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Digital R&D

The Next Frontier for Biopharmaceuticals

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Editors
Sastry Chilukuri
Ann Westra

For more info please contact *Ann_Westra@mckinsey.com*

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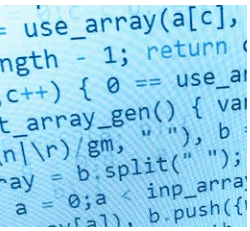

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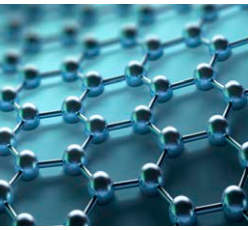

Contacts and references

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Digital in R&D: The $100 billion opportunity

Sastry Chilukuri, Edd Fleming, and Ann Westra

Digital promises to transform R&D productivity over the next decade. What will it take to realize this potential?

Healthcare today faces extraordinary challenges as aging populations, an increasing chronic diseases burden, and growth in the middle class in Asia transform patient needs. These stresses are placing new demands on innovation as health systems world-wide increase their scrutiny on value to address rising costs. Simultaneously, we are witnessing an unprecedented explosion of breakthroughs in science and technology that are redefining society and the practice of medicine.

All these changes have profound implications for biopharmaceutical research and development. Today's clinical environment is evolving rapidly and presents specific challenges: for example, the rise of personalized medicine and artificial intelligence has led to increasingly complex protocols and new end points; trials are more frequently targeted at smaller and harder-to-find patient populations; and competition has increased across the board, making the battle for trial sites and patients even more fierce. Biopharmaceutical company R&D is a series of high-risk, high-investment decisions and the industry is facing a considerable productivity challenge in terms of identifying, testing, and bringing new drugs to market, especially in the context of the highly innovative therapies we seek today.

The R&D productivity challenge

With the average pre-tax cost of each new prescription drug estimated at almost $2.6 billion[1] (including failures and capital costs) the spotlight is firmly on R&D productivity. The issue, long recognized, is that R&D expenditures have been increasing while drug approvals have largely been in decline for almost 50 years.

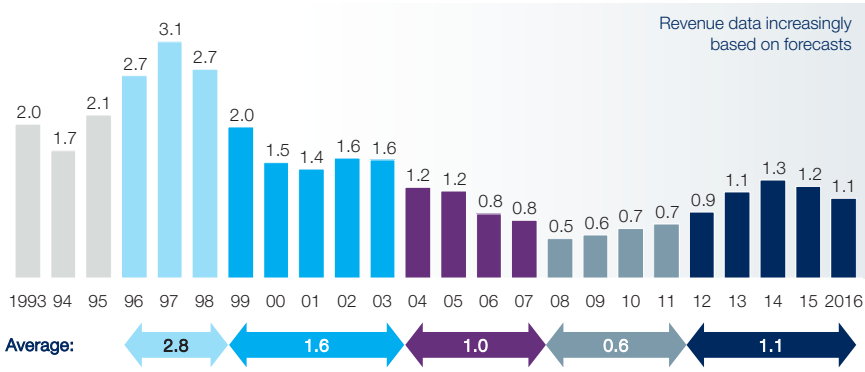
Digging further into this R&D productivity challenge in the biopharmaceutical industry, McKinsey analysis of the ratio of revenue to R&D spend shows that productivity reached its nadir between 2008–11—with return on investment (ROI) plunging to 0.5 in 2008—following a decade-long decline (Exhibit 1).[2]

Exhibit 1

Productivity is improving but there is uncertainty going forward

ROI vintage index over time

ROI vintage index = 7 years of revenues from NME launches[1,3] in a given year divided by the portion of R&D spend over the preceding 7 years corresponding to the given vintage[2,3]



1 NME-grade products, excluding generics, biosimilars, and NDA products (ie, new derivatives, reformulations, etc); launch year based on the global market entry and first reported/expected revenues; 3-year rolling average.
2 Assigned based on average R&D progression and proportion of spend attributed to different R&D stages.
3 Inflation-adjusted to 2017 US$; revenue values beyond 2016 are based on analyst forecasts.

Source: EvaluatePharma® May 2017; PhRMA 2016; McKinsey analysis

1 Tufts Center for the Study of Drug Development, "Briefing: Cost of Developing a New Drug," November 18, 2014, http://csdd.tufts.edu/files/uploads/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18,_2014..pdf.
2 The vintage index is defined as the ratio of the first seven years of revenue for all innovative launches in a given year to the corresponding portion of R&D investment over the previous seven years.

When we first analyzed this trend two years ago, the high failure rates for investigational compounds was the single largest driver behind the rocketing costs of launching a single successful drug.[3] Additionally, the blockbuster potential of new market entrants has often been exaggerated: an analysis found that 43 percent of consensus forecasts overestimated actual revenues by more than 40 percent.[4]

Encouragingly, however, the biopharmaceutical industry has found some recent reasons for optimism. Lately there has been a promising upturn in approvals and successful therapeutic launches, with productivity reaching a ROI vintage index of 1.3 in 2014. While the industry has not returned to the heady days of 1996–97, the ROI vintage index spiked at 3.1 in 1997. The signs of recovery in R&D productivity appear to be building some momentum. Developments in select therapeutic areas including oncology and the advent of technologies such as CRISPR[5] are opening up a new era of precision and personalized medicine—some of which is reflected in the rise in biotech valuations that we have witnessed recently. Yet, despite these silver linings, the cost of developing new drugs continues to be a cloud over the industry and the long-term R&D productivity challenge remains to be fixed.

So what lies behind this systemic decline in productivity and how is the transition to new science affecting R&D? In part, the industry's productivity problems stem

3 Kate Smietana, et al., "Improving R&D productivity," *Nature Reviews Drug Discovery*, June 12, 2015, pp 455–456, https://www.ncbi.nlm.nih.gov/pubmed/26065405. Kate Smietana, et al., "Trends in clinical success rates," *Nature Reviews Drug Discovery*, May 20, 2016, https://www.ncbi.nlm.nih.gov/pubmed/27199245.

4 Myoung Cha, et al., "Pharmaceutical forecasting: throwing darts?" *Nature Reviews Drug Discovery*, October 12, 2016, https://www.ncbi.nlm.nih.gov/pubmed/?term=sarraf+p%5Bau%5D+darts.

5 CRISPR: Clustered regularly interspaced short palindromic repeats.

from this very transition. While looking extremely promising for the longer term, realizing the possibilities of the genomic revolution has required considerable upfront investment to translate leads and potential into medicines that can benefit the patient. Moreover, the technology has generated an explosion of information, which has presented a new set of challenges for organizations—the equivalent of finding the proverbial needle in the haystack. Simultaneously, the hurdles relating to the regulatory requirements for demonstration of efficacy have also risen. Thus, balancing the risk-reward equation is becoming an increasingly significant factor for pharma: the failure costs of new molecular entities are climbing, which in turn are dramatically raising the overall cost of each NME.

The digital opportunity

Today we're witnessing the simultaneous maturing of numerous breakthrough technologies—genomics, nanotechnology, sensors and the Internet of Things, big data and advanced analytics, artificial intelligence (AI) and robotics, and 3D printing among others—that is unprecedented in human history. Broadly defined, digital is the application of these breakthrough technologies to radically reshape companies, industries and indeed broader society. This includes:

- Creating extreme winners and losers by industry
- Radically reshaping consumer to company interactions
- Transferring value to the consumer
- Dramatically lowering the cost base driven by technology/labor trade-offs across "processes"
- Dislocating the "role of the worker"

For businesses, it is paramount to reinvent the core and reimagine entire business models: products and services, research and development, sales and marketing, and channels. Within biopharmaceutical R&D, digital presents the opportunity to ensure better outcomes for patients via targeted therapies; significantly reduce the cost of drug development; and accelerate cycle times to get treatments to patients faster.

In 2013 we predicted that digital technology breakthroughs would transform biopharmaceutical R&D and the wider healthcare landscape.[6] At the time we anticipated a future where the following would not only be possible, but necessary.

- Predictive modeling of biological processes and drugs would become widespread as a result of R&D organizations using more diverse sets of molecular and clinical data. This would have a profound effect on the ability of manufacturers to identify molecules with the highest probability of successful development and to identify failures earlier.
- Patients would be matched to clinical trials using diverse data sources. They would be enrolled based upon factors such as genetic information—rather than via serendipitous visits to doctors' engaged in trials while the trials themselves would be smaller, shorter, less expensive, and generate better insights.
- Trials would be monitored "live" including using a diverse ecosystem of sensors and wearables around the patient to rapidly identify safety or operational signals requiring action, thus reducing costly delays.
- Data would flow freely among functions within pharmaceutical companies as well as to partners such as academia and contract research organizations, substantially speeding analysis and value generation.

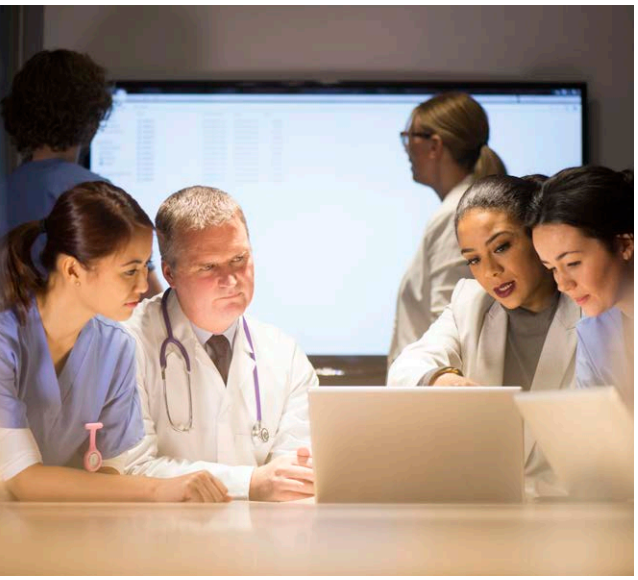
The only surprise for us today is just how much change there has been already and how fast these innovations have arrived.

Our vision for the future

Now, as we look toward the future of R&D ten years ahead, we glimpse an entirely new vista: a world where drug discovery is driven by machine learning and advanced analytics mining large data sets, enabling us to understand and visualize interaction with targets and to predict in silico a molecule's likelihood of success and reach approval in the market. Among many other innovations,

6 Jamie Cattell, Sastry Chilukuri, and Michael Levy, "How big data can revolutionize pharmaceutical R&D," April 2013, McKinsey.com.

we will see mainstream use of real-world evidence (RWE) to demonstrate the efficacy, safety, and outcomes of products with regulators, payors, and providers; a new model for conducting clinical trials where patients are enrolled as part of their routine care and rich data is collected through non-interventional means to improve the speed, cost, and quality of operations; the widespread use of sensors to collect rich information continuously from patients, and the broad-based application of artificial intelligence and deep learning to diagnose and treat patients.



This is a world that is completely digital—not simply digitized. While the latter applies digital technologies to current approaches (for example, moving from manual processes to paperless systems), going digital requires a complete rethink: deploying digital technologies to reimagine value chains and drive new innovation. Done right, we believe the size of the opportunity is $50-150 billion of EBITDA across the industry.[7] Given the nature of R&D, we think this journey will unfold over the next decade.

Achieving this vision

What then needs to be done and how do we set about architecting the digital transformation to achieve this vision? We believe that there are three key areas of focus that will unlock success[8]: the first two concentrate on areas of disruption that will transform R&D productivity, while the third targets the technology processes, culture, and mind-set that will underpin this transformation at scale.[8]

7 McKinsey analysis.
8 Sastry Chilukuri and Steve Van Kuiken, "Four keys to successful digital transformations in healthcare," April 2017, McKinsey.com.

1. **R&D in the age of analytics.** Companies that succeed at big data and advanced analytics outperform their competitors in every sector—for instance, Amazon in retail and Capital One in financial services—and we are currently at the start of the revolution in drug development. We see a wide range of use cases spanning R&D, including:

    - Mainstream use of real-world evidence for regulatory, payor, and medical applications
    - Use of data and analytics for next-generation clinical operations
    - Insights from in silico studies and analysis of diverse datasets to accelerate research and early development through more informed decision making, including smoothing the repurposing of existing drugs for new therapeutic areas
    - Building active surveillance capabilities to enhance pharmacovigilance (PV) operations and improve patient safety

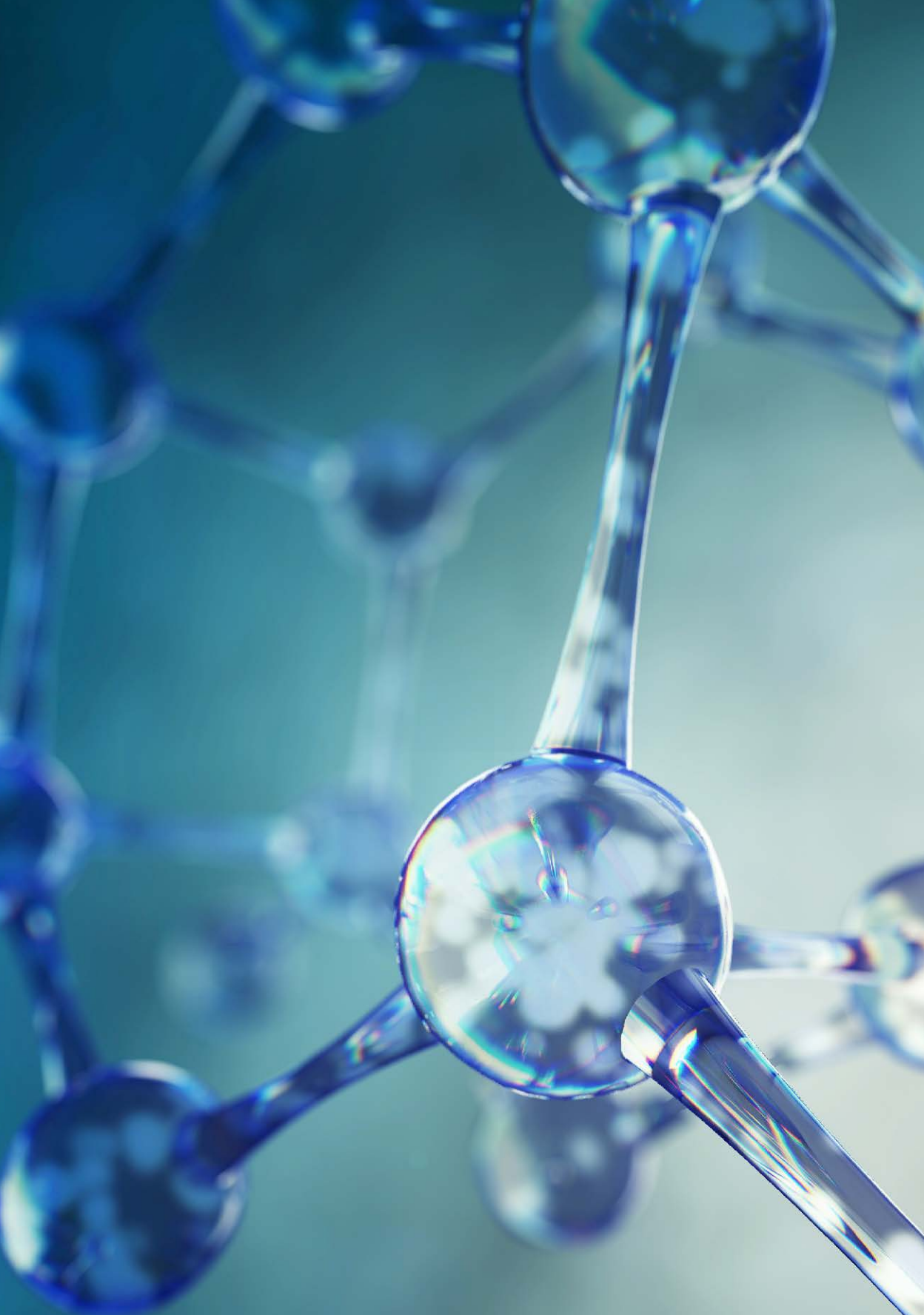
2. **Connecting with the individual customers.** It is no secret that the true impact of digital has been about reinventing the customer experience. Apple has successfully changed human behavior many times over, and technology winners such as Facebook, Netflix, Uber, and Amazon have simultaneously eliminated transaction costs while offering a delightful customer experience. A significant value driver within R&D will be reinventing how companies engage physicians, patients, and investigators at a granular level.

    - Through digital, medical affairs teams have the opportunity to understand the requirements of individual physicians (as well as other stakeholders) and to deliver precise information on demand.
    - Digital provides the opportunity to reimagine clinical trials around people. Patients will benefit from our greater understanding of their journey to improve their outcomes and trial experience including participation and adherence. Additionally, the use of wearables and other connected devices offers the opportunity to collect richer data automatically and enhance the experience of both patients and investigators.

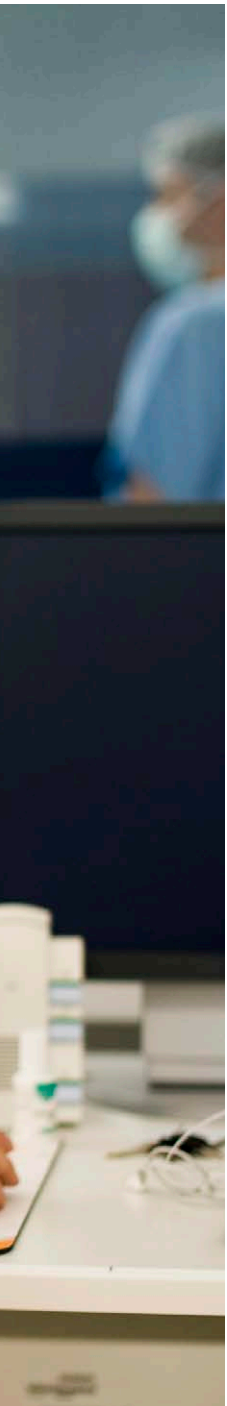
- Equally, adopting a partnership approach with investigators—understanding their specific pain points and deploying digital to streamline protocols and processes—will undoubtedly benefit sponsors in today's increasingly cluttered landscape of more complex trials.

3. **Designing the digital transformation at scale.** Most pharmaceutical companies are digital laggards compared with companies in other sectors such as media, retail, and telecommunications. Their digital-transformation efforts can stall for many of the same reasons these efforts are thwarted for others—for instance, a limited understanding of the specific ways that implementation of new technologies can create business value, a shortage of native digital talent, and insufficient focus on digital topics from senior leadership. Our experience with companies inside and outside the healthcare ecosystem suggests there are four core principles for succeeding with this kind of all-encompassing change program. First, healthcare companies (and R&D organizations) need to identify and prioritize their critical sources of value; they need to identify the capabilities that lead to competitive differentiation and those that would benefit most from digitization. Second, they must build their service-delivery engines—not just in managing new digital technologies but integrating agile, data science, and experience design into the fabric of the organization. Third, healthcare companies should look for ways to modernize their IT foundations: for example, moving to digital platforms such as cloud and Software as a Service, managing data and knowledge as a strategic asset, and improving security protocols for the company's crown jewels. Finally, companies must ensure that they build and maintain core management competencies including governance, financial processes, and organizational health—in other words, all the enablers that allow them to pursue a successful digital agenda.

These are the challenges and opportunities that lie ahead and we note that realizing the digital opportunity is no simple task—it represents a new innovation capability for the entire organization. What follows maps to each of these components to provide a broad-brush picture of how these momentous changes will play out in R&D over the next ten years or so, enabling us ultimately to plot a course through these uncharted waters.



R&D in the age of analytics



Real-world evidence: From activity to impact

Olivia Cavlan, Sastry Chilukuri, Matthias Evers, and Ann Westra

While there is general agreement that real-world evidence could significantly improve healthcare decision making, expanding its use requires action by multiple stakeholders.

Healthcare is rapidly transitioning to a new world of patient choice with a laser-like focus on outcomes and value. Indeed, healthcare systems that have traditionally focused on medical interventions driven via episodic interaction with the patient are now recognizing the need to fully understand exogenous factors and deliver continual care.

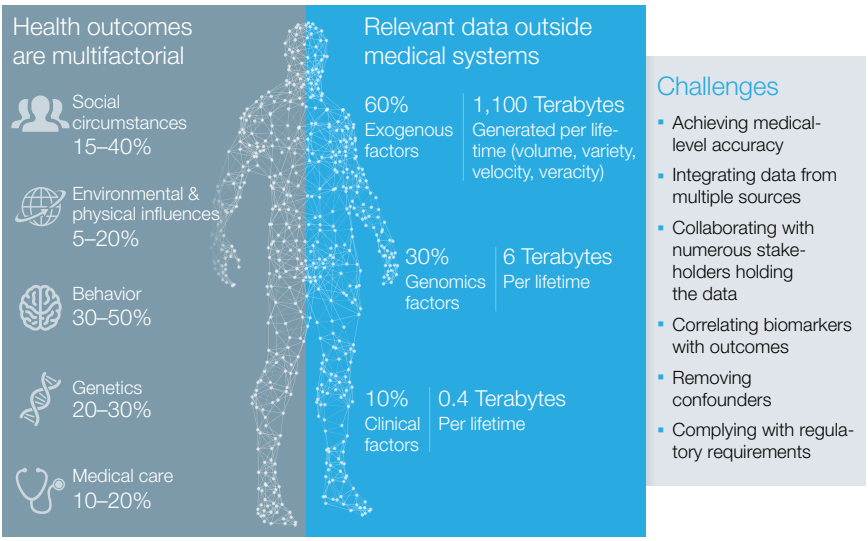
Exogenous factors such as genomics, behavior, and social and environmental influences play a critical role in delivering outcomes and value for patients and health systems; meanwhile, technology is finally allowing the capture and analysis of such real-world data (Exhibit 1).

Researchers from the US Food and Drug Administration (FDA) define real-world evidence (RWE) as: "Healthcare information derived from multiple sources outside of typical clinical research settings, including electronic medical records (EMRs), claims and billing data, product and disease registries, and data gathered by personal devices and health applications." They acknowledge that these datasets can "effectively complement the knowledge gained from "traditional" clinical trials, whose well-known limitations make it difficult to generalize findings to larger, more inclusive populations of patients, providers, and healthcare delivery systems or settings reflective of actual use in practice."[1]

1 U.S. Food and Drug Administration, "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices," August 31, 2017, https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm513027.pdf.

