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CERTARA MARKET ASSESSMENT

The Shifting Landscape for Outcomes-Based Contracting

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Certara Market Assessment

The Shifting Landscape for Outcomes-based Contracting

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Methodology

This paper is part of a series based on 15 semi-structured interviews with managed care experts and pharmaceutical executives, a comprehensive review of secondary research, survey data and grey literature including more than a dozen contract case studies and industry presentations.

Data analysis was supported by an innovative contracting team of Certara consultants with experience in the design of performance agreements in the US, Italy, France and UK. To preserve confidentiality, the managed markets interviewees for this research are not quoted in this release of the report. Any specifically attributed statements in this document are sourced from media reports or other material already available in the public domain.

The Shifting Landscape for Outcomes-based Contracting

The Surge of 'Paying for Value' as the new Reimbursement Paradigm

> *50% of all Medicare payments will come from alternative payment models by 2018. It is only logical to share risk beyond hospitals and physicians.*
>
> **HAROLD PAZ**, Chief Medical Officer, ***Aetna***

The 2010 Affordable Care Act, with its bundled payments and incentive programs, ushered in a new era of so-called alternative payment models: The Centers for Medicare & Medicaid Services (CMS) is set to make half of its Medicare reimbursement through performance-based agreements by this year. It is still unclear to what degree demonstration projects and initiatives will continue to emanate from the Center for Medicare & Medicaid Innovation (CMMI) under the Trump administration.

Irrespective of recent decisions to cancel major mandatory bundled-payment pilots (e.g., Comprehensive Care for Joint Replacement Model, Cardiac Rehabilitation Incentive Payment Model)[1], there is a widespread consensus among decision-makers that value-based reimbursement marks an irreversible trend.

A recent survey revealed that, in the eyes of senior sector leaders, the biggest driver for the transformation in healthcare is pricing pressures over the next 5-10 years. 47% of C-level executives cited the "adoption of value-based or risk-sharing pricing models" as their top choice, compared with 38% of respondents who listed "scientific breakthroughs".[2]

United HealthGroup, the largest health insurer in the US, released data showing that in 2017 about half of its $130 billion annual medical spending occurred through value-based models, a share the group seeks to increase to 60% over the next two years. UnitedHealth reports that nearly one in three of its plan members already receive care from providers in value-based arrangements.[3]

As health systems are driven to accept increasing accountability and downside risk, payers and providers are looking for the biopharmaceutical industry to share the risks around performance of their products – based on outcomes measured in the actual healthcare setting.

> *We need to put the pharmaceutical industry under the same responsibility as most other parts of the healthcare system are under now – and that is tying the value and price to outcomes achieved.*[4]
>
> **ROY BEVERIDGE**, Chief Medical Officer, ***Humana***

FIGURE 1
Major OBA driver: The accelerated path to value-based payments in healthcare

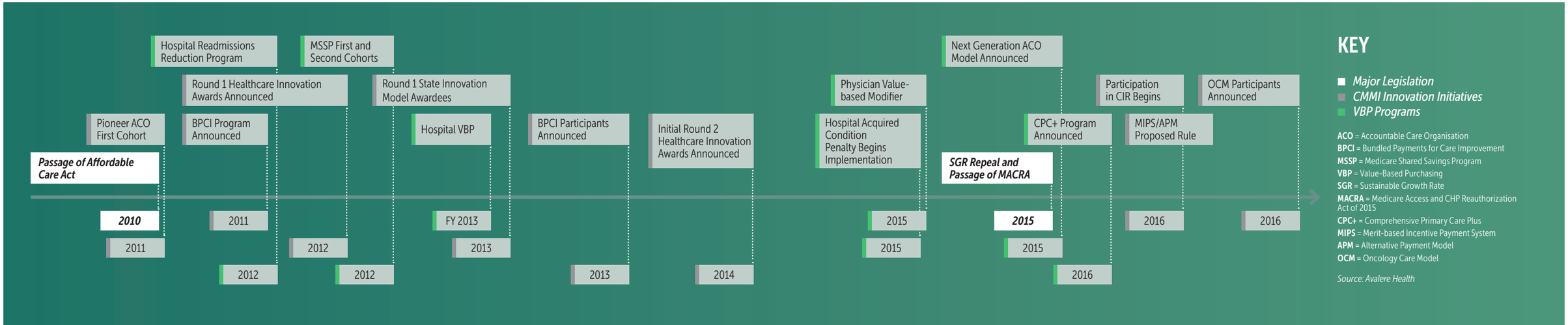
The Shift to Real World Demonstration of Effectiveness

The societal discussion around drug pricing and affordability of medicines has added additional pressure on payers and the biopharma industry to commit to value-based purchasing and the delivery of value for money. But as anyone working in the market access or HEOR domain would attest, 'delivering added value' to health plans is hardly a new priority for new treatments to attain adequate access. For sure, the perceived level of improvement of a new treatment and of genuine innovation relative to the standard of care has shaped pricing negotiations of launch products for many years – this is not a new phenomenon.

At the core of each debate about value lies the aim of demonstrating to the payer how a new product's attributes address an existing (unmet) need faced in routine clinical practice. Traditionally, this has been judged primarily by whether or not a new treatment has exhibited significant and meaningful improvements in key study endpoints in the randomized clinical trial (RCT). However, what has markedly changed in recent years is the demand for certainty on how that clinical data translates into the real world setting and what impact a new product promises (c.f. Figure 2) under such conditions.

Formulary decision-making is increasingly influenced by actual real world effectiveness considerations that go beyond RCT efficacy claims. As a result, instruments to support this value translation that may have previously fallen into the "nice to have" category (e.g., database analyses, economic models, surrogate validation) are now broadly considered "must haves" in the real world evidence discussion.

In a nutshell, payers are less and less inclined to accept 'theoretical arguments' to bridge perceived gaps between observed clinical trial efficacy and promised real-life value.



	UNMET NEEDS *"Problem"*		PRODUCT ATTRIBUTE *"Solution"*
Clinical	Disease progression	→	Product X delays progression in resistant pts
	High event/mortality risk	→	Significant relative risk reduction in RCT
	Lack of "safe" Tx options	→	Low rate of discontinuation for AE's
Humanistic	Impact on ability to work/function	→	Delayed progression improves function
	Impact on families/caregivers	? →	Fewer events lessens social impact
	Depression, negative QOL	→	Increased "self worth" from better function
Economic	Frequent healthcare visits	→	Controlled disease reduced need to switch
	Cost of disease progression	→	Delayed progression reduces cost
	Cost of managing AE's	→	Lower AE management cost

MUST HAVE **NICE TO HAVE**

- Evidence of disease burden/unmet need (in target patients)
- Strong RCT (representative population, key subgroups)
- Comparative effectiveness data, real world "effectiveness" program
- Evidence of value of surrogates
- Extrapolation of clinical benefit into real world context
- BI, CE models

FIGURE 2
New paradigm: Value translation demands increasing level of certainty on product benefits

In the absence of certainty on real world effects, outcomes-based agreements (OBA) offer a unique opportunity. They can be seen as the next chapter of the pay-for-value trend wherein the reimbursement for the pharmaceutical product is directly tied to the actual, measurable 'real world' value it provides in terms of predefined outcomes.

