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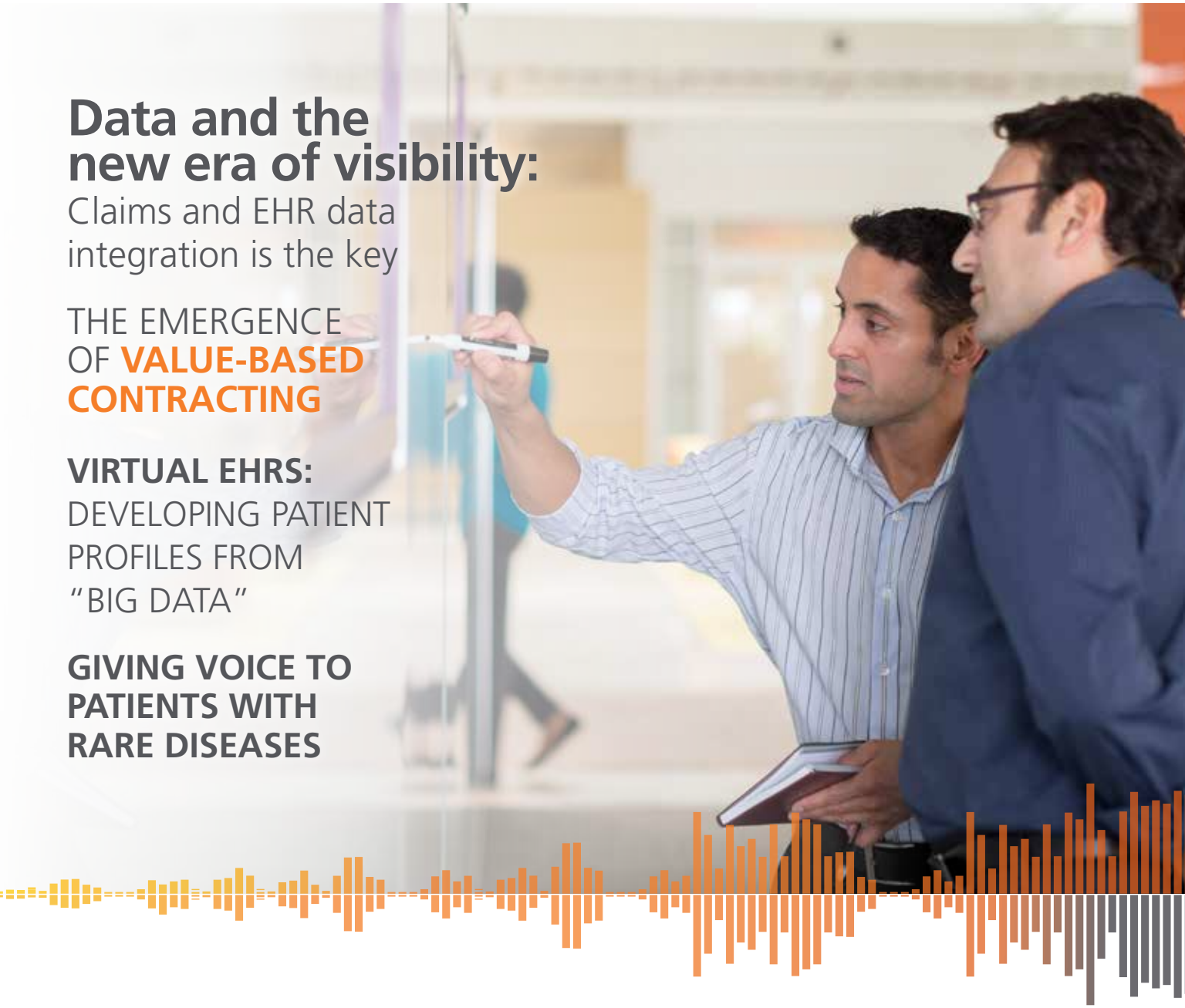

Data and the new era of visibility:
Claims and EHR data integration is the key

THE EMERGENCE OF **VALUE-BASED CONTRACTING**

VIRTUAL EHRS: DEVELOPING PATIENT PROFILES FROM "BIG DATA"

GIVING VOICE TO PATIENTS WITH RARE DISEASES

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Amplify is a publication of Optum®, a leading information and technology-enabled health services business dedicated to helping make the health system work better for everyone. With more than 80,000 people worldwide, Optum delivers intelligent, integrated solutions that help modernize the health system and improve overall population health.