Exhibit 1

Envision a holistic approach to healthcare where all relevant data shapes decisions real time



Source: Health policy brief: "The relative contribution of multiple determinants to health outcomes," *Health Affairs*, August 21, 2014

Real-world data traditionally comes from four sources—clinical data, administrative/claims data, patient-generated/reported data, and emerging data sources including social media and cross-industry data collaborations such as Project Data Sphere (see sidebar "The ever-expanding trove of real-world data").

The data environment continues to mature rapidly, with public-sector organizations, not-for-profit organizations, and commercial entities compiling expansive data pools. A number of developed countries have accumulated

The ever-expanding trove of real-world data

Real-world data sources generally fall into four categories (although these could expand in the future):

Clinical data

These are patient-level data pulled from electronic medical records (EMR) and patient registries that describe how patients are treated in the real world. They include lab values, diagnoses, notes, and other information from healthcare visits with physicians and other care providers. With more data from hospitals and entire health systems becoming digitized and more easily integrated across institutions, the power of these particularly rich datasets (for example, larger sample sizes, easier comparisons across systems) is increasing.

Administrative/claims data

Detailed patient-level data is also collected for non-clinical purposes, primarily for billing by providers to insurers and other payors, which can include diagnoses, services provided, costs, and other data required for the reimbursement of healthcare services. Other more administrative sources of data can also include data collected for tracking purposes, such as patient or population surveys.

Patient-generated/reported data

This category covers individual data describing the patient's experience and is typically both collected and shared/reported by the patient. Today this source of data is less prevalent than others but will likely expand due to the increased use of wearable devices that automate data collection and sharing. Online communities such as PatientsLikeMe encourage and enable sharing of patient-generated data with peers and investigators.

Non-traditional, health-related digital data sources

As digital becomes increasingly prevalent in our lives, new sources of patient-level health data are emerging. These span social media posts that have a rich trove of information, especially health-focused social media sites like Sage Bionetworks. Project Data Sphere is a pharmaceutical industry-sponsored platform to share, integrate, and analyze phase III comparator arm data from cancer trials to accelerate research.

large datasets containing information about several hundred million patients (Exhibit 2). In parallel, large corporations such as IBM and IMSQuintiles are offering rich data sets of their own. Unstructured data are starting to yield interesting insights as well. Online communities such as PatientsLikeMe afford unique views of patients managing their conditions in real time. Recently, Microsoft collaborated on an effort to extract insights from analysis of search records to predict pancreatic cancer.[2] Retroactive analysis of search content (such as symptoms) were found to clearly identify 5–15 percent of the undiagnosed population several months before a formal diagnosis was made. For this deadly condition, those months can make a huge difference.

Exhibit 2

Sample high-value real-world data pools in prioritized countries

	Database[1]		Lives covered, Millions	Industry access
Japan	MHLW	National claims database	126	Possible through academics, often requires significant data cleaning
US	CMS	Medicaid/Medicare claims databases	120	Possible through academics, but with limitations
France	SNIIRAM	National claims database	60	None, limited to academics and health policy experts only
	PMSI	National hospital claims database	60	Through academics only, but future unclear due to privacy concerns
UK	CPRD	Electronic medical record (EMR) data from 10% GPs	53	Open, 80% of pharma companies purchase access to raw data
	HES	English hospital EMR database	15	None, raw data previously available before "care.data" concerns
Germany	AOK, WIdO	Regional public sickness funds claims data	24	Possible through academics but long wait times and reluctant to share with industry
	Barmer GEK		9	
	TK, Wineg		7	
Denmark	sundhed.dk	National cross-linked healthcare databases	6	Possible through academics, but time consuming

1 CPRD (Clinical Practice Research Datalink), HES (Hospital Episode Statistics), MHLW (Ministry of Health, Labour, and Welfare), PMSI (Le Programme de médicalisation des systèmes d'information), SNIIRAM (Système National d'Informations Inter Régimes de l'Assurance Maladie), WIdO (Wissenschaftliches Institut der AOK).

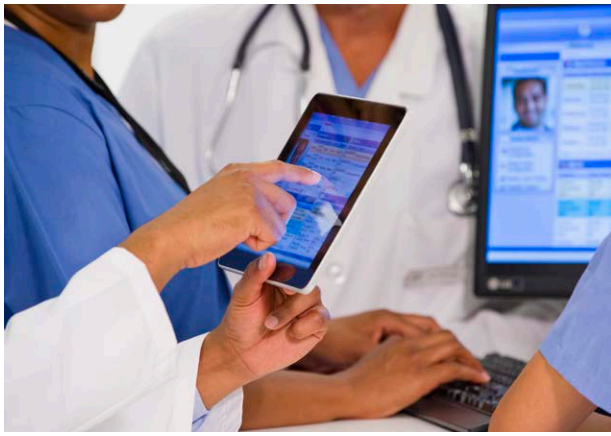
Source: Interviews with industry and other thought leaders; press releases; publications; websites

2 John Paparrizos, et al., "Screening for pancreatic adenocarcinoma using signals from web search logs: Feasibility study and results," *Journal of Oncology Practice*, June 2016, http://ascopubs.org/doi/full/10.1200/JOP.2015.010504.

Healthcare stakeholders are responding rapidly

The importance of real-world data continues to touch all areas of our lives, with stakeholders across the entire healthcare value chain—physicians, providers, payors, regulatory bodies, and pharmaceutical and medical device manufacturers—using real-world evidence to guide their decisions.

Physicians and providers rely on electronic medical records (EMR) data for physician-led clinical research while health system administrators use the same data to monitor the quality of care delivered across the system, including monitoring adherence to care pathways. Historically, many physicians have carried out chart reviews of their own patient populations, but with the growth of EMR, physicians can now quickly access the same data across a larger number of patients and institutions—an innovation that has transformed the impact of physician-led research. In the United States, consolidation of hospitals and healthcare systems has resulted in a larger scale of operations that in turn centralizes control over prescribing and requires a sharper focus on value as a consequence of risk-bearing contracts.



The United Kingdom is ahead of the trend, with the National Health Service already imposing value-based pricing for some therapies. For example, the NHS recently negotiated an arrangement with Janssen related to the use of Olysio (a Hepatitis C therapy) under which the NHS receives a rebate if patients are not cured after 12 weeks of treatment.[3] To improve results, Janssen offers pre-treatment blood tests to identify patients who might not respond to the treatment.

3 Eric Palmer, "Janssen agrees to rebate cost of Olysio to England's NHS if it doesn't work," *FiercePharma*, January 16, 2015, http://www.fiercepharma.com/pharma/janssen-agrees-to-rebate-cost-of-olysio-to-england-s-nhs-if-it-doesn-t-work.

Payors are analyzing their claims data to improve affordability of healthcare for members, and frequently integrate claims with EMR data to generate insights into the value and effectiveness of providers or protocols. More US payors are using outcomes-based contracts with providers: an estimated 80 percent of physicians and 100 percent of hospitals now have at least one such contract, and the percentage of payments that are value-based are estimated to have doubled from 10–15 percent in 2013 to 25–35 percent in 2014.[4] In Europe, health technology assessments are used to compare treatment patterns with National Institute for Health and Care Excellence (NICE) guidelines, and inform pricing and reimbursement levels. The UK's Systemic Anti-Cancer Therapy Chemotherapy dataset (SACT) was established in 2011 to document therapy across the United Kingdom, support treatment choices, and gain better insight into service provision and treatment patterns.[5]

However, when it comes to pharmacy costs, payors are still under immense pressure and continue to rely on traditional levers such as formulary status, co-pays, step edits, and prior authorizations to manage costs. Yet there has been movement recently with companies starting to enter into value-based partnerships with payors that link the net price of drug to expected outcomes. That said, while innovative contracts are growing in importance, they are not yet widespread.

Regulators use RWE to monitor the safety of marketed products through traditional pharmacovigilance tools (for instance, Periodic Benefit-Risk Evaluation Report, Periodic Safety Update Report, and Vaccine Adverse Event Reporting System) as well as newer digital aids such as the FDA Sentinel Initiative, a post-market active safety surveillance system.[6] Pre-approved use of RWE in efficacy decisions occurs today and there is potential for it to be used more broadly, such as in oncology, rare diseases, and pediatric conditions

4 Statistics derived from the following sources: Availity, Catalyst for Payment Reform, CMS, Health Affairs, MedScape.

5 Leela Barham, "Real-world evidence for pricing and reimbursement: the potential of Systemic Anti-Cancer Therapy (SACT) data," *Pharmaphorum*, January 15, 2015, http://pharmaphorum.com/articles/real-world-evidence-for-pricing-and-reimbursement-the-potential-of-systemic-anti-cancer-therapy-sact-data/.

6 *Sentinel Initiative Final Assessment Report*, September 2017, https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM577502.pdf.

when randomized controlled clinical trials are impossible or unethical to conduct.[7] In parallel, legislators are recognizing the value of RWE. In the United States, the 21st Century Cures Act passed in December 2016 establishes public-private partnerships to collect data and improve understanding of diseases, supports patient-focused drug development, and modernizes the design of clinical trials and their review process.

There is an emerging desire by regulators to make RWE much more central to their activities. This is reflected in the FDA's efforts to integrate data collected from electronic medical records, claims data, and registries to create a unified system for monitoring the safety of medical products.[6 (p 18)] Similarly, a National Institutes of Health (NIH) Common Fund has been established to build infrastructure, operational knowledge, and capacity for "pragmatic research" that incorporates electronic health records and other real-world data into large-scale distributed research networks to allow researchers to identify cohorts of interest more easily and expedite studies.[8]

Pharmaceutical companies have rapidly progressed in their use of real-world evidence. Generation I (circa 2011) had limited use of RWE and was heavily focused on safety and post-market. Generation II (2011–15) saw more integrated use of RWE across the end-to-end product lifecycle during which it was deployed to support regulatory decisions, advance disease understanding and clinical guidelines, and support outcome-based reimbursement decisions (Exhibit 3).

7 U.S. Food and Drug Administration, "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices," August 31, 2017, https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm513027.pdf; Scott Gottlieb, MD, "Advancing Public Health Opportunities with Real World Evidence," National Academy of Sciences, September 19, 2017, https://www.fda.gov/NewsEvents/Speeches/ucm576519.htm; Rachel E. Sherman, MD, MPH, et al, "Real-World Evidence — What Is It and What Can It Tell Us?," *The New England Journal of Medicine*, December 8, 2016, http://www.nejm.org/doi/full/10.1056/NEJMsb1609216.

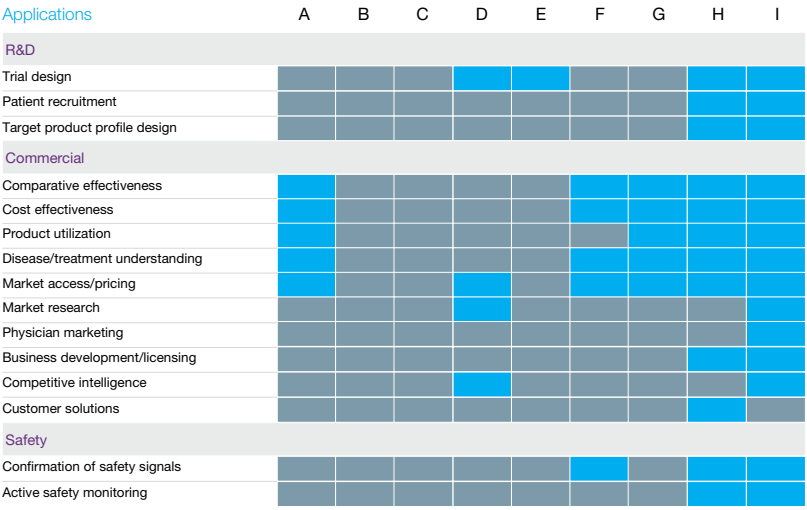
8 National Institutes of Health, Healthcare Systems Research Collaboratory, "About us," https://www.nihcollaboratory.org/about-us/Pages/default.aspx. Accessed September 15, 2016.

Exhibit 3

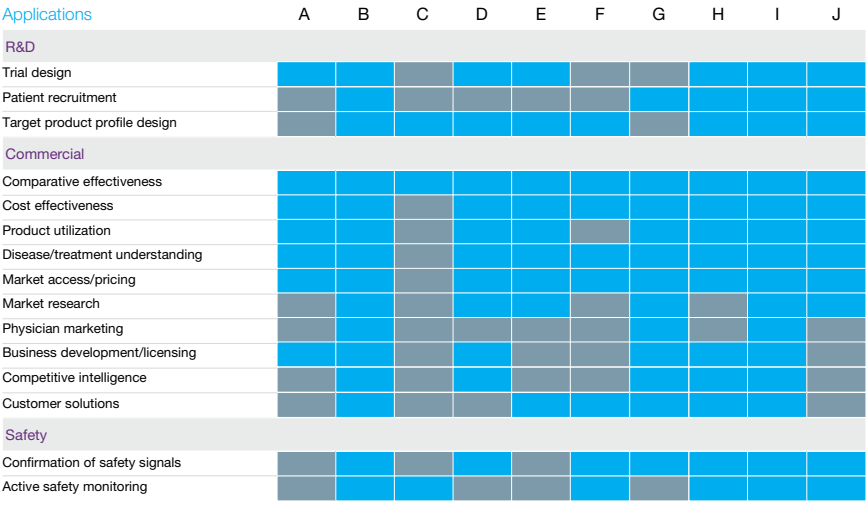
Evolution in the use of real-world evidence

RWE impact recognized
RWE impact not recognized

Generation I (2011): focus on safety and post-market



Generation II (2012–15): end-to-end product lifecycle



Source: McKinsey RWE benchmarking 2011 and 2013

In general, evolving RWE strategies over the past two to three years reflect companies' increasing recognition of the importance of these capabilities. Their efforts have been translated into organizational changes with the real-world evidence function becoming more centralized as companies seek to elevate standards and quality.

Today, we see a greater focus on the insights derived from real-world data, as well as recognition of the impact these can have on improving decision making and patient care both internally and by regulators, physicians, and payors (Exhibit 4). Indeed, the senior leadership in many pharmaceutical companies has invested in and built out centralized RWE capabilities around data acquisition, standards, and processes. Typically, these centralized teams sit in global medical affairs to promote the cultivation of more robust RWE science and support a broader vision for the real-world evidence function (Exhibit 5). That said, RWE capabilities around study design and management are more likely to remain scattered across the organization; this creates a challenge for RWE leaders to make a case for RWE with line leadership as compared with other, more traditional approaches to evidence generation (such as randomized controlled trials). Top talent engaged in RWE activity is broadly recognized as the key differentiating factor of leading RWE organizations—these organizations need people with deep knowledge of real-world data and analytics, business leaders with strategic vision, and communication skills to make a case for real-world evidence across the organization and externally.

Exhibit 4

Three generations of real-world evidence
Generation III (2016): Focus on insight and impact

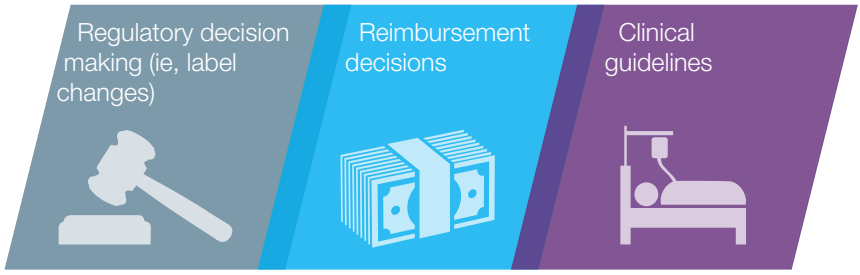
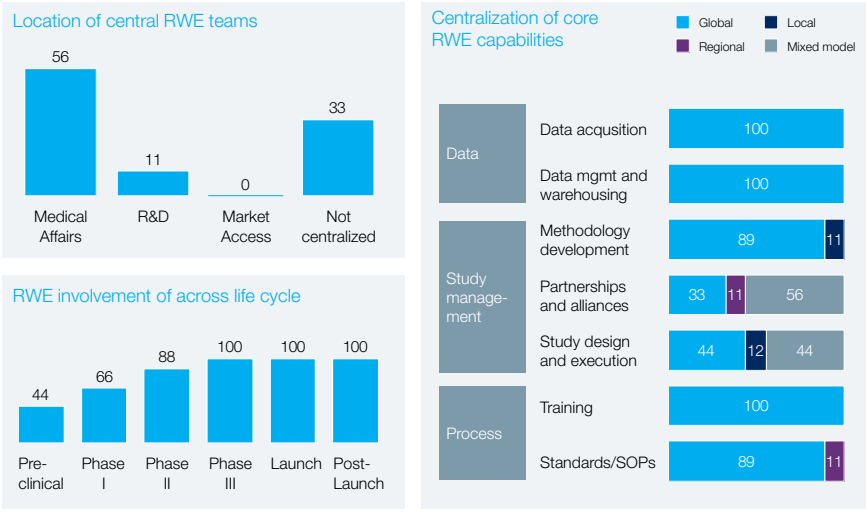


Exhibit 5

Approaches to centralization of RWE teams

% of companies



Source: McKinsey RWE Benchmarking (2017)

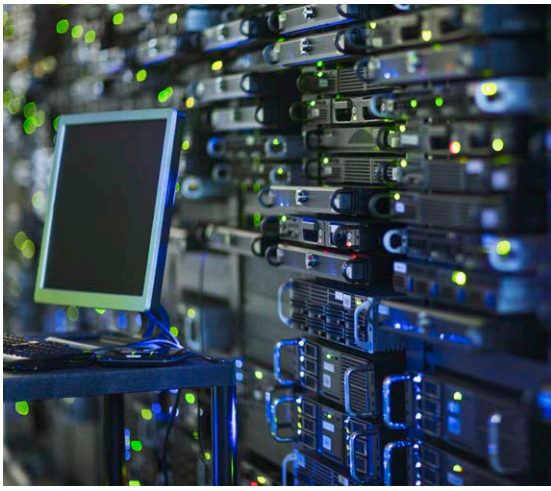
Barriers to increased use of real-world data

Among the most significant barriers to expanding use of real-world data is the consensus that randomized controlled trials (RCT) remain the gold standard for demonstrating the efficacy and safety of medical products and treatments. This consensus, shared by physicians, patients, payors, and regulators alike, creates significant hurdles to using RWE, even though there is a growing recognition that RCT alone cannot provide sufficient data for informed healthcare decision making in some situations. Because RWE can capture the use of medical treatments in real-life settings it could be used to better understand and characterize patients, and evaluate new treatments when randomization to placebo for clinical trials may be impossible, impractical, or unethical. In addition to the

preference for RCT, other barriers to developing and using RWE exist and need to be addressed to realize the potential of this data source.

Uneven quality of real-world data sources

Valuable real-world data exists in many countries, although it is most prevalent in the United States and Europe. Policies promoting collection of real-world data vary widely even within these regions, a reality that significantly impacts the quality of data, with data fragmentation remaining a major challenge. Some countries—such as those in the Nordic region—have developed rich databases cross-linking a patient's health data with other national databases, but these datasets reflect relatively low national populations. Bigger countries, such as France and Germany, have built large national databases covering millions of lives but generally these are narrowly focused on the claims data required to manage their healthcare system. It is critical to have policies and incentives in place to promote data capture by physicians and high-quality inputs into the database, especially in countries with nationalized healthcare systems, in order to build a database that can also be used for scientific research into public health.



Limits to access to real-world data

More uniform access to existing real-world databases for medical research could improve data quality. However, there is not consensus among patients, physicians, politicians, and the general public regarding the potential public health benefits of real-world data. Privacy concerns related to allowing access to these large datasets and the potential results of advanced RWE analytics have restricted both the collection and sharing of existing data. Although there is stronger support for access by independent academic research (in comparison with industry-sponsored science), data access remains one of the primary hurdles to advancing the science of RWE analytics.

Lack of standardization of RWE analytics

Despite the potential value of real-world data, it is also clear that a lack of standardized methodologies to develop RWE undercuts its broader use. Unlike RCT methodologies and practices (for example, Good Clinical Practices [GCP], and other practice quality guidelines), which are well developed and understood, the same cannot be said for RWE. Poor-quality analyses, limited transparency into methods, and bias in results are just a few of the issues that a lack of standardization brings. Rigorous, yet practical, methods and practices are needed to define how collecting, analyzing, and reporting real-world data should be done. Today, many RWE analytics are retrospective or observational—both of which are problematic. To be influential and useful, real-world data needs to be susceptible to robust analytics to confirm that data methods have eliminated biases, controlled quality, and allowed for integration of disparate data sources for both prospective and retrospective studies. Greater transparency around RWE study design and results is needed, similar to the publication of other pharmaceutical company studies through clinicaltrials.gov.

Varied public support for RWE

Even if the technical aspects of using real-world data ethically and responsibly for the benefit of public health are resolved, there remains a huge education task to convince stakeholders that the benefits of real-world data collection and analyses outweigh the risks of sharing such personal information. Some countries—for instance, Denmark—are having public discussions about developing a national health database; while, in the United Kingdom, general practitioner concerns about privacy and accountability are stalling the rollout of a real-world data platform. No country has resolved all the issues, but lessons can be drawn from current discussions to shape future policies.

While real, all these barriers can be overcome with concerted effort by stakeholders, particularly if stakeholders collaborate to advance RWE in partnership with data providers.

