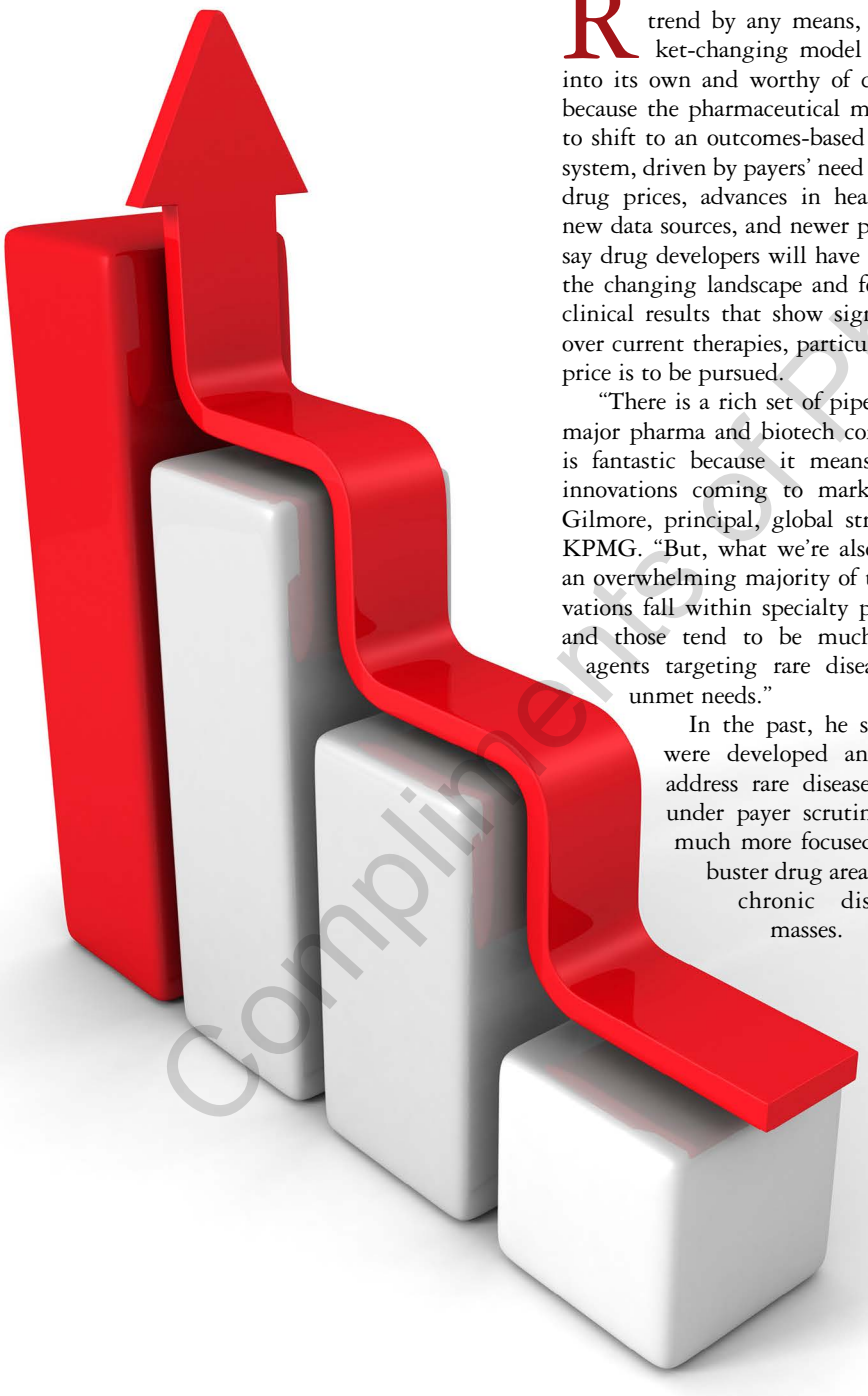
By Denise Myshko

# Trending 2018: Real-World Outcomes

The changing landscape for reimbursement of medical therapies is forcing developers to document outcomes and proven benefits of treatments.