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Welcome back to Amplify.

Welcome to the latest edition of *Amplify,* Optum Life Sciences contribution to the conversation about the future of health care. Inside you will find a number of articles and research findings that represent our latest thinking about what's next, and what that means for life sciences companies.

You may have already heard me say that data drives decisions, but it's worth repeating. The quality of the data we use — and how we use it — determines the success of those decisions.

But what makes some data more valuable than others? In life sciences, it is how well the data can help you identify, understand and address the priorities of patients and providers, as well as regulators and payers. It also means having the ability to ask, and answer, the right questions.

With the right data and proper analysis, you can gain competitive advantage and improve market agility. But make a misstep, and the repercussions can be costly and far-reaching. This is particularly the case now given the shift in the health care payment paradigm from fee-for-service to value-based reimbursement.

Our feature article, "Data and the new era of visibility," will delve into this topic in more detail. I also think you will find the other articles in this publication thought-provoking about what the future holds in this most challenging and exciting industry.

Curt Medeiros
President, Optum Life Sciences

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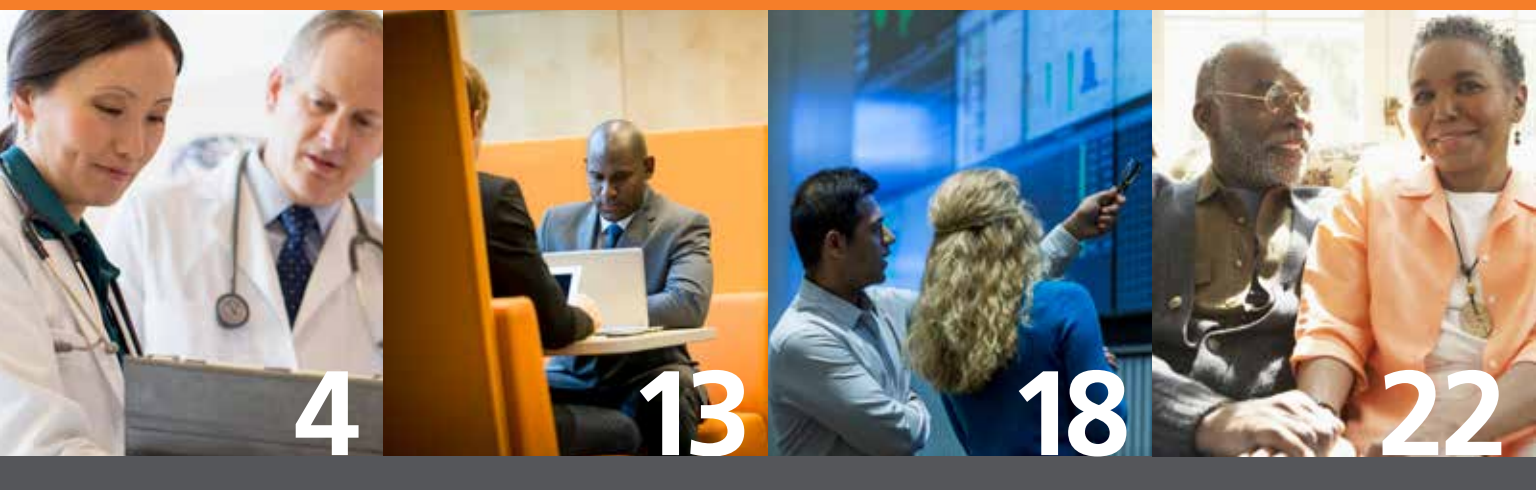


Data and the new era of visibility

Using data to drive decisions in life sciences

Data drives decisions. The quality of the data you use — and how you use it — determines the success of those decisions.