As one observer has pointedly put it to the authors of this report, OBAs constitute "value-based, not wish-based pricing".

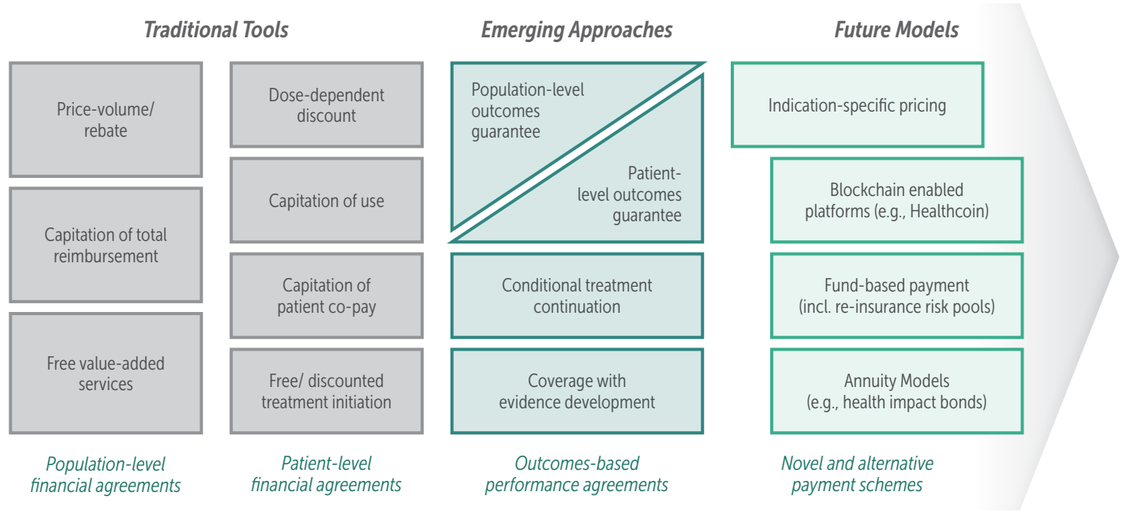
Agreements are characterized by the definition of an outcome (measure), collection of data after approval and a sys***tem of adj***udication agreed between the contracting parties. We will discuss in this report how OBA as a reimbursement tool can help manufacturers overcome challenges in addressing market access hurdles – in particular where questions about real world value remain, and uncertainty on the value translation isn't satisfactorily addressed through conventional evidence.

The Call for Innovation within the US Contracting Spectrum

Various reviews have been presented over the past few years with definitions, frameworks, and good practices around innovative contracting.[5] The widely-cited ISPOR task-force taxonomy distinguishes between financially-based agreements to manage the budgetary impact and performance-based agreements, separating between population- or patient-level focus, and further between those schemes that manage use or those designed to provide evidence. In short, academic frameworks tend to be a step removed from practical use.

In the reality of the US marketplace, contract categories are less clear-cut than such conceptualizations might suggest. Figure 3 places OBA along a simplified continuum of performance contracting options in the US. Most OBAs represent a tactical combination of financial rewards with a pay-for-performance measure (clinical, biomarker/surrogate as well as utilization endpoints). The clinical endpoint chosen for the OBA measure can but doesn't necessarily have to be identical with the one in the RCT that support the label.

FIGURE 3
OBAs within the continuum of performance contracting innovation



With respect to OBA structures, common deal parameters in the US context are:

1 adjustments of an additional rebate (above a base rebate) proportionate to pre-defined outcomes metrics;

2 financial guarantees to pay for plan beneficiaries who missed an outcomes performance threshold or were hospitalized (e.g., cost for impacted members pharmacy spent related to the product, total pharmacy costs of all utilized products relating to the condition, hospitalization costs for all patients on product if population-level);

3 total cost-of-care guarantees for patients on the manufacturer's product (e.g., on a per episode-basis or population-based per member per month) with applied outcomes data to adjust for the negotiated risk share of either payout (shortfall of the guarantee) or shared savings (in excess of guarantee).

> *As an ecosystem, we primarily still pay for pills, not better health solutions. The drug-makers that embrace novel payment models now will have an important first-mover advantage as paying for outcomes becomes institutionalized across the country.*
>
> **MICHAEL SHERMAN**
> Chief Medical Officer,
> ***Harvard Pilgrim***

Frequently also discussed under the banner of risk-sharing, OBAs are by design shifting the financial risk equation in terms of distributing the 'cost of uncertainty' between the payer and the manufacturer – a risk the health plan would have traditionally fully accepted at the point of purchase, and presumably priced into the agreed-upon rebate level and/or access conditions. OBAs still rely on negotiating a price at which the performing product is expected to be bringing value for money, however built into the agreement are upward and/or downward price adjustments based on observed effectiveness in the real world population which allow for mitigation of the cost of uncertainty. From a contracting perspective, the primary objective of an OBA is thus not to demonstrate clinical outcomes in clinical practice settings but an opportunity to address payer concerns that a product will be delivering the additional net benefit to cover its excess cost – without unduly restricting and or delaying patient access. To summarize, it is critical to understand that the absence of certainty is what creates the rationale for outcomes-based contracting.

A recent survey of managed care stakeholders echoes that innovation on the contracting front is a mutual priority. The research conducted with 189 AMCP members showed that 78% of the participants do not consider existing managed care tools to be sufficient to handle new high-cost therapies.[7] When asked about a range of half a dozen alternative tools to manage payer affordability, "risk-sharing over time" was selected by 37% of the stakeholders as the most promising solution to address future challenges – favored over direct price controls (21%) or indication-based pricing (14%) among others. It should be noted that possible future payment schemes, such as annuity models for certain breakthrough therapies, are likely to rely on pay-for-performance triggers as a key component.

> *The current model of payment for drugs is essentially transactional, fee-for-service payment and is the antithesis of the direction in which we will need to innovate to deliver sustained affordability of healthcare and prescription drug coverage. Drug manufacturers need to change their thinking...* [6]
>
> **WILLIAM FLEMING**, President, Healthcare Services, ***Humana***

OBA vs. Indication-based Pricing

Contrary to the belief that OBA and indication-based pricing (IBP) are dueling as alternative contracting concepts, we would suggest considering them as complementary approaches. Outcomes guarantees can be very useful in addressing the uncertainty that remains in IBP and would allow for more appropriately adjusted unit prices, rooted in the actual value the health plan has realized, as opposed to expectations based on pivotal trial results. For instance, a recent simulation of the use of trastuzumab (Roche's Herceptin) published in AMCP demonstrates that an efficacy-guided IBP (based on RCT data) would result in underpayment for metastatic breast cancer and overpayment for advanced gastric cancer treatment, compared to an IBP based on real world performance with outcomes guarantees.[8] The analysis, led by Dr. Yeung at the Kaiser Permanente Washington Health Research Institute, suggests that US payers may want to consider OBAs for an initial contracting period of 18 months to subsequently make more informed decisions on indication-based (a.k.a. differential) pricing.