Signs of growing acceptance of real-world evidence

Despite these hurdles, we see growing use of real-world datasets within a narrow set of circumstances. As detailed above, RWE is used most commonly by pharmaceutical companies, payors, and providers to better manage their organizations and make decisions about cost-effectiveness and comparative efficacy where other more robust data sources do not exist. Today, real-world data may sometimes be the best available source of safety data for on-market products as demonstrated by the preference of payors for their own data over clinical trial data, and by the FDA's Sentinel Initiative which uses claims and EMR data from many different databases to characterize and study potential safety risks of marketed products.[6 (p 18)]

Even so, realizing the vast public health benefits of these datasets will require broader use of this type of data. Real-world evidence can play a greater role in assessing efficacy, especially in situations where randomized controlled trials do not or cannot provide the data needed. However, large-scale expansion hinges on regulatory-approved approaches to RWE analytics. There are also some early signs that RWE is starting to be accepted by regulators, physicians, and patients for benefit decisions. Notably, this is occurring in a small subset of rare disease areas, such as oncology, orphan diseases, and similar therapeutic areas. Situations that support RWE are typically characterized by a lack of other therapeutic options, where the condition is seen as a life-threatening disease, where it affects a small population size, and/or the effect is easily measured. As RWE becomes increasingly accepted, we expect to see situations which meet some but not all these criteria supporting the use of RWE (see sidebar "Emerging regulatory use cases for real-world evidence in benefit assessment").

Incorporating RWE as an integral component of the data package on a product across the lifecycle (for example, from proof of concept to loss of exclusivity) would increase the knowledge of all stakeholders regarding potential benefits and side effects. With more robust data, improved methodology, and greater clarity about regulatory frameworks, RWE analytics in the short term could support:

- Therapeutic effectiveness, for instance by suggesting new and effective benefits for new products or for additional indications, assessing the optimal doses of approved products
- Understanding special populations that could benefit from a product, including protected populations such as the elderly, pregnant, or pediatric patients, while also enabling better understanding of effectiveness in patient sub-populations
- Fulfilling post-marketing requirements—for example, committing to RWE analytics after approval to further understand product benefit
- Enhancing the label to better inform patients and healthcare practitioners of important information not included in approved indication (such as adding benefit/risk information from observational studies)

Next steps

Real-world evidence could significantly improve healthcare decisions across the health system and ultimately improve patient care. Expanding its use, however, will require multi-stakeholder action on several priorities, as well as company-specific campaigns. The broad healthcare community is best equipped to make progress on the following goals:

1. **Increasing understanding and communication of RWE value drivers while focusing on high-impact use cases.** RWE analytics delivers valuable information, which frontline staff are responsible for getting, into the hands of payors, healthcare providers, and regulators to improve their healthcare decision making. A significant elevation of frontline capabilities across medical affairs, commercial, development, and health economics and outcomes (HEOR) will be required to share these analytics in a compliant and impactful fashion.
2. **Creating an operating model that drives integration and adoption of RWE and manages risk.** This should include coordinated funding linked to milestones, an integrated evidence plan, and a governance process to

Emerging regulatory use cases for real-world evidence in benefit assessment

Looking forward we see five use cases emerging for using real-world evidence in the benefit assessment by regulators.[7 (p 19)] Companies are just starting to include RWE in regulator submission packages that meet the following criteria.

1. **RWE used to establish historical controls.** When patients cannot be randomized to placebo such as in life-threatening orphan diseases with no adequate therapeutic options, historical controls are needed. Before the advent of EMR, physicians would physically scour old patient charts to build historical controls for regulatory submissions. Now with the advent of electronic medical records, this patient-level data can be assessed on a larger number of patients more easily and effectively.
2. **Early approval with RWE post-market monitoring.** In these cases, drugs for life-threatening diseases without adequate treatment options would be approved based on strong early clinical evidence (for example, approval based on only phase II or III randomized clinical trial) and be required to complete post-market monitoring via RWE only. In these disease states, some companies have struggled to recruit sufficient numbers of patients within a reasonable time frame to meet regulatory requirements for post-market randomized controlled trials; suggesting that RWE analytics may be a better approach in some cases.
3. **On-label RWE from another country submitted.** These are cases where a drug has already been approved outside the United States. For example, after an initial rejection for an expanded indication, NovoSeven was approved for those indications based on RWE collected through registries located primarily in Europe and Canada.[9]
4. **Medically accepted alternative-use RWE submitted for new indications.** Electronic medical records can contain rich data on drugs being used off-label for medically accepted alternative uses (for instance, based on recommendations in clinical guidelines developed by physicians). Today, this data has been included in a handful of successful regulatory submissions, but this is likely to increase.
5. **Medically accepted alternative-use RWE submitted for expanded populations.** Similar to RWE supporting use for new indications, electronic medical records contain rich data on drugs being used off-label for new populations (for instance, those not included in initial approval such as children, pregnant women, and also disease sub-populations such as patients with less severe disease). RWE was the sole data source evaluated by the FDA for the approval of the Sapiens transcatheter heart valve for an expanded patient population.[10]

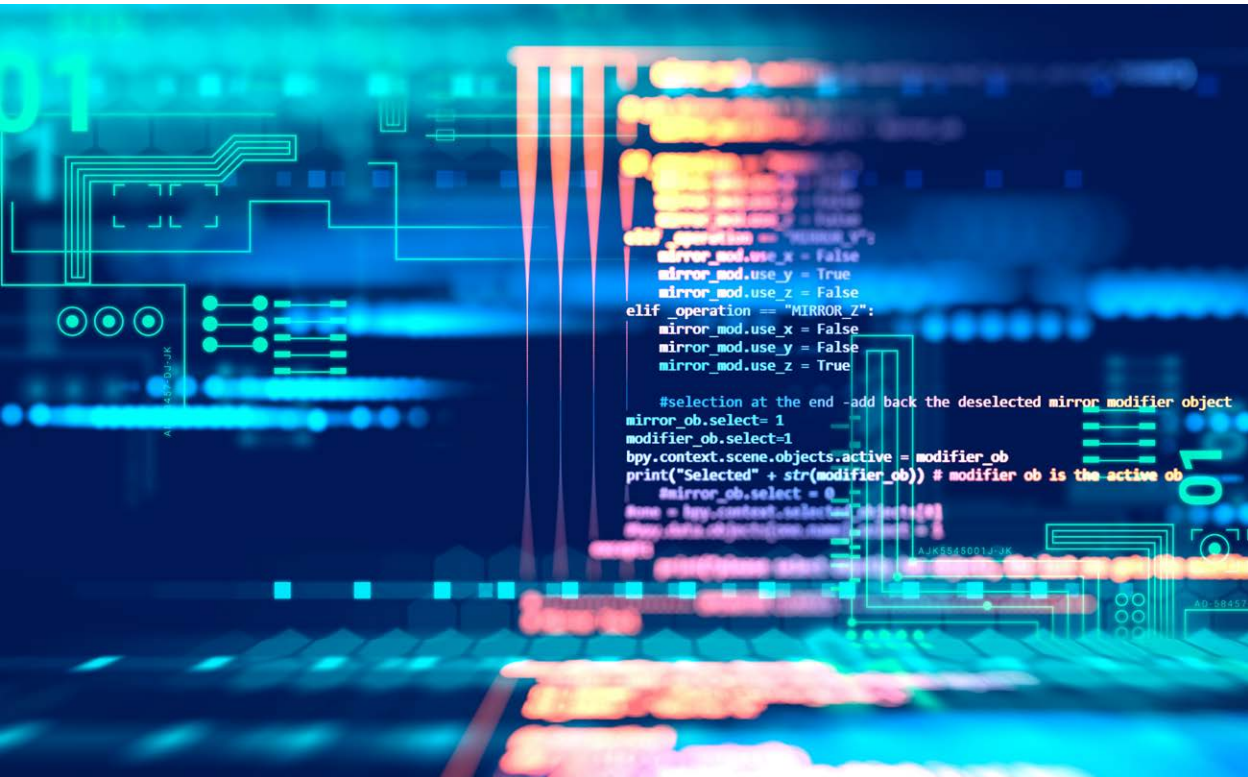
9 Novo Nordisk, "FDA Approves NovoSeven® RT for the Treatment of Glanzmann's Thrombasthenia (GT) With Refractoriness," July 7, 2014.
10 Jeffrey Shuren, MD, JD, and Bram Zuckerman, MD, "How Creative FDA Regulation Led to First-in-the-World Approval of a Cutting-Edge Heart Valve," *FDA Voice*, June 14, 2017.

manage risk from RWE activities. An integrated evidence plan (IEP) can link CDT/GCT, regions, and countries which clarifies collaboration and establishes a dossier. Accountable directly to GOC to oversee RWE operating model, RWE leaders will need to establish processes to manage risk especially in small countries and across functions (for example, commercial) as this output is typically not included in the product label, yet may be critical information for physicians, patients, payors, and others to improve healthcare decisions and patient outcomes. Additionally, an "Early Patient Insight and Value Output Team" (led by a DAS commercial leader) can coordinate across stakeholders and regions to uncover insights and architect solutions. RWE leaders must ensure the appropriate mix of non-interventional studies, and build internal capabilities across multiple study designs to improve internal decision making. Ultimately, RWE leaders are needed who can develop a RWE strategy, lead the execution of a RWE study, and communicate the outputs across the entire range of non-interventional studies being carried out internally and externally.

3. **Shaping an integrated, adaptive partner ecosystem.** Companies will need to identify academic collaborations to ensure credibility and trust in analyses, as well as gain access to novel data sources. Unbiased academic experts are needed to address short-term concerns around credibility and trust of these analytics. Companies may also need to consider partnerships with subject matter experts that have defined roles, such as in analytics. In the long term, investment in building RWE expertise across the entire healthcare industry will be needed to elevate the science and methodology of RWE analytics so that it is on par or even better than RCT in specific situations. Similarly, partnerships with database owners will be required in the short term to use data in restricted access databases, especially large, government-funded databases of public health systems in Europe which typically restrict access to this data. In the long term, however, such partnerships could demonstrate the public-health benefits of RWE to both database owners and the public at large to build support for higher-quality real-world databases and expanded access to them.

4. **Building platforms at scale to manage and analyze data in a rapid, low-cost fashion.** RWE leaders must simultaneously capitalize on the benefits of RWE over RCT and address the inherent weaknesses of real-world data sets. Building platforms and capabilities—including data infrastructure and storage—to increase the turnaround time and decrease the cost of RWE studies is critical to being able to utilize this data for internal business decisions. Platforms can also incorporate standardized methodology, which can be applied across all studies, improving the robustness and credibility of outputs.

Making progress on these goals will establish the kind of culture where RWE innovation will flourish, while ensuring that necessary, complementary capabilities exist to support both traditional R&D activities focused on clinical trials and RWE research.



Randomized pragmatic trials: Can they fulfill their promise?

Arnaub Chatterjee, Sastry Chilukuri, Michael Pencina, Eric Peterson, Saif Rathore, and Vijay Vaidya

Thoughtful collaborations between industry and academia can help randomized pragmatic trials gain acceptance as we seek more efficient ways to conduct studies.

While the principles behind the conduct of a randomized pragmatic trial (RPT) seem intuitive, their translation into real-world examples can be hampered by real or perceived barriers. Too often, trials originally designed as "pragmatic" expand to full "bells and whistles" randomized pragmatic trials that lose their original nimbleness. This may happen for several reasons: traditional operational teams can drive the most pragmatic designs back to "standard procedures," researchers desire to answer more and more questions in a single study, or there can often be real or perceived regulatory requirements. Although many leaders of regulatory agencies have pushed for more pragmatic approaches, this message has not always been heard when decisions are taken regarding specific trials.

Equally, however, there are major factors facilitating more pragmatic approaches. The most significant of these may be the volume of data collected and made available for research. The nearly universal adoption of electronic medical records (EMRs) in the United States creates unprecedented opportunities for pragmatic clinical trials. These clinical data offer the potential of better study planning, easier patient identification and recruitment, ready baseline data collection, and easier follow-up. Effective use of this data, nevertheless, requires

a sophisticated understanding of appropriate uses of EHR, which is not widespread, particularly among pharmaceutical manufacturers.

Multiple RPTs have been successfully conducted, including the Salford Lung Study, MI FREEE,[1] and the ongoing ADAPTABLE trial, which compares the risks and benefits of two different low-dose aspirin regimens for prevention of cardiovascular disease. ADAPTABLE is a RPT that draws from EMRs, Medicare claims, and patient-reported outcomes.

It is important to realize that ADAPTABLE has several features that make it ideal to be run as an EHR-based RPT, which many other types of trial may not satisfy. The drug being evaluated here is over-the-counter, therefore, safety reporting and drug distribution are simplified. Additionally, the outcomes measured in ADAPTABLE are "hard" (clinical events) and thus easy to verify in hospital records (that is, hospitalizations for myocardial infarction and stroke).

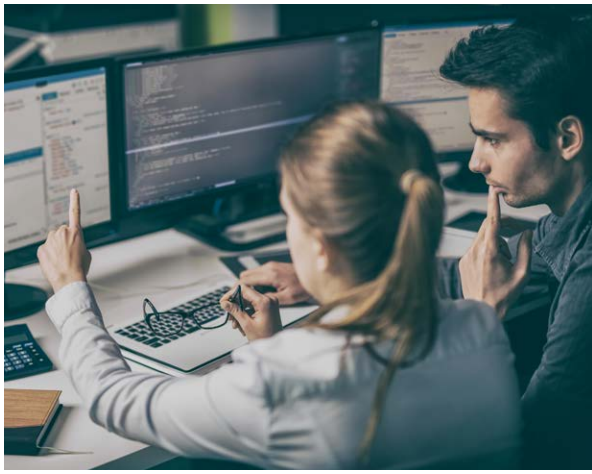
Another set of opportunities for RPTs lies in efficient trial design. The use of meaningful composite outcomes, "borrowing" of data from past experiments on the same population, different forms of trial adaptation, and early detection of unsuccessful treatment arms can all substantially decrease the number of patients who need to be randomized. Furthermore, limiting data collection to what is necessary, together with efficient interim monitoring that incorporates "quality by design," can result in better trials conducted for less money.

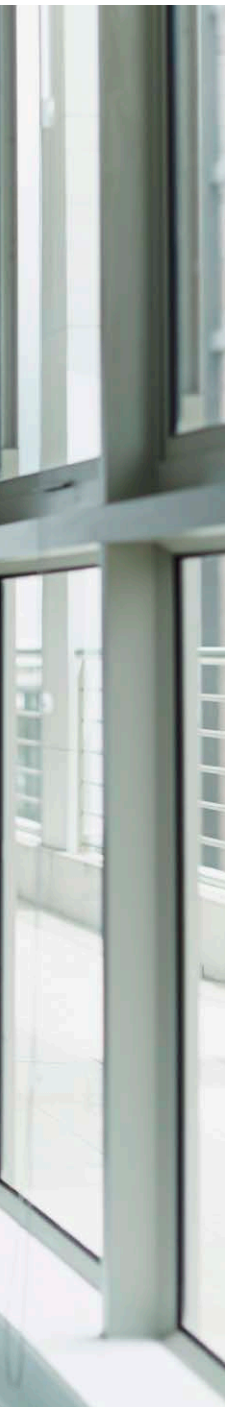
The most important step in enabling greater use of RPTs is a change of mind-set. This needs to occur within the organizations sponsoring clinical research, among those responsible for conducting the research, as well as among the regulators—a few successful examples of modern RPTs will go a long way toward paving the road. Engaging with those who are not afraid to innovate is necessary to achieve meaningful progress.

1 Niteesh K. Choudhry, MD, PhD, et al., "Full Coverage for Preventive Medications after Myocardial Infarction," *The New England Journal of Medicine*, November 14, 2011, http://www.nejm.org/doi/pdf/10.1056/nejmsa1107913.

Beginning the process of change will happen by ensuring that RPTs are aligned with questions that reflect clinical, economic, and policy priorities. Accordingly, ensuring that RPTs are well designed, built upon the correct data infrastructure, reflect meaningful clinical outcomes, and incorporate robust analytical capabilities will be necessary. This approach, particularly when framed in the context of strategic priorities, is rarely found within pharmaceutical manufacturers today.

Bridging this gap will require manufacturer, academic, and strategic collaborations that draw on each group's strengths. To that end, industry-sponsored RPTs can play an important role. By demonstrating that RPTs can be used to evaluate patented agents, these studies would begin to break down assumptions surrounding regulatory barriers to approval. RPTs can provide more tangible measures of effectiveness and assess the real-world outcomes that payors are increasingly requesting. Sponsors should not be afraid to invest in trial innovation and understand that this investment may not pay off in the first few applications: there is a learning curve to successful disruption, and mistakes and inefficiencies will happen along the way. To navigate this process, sponsors will benefit from guidance from thoughtful collaborations between academia and industry, such as between Duke Clinical Research Institute and McKinsey & Company. Through an iterative process, these collaborations can provide guidance in understanding the role of RPTs, preparing for RPTs, and aligning RPTs with strategic priorities. We are at an important junction in the history of clinical research where the role of RPTs is still being defined. RPTs cannot replace randomized controlled trials for answering definitive questions around efficacy. Yet, in the context of untenable costs, increasing demand for relevant evidence, and ample sources of new data, it is clear that RPTs have a role to play.





The next generation in clinical operations performance

Sastry Chilukuri, Edd Fleming, Eoin Leydon, Fareed Melhem, and Michael Steinmann

The potential impact of advanced analytics in clinical operations is significant and wide-ranging: from faster, lower-cost trials to higher data quality.

Challenges facing clinical development

The clinical environment is changing rapidly and simultaneously becoming more complex: the rise of personalized medicine has led to increasingly complex protocols; trials today are more often targeted at smaller patient populations that are also harder to find, while competition for sites and patients is becoming ever more fierce; meanwhile, continuing globalization of clinical operations requires a coordinated effort across countries; meanwhile, clinical operations continue to globalize, requiring a coordinated effort across countries.

Against this backdrop, then, it is no surprise that the execution of clinical trials has become increasingly challenging. A recent report from the Tufts Center for the Study of Drug Development estimated the capitalized cost per approved new molecular entity (NME) at over $2.5 billion—a 500 percent increase over the past 20 years.[1] While attrition rates account for some of this increase, the per-patient cost of clinical trials is also a major driver, consistently rising more than 10 percent a year over that same period. Not only is it more expensive

1 "Tufts CSDD Assessment of Cost to Develop and Win Marketing Approval for a New Drug Now Published," Tufts Center for the Study of Drug Development, March 10, 2016, http://csdd.tufts.edu/news/complete_story/tufts_csdd_rd_cost_study_now_published.

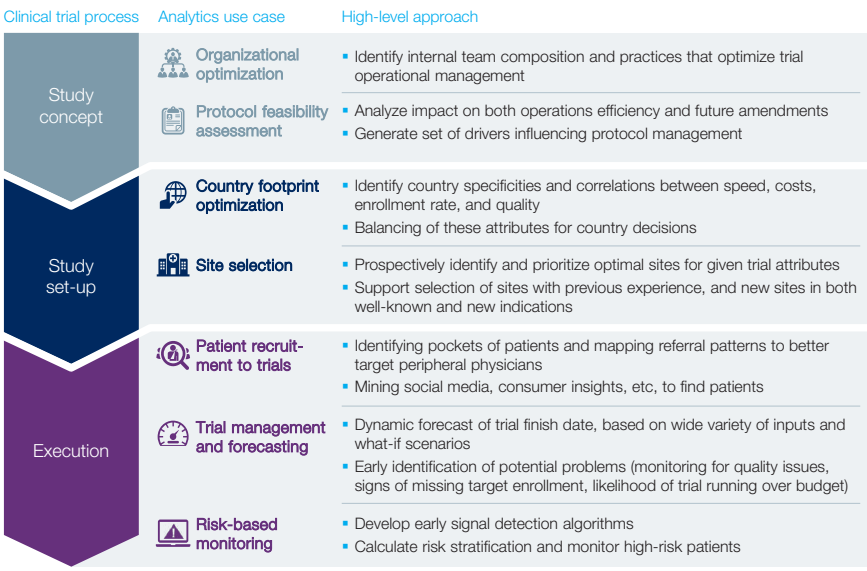
to run trials, it is also increasingly more difficult to do so successfully as a multitude of new drugs in a wider range of therapeutic areas makes patient recruitment more challenging: 80 percent of trials fail to meet enrollment timelines, directly impacting revenues, by reducing the time at peak sales.[2]

Advanced analytics provide an enormous opportunity to improve the way trials are designed and run. We have seen significant improvements across the trial value chain, from protocol design, footprint optimization, and site selection to patient recruitment, and through trial management and quality monitoring (Exhibit 1).

Here, we lay out the most exciting applications of advanced analytics in clinical trials and discuss what it takes to execute and capture value.

Exhibit 1

Analytics use cases in clinical operations



2 Jim Kremidas, "Recruitment roles," *Applied Clinical Trials*, September 1, 2011, http://www.appliedclinicaltrialsonline.com/recruitment-roles.

Advanced analytics use cases in clinical operations

Advanced analytics can drive performance improvement along the length of the clinical trials process.

These use cases have moved from theory into practice in recent years, enabled by advances in data, analytics, and technology:

1. An explosion in the volumes and variety of data collected (such as operational, quality, finance, communications) and new methods of translating unstructured data into machine-readable forms (for example, natural language processing, fuzzy matching, image processing)
2. Advances in analytic techniques to find patterns and make sense of the data (for instance, machine learning, deep learning)
3. Scalable cloud technologies and distributed programming frameworks, which have slashed the time and cost to set up an environment to host massive linked data and apply the necessary computing horsepower to crunch through complex algorithms

Thanks to technological advances, data and analytics can unlock hidden opportunities for efficiency. By finding and identifying and aggregating the smallest variations in performance, data can now provide executives with new capabilities to manage clinical trials. Bioharmaceutical companies that view their data as an asset and develop new capabilities in machine learning and predictive analytics can fundamentally transform their clinical trials across multiple locations. The impact can be far reaching—optimizing tasks from finding suitable patients and managing limited resources across their portfolio to meeting strategic and regulatory requirements. Across a clinical trials network even small improvements in these areas can add up to huge cost savings.

1. Protocol optimization

Recruitment challenges often begin with protocol design. Overly complex protocols can severely slow trial completion times and lead to an explosion of costs; however, pharmacos must balance a desire for simplicity with the increasingly complex nature of their products and the accompanying data.

Advanced analytics can support decision making through scenario planning, helping to frame trade-offs. Natural language processing and machine learning has opened the door to conducting in-depth analysis of protocols to better measure the impact protocol features have on enrollment rate and patient attrition. We can now better understand the incremental effect of an additional inclusion criterion or data collection feature (for example, a lab test) on overall trial performance; this enables clinical leaders to more fully understand the tradeoffs between clinical desires and operational impact. Leaders in the space have analyzed troves of past protocols and are developing predictive models to estimate the impact that specific protocol decisions would have on enrollment.