Real-word outcomes is not a new trend by any means, but it's a market-changing model that is coming into its own and worthy of covering. That's because the pharmaceutical market continues to shift to an outcomes-based reimbursement system, driven by payers' need to rein in rising drug prices, advances in health technology, new data sources, and newer players. Analysts say drug developers will have to stay ahead of the changing landscape and focus on data in clinical results that show significant benefits over current therapies, particularly if a higher price is to be pursued.

"There is a rich set of pipelines across the major pharma and biotech companies, which is fantastic because it means a lot of new innovations coming to market," says Peter Gilmore, principal, global strategy group at KPMG. "But, what we're also seeing is that an overwhelming majority of these new innovations fall within specialty pharmaceuticals, and those tend to be much higher-priced agents targeting rare diseases with high unmet needs."

In the past, he says, drugs that were developed and launched to address rare disease states weren't under payer scrutiny. Payers were much more focused on big blockbuster drug areas that addressed chronic disease for the masses.

"Now, increasingly we're seeing a significant budget impact as the collective body of these specialty drugs are priced from $10,000 to $50,000 to $100,000 per patient, per year depending on the disease state," Mr. Gilmore says. "These therapies are definitely under scrutiny by payers."

Payer groups want to learn how to keep their patient populations healthier at lower total costs. As such, payers will continue to shift their focus toward demonstrating if long-term outcomes, i.e. value, can be achieved, says Ron Lacy, senior director, commercial insights and analytics, UBC.

"Payers want to see outcomes that demonstrate the manufacturers' therapy and services improve overall health while reducing the total healthcare spend," he says. "Payers will want to see results from registries and postmarket launch research. This means the manufacturers will need to not only show comparative effectiveness of its therapies, but also the effectiveness of services delivered and in care settings."

Physician and patient access to new and valuable therapies had long been governed by regulatory agencies, including FDA, EMA, and others. Today, however, regulatory approval is just the starting line, says Joshua Schultz, senior VP and worldwide head of Parexel Access.

"Access today is driven largely by payers' willingness to reimburse for approved prod-

> Payers want to ensure that endpoints from clinical studies actually translate into real patient benefits in clinical practice, and they need real-world evidence to demonstrate this.
>
> **JOSHUA SCHULTZ**
> Parexel Access

Contracts that focus on the intended outcome associated with a therapeutic adds significantly to the complexity.

**KARLA ANDERSON**
PwC

ucts," he says. "And, as economic factors weigh more heavily in healthcare decision-making each year, payers' influence can only be expected to grow. This influence is leading to an interest in shifting from traditional charge-for-service models to outcomes-based approaches. Underpinning this change is a dramatic increase in the need for outcomes endpoints in a real-world setting — either as part of the regulatory approval package or as 'fast-follower' information upon approval."

Mr. Lacy says there is beginning to be a real shift toward a pay-for-performance model as pharmacy benefit managers look for more ways to align the cost of treatment with outcomes.

"Some programs allow payers to pay different rates for the same drug that can be used to treat different types of cancer that have different total costs of care," he says. "The pharma industry will need to adopt value-based pricing models with evidence tailored to the disease state, not just the therapy itself."

What this means is that manufacturers can no longer look at just their drug products; they also need to consider services that wrap around those products and the outcomes that the combined therapeutic and service delivers to patients.

"Pharma companies are investing in next-generation technologies that enable de-identified research that includes a wide substrate of linked data ranging from administrative claims, EMR records, lab requests and results, to patient-support services," Mr. Lacy says. "Organizations that know how to leverage these wide data sets with machine learning tools, statistical analysis, and visual analytics will gain an advantage in being able to deliver outcomes research at a lower cost and higher quality."

Payers aim to address two key questions about new drugs: is the drug better than current treatments, and how much should we pay for it, says Stephen Lubiak, senior VP, business intelligence and analysis, Ogilvy CommonHealth Worldwide, a WPP Health & Wellness company.

"Payers often require more clinical evidence than what is in the label, and may even desire economic information (recently approved for limited communications by the 21st Century Cures Act)," he says. "Payers prefer head-to-head, real-world, clinical studies because in many cases new drugs are competing with incumbent treatments. While recent advances in immuno-oncology provide a great example of superior clinical performance and value, in many other disease states the advantages of newer drugs are less apparent, and may even be considered 'marginal.' So, more proof or evidence is required by payers to demonstrate both clinical and economic value."