Combining outcomes guarantees with IBP has international precedents, most notably in Italy where OBAs in oncology have led to different net prices of a drug with single list price, depending on the prescribed indication. The process is driven by the availability of indication-specific patient registries. A classic example is bevacizumab (Genentech's Avastin) which is approved for use in at least seven different oncology indications. In Italy, Genentech negotiated with AIFA to create a different MEA agreement for the use of Avastin in each separate indication. Each agreement is said to reflect bevacizumab's value in different therapeutic settings, and ensures complete market access to the drug while the cost to Italy's health system of each indication is differentiated.[9]

A report by the Institute for Clinical and Economic Review (ICER) adds experiences from Australia, Germany and England which have explored differential pricing approaches for multi-indication products where an estimate-based, single "weighted-average" price is reconciled via retrospective rebates, based on actual utilization within the respective patient subpopulations.[10] However, challenges around data capture and infrastructure, legal, and regulatory hurdles currently pose limitations to the wider adoption of price discrimination across most of the EU-5. In the US context, the challenges for IBP are similar to those faced with the implementation of OBA.

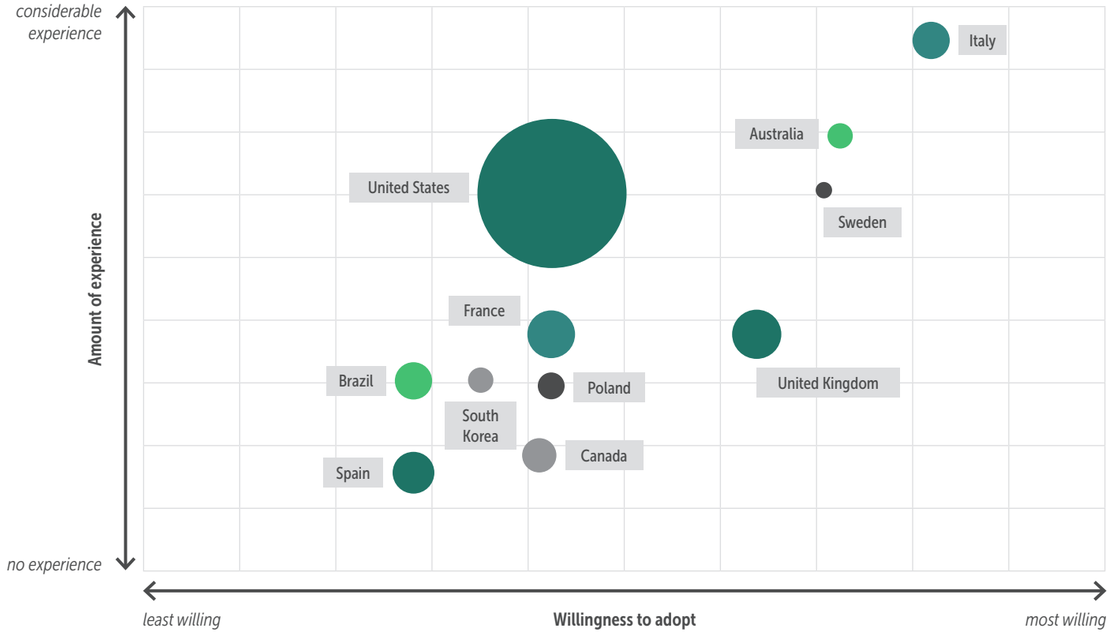
Although hitherto only adopted in exploratory fashion in the US market by PBMs (e.g., CVS Health or Express Scripts' Care Value Programs), IBP without OBA components would inherit the flaw of failing to match drug prices with the actual value new products provide in real world settings, a reason often cited by proponents in favor of the IBP approach. Without the outcomes component, IBP does little to remove any uncertainty on the question of value and patient health benefits and does not help to manage downside risk for payers.

The International Experience

Innovative contracting has been adopted in risk-sharing schemes under different names across health systems internationally for years (i.e. as Managed Entry Agreements, Patient Access Schemes, or Risk-Sharing Agreements). With the exception of Italy, a majority of these agreements in Europe have historically been financial schemes and, as such, have proven to be less costly to implement and monitor than OBAs.

Figure 4 offers an illustration of the level of experience of selected systems with innovative contracting agreements, contrasted with their pereceived willingness to adopt them (the size of the circle represents the volume of the respective pharmaceutical market). We should note that any attempt to categorize a country's positioning towards innovative contracting, and OBAs in particular, may render a useful visualization but is bound to a subjective interpretation of the data at hand. We will outline later that this is due to several unknowns when mapping the OBA landscape, in part driven by the different disclosure rules that govern the publication of agreements with private manufacturers across different health systems, as well as the level of ambiguity of future decision-making (such as dissonance between official policy and practical implementation of risk-sharing in the market).

FIGURE 4
Visualizing the current spread of adoption of innovative contracting[11]



We have seen that experiences with the adoption of OBAs across the various health systems are nuanced and heterogeneous. For brand teams trying to secure such contracts, navigating the different procedures between the US and the European payer ecosystems can be challenging. In the US, a fractured landscape of multiple payer archetypes requires concurrent managed markets effort to create separate, highly individualized negotiations and confidential contract terms with different payers for the same product. Seeking these contracts in the European environment, on the other hand, demands a sophisticated understanding of the respective national systems and national/ regional HTA procedures.

Recent analyses that incorporate payer research beyond publicly made statements by executives attest to a growing interest to include outcomes guarantees across Europe.[12] Evidence suggesting a moderate uptake of OBAs in Europe include the recently adopted national framework in Spain, the expected finalization of a similar one in the UK, the impact of a French framework introduced in 2013, and growing discussion on the part of sickness funds in Germany, all driven by global factors such as growing budget pressures. That the experience isn't universal shows in the example of the Netherlands where it has been found that OBAs are incompatible with market dynamics and data infrastructures and thus application was ceased.[13]

In any global comparison, Italy stands out as one of the earliest and most prolific adopters of outcomes-based contracts. The country's central national regulatory agency, Agenzia Italiana del Farmaco (AIFA), and the centralized National Health Service (NHS), manage all innovative contracting arrangements – they are not run by the various regions. AIFA's Prices and Reimbursement Committee (CPR; Comitato Prezzi e Rimborso) carries out the activity of negotiation with pharmaceutical companies for the setting of prices of products reimbursed by the NHS. Notably, our recent conversations with Italian stakeholders around AIFA suggest potential for a reverse move on the part of Italian decision-makers, that is to back away from the dominance of agreements with outcomes collection. No such move has been finalized.