What makes some data more valuable than others? In life sciences, it is how well the data can help you identify, understand and address the priorities of patients and providers, as well as regulators and payers. It also means being able to ask the right questions.

Use the right data and analyze it properly, and you can reap the rewards in terms of better patient and financial outcomes. Make a misstep, and the repercussions can be costly and far-reaching. This is particularly the case now that we're seeing a historic shift in the health care payment paradigm from fee-for-service to value-based reimbursement.

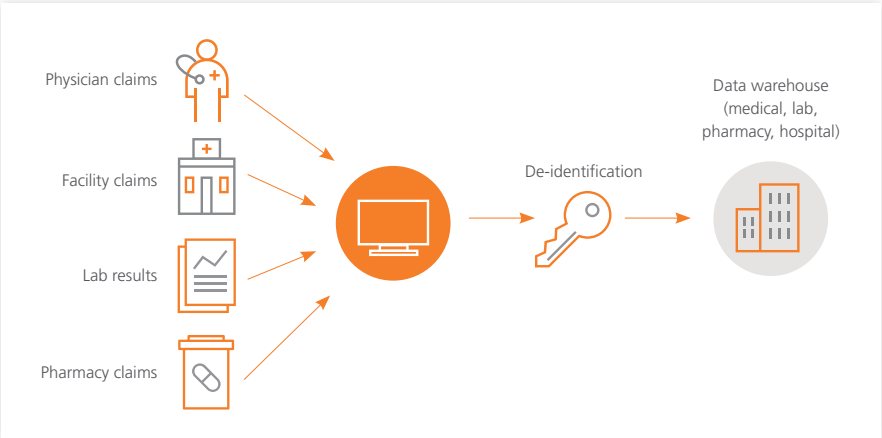
Uncover the truth behind resource utilization.

The breadth and scale of Optum data help you ask, and answer, the right questions. Our data comes from the nation's largest health care claims database and includes data on more than 120 million lives, dating back to 1993:

Physician claims | Facility claims | Lab results | Pharmacy claims

Our claims data contains complete member information for medical and pharmacy benefits, including enrollment dates, plan design details and cost information. This is extremely valuable in analyzing resource utilization and associated costs across the entire health care continuum. We also use a person-level de-identification algorithm to ensure our data is compliant with HIPAA and other privacy regulations.

Optum data is eligibility controlled, meaning the database it comes from is a closed system, which ensures it is accurate and precise. We're also expanding our claims database with the addition of a third-party vendor, which will enhance our database with over one billion prescriptions annually.



"One of the biggest setbacks for our clients is that they've stopped asking the questions that they haven't been able to answer. Our data enables them to answer questions that they need answers to — but may have stopped looking for."

Steve Davis
Senior Vice President,
Data and Advanced Analytic
Tools, Optum Life Sciences

Answer "why" with EHR data.

Claims data is valuable because it tells us what happened and how much it cost, but it misses a critical piece of the puzzle: "Why?"

Why did it happen? Why was the patient seen? Why did the doctor choose to prescribe a particular treatment over another?

The answers to questions like this provide critical insight into what is motivating stakeholder decisions throughout the health care timeline. Unfortunately, it isn't the kind of information you can find on a claim form because it comes from those one-on-one provider/patient interactions.

While you can't be a fly on the wall during those encounters, Optum offers the next best thing — access to electronic health records (EHR) data of more than 80 million individuals. Through our strategic services relationship with provider groups, our EHR data comes from 79 different clients spanning all 50 states, representing over 140,000 providers, 6,500 clinics and 600 hospitals. On average, it includes four years of patient history with a full spectrum of inpatient and outpatient treatments. Our EHR data includes both structured data (vital signs) and unstructured data (provider notes).