Mr. Schultz says this evidence can include data from diverse and heterogeneous patients who reflect the true range of patient profiles, behaviors, and treatment patterns that payers might see in their own patient populations.

"While the focus heretofore has been on study designs, such as comparative effectiveness studies, it is now shifting toward expanded sources of data that assess the impact of a treatment in the real world," he says. "Pharma needs to embrace innovation in the use of secondary data, wearables, and electronic health devices to meet these needs."

## Assessing Outcomes

Leveraging real-world data to provide evidence that supports both medical product development and patient care is a tremendous opportunity. While this opportunity might be driven by the increased power of the payer — or the corollary of high drug prices — other factors are spurring its adoption, says Sandy Allerheiligen, Ph.D., Certara senior VP of health economics and education.

"We see the real-world data opportunity as the ability to provide another avenue to ask 'what is the question we are trying to answer,'" she says. "Until now, those questions have been largely focused on safety, efficacy, and quality for regulatory approval. Those same approaches can now be expanded to address the hurdle of value and affordability needed

## HEOR Will Continue to Grow in Importance With Real-World Evidence Taking Center Stage

**NANCY BERG**
**CEO and Executive Director, ISPOR — The Professional Society for Health Economics and Outcomes Research**
**@ISPORorg and @NbergBerg**

As health economics and outcomes research (HEOR) continues to grow in importance around the world, one of the key areas that will be at the forefront of the field in 2018 is real-world evidence. Technology has made real-world data increasingly abundant — from claims data to electronic health records to wearable devices. While randomized, controlled trials are still considered the gold standard in research, interest in converting real-world data into real-world evidence for healthcare decision-making has never been greater.

Real-world evidence is attractive because it offers timely data at a reasonable cost. The large sample sizes in real-world trials allow for more refined analysis of treatment patterns, subpopulations, and adverse events. Additionally, real-world trials are typically more representative of what patients are actually experiencing.

Real-world evidence, however, can be viewed as a double-edged sword. Critics point to the potential for bias due to the lack of randomization, the lack of confidence in data quality, and the potential for data mining.

To address these issues, ISPOR recently partnered with the International Society for Pharmacoepidemiology (ISPE) to establish the Real-World Evidence in Health Care Decision Making Initiative. The objective of this joint initiative is to help improve the standards for the analysis and reporting of real-world data. The initiative's task force has recently published two companion papers that, as part of our Societies' respective missions, are freely available at www.ispor.org.

Payers are skeptical that pharma companies want to entice them into very complex contracts as a way to generate more sales. We don't often see the intentions of these two big stakeholder groups aligned.

**PETER GILMORE**
KPMG

Real-world scenarios are not mirror images of the therapeutic experience within the controlled clinical trial protocol.

**PATTY ZIPFEL**
MicroMass Communications

to gain acceptance and payment by health authorities."

Patty Zipfel VP, scientific strategy, MicroMass Communications, believes the pharma industry needs to help patients achieve optimal outcomes once efficacy has been demonstrated in a clinical trial.

"Real-world scenarios are not mirror images of the therapeutic experience within the controlled clinical trial protocol," she says. "During the clinical study, patients are offered support and a framework, whereas when patients start on a new drug, they often don't have the necessary support to work in meal requirements, for example, into their daily schedule."

Ms. Zipfel says pharma companies should provide solutions that change patient behaviors and address barriers to achieving ideal efficacy in the real world. This includes ways to improve therapy adherence, maximize patient self-efficacy, and achieve optimal therapeutic efficacy.

## Payer Partnerships and New Contract Models

Pharmaceutical companies are creating partnerships with payers to assess outcomes. For example, in October Anthem, HealthCore, and Boehringer Ingelheim initiated a trial to study COPD in a real-world setting. The AIRWISE trial hopes to provide understanding of the role of long-acting muscarinic antagonists, long-acting ß-agonists, and inhaled corticosteroids in reducing the risk of COPD exacerbations. Results from the trial will be available in 2020.

Merck is another company looking to improve outcomes through a partnership agreement. The company is collaborating with Aetna on the insurer's AetnaCare, a personalized, patient-centric approach to care. The agreement is for the type 2 diabetes medications Januvia and Janumet.