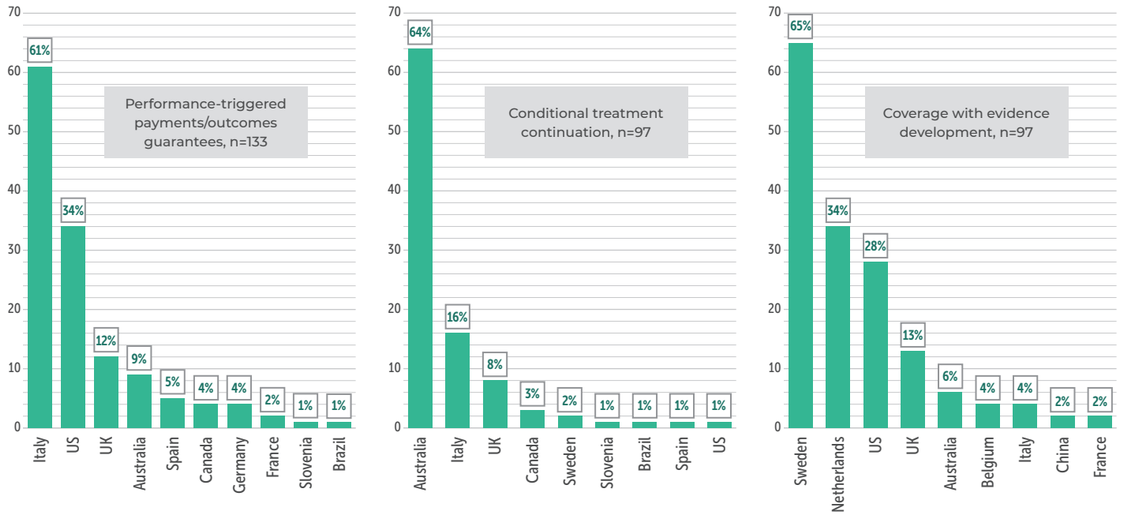
A recent study surveyed agreements in 16 countries of Central and Eastern Europe where limited comparative information has been transparently available. It concluded that financial agreements are now relatively well-established and that their use has increased over time in response to higher prices (in particularly in cancer and orphan drugs) and the need for payers to work within finite budget limits. Health systems' interest in resolving uncertainty of real-life effectiveness and utilization through outcomes guarantees is reported to be low however, and confined mainly to Hungary and Poland.[14]

As a rule of thumb, outcomes-based contracts have predominantly been initiated by health systems in Europe, and by manufacturers in the US. However, in recent years, the proverbial pendulum has begun to swing in the other direction in both parts of the world – with more payer-initiated OBAs now being pursued in the US and a momentum for pharma-initiated OBAs in Europe.

> *In Italy, we've definitely noticed a change. When drug developers realize that their product's pricing is creating a barrier to entry (knowing they cannot go much lower on price if they are to recoup their investment), they increasingly approach the payer to with some sort of MEA proposal. From the company perspective, this is often seen as the appropriate strategy as it allows to protect the official price that is published. Other countries in Europe often reference Italy when they set their own prices, so creating a 'pay-by-results' type approach is one way to protect the official published price in the market. The contracts we're doing in Italy vary. In one type of pay-for-performance scenario, the government payer would reimburse for the medication only for those patients who experienced a positive response after, say, two cycles of therapy. If the patient's response to therapy is positive, the health agency would keep paying for the drug. But if after two cycles, the patient was deemed to be a non-responder, not only would the payer not reimburse, but the drug maker would have to offer a payback for the first two cycles of therapy. It still makes strategic business sense for some brands to be bullish about taking the lead and to seek MEA arrangements with government payers in Europe. Without being open to these agreements, they may risk either having a hugely discounted list price imposed by the payer, or potentially even being excluded on that country's drug formulary altogether.*
>
> **PATRIZIA BERTO, PharmD, MBA**, Senior Global Consultant, ***Analytica Laser***

Globally speaking, agreements can be categorized into three major archetypes: (a) Performance-triggered payments, (b) conditional treatment continuation and (c) coverage with evidence development (Figure 5).

FIGURE 5
Total distribution of OBA across the three global archetypes



Sources: Analytica Laser Internal Analysis, UWA PBRSA Database, PubMed, Government agencies, Public Reporting (Fall 2017)

- **Performance-triggered payments** represent the major focus of our analysis as the dominant archetype for private-sector pharmaceutical OBAs in the US. As further outlined in subsequent sections of this report, reimbursement is tied to a clinical outcome measure in the real world, reached in a plan population or certain target patients.
- **Conditional treatment continuation** describes a scenario where coverage is dependent on certain short-term treatment responses, benefit or continued benefit (e.g., tumor response). The manufacturer commits to discontinue and switch patients that don't reach the outcome and, as in several of these schemes, provides funding or discounts during treatment initiation (e.g., MS in the UK, or Alzheimer's products in Italy that may be covered for three months by the manufacturer until certain goals are met and reimbursement will be continued and/or expanded by the national system).
- **Coverage with evidence development** rests on the collection of evidence in the real world, whereas reimbursement of the product may be discontinued if the outcome is not demonstrated in a well conducted study in an actual clinical practice context. In the US, this type of agreement has mainly been used for devices and diagnostics coverage with CMS due to the fact that pharmaceutical spend for Medicare largely falls into the responsibility of individual Part D payers.[15] It must be noted that due to limitation to publicly released information, US agreements without public payer component are underrepresented in any international comparison.

Which of the three global categories a particular OBA falls into is defined to a large extent by what needs to be demonstrated to the health system. If the treatment is understood to be effective, but what you need to assess is how effective it is under real world conditions, then outcomes guarantees are most adequate to address the uncertainty as previously outlined. If you know the treatment is effective and tends to work in an "all or nothing way", then the main goal is to identify the responders and exclude the non-responders, and conditional treatment continuation appears most suitable. Finally, if the relative effect of your treatment vs. the standard of care is uncertain and needs to be proven through research, then a coverage with evidence development is likely to be the best option over "no coverage".

> *It's time to take the outcomes-based commissioning out of the "too difficult" box. What we are trying to achieve is a new focus on outcomes for patients and better value for our tax payers.*
>
> **SIMON STEVENS**
> Chief Executive, ***NHS England***

The Recent Acceleration of OBA Uptake in the US

In 1998, Merck decided to compensate prescription costs for simvastatin if the drug failed to lower LDL. There have been approximately 70 publicly known OBAs in the US since then – and likely double that number if all confidential deals were to be included. Our estimates indicate that up to 50 agreements are entering the market every year globally, with at least a dozen new OBAs to emerge in the US annually. Noticeable is the recent uptake of activity in the US – while only 7 private sector deals were publicized between 1990 and 2013, 20 contracts where publicly announced since 2015 (Figure 6).

**Multiple drugs from Biogen's MS portfolio: Tecfidera, Tysabri, Plegridy, Avonex*

With respect to the publication of agreements in the US it makes sense to view current OBAs as trade agreements – and with trade agreements, the parties are not usually incentivized to engage in an exercise of public disclosure, it is likely that for the time being, the most advanced and successfully negotiated contracts will be those kept confidential between the parties.