To successfully mine the gold in provider notes and put you in the middle of the provider/patient conversation, Optum uses natural language processing (NLP) to bring to light invaluable details and insights, including:

- Provider observations
- Patient history, statistics, labs and vitals
- Original date of diagnosis
- Signs, diseases and symptoms (SDS)
- Prescribed and OTC medications
- Treatment rational and plans

"This new data allows a transformative shift in the market from data being simply insightful, to data being actionable."

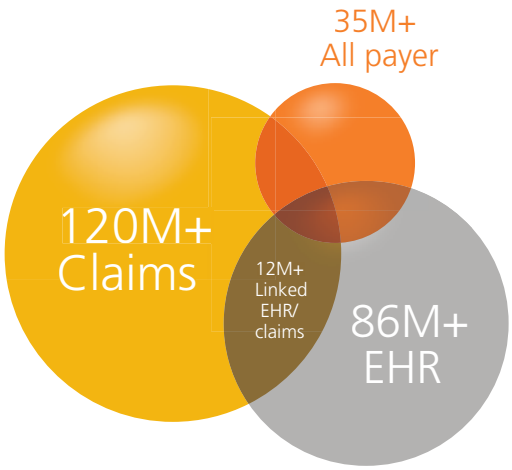
Steve Clark
Senior Vice President,
Optum Life Sciences

Solve the patient care puzzle.

Through a first-of-its-kind database containing linked claims and EHR data on some 12 million lives, Optum offers you an unparalleled volume of linked data. As a result, we can provide a much more detailed view of the clinical profile of patients, including those important interactions between the physician and patient.

Industry-leading real-world data assets

One of the largest and most complete claims data assets in the United States



One of the largest and broadest EHR data assets in the United States

First of its kind deterministically-linked EHR/claims data assets

"This data provides new and differentiated value in terms of visibility into the clinical profile of the patient and their interactions with their physician on a day-to-day basis. It also allows us to see more broadly across the entire health care system."

Curt Medeiros
President,
Optum Life Sciences

Succeed in the pay-for-value paradigm.

The transition to pay-for-volume to payer-for-value is aligning financial incentives and rewards for all stakeholders. When the right patient gets the right treatment at the right time, patients get the best, most cost-effective care and payers, providers and life sciences companies all maximize their financial rewards.

Achieving greater success in this new paradigm is easier when you understand how and where your medication is providing the most benefits, and which performance metrics are going to best reflect your impact on the patient population. Optum data provides the insight that helps you determine which strategies to employ to maximize those benefits.

Create a healthier world.

To satisfy all the stakeholders in the health care continuum, life sciences companies must meet incredible information demands. Depending on the audience, they must prove that their product:

- Works and causes no harm
- Will contribute to controlling costs
- Is affordable/accessible
- Will create healthier/happier patients
- Will ultimately cure or manage the condition that is impacting the quality of a patient's life

Along the way, they must make critical decisions with incredible financial consequences as they develop and market their product. That presents a huge challenge that requires reliable data and expert analysis. Optum provides both.

Integrated data from Optum adds clinical specificity to eligibility-controlled health care resource utilization and cost information on an enormous scale that is unmatched in the industry. Add to that the skill and experience of our world-renowned analysts, and you'll have the data and know-how you need to develop and market products that can define the marketplace and drive real clinical change.

Optum data in action

Take a look at these real-world examples to learn how others are putting our data to work.

Understand the competitive landscape

THE CHALLENGE

A commercially-focused team promoting its brand in the immunology space wanted to better understand the competitive landscape across six different indications: rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, Crohn's disease and ulcerative colitis.

THE APPROACH

Rather than adopt a product attribute approach, Optum analyzed its EHR data to identify products that providers use to meet a similar clinical need in the real world:

Line of therapy
Understanding when each product is typically introduced to immunology patients illuminates the competitive set of products that prescribers consider for therapy.

Switching
Identifying products that have a high degree of mutual switching underscores products that prescribers view as treating a similar clinical need.

Clinical profile
Comparing the clinical profile of immunology patients prescribed each product shows how providers treat based on the clinical presentation of patients.