Amgen and Humana have also teamed up to assess and improve outcomes. Six projects are currently under way or planned, with more expected. The collaboration initially targets multiple serious conditions, including cardiovascular disease, osteoporosis, neurologic disorders, inflammatory diseases, and cancer.

Amgen and Humana researchers are combining available sources of real-world evidence with data from wearable technology, digital apps, and Bluetooth-enabled drug delivery devices. Prospective observational studies are also being planned.

Payers' focus on outcomes-based reimbursement has started to change how pharma brings products to market, says Jeff Terkowitz, senior director, product, Inspire.

"Life-sciences companies have always been concerned with formulary placement in the United States, but the focus on evidence of success has made a major difference to data construction as part of the approval process."

In the United Kingdom, Mr. Terkowitz says, for some novel oncology treatments, life-sciences companies have been forced to accept arrangements in which they are only paid if the treatment is successful. These payment arrangements that focus on outcomes and approvals that are more contingent on comparative effectiveness are forcing the life-sciences companies to spend more time during preapproval trials demonstrating that the medicine is not just superior to a placebo, but that the treatment is superior or comparable with other treatments currently on the market.

Mr. Schultz says pharma companies today must think more broadly about their product-development plans, with a focus not just on product approval, but also with an eye toward meeting the market-access demands that will drive product success post-approval.

"Product development today requires a coordinated plan that includes both the critical pivotal trials, as well as the real-world evidence and economic analyses that will support payer

### Challenges for Value-Based Pricing Implementation

- Defining outcomes: The outcome set is the key component of the value-based pricing agreement. It is crucial to collaborate with hospitals, doctors, and professional societies, to select outcomes and clearly define inclusion and exclusion criteria for patients, as well as gain support and buy-in. The next hurdle is estimating causality between the product and outcome. This is because outcomes in a real-world setting often partly depend on various externalities (lifestyle, compliance, etc.).
- Measuring outcomes: Ideally, the infrastructure to measure outcomes will already be largely in place; if this has to be built however, it can push up costs. Clinical registries or patient reported outcomes are already available in numerous therapeutic areas (e.g. oncology) and geographies.
- Regulatory and legal barriers: Many countries set drug prices centrally. Without specific provisions for value-based pricing arrangements, there is no clear route for payers to negotiate separate value-based pricing schemes in such systems. Some health systems explicitly prohibit payments outside of legally mandated reimbursement systems. Many countries already have some value-based pricing arrangements in place.

Source: KPMG

4TH ANNUAL

# IMMUNO-ONCOLOGY 360°

## FEBRUARY 7-9, 2018 • NEW YORK, NEW YORK

THE PREMIER MEETING ACROSS ALL STAKEHOLDERS IN IO

CLINICAL • SCIENTIFIC • BUSINESS

**Axel Hoos, MD, PhD**
GlaxoSmithKline

**James Gulley, MD, PhD**
National Cancer Institute

**Andrew Baum, MD**
Citi

**Greg Simon, JD**
Biden Cancer Initiative

**Dolores Schendel, PhD**
Medigene AG

**David Lebwohl, MD**
Novartis Pharmaceuticals

**Roy Baynes, MD, PhD**
Merck Research Laboratories

**Dario Campana, MD, PhD**
National University of Singapore

**Christine K Ward, PhD**
Bristol-Myers Squibb

**Jeffrey Weber, MD, PhD**
NYU Langone Medical Center

**Lisa Butterfield, PhD**
University of Pittsburgh / SITC

**William Grossman, MD, PhD**
Genentech

PharmaVOICE readers receive **15% off** registration with code **PVCE15**

Learn more at THECONFERENCEFORUM.ORG

IO360

5TH ANNUAL

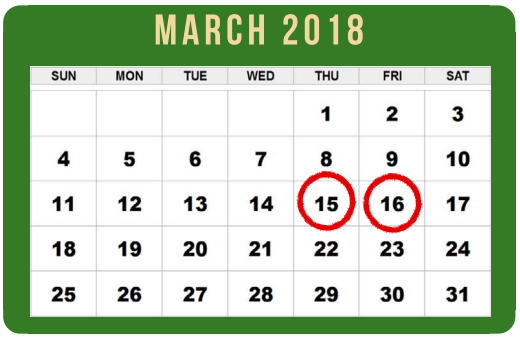
# PATIENTS AS PARTNERS US

## March 15-16, 2018 • Philadelphia, PA, USA

**Turning Discussion Into Action:**

Incorporating the patient perspective throughout the entire clinical trial continuum

SAVE THE DATE!