FIGURE 6
Significant momentum: Selection of recent OBAs in the public domain

Competitive Secrecy: OBAs are Trade Agreements

A major limitation for a quantitative assessment of the US OBA landscape today is that we can only list agreements selected for public consumption and, unfortunately, empirical evidence on their performance has been slow to materialize. In some instances, this may be complicated by the common notion that 'success is public, and failure remains private'. Grappling with their own internal learning curve and being involved in trial-and-error partnerships with payers, manufacturers' 'hard learning' tends to take place in private. While little is public about the financial implications of agreements we can report, nothing can be said about agreements out of the public domain that might have to be considered a failure.

Let's take another angle on why we should be aware of imperfect knowledge here: Some analysts have frequently questioned Novartis' financial benefit from its agreement for sacubitril/valsartan (Entresto) with Cigna, Aetna and Harvard Pilgrim. We should note that even if the deal terms are not disclosed, preferred formulary status and overall prescriptions uptakes are only partial indicators of performance. Whether this agreement, or any OBA for that matter, was indeed successful may entirely depend on the counterfactual, i.e. the projected result of the realistic contracting alternative the company could have reached with respective payers in relevant markets. What is the value health plans might have attached to the 20% relative risk reduction in death or hospitalization one of the pivotal trials showed? How would the traditional rebating approach have incorporated this benefit as far as these payers were concerned? Given that such information isn't part of the public knowledge for even those agreements we can identify, any conclusions should have a caveat: We know that public accounts only offer part of the picture.

Not surprisingly, a few pharma respondents in this research confirmed that their companies aggressively pursue OBAs but, as a matter of competitive strategy, prohibit the announcement of any specific deals whatsoever. Pioneering companies that are exploring innovative contracting as a commercial opportunity would indeed be ill-advised to disclose pillars of their strategic approach upfront. Notably competitive players include both manufacturers as well as other payers, who may shift to demand OBA and ledge on to announcements once deal parameters for a new branded product OBAs have made public. That said, there could be advantages to disseminating real world effectiveness data when it comes to addressing the audience of prescribers, which means that the implications and timelines of non-disclosure terms should be carefully studied by the brand teams.

> *The explicit NDA terms that are negotiated relating to the disclosure of the clinical and financial results of a performance-based contract are a two-sided coin. Drug makers may have a vested interest in publishing the real world data that is collected within the context of an agreement – especially if it demonstrates that the drug is performing better than it did in the clinical trials in which case they will want to explore NDA terms that allow for such flexibility if sought. If the data shows that the drug is performing even better than the clinical trial benchmarks, or particularly well for a certain group of patients, then those findings could work as a multiplier, encouraging more physicians to prescribe the treatment. Of course, real-life data may also show that the drug underperforms in clinical practice.*
>
> **PATRIZIA BERTO, PharmD, MBA**, Senior Global Consultant, ***Analytica Laser***

Another reason for the limited knowledge of actual performance results is that hard evidence on more recent OBAs is only now coming out. Considering the recent wave of OBA contracts in the US, many have been inked over the last 18 months, it's early days for demonstrable, statistically sound data to emerge. This is due in part to the time it requires to negotiate the first pilot OBAs, to put in place the necessary infrastructure to collect and analyze real world data and the fact that the availability of claims and medical data for analysis may often lag, by up to six months, the drug's use by patients. That is still before adjudication processes have begun. It's not surprising then that it has become a recent priority for industry to build decision-analytics platforms that integrate clinical and financial data points from the early experience to help ensure both a more systematic and faster prediction and measurement of performance of future OBAs.

Structural Hurdles Curbing OBA Expansion

What would you consider the biggest challenge with OBAs?

Electronic poll during analytica ISPOR Educational Symposium May 2017, n=53

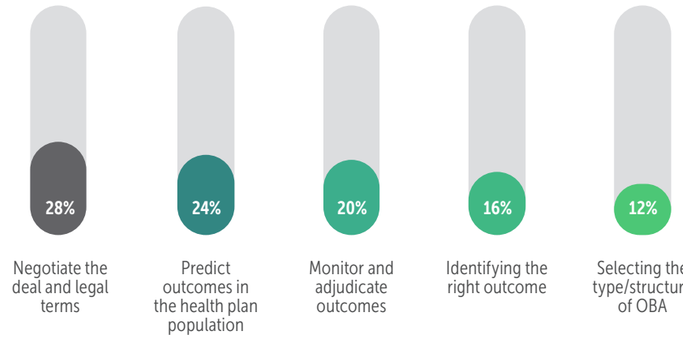


FIGURE 7
Spread of practical challenges with the OBA approach

Structural hurdles remain for wider OBA adoption and need to be considered as factors impacting the design and implementation process as we will further address in our practical recommendations (Chapter III).

KEY FACTORS

Stakeholder-cited challenges with OBA implementation

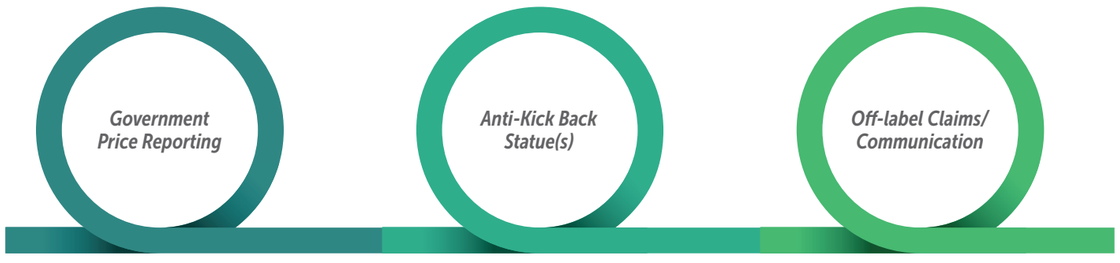
- Assessing risk upfront due to uncertainties around real world performance
- Managing lack of control (over outcome, proper dosing, product use, adherence…)
- Finding adequate time horizons in fragmented multi-payer insurance market
- Managing resource requirements to set up and adjudicate compared to traditional rebates and discounts
- Leveraging data infrastructure adequate for measuring / monitoring relevant outcomes
- Reaching contractual agreements b/w all stakeholders
- Managing risk of potentially burdening physicians with uncompensated data collection

First, a known challenge lies in matching outcomes measurement with the limited time horizons in the fragmented multi-payer US insurance market which is notoriously characterized by significant member switching between health plans. OBAs would certainly benefit from longer time horizons than the (year-end) time frame payers tend to rely on given these dynamics. The situation is complicated by the disconnect between initial, front-end costs and back-loaded benefits for certain therapies.[16] Solutions have been proposed but require a transformation in the insurance landscape; for instance, payers could begin to design pooling mechanisms for switching beneficiaries over time as a broader adjustment for stability on the exchange markets. Other propositions to address the flaws of a competitive insurance market are merely in the conception stage (e.g., health currencies such as HealthCoin, cure funds and/or multi-year reinsurance models).