THE PAYOFF

Optum in-house clinical experts were able to define the metrics of interest across five different categories used in this analysis:

1. Lab results (from structured EHR)
2. Quantitative pain scores (from structured EHR)
3. Quantitative severity scores from provider notes
4. Qualitative symptomatology from provider notes
5. Qualitative pain characterization from provider notes

"In order for our clients to be successful in this new pay-for-value paradigm, they need to understand where their medication does the most good. They need to understand what performance metrics are going to best reflect their impact on the patient population. And then they need to understand what strategies they can employ, what levers they can pull to really maximize those benefits."

Meg Good, PhD
Vice President of Health Economics and Outcomes Research, Optum Life Sciences

Evaluate the market for NOACs

THE CHALLENGE

To find growth opportunities for a manufacturer of a new oral anticoagulant (NOAC).

THE APPROACH

Optum used a combination of claims and EHR data to conduct a comprehensive, in-depth study of the NOAC market. The study examined how the profile (age, health, riskiness) of atrial fibrillation patients using NOACs has evolved since the introduction of the medication and identified the brand market share drivers for NOACs. We also examined how provider brand preferences related to a patient's profile, what the relationship was between cardiologist and PCP prescribing patterns, and what those patterns suggested about the influence cardiologists have on those PCPs.

THE PAYOFF

We found a number of possible growth avenues, including opportunities with untreated, one-fill-only and primary non-adherent patients. We also found opportunities with relatively healthier and comorbid patients who were new to NOACs or who could be switched from one drug to our client's. Our findings also pointed toward taking a different approach when communicating with PCPs vs. cardiologists based on their NOAC preferences.

Drive market expansion

THE CHALLENGE

A company experiencing delays in its diabetes pipeline wanted to expand the market for its existing diabetes drug.

THE APPROACH

Using Optum EHR data, they found that the clinical profile of patients who use their drug was not what they assumed it was. The company was under the impression that their drug was being used by patients who have clinical profiles similar to those taking GLP1 and basal insulin products. What they found was that there was a much closer connection between the clinical profiles of patients taking their drug and patients taking SFUs.

THE PAYOFF

This allowed the company to expand its market by also targeting patients using SFUs.

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Data is essential to understanding where your product goes from here. The insights we gain from data help us understand which products are on the right path to improving patient outcomes, what adjustments if any are needed, and where we fall in line with competitors. With integrated claims and clinical data from Optum®, the path to pinpointing the real-world impact of your product becomes clearer.

optum.com

By Brian Solow, MD
Chief Medical Officer,
Optum Life Sciences

The emergence of **value-based contracting**

Medicare payments will increase from **30% to 50%** in VBR by 2018.

New England Journal of Medicine, March 5, 2015, Sylvia M. Burwell, U.S. Secretary of Health and Human Services.

As the U.S. health care system continues its transition to value-based care in an effort to stem the rising costs of care, the current contractual agreement landscape between payers and pharmaceutical manufacturers is giving way to a more innovative reimbursement methodology — **value-based contracting (VBC).**

Regardless of the term used — value-based contracting, outcomes-based pricing or risk-share agreements — the goal of VBC is to lower costs while improving both quality of care and member experience. This is achieved by tying reimbursement with how well the drug or medical device performs its intended use. VBC isn't exactly new to the pharmaceutical/device industry, but it has been slow to take off. So why all the attention now?

MANUFACTURER pain points

As prices increase and payers begin focusing on the clinical value, access to patients and providers becomes more challenging.

Rebates are becoming unsustainable for manufacturers due to increasing rebate rates and culmulative price protection models.

PAYER pain points

Payers need supplemental means in addition to rebates to offset the significant costs of medications.

Payers are struggling to qualify and quantify the clinical value of products and robustly correlate them to health care resource utilization.

SHARED pain points

There is a need to quantify clinical outcomes and to find a common value metrics between payers and manufacturers.

Pipelines are dominated by specialty products, forcing payers to focus on heavy control and favoring exclusions.