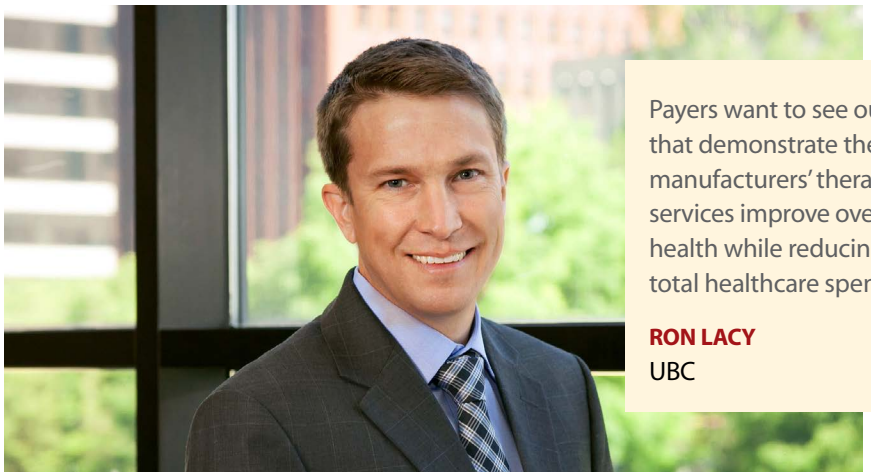

ASK THE PATIENT

"Ask the Patient" returns to Patients as Partners, a program representing a group of individuals who've experienced a clinical trial, where patients are available to answer questions about their clinical trial experience.

PharmaVOICE readers receive **15% off** registration with code **PVCE15**

Learn more at THECONFERENCEFORUM.ORG

PATIENTSASPARTNERS



Payers want to see outcomes that demonstrate the manufacturers' therapy and services improve overall health while reducing the total healthcare spend.

**RON LACY**
UBC

Leveraging real-world data to provide evidence that supports both medical product development and patient care is a tremendous opportunity.

**DR. SANDY ALLERHEILIGEN**
Certara

decisions — ideally starting at the very early stages rather than during post-approval," he says.

Madhur Garg, director, real-world evidence and market access at Sciformix, says the main impact of the increased focus on real-world outcomes has been in the way R&D of new drugs is structured.

"Regulatory approval alone is not the end goal anymore, so the R&D program has to account for payers' needs and evidence requirements," he says. "R&D programs are not just limited to randomized clinical trials; they also now include real-world studies to analyze efficacy-to-effectiveness translation of a given healthcare intervention."

The shift to outcomes-based reimbursement, while still evolving, has also led to innovative contracting approaches and more robust techniques for quantifying the risk associated with forecasting real-world outcomes of new technologies.

With intense pressure on drug prices, the pharmaceutical industry is turning to value-based contracts, also known as outcomes-based contracts. Value-based contracts are designed to tie prices to how a drug performs in the real world.

Although not yet common, analysts say there will be more of these types of arrangements as payers continue to bear the burden of all these high-cost therapies and begin to restrict access. Only one-quarter of pharmaceutical executives recently surveyed by PwC have participated in a value-based contract.

"The industry is beginning to embrace the imperative to collect real-world data with much of the cutting-edge activity occurring in the area of study design, mobile/sensor-collected data, secondary data assets, such as EMR and claims, and incorporating real-world approaches earlier into the development process," Mr. Schultz says. "Innovative contracting includes experimentation with a range of different models to allocate risk with the most innovative companies considering approaches that also enable behavior change at the physician/patient interface."

Mr. Schultz says outcomes-based pricing requires an ability to quantify likely performance in a real-world setting that is unlikely to be the same as experienced in pre-approval clinical trials.

Using a range of data sources and clinical expertise to reduce the potential variability on likely real-world outcomes has become a critical skill to support the creation of outcomes-based approaches.

Mr. Gilmore says it's too early to tell whether these contracts have been successful. "They've been done on a small scale and the results are not broadly publicized," he explains.