Second, substantial efforts are required to establish OBAs compared to traditional rebates and discounts. The achievement of contractual agreements between all stakeholders (e.g., on the selection of outcomes, patients, data collection methods) is cumbersome, time-consuming and requires strong trust building as well as highly complex negotiations (with multiple legal parties given additional re-insurance needs). Resource requirements and costs associated with ongoing adjudication are not insignificant, while data collection may need to be expanded if existing infrastructures are limited. Further, the process for rebate adjudication is an exclusive service provided by pharmacy benefit managers (PBM) today, so the adoption of OBAs beyond targeted pilots remains contingent on the ability for such agreements to work in a PBM framework.

Third, as shown in Figure 8, current legal requirements and regulations dampen manufacturers' appetite for the adoption of the OBA approach (e.g., Government price reporting: Medicaid's best-price rules, 340B Ceiling Prices; the FDA's off-label communications policies; state and federal anti-kickback statutes; concerns around data privacy and state laws, e.g., insurance, corporate practice of medicine, fee splitting). A thorough demonstration of the limitations of the current legal environment can be found in joint memoranda published by the manufacturer Eli Lilly and Company and insurer Anthem, and more recently recommendations from a stakeholder initiative at the Duke Margolis Center for Health Policy.[17]

FIGURE 8
Major legal and regulatory hurdles for OBA adoption



- Reporting requirement w/ CMS for calculation of Medicare Part B average sales price (ASP) and Medicaid best-price as (effectively) lowest-price offered to any non-excempt purchaser
- Most recent revision of best-price rule with commitment to offer **further guidance**, CMS recognizes value of OBAs as 'unique arrangements' (April 2016)

- Prohibits exchange of value to induce/reward service paid by federal government – this includes business with Medicare and Medicaid programs
- Acknowledged limitations of current safe harbors provisions during HHS OIG latest annual solicitation (Dec. 2016), concerted **call for safe harbor expansions**

- 21st Century Cures greatly expanded scope of pre-approval HCEI and audiences, also regarding off-label use
- FDA 2018 guidance regarding exchange of HCEI/pharma-payer communication re-defined agency position
- Choice of other endpoints for OBA adjudication than those leading to FDA label is possible

We should note though that despite valid legal concerns on all sides, the lack of safe-harbor legislation, for example, may complicate but not prohibit the development of innovative arrangements in the current US environment. Practically speaking, deal structures in the market tend to feature added complexity to avoid best price implications or delivering price adjustments in the form of "contingent discounts" based upon the achievement of a data metric. Without providing further guidance, CMS has recognized OBAs as unique and valuable while the FDA has emphasized that it neither regulates the terms of manufacturer-payer contracts, nor the practice of medicine. The most recent 2018 FDA Guidance offers answers to important questions as to what communication outside the four corners of the labels is acceptable when it comes to exchange of the healthcare economic information (HCEI) between pharma and payers that underpins many aspects of pre-launch OBA negotiations.

> *The inherent complexities of outcomes-based contracts should not serve as a deterrent. Rather, they should compel all involved entities, both public and private, to collaborate on and devote resources to addressing cost, data, and access challenges.*
>
> **MARC WATROUS**, SVP Managed Care and Customer Operations, ***Genentech***

The Outlook for OBA Growth in the US Marketplace

We have voiced the caveat earlier that estimates of the current OBA activity remain partial to charting the perspectives of those with inside knowledge. So, how can we best map the adoption of OBA in the US based on our interviews and client experiences – even if only for illustration purposes? The classic bell curve of innovation offers a method. Following Roger's concept of the diffusion of innovation, Figure 9 visualizes the spread of OBA adoption at a company level (as percentage of the total OBA market).

The key point: OBA adoption hasn't come anywhere near saturation point, basic pilots are considered by an early majority, more complex agreements (in terms of measurement scope or adjudication regime) are very much in their infancy with a few innovating organizations. At the same time there are today only very few pioneering companies with an approach "at scale" (such would include simulating OBAs as standard contracting option across the portfolio, employing a guiding framework, leveraging integrated OBA councils across franchises etc.)

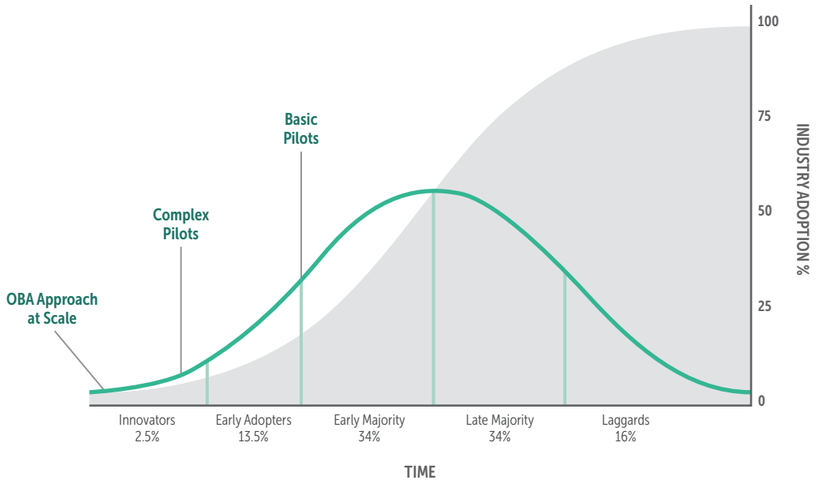


FIGURE 9
Have OBA crossed the chasm? Illustrating pharma's level of adoption following Rogers Innovation Model

According to the executives we consulted in late 2017, several major biopharma companies are each planning to launch more than a handful agreements in 2018. Despite hearing about a number of challenges, we also heard that the 'early adopters' were so-far satisfied with the return on their OBA pilots. The optimistic outlook is broadly in line with recent survey data (Figure 12).[18]

> *We've been tooling up for the last several years to do exactly the kind of thing we're talking about now. You have to trust each other, and it has to be simple and clear when the contract is working and then how well it's working.*
>
> **ROBERT McMAHON**
> US President, ***Merck***

The focus for OBA uptake remains particularly strong in high-cost and specialty therapeutic areas. Consider an unpublished poll of mid-level pharmaceutical directors with US market access responsibilities conducted in January 2017. It indicated that 53% of respondents believe risk-sharing will become one of the standard contracting methods in under 2 years in oncology. Another 38% told us they believe that it will take 3-5 years. Our online survey was based on a convenience sample of 205 industry respondents with roles in market access/ pricing, account management and HEOR who indicated the topic of value-based contracting for oncology products as a focus of their interest. Participants spread across 40 of the largest biopharma companies.

Global Category Leader: OBAs in Oncology

Considering the global category leader for OBA, Oncology, we only find a very limited number of agreements for cancer products in the market (c.f. Figure 10 for a selection). According to annually published data[19] from the manufacturer EMD Serono, US health plans take a somewhat cautious stand here.