We can also use advanced analytics to understand the implications of trial design on data variability and strength of signal. For example, analyses can be undertaken to look at the variability in end points based on sites selected, inclusion criteria including specific patient populations, and decisions around sample size. These can help inform specifics of the protocol, as well as impact of potential site-level variability on outcomes.

2. Footprint optimization and site selection

Today, companies tend to select trial sites based on recent experience or internal connections. Increasingly, companies are also using historical benchmark data to guide decision making. However, such methods do not work because of one simple fact: past site performance is not predictive of

future performance, even in the same disease area. Our analysis shows that a site's historical performance only accounts for 10–30 percent (depending on disease area) of expected performance in the next trial. A number of other factors are critically important in determining how a site will perform, including:

- **Complexity of protocol and screening approach**—Sites perform differently on ability to execute depending on both the overall complexity of the protocol and the specifics of the procedures required.
- **Site congestion**—The number of ongoing trials at a site impacts both enrollment rate and default rate, although not always intuitively. For example, in certain therapeutic areas having multiple trials at a site actually improves the enrollment rate, as those sites become hubs of patient flow. In other therapeutic areas, however, we don't see that effect.
- **Patient density and referral patterns**—Mapping patient populations and how they flow into sites can help identify sites likely to see more patients. This is especially powerful when overlaid with competitive trial maps, which account for competing trials at both the site and in the region.
- **Drug scientific excitement**—We have also seen a segmentation across sites and investigators in terms of how they perform, depending on the excitement generated around the molecule. Some sites are more attracted to the most talked-about or scientifically interesting molecules while others perform more consistently regardless of the molecule.

Counterintuitive learnings

- Historical performance only predicts 10–30 percent of future performance, missing significant value.
- Overlap in sites selected between trials for the same indication is often below 20 percent even within a company, suggesting a real opportunity to improve how we identify and allocate top sites.
- The impact of site congestion is complex, and varies by therapeutic area and indication. For some TAs, having multiple active trials at a site actually speeds enrollment.
- Even in lowest-cost countries, operations can vary dramatically; there is a five-fold variation in enrollment rates among the lowest-cost countries.
- Predictive quality risk monitoring can improve effective auditing by four times, and can also spot signs of trial and site quality risks earlier.

Integrating all of these different drivers—not to mention layering on country footprint requirements—would be a near impossible task using the typical approach. However, by integrating internal company data (clinical trial management system, electronic data capture) with external data sets, including real-world data and publicly available trial data, we can develop algorithms that are significantly more predictive of site-level performance. One client was able to improve enrollment rate 20 percent by applying these techniques.

3. In-trial forecasting and early signals of delays

Ensuring that trials are completed on schedule depends on meeting trial milestones, and taking proactive interventions to resolve issues before timelines start to slip. The enrollment phase of trials is the hardest to manage because activities are happening at site and country level, so often biopharmacuetical companies are not aware of a problem until deadlines are approaching or are missed which leads to delays and the need for costly "rescue" sites.

Traditional methods for monitoring enrollment rely on experts assimilating information from across a wide range of sites, relying on personal experience, and basic performance metrics to make judgments on the future trajectory. These judgments tend to be optimistic—the classic "J-curve" for how enrollment is just about to pick up—and the overall picture of trial-level delays only emerges late in the process.

Some companies are now taking a machine-learning approach, enlisting algorithms that can learn from the tens of thousands of historical cases of site enrollment and incorporate all measurable drivers, and then applying them

to active trials to obtain much more accurate predictions much earlier in the process. This increase in accuracy and timeliness means that trial leaders are warned of upcoming delays much earlier—between 25 and 50 percent of the way through the trial—and can take action to get a trial back on track.

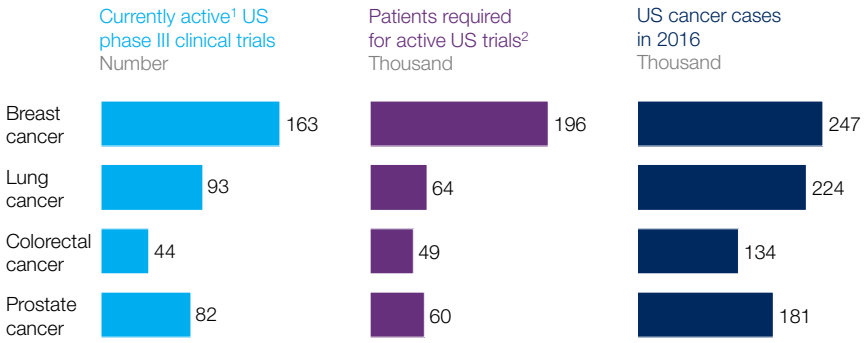
4. Patient recruitment

Patient recruitment is an increasingly acute challenge for sponsors as the number of trials continues to multiply faster than the population cohorts that participate in them. If we take oncology as an example, we see a number of indications where the patients required for trials is close to the total number of patients available (Exhibit 2).

Exhibit 2

Competition for patient recruitment is becoming a critical challenge as therapeutic areas are increasingly crowded

ONCOLOGY EXAMPLE



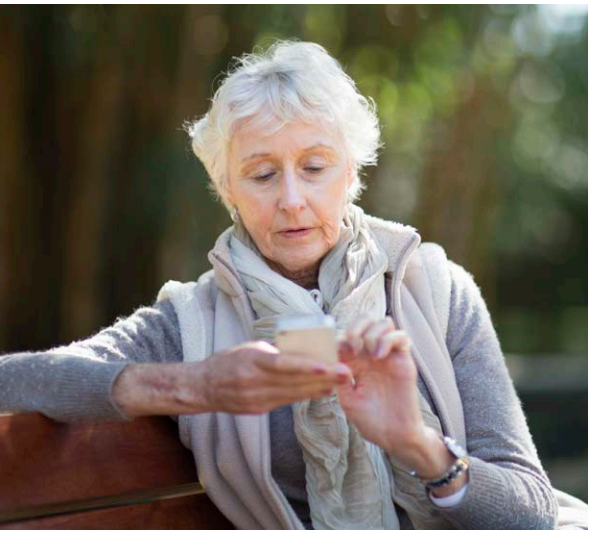
1 As of 21/11/16 and includes trials where recruitments status is one of the following: recruiting; active, not recruiting; enrolling by invitation.
2 Total interventional trials with above recruitment status compiled from Clinicaltrials.gov online database. Includes enrollment for all locations, also beyond US.

Source: American Cancer Society; ClinicalTrials.gov

A simple analysis of data from clinicaltrials.gov suggests that this is true for several other indications as well. Indeed, one study found that 19 percent of

trials terminated due to failed accrual, or completed with less than 85 percent expected enrollment, seriously compromising their statistical power.[3]

When patients are scarce and hard to find, analytic approaches can greatly improve on traditional methods by delivering insight at a granular level into where patients are and how they end up at trial sites. Using real-world data derived from claims and/or electronic medical records (EMRs), we can create local area maps that include patient populations and also track referral flows into sites. By mapping referral flows, it is possible to identify breakages in the chain where specific physicians are either not referring at all or referring only a few patients. Using this information, it is possible to target awareness messaging at these physicians to drive referrals.



Additionally, analytics and digital are creating new avenues to go directly to individual patients, who are increasingly taking charge of their own health decisions. Perhaps the simplest use of digital to speed recruitment is through dissemination of information via online, mobile, and social channels. Most sponsors and investigative sites now have searchable online databases of ongoing trials that direct patients to investigators. Increasingly, we are seeing that a more targeted approach to using social media for trial recruitment is needed—one that uses specialized social networks for specific patient populations. Several patient advocacy groups, as well as independent companies, have set up these patient-centric social networks. In addition, online communities devoted to a specific condition provide a useful recruitment source for trials, and are actively used by some sponsors.

3 Carlisle, B., et al., "Unsuccessful trial accrual and human subjects protections: An empirical analysis of recently closed trials," *Clinical Trials*, 2015, 12(1), pp. 77–83, https://www.ncbi.nlm.nih.gov/pubmed/25475878.

Data-driven trial matching is another approach to improving recruitment. Assuming patients consent to having their health information used, health records data can be mined to identify patients who would benefit from a given trial, with alerts then sent automatically to clinical staff. This approach has been used to great effect by single investigative sites, and some specialized EMR vendors are exploring broader use as well. Population health management companies, laboratory service providers, and contract research organizations (CROs) also have a wealth of data that can be mined for this purpose, and the potential has resulted in major strategic partnerships and acquisitions.

5. Predictive site quality risk

Ensuring quality and mitigating risk in the context of clinical trials is a critical issue for pharmaceutical companies, affecting patient safety as well as the integrity of data underpinning trial results. Risk-based monitoring is well established, deciding on monitoring resources across trials and sites based on the overall assessment of risk. However, it is now possible to take this to the next level, by using in-trial data processing and predictive analytics to dynamically reassess the risk and nature of issues at the site level.

The first challenge is collecting all of the relevant information about site quality, and translating this into machine-readable form. For example, issues captured in site visit reports are written in free text with only a small fraction of the information in a structured format. Using Natural Language Processing, algorithms can now identify themes in this text, and label the specific issues that are being raised. Applying this technique across thousands of active sites—and tens of thousands of sites on historical trials—delivers a data source that can then be properly analyzed, and combined with other flows of information from sites to develop a comprehensive view of the situation.

The next stage is to use this data to improve performance and better manage risk. Companies are now starting to develop and use predictive risk models to identify the likelihood of quality issues occurring at a site, similar to the way banks assess the risk of default. This analytical lens enables monitors to prioritize which sites to visit, and which risks to focus on; at a country and global level it provides the company with the opportunity to improve quality, while simultaneously managing resources better.

Achieving sustainable impact

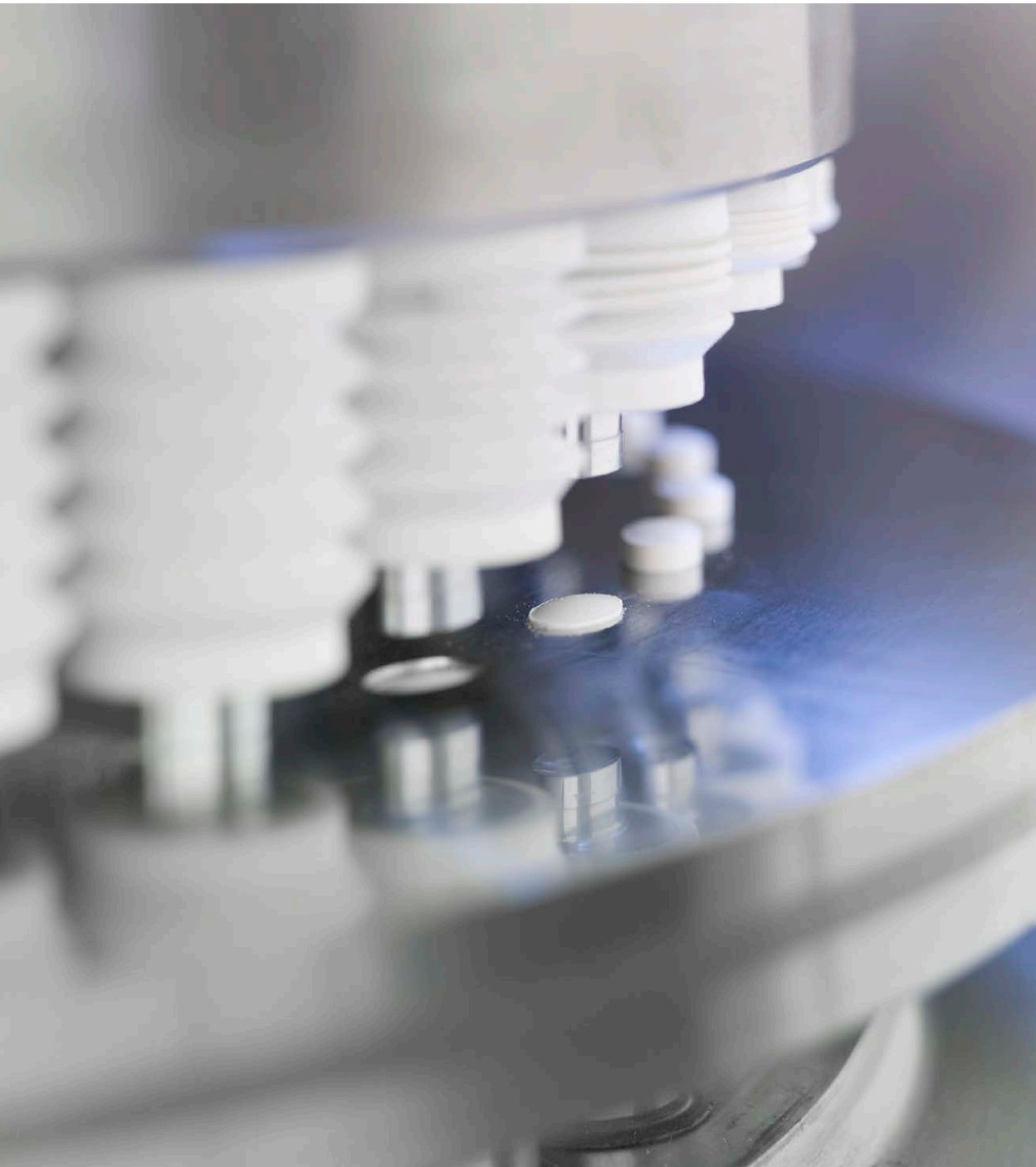
The potential impact of advanced analytics in clinical operations is enormous—from significantly faster trials, to lower cost, and higher data quality. This is critical irrespective of whether you are looking to optimize your insourced trials or seeking to monitor your CROs. Nevertheless, achieving success is not simple. We have seen several instances where promising pilots have withered on the vine either because they didn't solve a core problem or they didn't have organizational buy-in. To drive better decisions through analytics, we have identified a number of key success factors:

- **Take a fresh look at your own performance first to understand where the biggest opportunities are, and develop a use case–first approach.** It is common for leaders in clinical operations to feel like they already know all of the available trial sites and drivers of performance. This may not be totally unfounded, as deep institutional knowledge and personal familiarity with investigators and sites resides in most companies. Nevertheless, while this can certainly be an asset, it can also be detrimental when people get stuck in routines. Through our analytics work we have found many results that are surprising, even counter-intuitive. Start with an open mind; take an evidence-based approach to your self-assessment and prioritize a handful of opportunities that would be most impactful to your business.
- **Understand the relevance of data and analytics on your specific situation.** There are a large and growing number of off-the-shelf solutions targeting many of the use cases we have discussed. While these can be useful tools, we believe the greatest impact comes from the integration of company internal data with external data, and the development of algorithms on top that are specific to the company's unique circumstances and internal practices. Succeeding in these areas requires the ability to identify and integrate multiple data sources relevant to your needs, develop tailored algorithms, and integrate changes into workflows to drive better decisions.
- **Do not wait for the perfect data set because it will never arrive.** The data you generate as part of day-to-day operations is one of your most important assets, so work out how you can make use of it now. The two

most important lessons we have learned from helping companies make use of their data for business improvement are: 1) the power of linking a wide range of data sources; and 2) making the best use of your current data, and then improving over time. Advances in data-processing techniques mean that you can now create links between previously disconnected legacy systems, and transform unstructured data. Meanwhile, we see countless situations where organizations embark on multiyear programs to fully transform and integrate data systems—while the business waits. Such IT transformation and "data hubs" are needed, and will prove valuable when delivered, but they should not delay innovation. Start now with your priority analytics use cases and improve them over time as data improves. New data sources can be added as they come online.

- **Do not separate analytics out of the business.** Analytics should be viewed as a core capability, and a central part of the business decision-making process. Ensure analytics are developed in a way that supports decision makers. Analytics for analytics' sake don't help.

- **Do not underestimate change-management requirements.** These techniques will be foreign to much of your organization, and at times will challenge the established way of doing things. Engage your business leaders both at the global and country level early in the journey to build understanding and gain buy-in. As you develop, these predictive and optimization analytics pilots will transform into new capabilities that allow you to do things that were previously not possible; meanwhile, your business processes, and your people, will need to adapt in step to fully capture the value.



Moving beyond serendipity in drug discovery

Sastry Chilukuri, Leeland Ekstrom, Jonathan Usukura, and Ann Westra

A systematic approach to drug repositioning is poised to reinvigorate pharma.

As the biopharmaceutical industry strives to improve R&D productivity and meet the twin challenges of rising development costs and patent expiration, the opportunity beckons to reposition existing compounds to benefit more patients. Several firms have extended the protection of existing molecules this way, capitalizing on their known safety profiles while repurposing them for new use cases; at the same time, companies specializing in drug repositioning or repurposing are expanding.

There have been several high-profile and somewhat surprising repositioning success stories.

- Perhaps the most well known is Sildenafil, which failed phase II clinical trials for angina, only to be reborn as Viagra to treat erectile dysfunction due to its unanticipated "beneficial side effects."[1] Later it was repurposed again for pulmonary arterial hypertension.
- Thalidomide was thought to be a dead molecule when its use was tied to birth defects, yet its successor variation Thalomid is a leading therapy to treat multiple myeloma as well as other cancers.[2]

1 Miranda Hitti, "Viagra Ingredient OK'd for Lung Problem," *WebMD*, June 8, 2005, https://www.webmd.com/lung/news/20050608/viagra-ingredient-okd-for-lung-problem#1.
2 Stacey L. Adams, "Thalidomide: the teratogenic drug that found a role in cancer treatment," *HemOnc Today*, April 10, 2009, https://www.healio.com/hematology-oncology/news/print/hemonc-today/%7B29d6f4c4-0398-4cb4-aedf-c6d816d95a9c%7D/thalidomide-the-teratogenic-drug-that-found-a-role-in-cancer-treatment.

It is estimated that repositioned and rescued drugs now represent 30 percent of drugs approved and 25 percent of current pharmaceutical industry revenues.[3] Yet, despite the known successes and the support available to biopharmaceutical firms to undertake repurposing, there are significant barriers to implementing in practice.

- First, many companies are not structured—nor are their R&D teams resourced—to facilitate repurposing. Moreover, even if the resource gap could be closed, the mind-set shift required of teams typically focused on discovering new molecules is significant.
- Because of the customer and financial benefits of repositioning, companies need a strategy to integrate basic repositioning practices into their R&D operations rather than banking on serendipitous discovery of new uses for molecules (see sidebar).

Organizations, both public and private, are now mining data such as molecular pathways, DNA mutations, and gene expression to enable better prediction of potential new indications for a molecule. The combination of ever-expanding data sources, increasing computational power, and growing technical and analytical sophistication of several service providers can make repositioning a compelling component of a biopharmaceutical company's strategy.

Nonetheless, both practical and emotional barriers exist to maintaining repurposing capabilities in large biopharmaceutical companies.

- On a practical level, once a drug fails an initial trial the discovery team frequently breaks up. Without a clearinghouse or defined process to investigate different uses, there is no "owner" to try to resuscitate the molecule for a secondary purpose.
- On an emotional level, it's difficult for scientists to maintain enthusiasm for a molecule that has the stain of failure—fear of a second failure and anxiety about what was missed in the initial brief often combine to motivate scientists to distance themselves from a molecule—even though they are the most obvious sources to try to rescue it.

3 Dr. Stephen Naylor, et al., "Therapeutic Drug Repurposing, Repositioning and Rescue," *Drug Discovery World*, Summer 2015.

Risk and reward

Advanced analytics enable companies to move from obvious adjacent indications to uncovering more innovative opportunities with greater intellectual property and commercial potential. We view repositioning as a continuum of potential risk and reward.

- **Serendipitous—**Responsible for many current examples of repositioning, serendipitous discovery typically relies either on observation of side effects or off-label usage of the molecule in clinical trials or the market.
- **Rational—**Rational repositioning is typically based on screening other drugs with the same mechanism of action. For example, psoriasis and multiple sclerosis are related by immune and inflammatory mechanisms, suggesting the potential for a molecule like DMF to act on both.[4] Another example, imatinib was expanded from Chronic Myelogenous Leukemia (CML) to five other indications based on understanding the mechanism of action of tyrosine kinase inhibitor.[5]
- **Systematic—**Systematic discovery extends rational discovery with the data sources, analytical capabilities, and organizational constructs needed to make it happen at scale. Increasing industry interest has spawned new biotechs, technology startups and academic centers focused on repositioning. Leading large pharmaceutical companies are acquiring, partnering with, and investing in capabilities to support repositioning. Novartis[6] is partnering with Cyon, and Lilly[7] with Denovo Biopharma.

4 Ratul Kumar Das, et al., "Recent advances in the biomedical applications of fumaric acid and its ester derivatives: The multifaceted alternative therapeutics," *Pharmacological Reports*, April 2016, Volume 68, Issue 2, http://www.sciencedirect.com/science/article/pii/S1734114015003448.

5 *Journal of Market Access & Health Policy*, 2013, 1: 21131.

6 Stacy Lawrence, "Novartis licenses its anti-PCSK9 to sepsis startup Cyon," *FierceBiotech*, August 23, 2016, http://www.fiercebiotech.com/biotech/novartis-licenses-its-anti-pcsk9-to-sepsis-startup-cyon.

7 "Denovo Biopharma Licenses Late-Stage Neuroscience Drug From Lilly For Development As A Personalized Medicine," *Cision PR Newswire*, March 3, 2015, https://www.prnewswire.com/news-releases/denovo-biopharma-licenses-late-stage-neuroscience-drug-from-lilly-for-development-as-a-personalized-medicine-300043642.html.

Adopting a systematic approach would address these realities by providing resources and capabilities for developing and managing the lifecycle of a molecule, including repositioning efforts.

Benefits of repositioning

The very real benefits of repositioning make it an important lever for biopharmaceutical companies committed to improving R&D productivity.