Analysts say value-based pricing has a real potential to bring value to pharmaceutical companies, payers, patients, and providers in advanced health systems. But this can only happen when stakeholders define and measure outcomes effectively, choose appropriate patients, and manage costs efficiently.

Novartis, along with Cigna and Aetna, was one of the first pharma companies to announce a pay-for-performance arrangement in early 2016, for the heart failure drug Entresto. In this arrangement, Novartis has agreed to pay addi-

## Ensuring Patient Access

**MADHUR GARG**
**Director, Real World Evidence and Market Access, Sciformix**

Payers are already playing a crucial role in patient access to healthcare across the reimbursed markets.

Many emerging markets are now embracing health technology assessment (HTA) in various forms throughout APAC and LATAM, for example Brazil, China, and Taiwan.

As healthcare financing comes under increased scrutiny, both socially and politically, payers will be held accountable for every healthcare penny spent. Thus, there is an increased focus by payers on identifying, measuring, and incentivizing the right healthcare outcomes both at an individual patient level as well as the larger health system level. Payers are becoming increasingly technology and data savvy and will have to explore innovative models to partner with healthcare providers and manufacturers.

Already, payers are working in closer collaboration with regulatory agencies, which is likely to continue in the future. Further, payers see manufacturers as partners in ensuring patient access to the best of healthcare technology.

That being said, it has been an evolving relationship with mixed outcomes. Now more than ever, the industry is proactively engaging in earlier and more impactful conversations with payers to better understand payer needs and decision drivers. This can be seen in the numerous early advice schemes that payers such as NICE and IQWIG have in place to facilitate early dialogue with the manufacturers. Both are becoming more outcomes focused and ready to explore innovative patient access models. Not only payers but even regulators are recognizing the value of real-world evidence in drug development and regulatory approval process.

Life-sciences companies have always been concerned with formulary placement in the United States, but the focus on evidence of success has made a major difference to data construction as part of the approval process.

**JEFF TERKOWITZ**
Inspire

tional rebates, depending on whether hospitalizations of patients for congestive heart failure are reduced, and the overall savings to payer.

Another payer, Harvard Pilgrim, has signed agreements that cover the rheumatoid arthritis medicine Enbrel, made by Amgen, and Lilly's osteoporosis medicine Forteo.

Harvard Pilgram's contract with Lilly rewards improvement in persistence in medication use as compared with the baseline level of adherence seen in the Harvard Pilgrim population. If meaningful improvements to Forteo persistence are realized in Harvard Pilgrim's patients, Lilly will reduce the cost of the drug for Harvard Pilgrim. Harvard Pilgrim will work with its pharmacy network and Lilly to drive improvements in patient persistency.

The complexity of these contracts is a barrier, says Karla Anderson, principal in pharmaceutical and life sciences practice at PwC.

"Contracting, from a historic standpoint, was either with PBMs or with payers, and it has been fairly focused on a rebate model, meaning that the manufacturer charges a certain price and, based on the volume that a payer uses, the manufacturers apply a discount," she says. "Contracts that focus on the intended outcome associated with a therapeutic adds significantly to the complexity."

Value-based contracts involve a lot of data that need to be collected, and there has to be an operational mechanism to collect and assess that data.

Ms. Anderson says payers now see an advantage of these contracts for high-cost specialty products.

"The administrative burden of doing value-based contracting is seen as warranted for specialty drugs, which it hadn't been for drugs, such as those for diabetes and cardiovascular disease, used for larger audiences," she says. "These contracts work nicely for certain drugs that prevent hospitalization, as an example. Probably, one of the cleanest types of value-based contracts is for asthma. If patients take their medicine according to the intended prescription, they can stay out of the hospital."

Mr. Gilmore says payers are skeptical that pharma companies want to entice them into very complex contracts as a way to generate more sales, which is another barrier to overcome.

"We don't often see the intentions between these two big stakeholder groups align," he adds. "This certainly has to change. Manufacturers have to give a clear case to payers that engaging in these value-based contracts is beneficial and that they will actually reduce the overall cost of care."

Ms. Anderson says in general, value-based contracts are highly customized.

"There is a lot of activity going on in pricing and contracting in general to introduce robotics process automations, artificial intelligence, and Blockchain to ease some of the burden," she says." PV