Eight of the 58 commercial plans surveyed had at least one OBA for an oncology product in the market in the plan year 2016. Fifteen other plans were aiming to introduce an OBA in 2017 for oral oncology agents, and another 10 plans for IV or injectable products. While roughly two thirds of plans were not planning to launch any OBAs in 2017, the interest was generally highest among the largest plans (over one million covered lives), and higher among medium plans (400,001-999,99 lives) than small plans (fewer than 400,000 lives). This finding is hardly surprising as smaller payers have only limited bandwidth to do multiple deals simultaneously given that the burden of data collection tends to largely fall into their responsibility. While the adoption numbers here represent only a small percentage of overall specialty contracts, it is notable that outcomes-based agreements, as a utilization management tool, have seen an increase in use of 55% since 2014, considerably more than electronic Prior Authorizations or partial fill programs in comparison.[20]

FIGURE 10
Selection of agreements in Oncology in the US

Eloxatin; Camptosar; Erbitux; Avastin (2005) Sanofi, BMS, Pfizer, Genentech | *CMS*	**OncotypeDx (2007)** Genomic Health | *United Healthcare*	**Avastin (2015)** Genentech | *Priority Health*	**Iressa (2016)** AstraZeneca | *Express Scripts*	**Kymriah (2017)** Novartis | *CMS*
Disease Area: Colorectal cancer (2005) **OBA Terms:** ■ Group contract, CMS promised to cover oxaliplatin, irinotecan, cetuximab, or bevacizumab for treatment of colorectal cancer on the condition that these drugs show a satisfactory level of efficacy in registered clinical trial ■ Coverage with evidence development	**Disease Area:** Breast cancer **OBA Terms:** ■ United agrees to reimburse test for 18 months, while results will be monitored ■ If number of patients receiving therapy exceeds agreed threshold, even if the test suggests they do not need it, United will negotiate a lower price due to test not having the intended impact on actual medical practice	**Disease Area:** Non-small cell lung cancer **OBA Terms:** ■ Genentech not required to pay Priority Health rebate if patient remains progression-free for longer than 6 months ■ If patient has to change treatments (because of toxicity or disease progression), Genentech provides rebate adjusted for the length of their PFS	**Disease Area:** Breast and lung cancers **OBA Terms:** ■ AZ reimburses Express Scripts (who will refund plan sponsors) for cost to treat first-line patients who discontinue before 3rd prescription refill	**Disease Area:** Pediatric leukemia **OBA Terms:** ■ CMS to allow for payment only when pediatric/ young adult when the patient responds by the end of the first month of therapy ■ CMS clarified that expansion to other indications would be priced differently

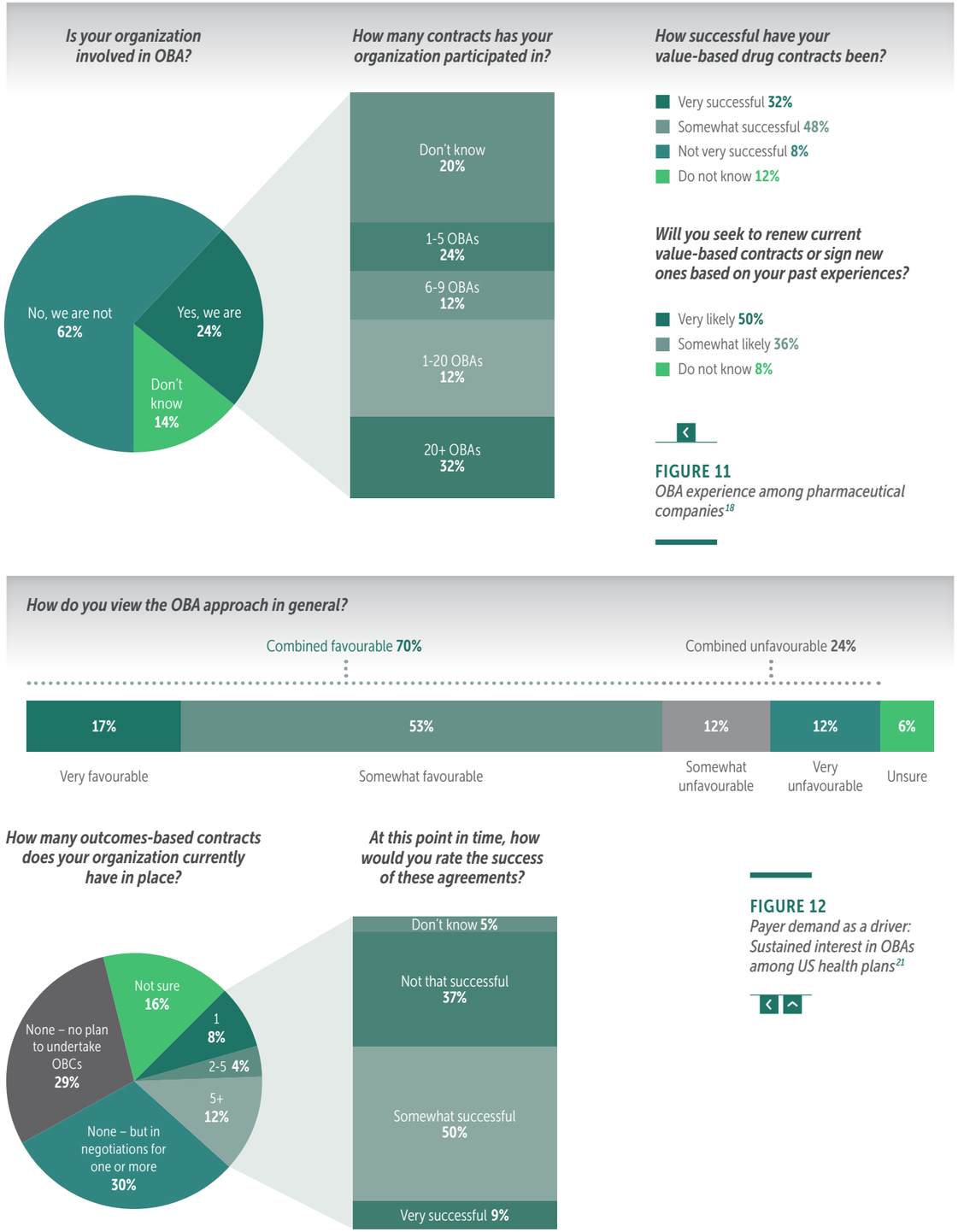


FIGURE 11
OBA experience among pharmaceutical companies[18]

FIGURE 12
Payer demand as a driver: Sustained interest in OBAs among US health plans[21]

> *While not the only approach we take to help ensure members are getting the value they deserve from the drugs they take, outcomes-based contracts are integral to our contracting strategy. Several contracts we've added in recent months demonstrate Prime's continued commitment to align manufacturers, members, payers and providers around the goal of improving health by helping to ensure drugs work as they are intended.*
>
> **ALEC MAHMOOD**, Chief Financial Officer, ***Prime Therapeutics***

There was overall agreement among those participating in conversations for this report that while pharma companies will proactively pursue OBAs as a contracting innovation (under less than ideal legal circumstances, and where strategically appropriate), a broad uptake will be triggered when as payers are consistently demanding OBAs. A former Aetna executive told us that all major payers should be interested in such arrangements partly because payers like to be seen as data-driven information and service companies, and partly because contracts that are value- and outcomes-driven send important messages in the competition for customers. Furthermore, wasted healthcare expenditure due to medication non-adherence is considered to be up to $300 billion every year – a challenge to be confronted together with industry and a possible lever for further OBA uptake. As we will argue in the next chapter of this briefing, agreements that work out favorably for both sides of the agreement are achievable – not just on paper.