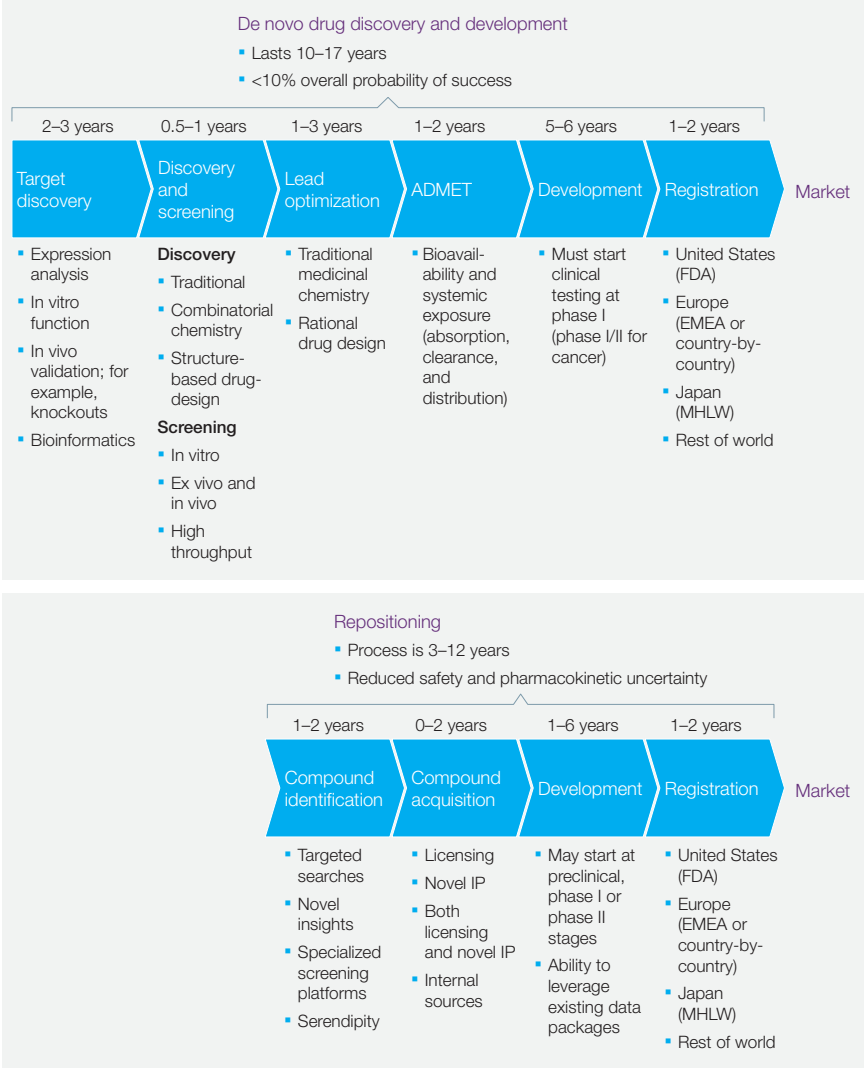
Repositioning enables R&D teams to:

- **Accelerate development and reduce risk—**Repositioning by definition has already jump-started development, and can reduce the end-to-end process from the typical 10–17 years for a de novo drug to as little as 3 years for a phase IIb drug with established safety (Exhibit 1). In addition, repositioning projects carry lower risk because a molecule's safety and pharmacokinetic profiles are known, which reduces the probability of failure at each stage of development.
- **Enhance revenue and recover investment—**Repositioning can identify more lucrative indications or salvage an abandoned project.
- **Extend IP protection—**Novel uses for an existing molecule can result in longer patent protection, depending on the level of novelty and whether any reformulation is involved. Additionally, proactively identifying indication expansion opportunities earlier in development can lead to greater revenue during the period of exclusivity.

Capturing these benefits requires that repositioning become a central element of the drug development and lifecycle management toolkit, ideally using non-replicable proprietary patient-level clinical data of the founding company. Other tools and resources such as commercial knowledge (for example, healthcare providers' suggestions for possible uses) or publicly available datasets and computational tools are also helpful, but are less controllable than proprietary data.

Exhibit 1

Development timelines for de novo vs repositioned molecules



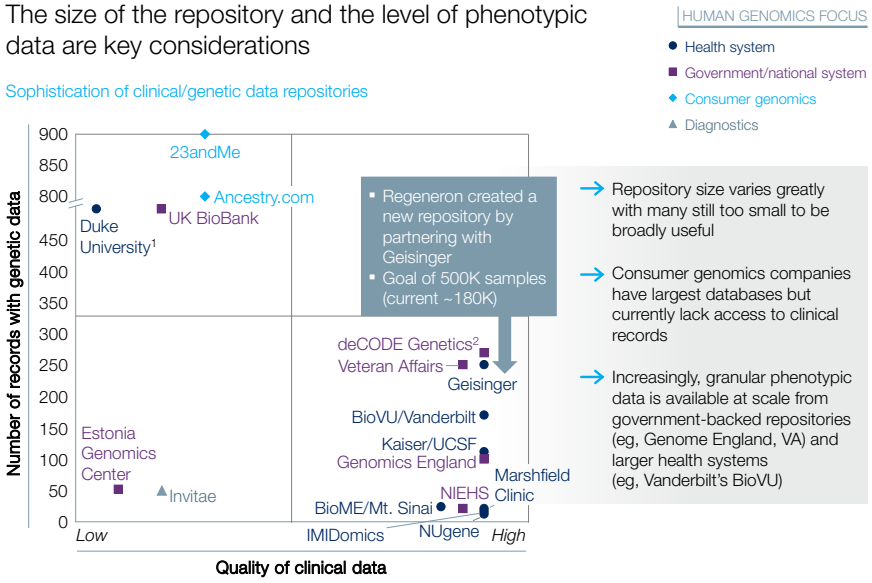
Proprietary patient data

A number of institutions have amassed large-scale biological databases consisting of tens of thousands of samples and corresponding patient data—unique source material that can be used for repositioning. Assuming the required level of clinical data needed is available, these datasets have the potential to yield deep insights based on real-world clinical evidence and experience. The integration of clinical and human genomic data complements traditional in vitro or animal in vivo studies. Exhibit 2 identifies the size and data types of known repositories that are used for repositioning.

Biopharmaceutical companies have demonstrated a strong interest in developing, accessing, and integrating proprietary datasets, as recent merger and acquisition activity in this space reveals.

Exhibit 2

The size of the repository and the level of phenotypic data are key considerations



1 May include pathology samples and cell lines.
2 deCODE bought by Amgen in 2012 and therefore data no longer available.
Source: Company websites; McKinsey analysis

- Amgen's 2012 purchase of deCODE Genetics represents an investment in building proprietary genomic datasets and the belief that even a small improvement in drug success rate, speed to market, and differentiation of early- and late-stage therapies would justify this expenditure.[8]

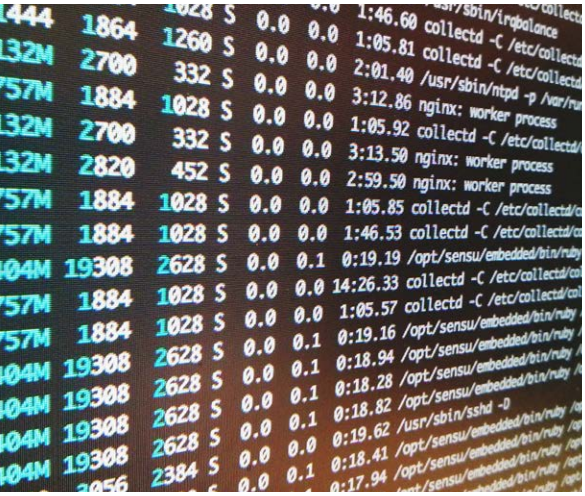
- In 2014, the Geisinger Health System and Regeneron announced a five-year collaboration to collect and sequence data via the Regeneron Genetics Center (RGC). One large-scale analysis of almost 51,000 exomes of patients and their electronic health records has revealed clinically actionable variants in 3.5 percent of individuals as well as a number of known and potential drug targets.[9] To date the RGC has paired the sequenced exomes and de-identified electronic health records of more than 180,000 people, for use in target discovery and drug-development programs.

- Genomics England is partnering with ten biopharmaceutical and biotech companies to create the Genomics Expert Network for Enterprises (GENE) Consortium.[10] The 28 teams of the consortium include leading scientific researchers, who will analyze the 100,000-genome dataset and identify new scientific and medical breakthroughs.

- Vanderbilt University Medical Center has been exploring repurposing applications with its BioVU repository. Over the past decade, Vanderbilt has invested tens of millions of dollars to amass a dataset of over 2.6 million de-identified patient records with an average of ten years of longitudinal data. Vanderbilt also collected biological specimens from 225,000 patients so it has the ability to match genetic with clinical data.[11] The effort seems to have paid off: researchers in one study used the Phenome Wide Association Study (PheWAS)—a methodology that finds relationships between genetic markers such as SNPs and phenotypes—and found 63 novel associations compared with prior genome wide association studies (GWAS)

8 "Amgen to Acquire deCODE Genetics, a Global Leader in Human Genetics," Amgen press release, http://investors.amgen.com/phoenix.zhtml?c=61656&p=irol-newsArticle&ID=1765710.
9 "Analysis of nearly 51,000 Geisinger patient exomes, EHRs reveal actionable variants, drug targets," *GenomeWeb*, December 22, 2016, https://www.genomeweb.com/molecular-diagnostics/analysis-nearly-51000-geisinger-patient-exomes-ehrs-reveal-actionable-variants.
10 Genomics England, https://www.genomicsengland.co.uk/.
11 "What is BioVU?," Vanderbilt University Medical Center, https://victr.vanderbilt.edu/pub/biovu/.

of the same SNPs.[12] BioVU is creating a spinoff, Nashville Biosciences, to serve biopharmaceutical clients for repositioning at each stage of the development cycle (from preclinical indication exploration to late-stage rescue opportunities).



Commercial in silico offerings

As an alternative to building internal tools or integrating those coming out of academia, there are a growing number of commercial products and partnership options within the in silico discovery and repositioning space. These typically build on the methods discussed above. A number of specialized companies such as Elsevier's Pathway Studio and Qiagen's Ingenuity Systems[13] offer virtual screening products for discovery and repositioning. A few general technology players have also entered the arena. For example, cloud computing vendor Cycle Computing and predictive analytics firm Ayasdi both offer products focused on drug discovery.[14] These platforms—or something similar—are a necessary part of indication selection and repositioning efforts.

Biopharmaceutical companies that partner with companies that provide repositioning services gain access to more cutting-edge analytics methods and

12 Joshua C. Denny et al., "Systematic comparison of phenome-wide association study of electronic medical record data and genome-wide association study data," *Nature Biotechnology*, December 31, 2013, pp 1102–1111, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3969265/.

13 "Elsevier Launches Web-Based Pathway Studio and Adds New Molecular Data from Its Biology = Journals to Boost Early Discovery Research," Elsevier, March 26, 2013, https://www.elsevier.com/about/press-releases/science-and-technology/elsevier-launches-web-based-pathway-studio-and-adds-new-molecular-data-from-its-biology-journals-to-boost-early-discovery-research; "Qiagen Buys Genomic Data Analysis Firm Ingenuity Systems for $105M," *genomeweb*, April 30, 2013, https://www.genomeweb.com/informatics/qiagen-buys-genomic-data-analysis-firm-ingenuity-systems-105m.

14 Jason Zander, "Microsoft acquires Cycle Computing to accelerate Big Computing in the cloud," Microsoft, August 15, 2017, https://blogs.microsoft.com/blog/2017/08/15/microsoft-acquires-cycle-computing-accelerate-big-computing-cloud/; Pek Lum, "Ayasdi Cure: Accelerating Drug Discovery, Advancing Precision Medicine," Ayasdi, April 19, 2014, https://www.ayasdi.com/blog/bigdata/ayasdi-cure-accelerating-drug-discovery-advancing-precision-medicine/.

more integrated data sources than the typical biopharmaceutical company could assemble in house. For example, BioVista and Excelra have advanced analytics engines that integrate typical literature mining and simulation approaches and add data sources such as electronic medical records (EMRs).[15] As a consequence, companies have a large dataset available for correlating drugs, pathways, and outcomes to rapidly screen indications. Another company, InSilico Medicine developed a neural network–based solution that processes research publications and patient data into pathway activation profiles used to search for repositioning candidates.[16]

Pharma-tech partnerships can take a variety of shapes. Nimbus Therapeutics was co-founded by Schrödinger to develop drugs using Schrödinger's technology platform, recently entering into a licensing agreement with Genentech.[17] Molplex, which uses artificial intelligence to discover drugs, has a partnership with AstraZeneca.[18] These partnerships underscore the growing importance of having advanced, dynamic analytic platforms available for drug discovery.

Publicly available datasets and computational tools

Numerous computational tools to perform drug-repositioning screens already exist. Fortunately, they are also in the public domain as many were generated by academic labs or in response to government initiatives. Accordingly, R&D groups can take advantage of these public datasets and existing algorithms to help expedite drug-repurposing efforts by using the following sources and in silico techniques:

15 "Results of Biovista Work Released," *ProHealth*, January 19, 2016, http://www.prohealth.com/library/showarticle.cfm?libid=22775; Nick Paul Taylor, "Astellas continues IT-enabled drug repurposing deal drive with Excelra hookup," *FierceBiotech*, June 10, 2016, http://www.fiercebiotech.com/it/astellas-continues-it-enabled-drug-repurposing-deal-drive-excelra-hook-up.

16 "Insilico Medicine launches a drug discovery platform ALS.AI," *Eurekalert!*, June 1, 2017, https://www.eurekalert.org/pub_releases/2017-06/imi-iml053117.php.

17 Damian Garde, "Genentech co-signs Nimbus' computer-aided R&D with an oncology pact," *FierceBiotech*, October 20, 2015, http://www.fiercebiotech.com/partnering/genentech-co-signs-nimbus-computer-aided-r-d-an-oncology-pact.

18 "Molplex Pharmaceuticals And AstraZeneca PLC To Collaborate On New Oncology Research Programme," *BioSpace*, January 14, 2015, https://www.biospace.com/article/releases/molplex-pharmaceuticals-and-astrazeneca-plc-to-collaborate-on-new-oncology-research-programme-/.

- **Knowledge-mining—**Information from peer-reviewed journal databases (for example, PubMed) and patent documentation can be extracted by text-mining algorithms (such as MANTRA and CoPub) to identify novel drug-target relations.

- **Biochemical—**Drug and protein structures found in online databases (for example, ChemSpider, Protein Data Bank) are used by inverse docking algorithms (for example, AMIDE and MDOCK) to computationally dock a small molecule of interest against a library of potential protein binding partners.

- **Genetic—**Several sources are available linking genetic variation to phenotypes and health: for example, ClinVar and dbGaP published by the National Center for Biotechnology Information (NCBI). Studies can also be undertaken to associate indications with genetic risk loci and nearby putative disease-causing genes (termed genome-wide association studies or GWAS). In fact, specification of candidate risk genes that are the target of an approved drug for a separate indication is a key approach for drug repurposing.

- **Gene expression profiles—**Both microarray and sequencing-based gene expression data across a multitude of normal, disease, and drug-treated cell lines and patient samples are available on NCBI-curated databases (for example, Gene Expression Omnibus and Sequence Read Archive). These data can be leveraged to identify negative correlations between drug and disease gene expression signatures, suggesting drug repurposing may be successful. Such functional association hypotheses can be generated from gene expression data using Connectivity Map, Library of Integrated Network based Cellular Signatures (LINCS), Drug versus Disease (DvD), and others.

- **Clinical—**Drug-related adverse effect phenomes can be compiled from package inserts and patient-reported health outcomes data (for example, Side Effect Resource). Mining for side effects of drugs that may ameliorate the symptoms of a separate disease could identify new avenues for repurposing.

While the tools described and the troves of data they utilize have great potential for drug repurposing, there are several challenges to their successful use in a commercial setting. First, data specific to the drug, drug target, pathway, or disease of interest may be limited. For example, when exploring a drug-protein docking approach, a major limitation is the number of protein targets with solved structures. Second, it is wise to have a portfolio of several in silico opportunities that span therapeutic areas (TA) rather than focusing on a single molecule. More targets will yield promising leads to be validated with in vitro or in vivo studies.

Don't reinvent the wheel

A systematic approach to repositioning depends on assembling the right data and analytical approaches appropriate for the therapeutic area. For example, McKinsey's Disease Navigator integrates publicly available genetic, chemical, and clinical data to identify novel drug repurposing insights. In Disease Navigator, integration of monogenic disease genetic variants, GWAS correlations, and animal knockout study data yields a genotype-phenotype association score between the drug of interest and all potential indications. Additionally, drug-target data and clinical trial stage information reveal the competitiveness of the clinical pipeline in each indication.

Developers of datasets have pivoted from offering their insights to industry clients to becoming biotechs themselves. 23andMe provides Genentech[19] and Pfizer[20] access to data to derive insights for certain disease areas, specifically Parkinson's disease in the case of Genentech. Clearly there is ongoing interest in data- and analytic-driven partnerships that have the potential to change the paradigm of drug development if applied broadly.

Testing and executing a repositioning strategy

The major issue for biopharmaceutical companies is *how* to execute a repositioning strategy that captures potential benefits. Assembling advanced technical sophistication, diverse data sets, and commercial expertise requires disparate groups in a biopharmaceutical organization to work together. Aligning these capabilities and assets in one harmonious group can be an organizational

19 Matthew Herper, "Surprise! With $60 Million Genentech Deal, 23andMe Has A Business Plan," *Forbes*, January 6, 2015, https://www.forbes.com/sites/matthewherper/2015/01/06/surprise-with-60-million-genentech-deal-23andme-has-a-business-plan/#f144a0c2be97.

20 Caroline Chen, "23andMe Turns Spit Into Dollars in Deal With Pfizer," *Bloomberg*, January 12, 2015, https://www.bloomberg.com/news/articles/2015-01-12/23andme-gives-pfizer-dna-data-as-startup-seeks-growth.

challenge when focused on de novo discovery. As discussed previously, researchers can view repositioning as less innovative and the activity may even carry the "stench of failure," making staffing more difficult still. Consequently, before embarking on or scaling repositioning efforts, leaders should consider several key questions to ensure success.

1. Where does repositioning fit into the company's portfolio? Companies with molecules at the end of IP protection typically focus on repurposing to extend patent life, while others may find more value from indication selection or expansion earlier in the lifecycle.

2. Which assets should be the focus of repositioning efforts? Will repositioning apply to all molecules or only to failed molecules? Leaders will want to agree on whether the company is interested in repositioning its own assets or whether finding new opportunities to in-license should also be considered.

3. What is the company's appetite for entering new therapeutic areas? Repositioning analyses can identify indications in any therapeutic area, often outside the initial TA or even beyond the strategic focus of the company. Companies will need to be comfortable pivoting into a new area or developing a dedicated process for out-licensing in new indications.

4. What level of investment is the company prepared to make? Publicly available and other common data sources will increasingly become "mined out" as their usefulness becomes exhausted. Accordingly, companies with proprietary data assets and methods will have an advantage.

5. Where in the organization should repositioning sit? Given the applications across TAs and lifecycle stages—as well as across clinical and IT, commercial and R&D—finding a natural "owner" or champion to drive repositioning efforts can be challenging. Extensive repositioning initiatives may require stand-alone divisions that are well integrated.

For many biopharmaceutical companies, the science of repositioning may be relatively easy compared with the organizational issues involved in standing up a repositioning team. For this reason, biopharmaceutical leaders will need

an approach to promoting and adequately protecting repositioning resources, perhaps by offering unique incentives to team members until the team's efforts yield success and their value gains traction.

Repositioning can impose unique commercial and stakeholder management demands on an organization. Successful reintroduction of a molecule can include:

- Development of a roadmap describing a wide variety of indications for the molecule
- A demonstration of desired inhibiting activities for a targeted list of disorders
- A new understanding of drugs derived from the use of the repositioned molecule and how the drugs could impact disease areas, especially those with high levels of medical need

The tenacity of the team and a strong rationale for repositioning the drug will be required to overcome resistant investors, commercial teams, R&D teams, and prescribers.

Conclusion

The next three to five years will be a critical period for life sciences organizations as they design strategies to enhance their existing R&D programs. We believe that launching a systematic repositioning effort can be an integral component of R&D strategies—one that could impact all stages of a company's pipeline and result in much higher returns on investment than the opportunistic or serendipitous approach to repositioning used previously. Having a more systematic approach, however, requires life science leaders to make critical choices regarding which tools and datasets to use, which partners are the right fit, and how to integrate both into their organizations. Nevertheless, given the relatively low investment needed and high potential returns, developing an actionable, coherent approach to repositioning can pay off handsomely.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Digital vigilance: Building the backbone for insight-driven safety

Kate Chavez and Brandon Parry

Innovative data analytics has the capacity to enhance patient safety and unleash the strategic potential of pharmaceutical drug safety organizations.

Pharmacovigilance (PV)—though rarely celebrated—has always played an essential role, quietly and continuously monitoring a variety of data sources to detect, analyze, track, and report potentially adverse safety signals resulting from medical product use. In recent years, however, PV has experienced something of a renaissance, due in part to rising regulatory expectations, some high-profile and public drug safety "failures," and an emerging appreciation of the strategic potential the function holds. Indeed, some in the healthcare sector prefer the term "patient safety" to reflect the increasingly holistic and strategic role PV plays in many pharmaceutical companies.

Yet, while expectations are changing, it is also becoming increasingly difficult for PV groups to safeguard patients as the volume and types of data requiring analysis far outstrip companies' capabilities to analyze them. Compounding the challenge, PV groups have not been among the first to adopt innovative data science tools and techniques, even as most leaders acknowledge that traditional analytical methods—such as Individual Case Safety Report (ICSR) monitoring—are no longer fit for the purpose of sensing safety signals in all the forms in which they might appear.

PV today is a labor-intensive yet data-rich portfolio of activities. Recognizing the need to innovate cumbersome work processes

A number of forward-thinking companies are investing in disruptive—if still unproven—innovations. These innovations will need to simultaneously meet higher compliance expectations of regulators and equip companies with the best data and supporting analytics to defend and differentiate products.

and an opportunity to capitalize on rich datasets, a number of forward-thinking companies are investing in disruptive—if still unproven—innovations. These innovations will need to simultaneously meet higher compliance expectations of regulators and equip companies with the best data and supporting analytics to defend and differentiate products.

