ahead of the curve-Recommendations for accelerated access pathways and a flexible pricing and reimbursement framework. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/514445/AAR_Proposition.pdf: 2016.
7. Klemp M, Fronsdal KB, Facey K, Forum HP. What principles should govern the use of managed entry agreements? Int J Technol Assess. 2011;27:77-83.
8. Montilla S, Xoxi E, Russo P, Cicchetti A, Pani L. MONITORING REGISTRIES AT ITALIAN MEDICINES AGENCY: FOSTERING ACCESS, GUARANTEEING SUSTAINABILITY. International Journal of Technology Assessment in Health Care. 2015;31(4):210-3.
9. Palace J, Duddy M, Bregenzer T, Lawton M, Zhu F, Boggild M, et al. Effectiveness and cost-effectiveness of interferon beta and glatiramer acetate in the UK Multiple Sclerosis Risk Sharing Scheme at 6 years: a clinical cohort study with natural history comparator. The Lancet Neurology. 2015;14(5):497-505.
10. Boggild M, Palace J, Barton P, Ben-Shlomo Y, Bregenzer T, Dobson C, et al. Multiple sclerosis risk sharing scheme: two year results of clinical cohort study with historical comparator. BMJ. 2009;339:b4677.
11. Palace J, Bregenzer T, Tremlett H, Oger J, Zhu F, Boggild M, et al. UK multiple sclerosis risk-sharing scheme: a new natural history dataset and an improved Markov model. BMJ Open. 2014;4(1).
12. Raftery J. Multiple sclerosis risk sharing scheme: a costly failure. BMJ. 2010;340:c1672.
13. McCabe C, Chilcott J, Claxton K, Tappenden P, Cooper C, Roberts J, et al. Continuing the multiple sclerosis risk sharing scheme is unjustified. BMJ. 2010;340:c1786.
14. Boon W, Martins L, Koopmanschap M. Governance of conditional reimbursement practices in the Netherlands. Health Policy. 2015;119(2):180-5.
15. Gaultney JG, Franken MG, Uyl-de Groot CA, Redekop WK, Huijgens PC, van der Holt B, et al. Experience with outcomes research into the real-world effectiveness of novel therapies in Dutch daily practice from the context of conditional reimbursement. Health Policy. 2015;119(2):186-94.

16. Garattini L, Curto A, van de Vooren K. Italian risk-sharing agreements on drugs: are they worthwhile? The European Journal of Health Economics. 2015;16(1):1-3.
17. Navarria A, Drago V, Gozzo L, Longo L, Mansueto S, Pignataro G, et al. Do the Current Performance-Based Schemes in Italy Really Work? "Success Fee": A Novel Measure for Cost-Containment of Drug Expenditure. Value in Health. 2015;18(1):131-6.
18. Cancer Network Pharmacist Forum. A Report into the Uptake of Patient Access Schemes in the NHS. http://www.bopawebsite.org/contentimages/publications/Report_into_Uptake_of_Patient_Access_Schemes_8_11_09.pdf: 2009.
19. Towse A, Barnsley P. APPROACHES TO IDENTIFYING, MEASURING, AND AGGREGATING ELEMENTS OF VALUE. International Journal of Technology Assessment in Health Care. 2013;29(4):360-4.
20. Drummond M, Pouvourville G, Jones E, Haig J, Saba G, Cawston H. A Comparative Analysis of Two Contrasting European Approaches for Rewarding the Value Added by Drugs for Cancer: England Versus France. PharmacoEconomics. 2014;32(5):509-20.
21. National Audit Office. Investigation into the Cancer Drugs Fund www.nao.org.uk 2015.
22. Dixon P, Chamberlain C, Hollingworth W. Did It Matter That the Cancer Drugs Fund Was Not NICE? A Retrospective Review. Value in Health. 2016;in press.
23. Morrell L, Wordsworth S, Rees S, Barker R. Nicer in NICE? Impact of Cancer Drugs Fund reform on patient access to drugs. RDM Annual Symposium, Oxford University; Oxford2017.
24. Commercial Medicines Unit - move to NHS England [press release]. https://nhsprocurement.org.uk/news/commercial-medicines-unit-move-to-nhs-england/2017.
25. Buxton M, Longworth L, Raftery J, Sculpher M, Towse A. Reforming the Cancer Drug Fund. BMJ 2014;349:g7276 doi: 101136/bmjg7276 (Published 28 November 2014). 2014;349:g7276.
26. Morrell, L. What else did the Cancer Drugs Fund do for us? Real-world data? http://casmi.org.uk/2017/09/else-cancer-drugs-fund-us-real-world-data/ 2017.