It is evident from our review of case studies that for large national payers in the US, value-based contracting has already become a core business strategy. Cigna has been able to leverage its structure as an integrated health plan, PBM, and specialty pharmacy. Aetna, Humana or Anthem have all pursued several agreements and published details on some. A few regional plans are also fairly active – such as UPMC Health Plan, Priority Health, Regence Health Plan or Harvard Pilgrim in Massachusetts which has more than a dozen OBAs in place today (see contribution in next chapter) – while others like Blue Cross Blue Shield of Massachusetts or Tufts Health Plan have expressed preference for working through pharmacy benefits managers (PBM). Prime Therapeutics, the PBM owned by 18 Blue Cross Blue Shield plans/subsidiaries, has recently announced a number of agreements, such as for empagliflozin (Boehringer's Jardiance), liraglutide (Novo Nordisk's Victoza) or Biogen's portfolio of disease-modifying agent in multiple sclerosis, including interferon beta-1a (Avonex), peginterferon beta-1a (Plegridy), dimethyl fumarate (Tecfidera) and natalizumab (Tysabri). We would highlight as a trend that payers do not hesitate to have multiple agreements for competing products in one class, so manufacturers want to be enjoying a first mover advantage.

> *Innovations like Kymriah reinforce our belief that current healthcare payment systems need to be modernized in order to ensure access to new high-cost therapies, including therapies that have the potential to cure the sickest patients. Improving payment arrangements is a critical step towards fulfilling President Trump's promise to lower the cost of drugs.*
>
> **SEEMA VERMA,** CMS Administrator

We have little doubt that the focus on patient outcomes will continue to grow as the demand for 'value' and the 'thirst for real world evidence' has risen among each stakeholder group. Technological advances in digital data, health information exchanges and EHR interoperability (i.e. consequences of MACRA implementation) will further expand new and additional real-time data and patient tracking, while continued funding of large clinical data networks (e.g., PCORnet) presents opportunities to enable standardization in order to streamline data collection efforts.[22]

Despite the current lack of definite legal guidance, the US government has also expressed broad support when addressing value-based contracting. Some have suggested that – given its size – Medicare could serve as an ideal laboratory for risk-sharing schemes in the US. In 2016, CMS did propose a rule for Part B demonstration model that would have allowed CMS to enter voluntary agreements with manufacturers to link patient outcomes to price adjustments. However, in December 2016 the agency decided not to finalize the rule citing stakeholder concerns and complexity. Observers close to CMS have reasonable expectations that the facilitation of value-based contracting for medical products ranks among the top priorities given the new HHS leadership in 2018. Notably, in the fall of 2017 CMS had agreed to an unprecedented outcomes-based agreement with Novartis on tisagenlecleucel (Kymriah), the first FDA-approved, personalized CAR-T cell therapy for relapsed or refractory acute lymphoblastic leukemia: Treatment would be reimbursed only if patients respond after one month. In reply to Novartis' announcement of the unique collaboration on August 30, 2017, CMS made sure to emphasize that it aims to "alleviate regulatory barriers as may be necessary through the authority provided to the Center for Medicare and Medicaid Innovation (CMMI)... to test payment and service delivery models that involve value-based payment arrangements."[23]

The particular agreement was retired in 2018 following a review by HHS lawyers due to concerns around its genesis, while HHS leadership has made sure to re-iterate support for innovative contracting in general.

THE NEW FRONTIER IN US CONTRACTING

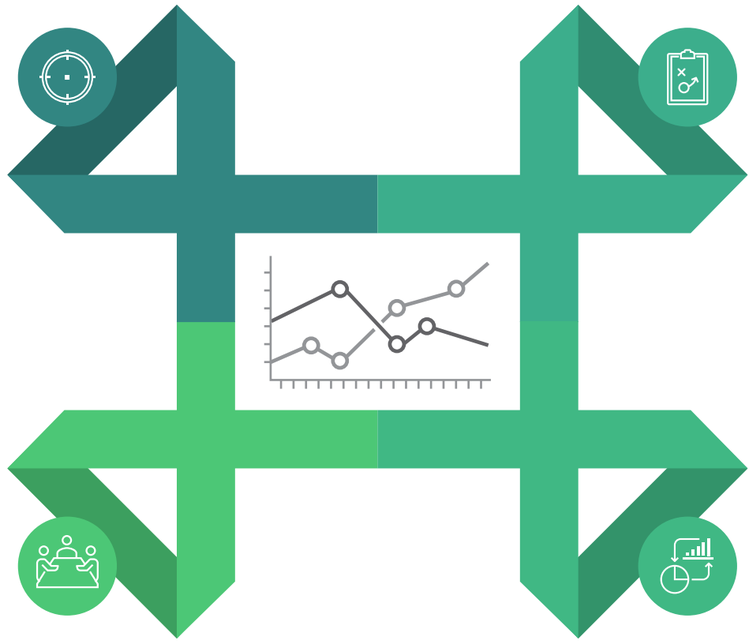
HOW YOU CAN SET UP FOR OBA SUCCESS

Definition of the Contracting Approach

- ✓ Evaluation of payers/health system position regarding different types of innovative agreements
- ✓ Clearly set out the benefits of the OBA for the respective payers
- ✓ Setting expectations in terms of improved access, lower base rebates, increased customer confidence in products, payer relationship building

Selection of the Right Design

- ✓ Investigation of outcomes interesting to respective payer(s)
- ✓ Assessment of which outcomes can be monitored
- ✓ Selection of time horizon and most adequate type of agreement
- ✓ Consideration of legal issues such as impact on Medicaid best price, Medicare Part D payment rates



Implementation and Adjudication

- ✓ Selection of data sources and methods most adequate to monitor real-world performance
- ✓ Developing plans to adjudicate results and trigger payments and define exceptional events that should lead to renegotiation
- ✓ Analysis of re-insurance modalities
- ✓ Decision of governance to ensure the long-term success of the agreement

Testing and Refining Deal Modalities

- ✓ Definition of key factors that could influence the outcomes/risk
- ✓ Simulation of the expected performance in the real world for the selected outcomes in the population covered by the plan
- ✓ Modelling of the expected financial impact compared to traditional pricing/rebating approaches
- ✓ Evaluation of contractual terms needed to limit risk

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- Conducted prediction and monitoring of real world outcomes for new lipid-lowering treatment
- Evaluated the real world risk of hospitalization for the implementation of innovative contract in asthma
- Prepared and facilitated senior management workshop on design and implementation of OBAs for top 5 global PharmaCo
- Measured real world outcomes in the context of an OBA for new treatment in schizophrenia
- Evaluated new price structures and financial risk-sharing scenarios for treatment in multiple solid tumors
- Led various educational symposia, i.a. ISPOR 21st (2016) and 22nd Annual Meeting (2017)

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