Determining the value of therapy interventions

The current contractual agreement system has been dominated by the traditional purchase discounts and rebate arrangement in exchange for product formulary access. The level of control through therapy interventions (step-edits, prior authorization, higher differential copay tiers) exhibited by a particular formulary is tied directly to a manufacturer's motivation to reduce the net drug spend through higher rebate payments.

Unfortunately, despite the advent of price protection terms in formulary contracts, the cost of many drugs has risen to an unsustainable level, and the true value of some medications is being called into question.

The term value depends on the constituency weighing it. Unlike Europe, where the quality-adjusted life-year (QALY) is routinely used in an economic evaluation to assess the value for money spent on medical interventions, there currently is no standard for the evaluation of the cost-effectiveness of drug therapy in the U.S.

For payers, value has a financial implication that is based on the cost of the medication or procedure and any cost offset that may occur as a result of the use of that medication.

For providers, the Centers for Medicare & Medicaid Services (CMS) is driving a fee-for-value reimbursement model with the intention to systematically improve care outcomes and reduce costs across the continuum of care through more collaborative and coordinated treatment. However, this shift in focus for providers will not be successful unless payers have a similar approach — emphasizing value of money spent on medical interventions as a basis for contracting with manufacturers.

Performance vs. outcomes

As drug prices continue to escalate, it is clear that the traditional model of purchase discount and rebate payments in exchange for access is not sustainable for many drug categories, in particular so-called specialty drugs.

While payers have long been utilizing levers that shift the financial responsibility for the cost of medications to the patient, employers recognize that there is a limit to this strategy. In response, payers have been experimenting with new contractual agreements that focus on the performance of a drug. It is an important distinction to use the word "performance" rather than "outcome." An "outcome" implies a broader view of care, often in a longitudinal setting, which may draw conclusions of

a pharmacoeconomic nature (for example, patient or disease state morbidity and mortality). For that reason, contractual agreements aimed squarely at evaluating the performance of a drug in the real world setting are using the moniker "value-based" rather than" outcome-based."

Given all the requisite caveats associated with the real-world use of medicines, the primary aim of VBC is to manage cost more effectively through tying reimbursement to the actual performance of the drug. Currently, there is no recommended standard for contracting in this manner.

While many payers have claimed to have multiple value-based contracts in place, this contracting effort is in its infancy with many key questions yet to be addressed, including:

- What metrics should be used (subjective vs. objective) for drug performance?
- What is the timing of reported data for rebate payment?
- How should rebate payments be structured to associate with drug performance?

Even if the basic construct is easily built, the challenges of potential financial impacts to government pricing calculations for the manufacturer, as well as avoidance of anti-kickback statutes and privacy concerns, remain.

When value-based contracts work

Value-based contracting works when great care is taken to ensure it a collaborative process among all stakeholders — and when stakeholders are engaged early in the process. It has been our experience that an effective and executable VBC incorporates flexibility and alignment of both clinical and business perspectives.

When executed correctly, a value-based contract offers significant benefits to both the payer and manufacturer in the ways that it:

- Quantifies clinical value into meaningful metrics between payers and manufactures
- Reduces the burden or supplements rebates
- Provides an objective evaluation of a products, impact on overall health care
- Enables payers to quantify/qualify clinical value
- Is design-driven and supported by robust data

The right VBC partner

Optum is uniquely positioned to help you design and develop value-based contracts with payers. The life sciences value-based contracting team at Optum offers an end-to-end contract development service from strategy inception to contract execution. We use a three-stage process to target appropriate assets and build meaningful contracting strategies that are operationally feasible and applicable across multiple payer archetypes. This approach also helps you engage stakeholders to ensure alignment and progression toward contract execution.

With deep experience negotiating contracts for a leading PBM, our core team is complemented by a broad range of expertise in data and analytics, health economics and outcomes research, and actuarial analysis.