Viewing pharmacovigilance through both these lenses—as a path to compliance and as a way to establish true product differentiation—should provide the incentive needed to invest in more innovative ways of working. However, adopting this dual view of PV also requires companies to invest in identifying the solutions that can deliver the data management and analytic horsepower necessary, and to have the patience and persistence to isolate reliable solutions.

Great expectations: PV in the era of big data analytics

Luckily, we have some excellent public examples of disruptive innovations that aim to transform PV's core practice of reactively processing reported events and turning them into insight. The US Food and Drug Administration (FDA) has undertaken a multi-year journey to build active safety surveillance capabilities via its Sentinel Initiative.[1] In the private sector, IBM Watson Health represents a significant step forward, offering "the first commercially available cognitive

1 *Sentinel Initiative Final Assessment Report*, September 2017, https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM577502.pdf.

computing capability," which understands natural language, generates hypotheses based on evidence, and integrates real-time data to continually refine results. Watson Health recently announced collaborations with Celgene, Siemens Healthineers, and the government of Finland to improve public health management and safety monitoring.

Both Sentinel and commercial solutions demonstrate that much of the labor-intensive PV data identification and aggregation, which used to be a barrier, can now be automated, allowing for a cost-effective way to generate insights from integrating heterogeneous data sets.

Sentinel has provided a jumpstart to a new era of safety analytics and makes it possible for the FDA to interrogate diverse datasets on a population level to detect safety trends and issues—a clear advance compared with what most pharmaceutical companies can do. The partnerships formed in connection with Sentinel have enabled the aggregation of data covering more than 223 million members from 17 different data partnerships, and the library of reproducible analytical methods grows by the day.[1 (p 62)] Indeed, the power of Sentinel's data and analytic platform permits us to contemplate a future where phase IV safety monitoring studies are a thing of the past.

Of course, the progress represented by Sentinel has come at significant cost—the US government invested hundreds of millions of dollars over five years to build the Sentinel capability—and significant further investment will be required to realize its full potential.

Despite this, Sentinel reflects a growing consensus that better safety information hinges on better, more comprehensive data tools and analytics and raises the bar for what safety data analytics could look like in PV organizations. Today, pharmaceutical companies need a PV strategy that reflects this new understanding and places novel data sources and analytical methods at the center of their plans for the future.

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The case for digital vigilance: Better patient safety and stronger product value propositions

PV leaders who accept the challenge of evolving their organization need a strong business case for doing so—and strong internal and external partnerships to execute. (Even a deeply resourced industry leader like Watson Health sought out Celgene to help it develop the beta version of its PV platform.) There are at least three strong arguments for making the investment sooner rather than later.

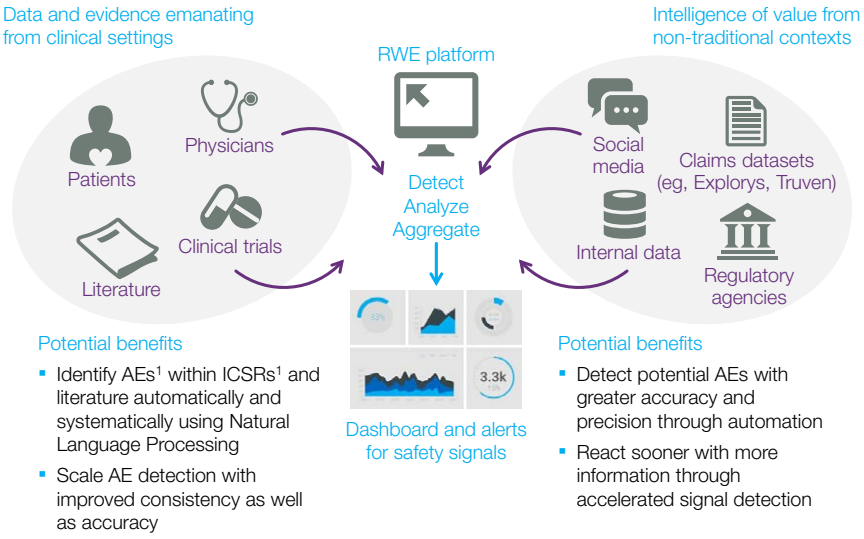
The most pressing rationale for upgrading and broadening safety data analytics is to ensure compliance with new safety reporting standards and expectations. To operate truly "global" PV systems requires the capability to analyze data generated from more conventional sources (for example, clinical trials, spontaneous reports, literature) in addition to less well-structured forms of data emanating from more real-world contexts (such as social media, patient support programs, market research, etc). Pairing and supplementing those datasets with acquired data—potentially electronic medical records (EMRs), claims sets, or other sources—only further reinforces analytical robustness. A capability that integrates and analyzes dynamic data from a variety of sources and allows safety teams to react as quickly as possible to developing safety trends is foundational to the discipline, central to full compliance, and critical to patient safety (Exhibit 1).

Beyond compliance and proactive safety management, an equally compelling argument for investment is that advanced analytics solutions allow companies to defend against potentially problematic findings and develop data-driven insights that could support product differentiation. The ability to ask and quickly gain answers to questions on a population level, which were previously unanswerable even a few years ago, is one of the greatest benefits of building advanced safety data analytics. This comes in on top of well-described benefits associated with automation of statistical analyses to shorten timelines and reduce the effort required to generate both periodic safety reports (such as Periodic Benefit-Risk Evaluation Reports and Periodic Safety Update Reports) and other routine analysis.

The ability to ask and quickly gain answers to questions on a population level, which were previously unanswerable even a few years ago, is one of the greatest benefits of building advanced safety data analytics.

Exhibit 1

Unified safety platforms detect, analyze, and aggregate safety signals



1 AEs = adverse events and ICSRs = individual case study reports.
Source: McKinsey analysis

The third reason to invest in upgrading PV capabilities is that doing so should have synergistic, cross-functional benefits for companies. The cost of acquiring supplementary datasets and building digital backbones to support advanced analytics can be significant. While it may not be financially viable to procure new datasets and enhanced services exclusively for safety or PV objectives, other functions such as health economics and outcomes research, regulatory affairs, and medical affairs could also benefit from the data and capabilities acquired—whether these are developed internally or through partnerships. Sharing the cost burden makes investments in advanced analytics of usage data more tenable, while offering the potential for novel insights to emerge from cross-functional teams working with the same underlying data.

Overcoming barriers to future-proof the PV function

Presuming there is appetite to invest in new capability, the change management challenge associated with making these changes shouldn't be underestimated. Pharmacovigilance is a statistical and medical science, and is sometimes considered unattractive due to perceived lack of opportunities and the repetitive nature of many PV tasks. It would not be surprising to find PV veterans who shrink from integrating content posted on social media platforms such as Facebook or Twitter into their analyses because it falls short of conventional assumptions about data reliability and integrity. The challenge is to find the right use of this information in ways that traditionalists can embrace. Companies such as Epidemico have chronicled[2] how using social media analytics for active surveillance can fill in data gaps and provide companies with actionable insight into product performance far earlier than captured in reports to the manufacturer, regulator, or healthcare provider. For example, analyzing search term trends can allow a company to identify potential signals related to drug combinations that involve its products and is usually faster, cheaper, and more effective than compiling EMR data.

The immediacy of social media analysis is a significant advantage, particularly because patients are more likely to turn to online platforms than contact a manufacturer with safety concerns. A recent survey by Novo Nordisk found that over half the patients responding knew little to nothing about what drug safety offices do and only 48 percent knew they could contact the manufacturer directly—but only 13 percent had had any contact with a safety office. If PV organizations are true in their commitment to patient engagement and patient-centricity, findings such as this have to be a call to action—and change.[3]

In tandem, R&D and PV leaders will also need to change their talent-management approach, with an emphasis on strategies that identify, attract, and develop talent that can meet new expectations. The PV team of the future will certainly include medical professionals and statisticians, but one can imagine data scientists, coders, and design experts having a meaningful role as well. Skill sets will need to evolve in lock-step, where team members

2 See "Social Media Listening for Routine Post-Marketing Safety Surveillance," *Drug Safety*, May 2016.
3 Puja Patel, et al., "Patient Drug Safety Reporting: Diabetes Patients' Perceptions of Drug Safety and How to Improve Reporting of Adverse Events and Product Complaints," *DIA*, 2017.

bring deeper business acumen, a working understanding of digital platforms, and comfort with epidemiological application of new datasets and analytic methods. At the same time, increasing operational complexity and shortened innovation cycles will place new emphasis on "soft skills"—such as learning agility, emotional intelligence, top-down communication, and active vendor management.

Conclusion

It's clear that the current PV analytic toolkit deployed by most companies is no longer sufficient for either its traditional safeguarding purpose or to assist in expanding commercial opportunities. The convergence of advances in data science and expanding stakeholder needs means that PV is poised for disruption—not only in terms of what it focuses on and why, but also in relation to the tools and techniques it uses, and the makeup and mind-set of the PV team itself. Investments by public sector and commercial entities have paved the way for PV organizations to chart a new course and deliver more value to patients and their organizations.

How big data can revolutionize pharmaceutical R&D

Jamie Cattell, Sastry Chilukuri, and Michael Levy

Pharmaceutical R&D suffers from declining success rates and a stagnant pipeline. Big data and the analytics that go with it could be a key element of the cure.

After transforming customer-facing functions such as sales and marketing, big data is extending its reach to other parts of the enterprise. In research and development (R&D), for example, big data and analytics are being adopted across industries, including pharmaceuticals.

The McKinsey Global Institute[1] estimates that applying big-data strategies to better inform decision making could generate up to $100 billion in value annually across the US healthcare system, by optimizing innovation, improving the efficiency of research and clinical trials, and building new tools for physicians, consumers, insurers, and regulators to meet the promise of more individualized approaches.

The big-data opportunity is especially compelling in complex business environments experiencing an explosion in the types and volumes of available data. In the healthcare and pharmaceutical industries, data growth is generated from several sources, including

1 Our work builds on insights from several reports and articles, all available on Mckinsey.com: James Manyika et al., "Big data: The next frontier for innovation, competition, and productivity," McKinsey Global Institute, May 2011; Peter Groves et al., "The 'big data' revolution in healthcare: Accelerating value and innovation," January 2013; and Ajay Dhankhar et al., "Escaping the sword of Damocles: Toward a new future for pharmaceutical R&D," *McKinsey Perspectives on Drug and Device R&D*, 2012.

the R&D process itself, retailers, patients, and caregivers. Effectively utilizing these data will help pharmaceutical companies better identify new potential drug candidates and develop them into effective, approved, and reimbursed medicines more quickly.

Imagine a future where the following is possible:

- Predictive modeling of biological processes and drugs becomes significantly more sophisticated and widespread. By exploiting the diversity of available molecular and clinical data, predictive modeling could help identify new potential-candidate molecules with a high probability of being successfully developed into drugs that act on biological targets safely and effectively.
- Patients are identified to enroll in clinical trials based on a wider variety of sources—for example, social media—than doctors' visits. Furthermore, the criteria for including patients in a trial could take significantly more factors (for instance, genetic information) into account to target specific populations, thereby enabling trials that are smaller, shorter, less expensive, and more powerful.

- Trials are monitored in real time to rapidly identify safety or operational signals requiring action to avoid significant and potentially costly issues such as adverse events[2] and unnecessary delays.
- Instead of rigid data silos that are difficult to exploit, data are captured electronically and flow easily between functions (such as between discovery and clinical development) as well as to external partners (such as physicians and contract research organizations [CROs]). This easy flow is essential for powering the real-time and predictive analytics that generate business value.

That's the vision. However, many pharmaceutical companies are wary about investing significantly in improving big-data analytical capabilities, partly because there are few examples of peers creating a lot of value from it. However, we believe investment and value creation will grow. The road ahead is indeed challenging, but the big-data opportunity in pharmaceutical R&D is real, and the rewards will be great for companies that succeed.

The big-data prescription for pharmaceutical R&D

Our research suggests that by implementing four technology-enabled measures, pharmaceutical companies can expand the data they collect and improve their approach to managing and analyzing these data.

Integrate all data

Having data that are consistent, reliable, and well linked is one of the biggest challenges facing pharmaceutical R&D. The ability to manage and integrate data generated at all stages of the value chain, from discovery to real-world use after regulatory approval, is a fundamental requirement to allow companies to derive maximum benefit from the technology trends. Data are the foundation upon which the value-adding analytics are built. Effective end-to-end data integration establishes an authoritative source for all pieces of information and accurately links disparate data regardless of the source—be it internal or external, proprietary or publicly available. Data integration also enables

2 Adverse events refer to harm to or death of trial participants.

comprehensive searches for subsets of data based on the linkages established rather than on the information itself. “Smart” algorithms linking laboratory and clinical data, for example, could create automatic reports that identify related applications or compounds and raise red flags concerning safety or efficacy.

Implementing end-to-end data integration requires a number of capabilities, including trusted sources of data and documents, the ability to establish cross-linkages between elements, robust quality assurance, workflow management, and role-based access to ensure that specific data elements are visible only to those who are authorized to see it. Biopharmaceutical companies generally avoid overhauling their entire data-integration system at once because of the logistical challenges and costs involved, although at least one global biopharmaceutical enterprise has employed a “big bang” approach to remaking its clinical IT systems.

Companies typically employ a two-step approach: first, they prioritize the specific data types to address (usually clinical data) and create additional data-warehousing capabilities as needed. The goal is to tackle the most important data first to obtain benefits as soon as possible. This step alone can take over a year and requires significant infrastructure and procedural changes. Second, the company develops an approach for the next levels of priority data, including scenario analysis, ownership, and expected costs and timelines.

To realize the benefits of consistent, well-linked and reliable data, companies must also integrate existing external data sources, specifically real-world

evidence which is the digital data collected on the real-world use of drugs and other treatments. To expand their data beyond clinical trials, some leading pharmaceutical companies are creating proprietary data networks to gather, analyze, share, and respond to real-world outcomes and claims data. Partnerships with payors, providers, and other institutions are critical to these efforts. These real-world outcomes are becoming more important to pharmaceutical companies as payors increasingly impose value-based pricing. These companies should respond to this cost-benefit pressure by pursuing drugs for which they can show differentiation through real-world outcomes, such as therapies targeted at specific patient populations. In addition, regulators and other government organizations have created incentives for research on health economics and outcomes.

Collaborate internally and externally

Pharmaceutical R&D has been a secretive activity conducted within the confines of the R&D department, with little internal and external collaboration. By breaking the silos that separate internal functions and enhancing collaboration with external partners, pharmaceutical companies can extend their knowledge and data networks and advance the science of big data analytics.

Whereas end-to-end integration aims to improve the linking of data elements, the goal of collaboration is to enhance the linkages among all stakeholders in drug research, development, commercialization, and delivery.

Maximizing internal collaboration requires improved linkages among different functions, such as discovery, clinical development, and medical affairs. This can lead to insights across the portfolio, including clinical identification and research follow-up on potential opportunities in translational medicine[3] or identification of personalized-medicine opportunities through the combination of biomarkers research and clinical outcomes; predictive sciences could also recommend options at the research stage based on clinical data or simulations.

External collaborations are those between the company and stakeholders outside its four walls, including academic researchers, CROs, providers,

3 Translational medicine refers to taking new scientific discoveries and turning these into effective health improvements and medicines.

and payors. Several examples show how effective external collaboration can broaden capabilities and insights.

- External partners, such as CROs, can quickly add or scale up internal capabilities and provide access to expertise in, for example, best-in-class management of clinical studies.
- Academic collaborators can share insights from the latest scientific breakthroughs and make a wealth of external innovation available. Examples include Eli Lilly's Phenotypic Drug Discovery Initiative, which enables external researchers to submit their compounds for screening using Lilly's proprietary tools and data to identify whether the compound is a potential drug candidate. Participation in the screening does not require the researcher to give up intellectual property, but it does offer Lilly a first look at new compounds, as well as an avenue to reach researchers who are not typical drug-discovery scientists.
- Collaborative "open space" initiatives can enable experts to address specific questions or share insights. Examples include the X PRIZE, which provides financial incentives for teams that successfully meet a big challenge (such as enabling low-cost manned space flight), and InnoCentive, which offers financial incentives for individuals or teams that address a specific problem (such as determining a compound's synthesis pathway).
- Customer insights can be used to shape strategy throughout the pipeline progression.

Some pharmaceutical companies have made inroads in improving internal and external collaboration, which involves addressing a number of challenges. These include putting in place communications systems and governance to enable appropriate and effective information exchange. Another challenge is to promote a shift in mind-set, moving away from withholding all data and toward identifying which data can be shared and with whom. In addition, pharmaceutical enterprises must understand and mitigate the legal, regulatory, and intellectual property risks associated with a more collaborative approach.

Some pharmaceutical companies start to improve collaboration by identifying data elements to share with specific sets of trusted partners, such as CROs, and establishing privileged and near-real-time access to data produced by external partners. Such steps are only the beginning, however, as they are essentially just a way to expand the "circle of trust" to select partners.

Leverage the latest technology

Technology continues to evolve with new R&D tools coming out frequently, making it a challenge for R&D leaders to decide where to focus limited funds and how to select the right platform for their portfolio and business challenges. A tight focus on improving both the efficacy of trials and internal decision making with an eye on the total spend (not just limited to technology spend) can help inform these decisions. The following digital R&D solutions look especially promising today.

1. Employ IT-enabled portfolio decision support

To ensure the appropriate allocation of scarce R&D funds, it is critical to enable expedited decision making for portfolio and pipeline progression. Pharmaceutical companies often find it challenging to make appropriate decisions about which assets to pursue or, sometimes more importantly, which assets to kill. The personnel or financial investments they have already made may influence decisions at the expense of merit, and they often lack appropriate decision-support tools to facilitate making tough calls.

IT-enabled portfolio management allows data-driven decisions to be made quickly and seamlessly. Smart visual dashboards should be used whenever possible to allow rapid and effective decision making, including for the analysis of current projects, business-development opportunities, forecasting, and competitive information. These visual systems

should provide high-level dashboards that permit users to examine the data deeply (including information to bolster managerial decision making) as well as at the tactical level to make asset performance and opportunities more transparent.

In addition to the technical requirements, portfolio decision making should follow a defined process with known timing, deliverables, service levels, and stakeholders. The people involved in the process should be given clear roles and authority (for example, their ability to make decisions should be defined). Resource allocation should be based on a systematic approach that accommodates top-down budgetary requirements and bottom-up requests. And innovation boards at the corporate level and at the business unit or therapeutic area level should review the portfolio regularly. The boards should assess, manage, and prioritize the portfolio based on the corporate strategy and changes in the business landscape or industry context.

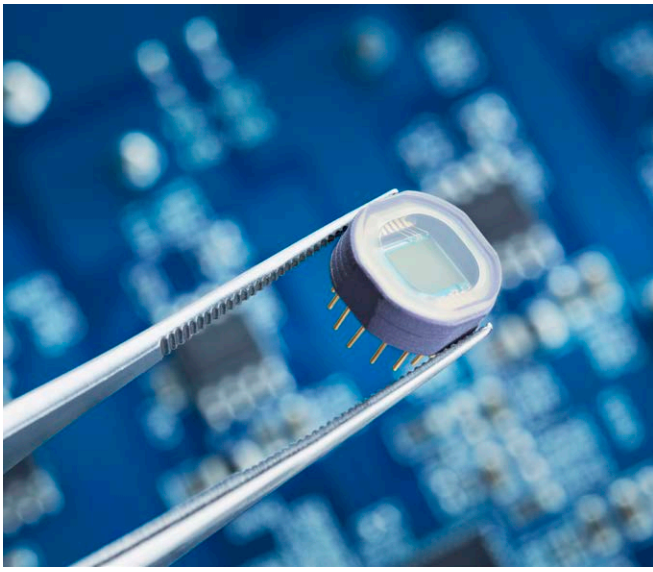
2. Leverage new discovery technologies

Pharmaceutical R&D must continue to use cutting edge tools. These include sophisticated modeling techniques such as systems biology and high-throughput data-production technologies—that is, technologies that produce a lot of data quickly. As one example, next generation sequencing will make it possible to sequence an entire human genome at a cost of roughly $100 within 18 to 24 months.

The wealth of new data and improved analytical techniques will enhance future innovation and feed the drug-development pipeline. Integrating vast amounts of new data will test a pharmaceutical company's analytical capabilities. For example, a company will need to connect patient genotypes to clinical-trial results to identify opportunities for improving the identification of responsive patients. Such developments would make personalized medicine and diagnostics an integral part of the drug-development process rather than an afterthought and would lead to new discovery technologies and analytical techniques.

3. Deploy sensors and devices

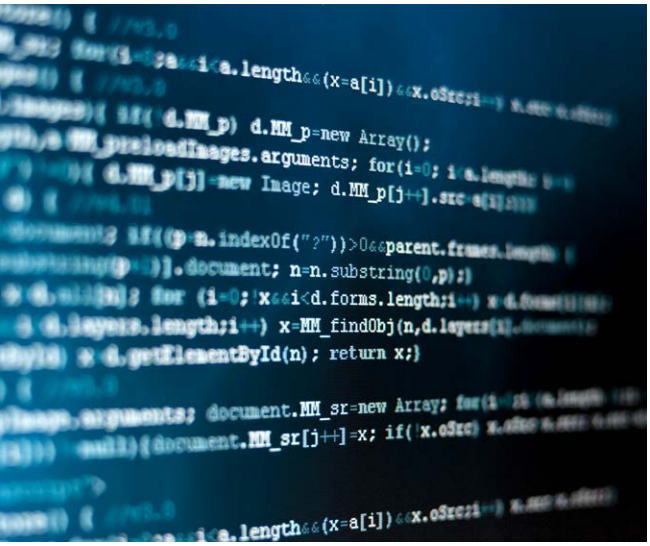
Advances in instrumentation through miniaturized biosensors and the evolution in smartphones and their apps are resulting in increasingly sophisticated health-measurement devices. Biopharmaceutical companies can deploy smart devices to gather large quantities of real-world data not previously available to scientists. Remote monitoring of patients through sensors and devices represents an immense opportunity. This kind of data could be used to facilitate R&D, analyze drug efficacy, enhance future drug sales, and create new economic models that combine the provision of drugs and services.