Using our depth of capabilities and expertise, we provide support in clinical and trade evaluation, data analytics and actuary analysis. Optum value-based contracts are developed from a payer perspective, which helps you save valuable time and expense.♦

Components of a successful value-based contract

1. **Creates** value for all stakeholders
2. **Balances short- and long-term opportunities and risks** — want more than a one-year deal
3. Brings together groups critical to **establishing value-based contracts** — HEOR, actuarial and across-Optum, risk-based contracting groups
4. Leverages claims and select clinical data to **ensure understanding** of outcomes and patient segments
5. Leverages a "simulation" to **test uncertainties** if there are significant unknowns
6. Adjudicates based on **defined outcomes,** and squares up at year end

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Big data can transform our perception of health care — as long as we have the ability to interpret it. As a health services and innovation company, Optum® powers modern health care by combining data and analytics with technology and expertise. We embed substantive knowledge and context into our applications and data products, adapting epidemiologic principles to big data to arrive at actionable insights.

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By Dave Dore, PhD
Vice President, Epidemiology

Virtual EHRs

Developing patient profiles from "big data"

The clinical vignette provided by the detailed, structured review of an individual patient has served as a basis for medical communication and a foundation of medical knowledge for thousands of years. Published case reports help illustrate important considerations in routine patient care, and highlight important observations that might easily be missed by the untrained eye, or become lost in a sea of data from large collections of patients.

The current cachet of "big data" is a reflection of the real promise offered by the ability to make connections among innumerable points of data. However, this power complements rather than replaces the insights that can be obtained from narrative case reports. Big data can also enable the modernization and scalability of case review and reporting by providing a means to rapidly and efficiently compile the virtual patient-level medical record histories.

What are vEHRs?

Virtual electronic health records, or vEHRs, are curated patient records of de-identified individual patient profiles from health care claims and/or EHR data. These patient profiles are drawn from large-scale repositories of electronic health care data and investigator-specified selection criteria to provide a chronologic listing of relevant claims utilization and EHR information, including free-text summaries derived from natural language processing (NLP) procedures.

What do vEHRs — and Optum — offer?

Scalable

A query-able centralized data repository of Optum extensive data assets enables the identification of cases for review from among tens of millions of EHR records and over 100 million claims records. This scale enables the identification of large case series, including cases of rare or potentially isolated conditions or cases of conditions complex in presentation, and the rapid compilation of the virtual medical records (profiles).

Efficient

Provide rapid compilation into structured chronological listings of the patient experience from a centralized data repository.

Detailed

De-identified patient profiles combine health care claims with structured and unstructured information from EHRs.

Accessible

Profiles can be directly accessed via a secure web interface.

Address uncertainty

"Big data" is variable and changes rapidly. vEHRs enable intuitive exploration of the data for feasibility assessments, case series review and a range of other applications. Optum offers this data as part of a services package that includes epidemiology research and clinical knowledge, which is necessary for valid case sampling, and for curation of the human-readable data interface via AbsTrak.

> The current cachet of "big data" is a reflection of the real promise offered by the ability to make connections among innumerable points of data.

What are the seven potential applications of vEHRs?

1. **Data exploration and education**
   - Study feasibility
   - Availability of information in the source data
   - Training clinicians or data analysts
   - No hypothesis and few assumptions needed

2. **Rare diseases**
   - Historically, compilation of a certain number of cases is challenging for any single study
   - We start from a large source population
   - Rich clinical information
   - Inexpensive relative to rare disease registries
   - In certain settings, feasible to observe patients over sufficiently long time to characterize disease trajectories

3. **Medical product safety surveillance, public health surveillance, etc.**
   - Detecting adverse effects of treatment
   - Characterizing rare adverse events of medical care
   - Recognition of new disease variants — in particular, rare manifestations[1]

4. **Verification of adverse events of interest**
   When applied to integrated data, vEHR is an alternative to medical record abstraction with claims-based studies.

5. **Enabling the creation of complex variable definitions**
   - Some variables are pre-defined in the existing data; others require more exploration.
   - vEHR profiles can be compared to candidate patient classification schemes (variable definitions) to determine the validity of the definition or to enable experts to identify appropriate changes.