Remote-monitoring devices can also add value by increasing patients' adherence to their prescriptions. Examples of devices that are under development include smart pills that can release drugs and relay patient data as well as smart bottles that help track usage. Technology and mobile providers are offering services such as data feeds, tracking, and analysis to complement medical devices. These devices and services, combined with in-home visits, have the potential to decrease healthcare costs through shortened hospital stays and earlier identification of health issues.

Improve safety and risk management

Pharmaceutical companies can use safety as a competitive advantage in regulatory submissions and after regulatory approval, once the drug is on the market. Safety monitoring is moving beyond traditional approaches to sophisticated methods that identify possible safety signals arising from rare adverse events. Furthermore, signals could be detected from a range of sources such as patient inquiries on websites and search engines. Online



physician communities, electronic medical records, and consumer-generated media are also potential sources of early signals regarding safety issues and can provide data on the reach and reputation of different medicines. Bayesian analytical methods, which can identify adverse events from incoming data, could highlight rare or ambiguous safety signals with greater accuracy and speed.

An early response to physician and patient sentiments could prevent regulatory and public-relations backlashes. The FDA is investing in the evaluation of electronic medical records through the Sentinel Initiative, a legally mandated electronic surveillance system that links and analyzes healthcare data from multiple sources. As part of this system, the FDA can now proactively assess the safety of products based on access to data from 223 million members through 17 different data partnerships nationwide. [4]

Better data, new technology, cross-industry collaborations, and an improved focus on safety will enable improvements in clinical trial design and outcomes as well as greater efficiency. Clinical trials will become increasingly adaptable to react to drug safety signals seen only in small but identifiable subpopulations of patients. Examples of potential clinical trial efficiency gains include the following:

- Dynamic sample size estimation (or reestimation) and other protocol changes could enable rapid responses to emerging insights from the clinical data. Efficiency gains are achieved by enabling smaller trials for equivalent power or shortening the time necessary to expand a trial.

4 *Sentinel Initiative Final Assessment Report*, September 2017, https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM577502.pdf.

- Adapting to differences in site patient recruitment rates would allow a pharmaceutical company to address lagging sites, bring new sites online if necessary, and increase recruiting from more successful sites.
- Increased use of electronic data capture could help in recording patient information in the provider's electronic medical records. Using electronic medical records as the primary source for clinical trial data rather than having a separate system could accelerate trials and reduce the likelihood of data errors caused by manual or duplicate entry.
- Next generation remote monitoring of sites, enabled by fluid, real-time data access, could improve management and responses to issues that arise in trials.

The challenges of a big-data transformation

For a big data transformation in pharmaceutical R&D to succeed, executives must overcome several challenges.

Organization

Organizational silos result in data silos. Functions typically have responsibility for their systems and the data they contain. Adopting a data-centric view, with a clear owner for each data type across functional silos and through the data life cycle, will greatly facilitate the ability to use and share data. The expertise gained by the data owner will be invaluable when developing ways to use existing information or to integrate internal and external data. Furthermore, having a single owner will enhance accountability for data quality.

These organizational changes will be possible only if a company's leadership understands the potential long-term value that can be unlocked through better use of internal and external data.

Technology and analytics

Pharmaceutical companies are now saddled with legacy systems containing heterogeneous and disparate data. Increasing the ability to share data requires rationalizing and connecting these systems. There's also a shortage of people equipped to develop the technology and analytics needed to extract maximum value from the existing data.

Mind-sets

Many pharmaceutical companies believe that unless they identify an ideal future state, there is little value to investing in improving big data analytical capabilities. Indeed, they seem to fear being the first mover, since there are few examples of pharmaceutical companies creating a lot of value from the improved use of big data. Compounding their hesitation is concern about increasing interactions with regulators if they pursue a big data change program. Pharmaceutical companies should learn from smaller, more entrepreneurial enterprises that see value in the incremental improvements that might emerge from small-scale pilots. The experience so obtained might yield long-term benefits and accelerate the path to the future state.

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PANELMARKET
Berlin
New Delhi
Canberra
Wellington

Connecting with the individual customer

Medical affairs: Key imperatives for engaging and educating physicians in a digital world

Matthias Evers, Ivan Ostojic, Brindan Suresh, Josh Weiner, and Ann Westra

Medical affairs teams have an increasing role to play in shaping product strategy as healthcare professionals seek more personalized, tailored, and user-friendly information—but only if they are able to engage physicians successfully. Five strategic imperatives can help them master customer engagement in a digital world: start with your customer, develop a channel strategy, build a content development engine, measure continuously, and become more agile.

As the trend toward medical affairs (MA) becomes an even more significant part of biopharmaceutical companies, MA teams have emerged as key players not only in advancing the success of their companies, but also in helping to improve patient outcomes. Underpinning this role is their ability to engage customers—especially physicians—effectively via digital channels.

Traditionally, however, MA teams have relied heavily on face-to-face interactions to fulfill their brief. Today, though, physicians are willing to invest less time in meeting people in person to obtain information, so the MA role is challenging as digital begins to transform the way teams engage customers. MA leaders are rethinking how they operate in an increasingly digital world driven by the following signs of the growth in digital in healthcare.

- **How physicians are consuming medical content is evolving.** As physicians have become digital consumers in their everyday lives, they are also changing the way they consume medical information in their professional lives and embracing the convenience of digital channels that provide content on demand.
- **There is an increasing need for education and high-quality information**, given the proliferation of specialty and more complex medicine. Moreover, there are escalating external demands to demonstrate the additive value of therapies, along with increasingly stringent requirements related to transparency and compliance. These requirements stem from a variety of sources, including legislation targeting the transfer of value, such as the European Federation of Pharmaceutical Industries and Associations (EFPIA) code and the Sunshine Act in the United States, which requires disclosure to the Centers for Medicare and Medicaid Services (CMS) of any payments or other transfers of value made to physicians or teaching hospitals.
- **Opportunities for using digital and delivering content are multiplying** with the availability of more sophisticated electronic channels and the advent of new technologies such as virtual reality. At the same time, the emergence of miniaturized devices and sensors, which enable collection of granular real-world patient data that can be integrated using analytics platforms, now affords greater transparency regarding product effects and their use.

Physicians' use of digital content for discussion, research, and collaboration continues to grow: nine out of ten physicians believe their time spent on digital for professional purposes will grow in the next year.[1] Today, physicians globally spend at least 1.5 hours online per day conducting research, with at least half of that on social media. We found that 72 percent of doctors believe that social media channels improve the quality of patient care and more than 30 percent use them for professional purposes, often preferring open forums to physician-only online communities. For example, in the neurological disease space, physicians who used SERMO—a social network for physicians to collaborate and share ideas—were 53 percent happier with the job they do. Meanwhile, 38 percent of physicians who do not currently use social media believe they will use it for professional

1 McKinsey survey 2016; average of responses from Canada, Germany, and the United States.

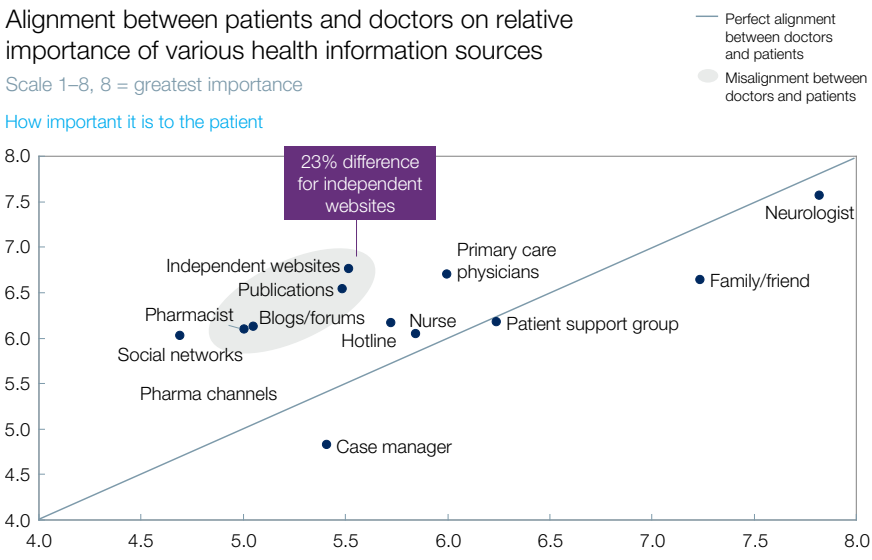
purposes in the next two years. Doctors' reasons for using various channels are even more fascinating. Today, physicians seek digital journals and publications to understand disease mechanisms and learn about new therapies; however, 61 percent of those using social media consider it an equally or more effective way to obtain answers to specific case-related questions or concerns.

Patients have long gravitated to digital with 90 million patients discussing health topics online. In the United States, 80 percent of patients carry out online research prior to a consultation, and four out of five patients would share their data to receive better care.[2] Interestingly, however, despite the emergence of digital for both patients and physicians, physicians do not always understand the role and importance that digital resources play for their patients (Exhibit 1).

Exhibit 1

Alignment between patients and doctors on relative importance of various health information sources

Scale 1–8, 8 = greatest importance



Source: McKinsey analysis

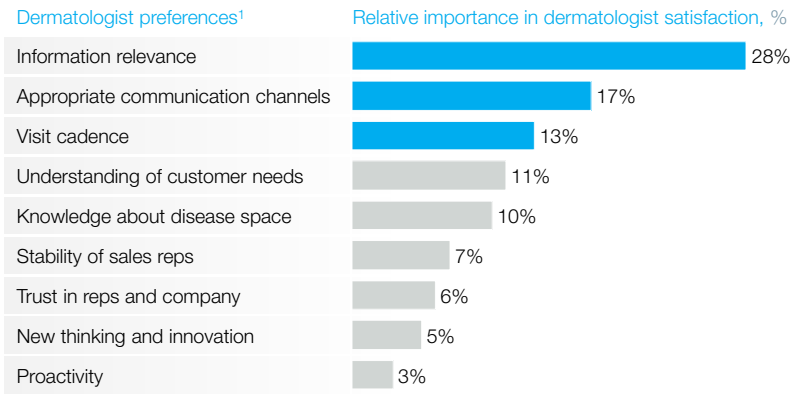
2 Susannah Fox, "The social life of health information," Pew Research Center, January 15, 2015, http://www.pewresearch.org/fact-tank/2014/01/15/the-social-life-of-health-information/.

Meanwhile, physicians' expectations for the quality of engagements continue to grow exponentially: 81 percent of physicians are dissatisfied with their interactions with biopharmaceutical companies, and over 40 percent no longer perceive a "need" for medical support from pharma. Driving this dissatisfaction is a perceived lack of personalized, relevant content (28 percent) and appropriate communication channels (17 percent), as Exhibit 2 indicates. This disruption has been caused, in part, by global advances in data availability and enhanced analytics capabilities, which have enabled companies across all industries to create personalized experiences. Indeed, there is a gap opening up in relation to the use of analytics to improve physician satisfaction between research and knowledge vendors on the one hand and biopharmaceutical companies' medical affairs organizations on the other; this will continue to commoditize what MA groups traditionally have provided, and apply pressure to use advanced analytics to be more effective in their engagement.

Exhibit 2

Personalized, relevant content and appropriate communications channels are priorities for physicians

DERMATOLOGY EXAMPLE



1 McKinsey HCP Survey n=300.
Source: McKinsey analysis

Despite these clear trends—and continuing discussion of how digital will transform the customer engagement model along with medical affairs' contribution to it—adoption has been slow, and its impact remains unclear. In fact, McKinsey research exploring adoption of digital by medical affairs teams at biopharmaceutical companies found that:

Despite these clear trends—and continuing discussion of how digital will transform the customer engagement model along with medical affairs' contribution to it—adoption has been slow, and its impact remains unclear.

- 50 percent of biopharmaceutical companies view their digital strategy as "conservative"—that is, preferring face-to-face interaction with limited deployment of new technologies.
- 40 percent support the "status quo"—that is, equipping medical science liaisons (MSLs) in the field with basic tablet technology, building customer tools, and slowly moving to virtual formats.
- Only 10 percent of pharmacos report that they are "investors" in digital for MA—that is, supporting tools that enable real-time exchange between corporate headquarters and field medical or facilitating immediate access to information for MSLs and opinion leader physicians, and moving relationships into virtual formats.

While opaque compliance regulations may account for some of this caution, other causes include the investment required to update technology infrastructure, as well as a widespread MA mind-set that views digital as a "nice to have" rather than critical, in order to support isolated initiatives.

The current rate of adoption is reflected in digital's limited impact, with many physicians dissatisfied with the current state of affairs. McKinsey research among physicians found that two-thirds of medical professionals complain they are bombarded with generic digital content and are seeking more personalized, tailored, and user-friendly information (for example, short videos). At the same time, there is an expectation that MA teams can do more to provide unbiased digital content.

These perceptions and unfulfilled needs raise a critical question for medical affairs: how should teams deploy digital technologies in their customer engagement model to help physicians and improve patient outcomes? Like all of us, doctors use digital as part of their daily lives, yet dedicated biopharmaceutical digital platforms have tended to fall flat in the eyes of physicians. In practical terms there is trade-off between building the perfect tool and making use of what exists or, indeed, small investments focused on actually making physicians' professional lives easier. For instance, digital MSLs were tried a couple of years ago but largely dropped because they weren't busy enough and there were over concerns around regulatory guidance—the consequence is that this has made medical leaders reluctant to act. Accordingly, it is clear that there is an opportunity to evolve the traditional physician engagement model to provide the right digital content—data or insights—to physicians, either directly through owned, proprietary channels, or through third-party channels, which fit in providers' workflow. What is less clear is the path to achieving a digital medical affairs model. A switch to a test-and-learn mindset would enable medical leaders to try out and learn from digital approaches to customer engagement, to identify the next generation of digital field medical teams.

This article proposes the stepping stones along such a path. We identify five imperatives that can help the medical affairs function to master customer engagement in a digital world.

1. Start with your customer.

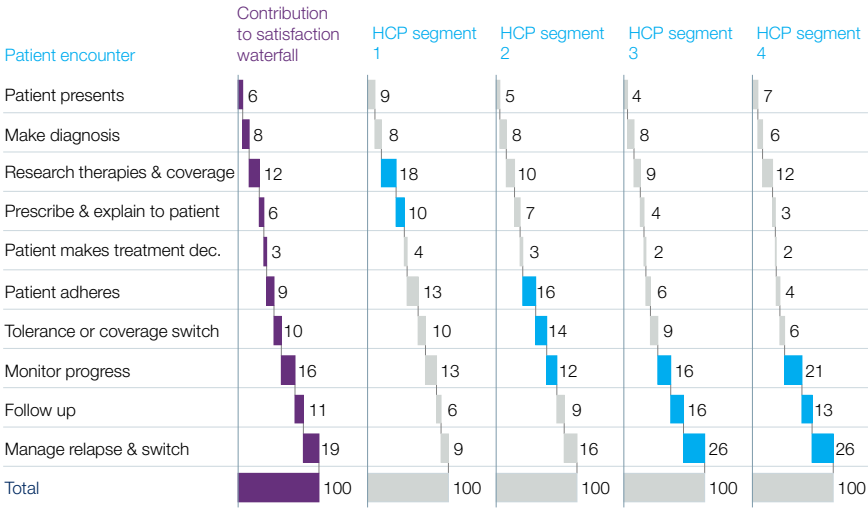
Every digital engagement design has to start with the customer at the center, while clearly making a link back to the product or disease area. Medical affairs teams are well positioned for this role with their detailed understanding of customers—physicians and patients—as well as the product. Such deep understanding of the customer allows MA teams to uncover insights that enhance product strategy, which can then be implemented by the commercial and medical affairs functions. Accordingly, companies should seek to develop clear processes that enable MA teams to maximize the benefits of their privileged position vis-à-vis physicians by uncovering and feeding back insights that shape commercial strategy to ensure it meets the needs of customers.

In this context, medical affairs teams need to develop a profound understanding of physician journeys in both quantitative and qualitative terms; general journey descriptions are useful but deeper understanding of individual journeys is even more useful. Combining the two (we call this "quantified experience design") can bring granular understanding of how physicians spend their day. This includes identifying when, how, and through which channels they consume medical information; how they interact with other stakeholders; and when they engage with biopharmaceutical companies.

Quantitatively, this can be achieved primarily by mapping the physician journey. To do this, we need to identify physician segments—machine learning being the most sophisticated way to achieve this—and link them to customer relationship management (CRM) data as well as other datasets to understand the core drivers of satisfaction. Each physician experiences two journeys: 1) the patient-encounter journey; and 2) the knowledge-accumulation journey. It is important to note that the various steps on the journey vary in their significance to different physician segments (Exhibit 3). Appreciating this is the first "step" toward understanding how best to satisfy the physician's requirements.

Exhibit 3

Different health care professionals (HCPs) value different steps of the patient encounter



Source: McKinsey analysis

To really get "under the skin" of why these steps contribute so much to satisfaction, we need to understand both the rational and emotional aspects of every stakeholder journey. These can only be revealed through deep immersion in the stakeholder experience. We can then seek to uncover unmet needs or identify "micro moments" during which there are opportunities to add value—so-called "moments of truth." Our research has shown that the current medical information world is fragmented and that physicians prefer to have a single source of information, which they can use when they need to make quick queries; for example, platforms like UpToDate are fairly handy for rapid information search. PhactMI, a collaboration of biopharmaceutical company medical information (MI) departments dedicated to supporting physicians in their commitment to provide quality patient care, is an important first step toward providing a comprehensive online information source—see sidebar "Collaborative platform phactMI aggregates information to speed responses

to health care professionals." Beyond this, physicians still rely largely on web searches and scientific publications, but acknowledge that information could be presented in a more engaging way such as short videos on personalized, modern platforms.

Collaborative platform phactMI aggregates information to speed responses to health care professionals (HCPs)

The not-for-profit platform, Pharma Collaboration for Transparent Medical Information, known as phactMI, was founded by 19 biopharmaceutical companies to improve awareness of the value that medical information (MI) teams deliver and to aggregate and provide access to medical information on many conditions through a single portal (www.phactmi.org). Physicians no longer have to search for product information across each member site individually; they can submit queries on specific brands and companies through the website, which are then routed to the appropriate company for response. Member companies (currently 24) are banking on the improved response and increased efficiency of delivering medical information to strengthen relationships with physicians. The platform is funded by members, and membership is open to most pharmaceutical and biotech companies, which meet the requirements for high-quality provision of medical information.

2. Develop a winning digital channel strategy, not a series of "one-off" efforts.

Armed with a deep understanding of its customers, as well their own team's position and capabilities, medical affairs organizations can then develop a winning engagement strategy for the digital world. This needs to be comprehensive and well coordinated—encompassing both digital and face-to-face channels when needed as part of an integrated strategy—rather than a collection of projects in isolation. One fundamental issue concerns which digital channels MA wants to own and which third-party channels could be used to build a presence where stakeholders already congregate. For example, forums where companies cannot control the content would require an effective partnership strategy. Other considerations include:

- How do you make content personal? Simply adding more "digital noise" to the already fragmented medical information/education system will neither help differentiate companies nor make information more visible.

- For owned channels, content needs to be "sticky" which means producing content in compelling formats such as physician preferred short three minute videos or advanced user-centric designs for digital channels and tools, including a simple but engaging interface and the ability to personalize content.

Clarifying these strategic goals and delivering a memorable customer experience, often by doing relatively simple things to achieve those goals, will enable MA to become leaders in digitally engaging physicians—much like companies from other sectors such as consumer goods or personal technology that have been able to achieve success with their customers.

3. Build a content-development engine that continuously delivers fresh insights.

A common pitfall for medical affairs is that there is too much focus on channels and too little focus on content strategy—content must be the cornerstone of every digital strategy with digital channels being the enabling tool. Moreover, content should clearly be high quality and unbiased, because these characteristics drive trust and adoption. Too often, biopharmaceutical companies publish generic content from common vendors, a policy that does not allow them to differentiate themselves. This leaves users dissatisfied and needing to look elsewhere for answers to their questions.

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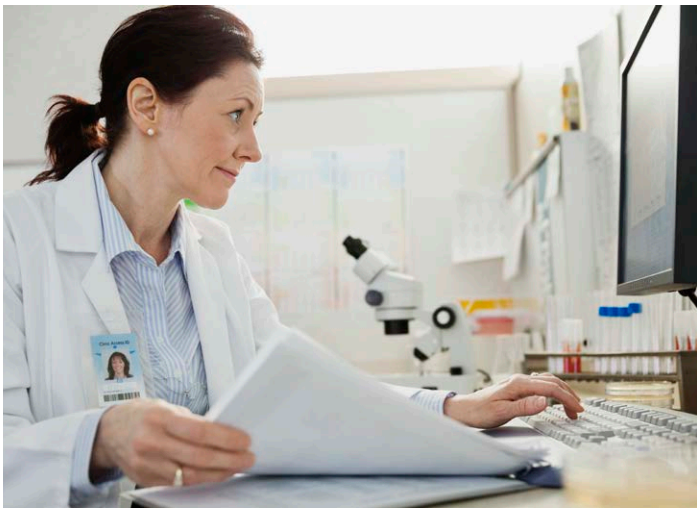
Furthermore, the status quo is now to offer curated content. With many of the digital sources that physicians are now using—whether for generic news or medical information—the content is tailored to their needs. However, the digital content offered by medical affairs is often lagging. When presented correctly, digital engagement can be more effective than traditional print media. Consider

how major newspapers such as *The New York Times* have gained over 60 percent more digital readers in their website this year and are on track to double digital revenue from 2014 to 2020.[3] The digital channel can be powerful, because it can be personalized in real time: the right message at the right time, based on physician patterns. This offers a perfectly tailored sequence of information, in sharp contrast to today's status quo—preparing material in advance and hoping it is the right content, in the right order.