6. **Clinical trial planning/eligibility pre-screening**
   - Assess provider or patient populations for matches to clinical trials eligibility criteria via queries of structured and unstructured patient data.
   - Profiles could be used for feasibility study and/or as a prescreening tool for potential trial participant recruitment to "find out what we don't know about real-world practice."

7. **Publication of case series**
   Once reviewed, profiles can be directly incorporated into a manuscript by describing features of the cases and their clinical course and care, a process that has been referred to as meta-analysis of case reports. In this way, the average age (and distribution) of cases can be provided with their gender mix and timing of symptoms, diagnoses and treatments, along with response. In certain scenarios, as in rare diseases, this could represent one of the first sets of patients so described and could make for a manuscript in itself. ♦

1. Whereas isolated case reports have limited use, the capability to rapidly query for and compile large numbers of case reports can allow for characterization (clinical presentation, management, and disease course; patient demographic characteristics) and contextualization (potential risk factors, exposure duration) to inform the early perception of an emerging public health concern.

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In this competitive market, it can be difficult to ensure the right messaging about your product's true value is getting through to stakeholders. Optum® experts leverage powerful techniques with considerable expertise in market access strategy and health economics modeling to effectively present your product's full potential. With the right market access strategy in place for your product, you're free to focus on what's most important — improving patient outcomes.

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By Martha Bayliss, MSc
Vice President, Patient Insights

Giving voice to patients with rare diseases

All drug development programs should have a firm scientific foundation, and understanding the natural history of a disease is an important element in this foundation.

It is unfortunate that many rare diseases are not well understood. According to the Federal Drug Administration's (FDA) 2015 draft guidance: Rare Diseases: Common Issues in Drug Development Guidance for Industry:

> *"Many rare disorders are serious conditions with no approved treatments, leaving substantial unmet medical needs for patients. FDA recognizes that rare diseases are highly diverse and is committed to helping sponsors create successful drug development programs that address the particular challenges posed by each disease…*
>
> *All drug development programs should have a firm scientific foundation, and understanding the natural history of a disease is an important element in this foundation. Because of the small numbers of patients affected, and with clinical experience dispersed among a small number of clinical referral centers, the natural history of rare diseases is often poorly described."*

The FDA's industry guidance goes on to encourage life sciences companies to address these challenges by developing a clinical trial strategy that chooses appropriate endpoints and develops a better understanding of the symptoms and experiences related to these conditions.

Another FDA initiative focusing on **Patient-Focused Drug Development (PFDD)** clearly states the agency's expectations for representing patients' perspectives in drug development. For some rare diseases, the PFDD has compiled patient data to inform selection of clinical trial outcome measures that mean the most to patients. In that same spirit, the patient insights group within life sciences at Optum offers a uniquely patient-centered solution for a better understanding of rare diseases. Our patient-reported outcome (PRO) scientists understand the complex landscape of health measurement for rare diseases, for which disease-specific measures are rarely available.

A new approach to understanding natural history of disease

One approach for better understanding these patients' natural history of disease and treatment experience is to conduct non-interventional, observational studies of patients across the disease and treatment continuum. Results from these types of studies can be of great help in advancing knowledge, or can be misleading if not well-designed and implemented or if the right patients are not recruited.

Michelle White, PhD, senior scientist explains, "One key feature of these studies is the ability to reach a large number of patients quickly — that can't be achieved in typical studies working with several individual clinical sites. We use a variety of recruitment strategies and online screening and data collection with our Smart Measurement® System, often partnering with patient advocacy groups to take advantage of their credibility and established reach into the patient community. Our targeted participant communication real-person contact teamed with our automated email reminder system ensures high retention rates in longitudinal studies."

Patient insights from Optum

Optum can help developers of drugs for rare diseases to:

Fulfill FDA recommendations to document the natural history of rare diseases.

Gather critical information about patient experience and unmet need for treatment.

Inform selection of endpoints for efficacy trials and definition of treatment success.

Engage meaningfully with patient advocacy groups.

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