Channels are important, of course, and the right content needs to be strategically placed throughout the year using the right channels, while taking into consideration factors such as information from medical conferences and journals. Having a high-velocity, disciplined content development process is critical, and this requires MA to make intelligent choices about sourcing and packaging of content. Tailored content can become very expensive, very quickly, so repurposing internal content or being creative about content sourcing (for instance, crowdsourcing of content through online medical community platforms) would be a smart approach. Overall, tailoring communications and content to the different physician segments (for example, opinion shapers, versus rising starts, versus general practitioners) is the key to effective engagement. These groups will likely require different types of content, level of detail, and sophistication to find the output appealing.



3 www.forbes.com, "*New York Times*' digital subscriptions continue to drive growth," May 4, 2017.

4. Measure, measure, measure.

Inferior and poorly targeted content does not engage the user and is ultimately wasted. So how do you know if your strategy is delivering the expected impact? Analytics is the answer—for example, linking CRM data on engagement and outputs with data on patient outcomes derived from electronic medical records. The ability to capture and interpret a variety of metrics is a prerequisite to both setting an initial digital strategy and adapting it in real time. Capturing the value of digital content to your stakeholders, and thus to your company, can be achieved using a variety of approaches.

- **Generating user insights—**The capacity to personalize platforms depends upon the ability to collect user experience information (in a manner that complies with privacy laws and terms of use) about how physicians engage with digital platforms and their content. Analyzing individual stakeholder patterns uncovers their preferences and enables content providers to make adjustments to best serve individual users as well as enhance overall digital strategy. Every digital interaction generates data that can be used to derive insight. Machine learning can be used to determine the perfect content pattern in order to answer questions such as "What does my physician want to discuss?" or "What is the most effective way to discuss it?". Natural language processing can be used to understand the most frequent things physicians are emailing and calling about. The feedback can then be used in the deployment of teams and content creation.

- **Measuring impact—**MA teams must also capture clear operational and impact metrics related to their digital offerings. Continuous measurement of operational usage includes number of visits and downloads, as well as time spent per page. Quality metrics such as content quality rating and usability ratings also provide valuable feedback. Best-practice companies would go further and look at the role digital engagement has on other channels in order to determine the downstream call rate, the repeat visit rate, and how sessions change from one to another.

- Finally, impact metrics such as sentiment and recommendation scores can provide insight into whether the content actually improved clinical practices or patient outcomes. Identifying a range of metrics to capture and monitor

will help MA teams determine whether their strategy is achieving its goals, and also whether the digital channel mix is optimal for those goals. Our observation is that very few biopharmaceutical companies continuously measure and optimize operational metrics such as visits, conversion rates, and time spent. All three of these metrics are needed in order to optimize digital engagement.

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- **Integrate measurements into a 360-degree feedback loop—**Even with measurement, many organizations fall short in their ability to bring the results back in, and "course correct." This can be achieved by establishing a "360-degree command center," a dedicated set of one or two teams who are reviewing the results globally and ensuring that the key findings are integrated into future strategy. This acts as a "SWAT team" to identify root causes of issues and key drivers of performance, with a mandate to guide local medical teams accordingly, based on global insights. Taking this a step further, firms could consider augmenting the command center with technical integration application programming interfaces (APIs) that ensure there is a feedback loop for digital channels.

5. Deploy digital to become more agile in anticipating and responding to needs.

Inevitably, however, organizations can spend too long developing and testing, rather than just implementing. Overall, we require a change in mind-set: we need to try out new ideas and keep learning rather than looking for the "perfect" solution, which can take so long to develop that it's no longer perfect—just a significant investment. Organizational agility takes many forms and can be enhanced both through the structure and culture of the organization as well as the tools and systems deployed. A successful digital culture inevitably includes early iterative testing of offerings with stakeholders. The mindset required is: "Don't let perfection be the enemy of the good." Instead of requiring a perfect

platform, agile teams will launch a prototype that can be continuously tested and refined through user feedback. This approach requires a mind-set shift for most MA teams: a "test, learn, and can do" attitude stands in direct contrast to traditional processes, which are heavy on committee consensus and long proposals. This fresh way of working is critical to developing a compelling digital experience.

In terms of tools and systems, one way to transform stakeholder engagement is to empower MA and MSLs with a physician "next-best-action" recommendation system. The veracity of data and effectiveness of machine learning can further empower medical affairs, whereby the insight generated can be integrated into a next-best-action system—a common practice in mature industries such as banking. Such analytically enabled next-best-action systems can transform the current outdated engagement model into one that is proactive by helping to prioritize visits for known opinion leaders and responding to proactive outreach.

Addressing common questions can create exponential value. Which physicians should we communicate with, and with what frequency? What is the best channel for the communication: is it face-to-face, email, video chat? What topic should be discussed, and explicitly how? What are the current specific pain points for my physician and how do I address them? All of these questions can be answered with machine learning, predicted in real time, for each physician to guide their engagement. MSLs could rely on daily use of the recommendation system as a new "brain companion" designed to help increase the effectiveness of the field medical team and, importantly, the satisfaction of the physicians they engage.

Another important element is forward-looking agility. Medical affairs' digital strategies are often largely reactive, based upon current physician preferences and stated interests, and addressing current sources of medical information, education, and engagement. However, while satisfying current user needs is obviously necessary, it is equally important to identify developing demand trends such as the desire to use patient-

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focused big-data analytics as well as new sources of medical content such as virtual reality for surgeries. Just as Uber has transformed the for-hire transport business by having private persons deploy their underutilized vehicles, we can imagine something similar emerging in the healthcare sector with the use of big data to profile patients, improve clinical decision making, and enhance medical information distribution and education.

Conclusion

These five imperatives can guide medical affairs toward achieving digital mastery. It should be noted that digital capabilities are also needed elsewhere in the organization, and would be difficult for MA to develop them in isolation. The medical affairs organization should work hand in hand with commercial to redesign the go-to-market model to integrate digital and non-digital channels more effectively. Furthermore, they should consider digitization to improve major multi-step, time critical processes such as material review, knowledge management, grant management, and digital knowledge management tools.

A winning digital strategy means taking a wider industry perspective. Medical affairs teams can and should find ways to collaborate with MA teams within other companies. Platforms can originate with specific biopharmaceutical companies and potentially evolve to become cross-industry platforms. At the same time, medical affairs organizations should be specific with regulatory bodies about what they are trying to achieve—in this way they can work to redefine compliance rules for the digital age.

Without a digital refresh, biopharmaceutical companies remain at a disadvantage and risk being disintermediated by new market entrants as the preferred source of healthcare information. New rules of engagement designed specifically for the digital world will spark innovation within MA to facilitate delivery of the tailored and unbiased content that physicians and other stakeholders are now demanding to help them improve patient outcomes.

Engaging patients during clinical trials

Montana Cherney, Amit Paley, Leslie Ruckman, and Kevin Webster

Digital provides the opportunity to reimagine clinical trials around patients, in order to improve participation and adherence.

It's clear that the wider healthcare landscape is changing both rapidly and fundamentally in response to a number of powerful forces. Science and technology is progressing swiftly, while payors and patients are quite rightly becoming ever more demanding as they seek better outcomes. Patients have more information than ever before at their fingertips and a greater range of choices as health consumers. In response, health professionals and providers, payors, and biopharmaceutical companies have been moving to position the patient at the center of their activities.

In the context of R&D, these forces have important implications for the way research is conducted and trials are designed. Patient centricity, in particular, is becoming an increasingly potent force for change within clinical trials, driven by several specific trends:

Competition. An explosion of clinical trial activity across the industry has sparked an arms race to recruit trial participants. Examples include therapeutic areas such as lung cancer, inflammatory bowel disease, and multiple sclerosis.

Patient empowerment. 1 in 20 Google searches are now for health-related information.[1] Consumerization of healthcare has given patients a greater stake in decision making about their care. Patients are taking a more active role in researching their options, especially when a physician recommends a clinical trial. They arrive

1 Google blog, "A remedy for your health-related questions: Health info in the Knowledge Graph," blog entry by Prem Ramaswami, February 10, 2015, googleblog.blogspot.co.uk.

in the clinic with more knowledge about themselves and their conditions, higher expectations, the desire to be treated as partners in their care, and will increasingly seek to evaluate multiple trials that may be available across numerous centers. Additionally, the growth of online advocacy and support communities has created a mechanism for patient experiences to be shared, making it all the more critical for a trial to engender a positive experience for its participants. If it fails to do this, a negative reputation and negative-feedback network effect may spell disaster for enrollment targets. For this reason it is also vital to engender appropriate habits among trial participants. Sustainable habit building relies on accurately designed tools and timely notifications to enable consumers and providers to successfully adjust to changes in daily routines and behaviors.

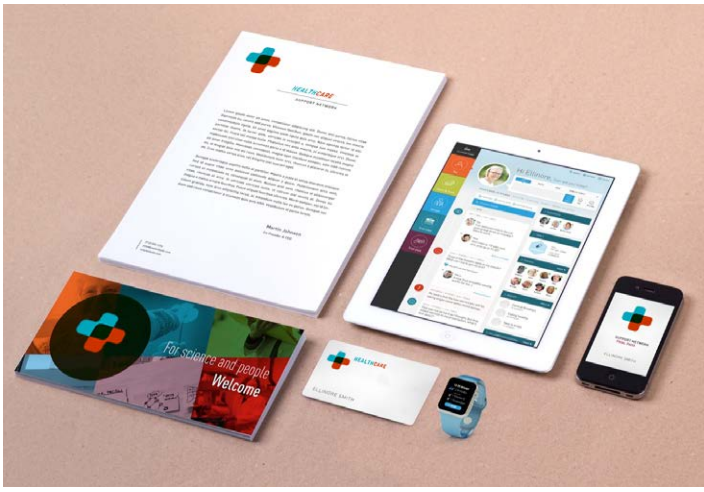
Trial registries. In order to support effective clinical development, many trade groups and government organizations are launching trial registries to provide transparency and some data sharing across multiple trials. One example was announced in September 2016 by former Vice President Joe Biden as a key component of his Cancer Moonshot Initiative, which is designed to marshal resources across the federal government to speed progress in cancer research and lead to improved cancer prevention, detection, and treatment. Biden announced steps to make it easier for participants to find clinical trial opportunities as quickly as possible, incentivize new ways of designing clinical trials to maximize participation while minimizing burden and risk, and strengthen the transparency of clinical trials and trial results. The National Cancer Institute (NCI) of the National Institutes of Health (NIH) has redesigned the way cancer clinical trial information is made available to patients and oncologists through its "trials.cancer.gov" site. Patients can enter a few personal details to find nearby NCI supported trials for which they may be eligible.[2]

To respond effectively to these challenges, we need to engender significant innovation within the clinical trial experience: first, to increase trial efficiency

2 National Cancer Institute, "Cancer Moonshot℠," https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative; The White House Press Office, "FACT SHEET: Vice President Biden Announces New Steps to Improve Clinical Trials Essential to Advancing the Cancer Moonshot," https://obamawhitehouse.archives.gov/the-press-office/2016/09/16/fact-sheet-vice-president-biden-announces-new-steps-improve-clinical.

and effectiveness; second, to enhance user experiences; and third, to improve patient engagement and thereby improve adherence and outcomes.

Toward patient centricity



While clinical operations teams are only recently shifting to become more patient-centric, commercial teams have been making many strides in this direction. One biopharmaceutical company's oncology business unit recently told us, "As oncology product discovery continues to develop through clinical trials, it's crucial to gain a deeper understanding of true patient experience to drive better engagement, compliance, and patient retention. Greater involvement of patients and patient advocacy groups in the entire drug development continuum is the way to achieve this goal."

A core component of becoming more patient-centric is the ability to interpret the patient journey or journeys (given the diversity of patient experiences). Understanding these journeys can help clinical groups design and operate their trials in ways that minimize pain points during trials. In particular, understanding an individual's reasons for joining a trial provides insights into how best to fulfill their needs both medically and in terms of their motivation. This enables clinicians to address issues such as what the patient is looking to gain from the experience beyond alleviation of symptoms—for instance, advancing scientific research and helping future patients or receiving quality care at a discount. Digital techniques can be deployed to apply analytics to better understand these journeys as well as to develop creative interventions that better satisfy patient needs and desires for joining the study. For example, if a key pain point in the patient

experience is remembering to take an oral drug twice a day, we can deploy apps that will provide push notifications on patient devices (such as an Apple Watch or a smartphone) or use new adherence-tracking smart devices (for example, GlowCaps) on the clinical trial.

There are a number of ways in which the clinical trial process can be made more patient-centric in order to improve patient experience and adherence. In order to understand the patient journey more comprehensively, we have developed a process that enables stakeholders to rapidly gain insights into the process by mapping out the patient's journey in terms of an iterative branching cycle of finding and completing a clinical trial.

The healthcare decision journey

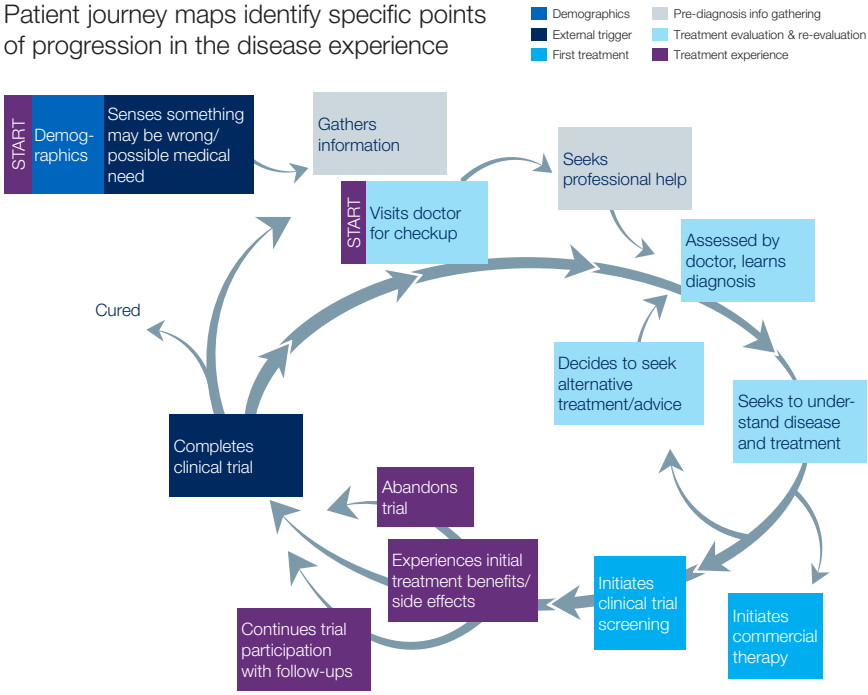
Most pharmaceutical marketers are familiar with the concept of conducting market research to create a "sales funnel" as a guide for marketing programs, where patients move in stages from product awareness to product purchase. Often, these use a linear or sequential logic to represent patient behavior. In the retail industry, that linear journey has been augmented in recent years by the consumer decision journey which recognizes that, in a world where consumers are empowered by information, the process involved in making a purchase is much more iterative.

For biopharmaceutical companies seeking to understand how consumers make healthcare decisions, the patient journey map is enlightening (Exhibit 1). It maps a patient's journey from first awareness of a problem to treatment, examining the factors guiding patient decisions at each stage. These insights enable clinicians and biopharmaceutical marketers to engage with patients in ways that feel natural and personal. That may mean providing information to help an important choice to be made, supporting the execution of that choice, or simply empathizing. For example, a patient's decision to enroll on a trial is one "success event" from the perspective of a trial manager, but just one of many points of influence in the patient journey map. Other factors are the patients' own research, their consultations with others, considerations of the

cost of treatment, scheduling of appointments, responses to side effects, or remembering to take medications. Some may be far more important personally for individual patients than the decision to enroll, such as the moment before the first time the patient self-injects a biologic (or the moment before the second time, when the patient remembers how much the first injection hurt). Every point in the patient journey map is potentially a vital point of interaction—by understanding it, trial managers can understand the relative importance of points and (re)allocate investment and attention accordingly.

Exhibit 1

Patient journey maps identify specific points of progression in the disease experience



The patient journey map above vividly illustrates the considerable branching and looping that can happen within each of five stages of a typical patient journey. The first group of instances relates to a patient's recognition of a problem (what we call the external trigger). The second is the process the patient goes through to gather information. The third represents the patient beginning to evaluate treatment options (which can be iterative). The fourth is the beginning of treatment and the fifth is the ongoing treatment. Patient behaviors and experiences at each point differ by disease and by patient, so the patient journey map has to be disease specific. For example, a map of psoriasis patients in the United States found that 58 percent had requested a specific brand of medication from their physician in the past year. This is twice as high as would be expected in the general patient population and illustrates the importance of communicating with certain segments of psoriasis patients before they visit a physician.

As we have seen, patient journey maps identify specific points of progression in the disease experience—the patient journey—and can be applied equally to the clinical trials process as to other elements of the biopharmaceutical product lifecycle. Exhibit 1 highlights some key stages in the patient journey in the context of clinical trials, and the decision processes that a patient may make. Clinicians and other stakeholders can use this map to identify key needs and stage gates during the trial process, and then devise corresponding mitigation strategies for the hurdles encountered. Some significant considerations are:

Knowing about a trial— Patients need to know about the availability of relevant trials and increasingly there are more options for trials a patient may be eligible for. Patients are increasingly looking to various sources such as online forums to identify trials of particular importance they believe have the best chance of significantly improving their condition.

Cost implications of trial enrollment— In certain markets, such as the United States, patients may wish to enroll in a clinical trial to reduce their cost burden of receiving treatment (for example, a patient may be uninsured and unable to afford the current standard of care therapy). Understanding the economic implications of trial enrollment in a compliant manner may be a critical factor for certain

conditions for some patients (for instance, moving to a long-lasting formulation of a drug to treat macular degeneration compared with the equivalent active agent in the current shorter-acting formulation).

Convenient trial location— While patients may change providers to enroll in a clinical study, each degree of removal will likely face significant attrition (for instance, if the trial is not active at the patient's current physician, or within the same facility, or geographically nearby). Understanding of this drop-off curve differs by disease state and expected trial clinical effect (for example, patients will travel far farther for a disruptive cancer therapy with curative potential than a biosimilar trial). Biopharmaceutical companies must then identify where critical patient pools lie and analyze data around how each of these sites is expected to perform on a trial to optimize site selection for the trial.

Burdensome screening protocols— Patient research can help inform the barrier to enrollment that invasive testing techniques may present, which will vary by disease and projected trial impact. Understanding this will help clinical trial designers weigh tradeoffs of potentially using less-invasive testing recognizing that may influence cost and breadth of sites eligible for the study (for instance, PET scan versus lumbar puncture for Alzheimer's disease).

Burdensome follow-up (too frequent, too long per visit)— The adoption of new technologies such as telemonitoring wearables can dramatically reduce the burden for patient monitoring on the trial, while also providing a much richer data set for analysis (for example, a Fitbit in conjunction with a periodic video conference for a heart-failure therapy with mobility as the readout).

Limited experience of ownership and appreciation of being on a trial— Being provided with the results of a clinical study after completion or receiving access to a patient's own data from a trial may significantly improve the participant experience and deliver genuine value—for example, where a cancer patient receives a full genomic sequence, this can be used later to guide care in a subsequent line of therapy. Other options include being invited to patient advocacy meetings or key conference proceedings where results are being published.

Devices offer new ways to engage with patients

The rapid advance of wearable sensors into the consumer market has created fundamentally new channels for clinical trial planners to engage with patients. Back in 2013 only a couple of dozen trials used wearables; today there are well over 100 incorporating this technology. Increasingly, we are seeing wearables and other connected devices used for real-time monitoring of patients' vital signs during trials, helping to reduce the cost of data collection, and to improve understanding of patient behaviors (such as adherence), and outcomes. For example, Stanford University was able to recruit 11,000 participants for a heart disease study in 24 hours using Apple's ResearchKit. A further study suggests ResearchKit is especially suitable for short-duration trials requiring rapid enrollment across diverse geographical locations, frequent data collection, and real-time feedback to participants.[1]

Beyond consumer devices such as Apple Watches and Fitbits, specialized devices are being developed to non-invasively measure key vitals where previously such activity required cumbersome visits. One example is GE's wireless "Band-Aid"-like skin sensor that analyzes sweat for hydration and stress levels.

Trial designers now have the potential to collect large longitudinal datasets in real-time from participants in a much less invasive fashion. To exploit these new technologies to the fullest, trial planners must first have clarity on what will be measured; identify the "fit-for-purpose" device technology, establish the supporting infrastructure required (such as training), collect the data into a centralized secure database, and prepare for the analytics needed to generate insights. At the same time they need to consider what will happen beyond the trial. Will the device continue to be provided once the trial has been completed and at what cost? Will the technological cycle be so quick that new generations of smartphone are no longer compatible with companion devices?

Adherence: a leading application for connected devices in trials

Adherence continues to be a significant factor in attaining positive outcomes for patients with chronic illness—low adherence during trials can restrict data, reduce efficiency, increase costs, and ultimately slow trials so that treatments take longer to reach the wider patient population. We see the emergence of new devices designed to track and improve adherence (for example, AdhereTech), which are initially applied in the commercial setting and then move into the clinical trial setting.

However, companies need to design devices that patients are not only "able" to use but also "want" to use. This applies equally to standalone systems or devices in combination with digital tools such as companion apps.[2] As with all technology, it is important to ensure that digital devices are user friendly: patients, carers, HCPs, and researchers do not need the added burden of dealing with a technological solution that requires significant setup and maintenance effort. For example, we are aware of one smartphone pilot during which there were device charging issues, problems with log-ins, and leakage of personal data—all of which the contract research organization had to fix for the trial to progress.

1 Malcolm Owen, "Asthma study using Apple's ResearchKit proven accurate when compared to existing research," AppleInsider.com, March 13, 2017.
2 Thomas Nilsson, "Combination products, companion apps and patient adherence," Veryday blog, http://veryday.com/aspect/combination-products-companion-apps-and-patient-adherence/.

Going forward

We definitely see wearables playing an important role in collecting usage patterns and driving patient engagement. However, it is not as simple as providing a device and hoping to improve adherence. In the future, we see two device archetypes emerging: 1) super-robust dedicated devices that work to collect data in a simple and affordable way; and 2) an already-existing massively distributed platform at scale—such as Apple—either working directly in the main device or through companion hardware.

We're likely to see more and more attempts to build devices and wearables into drug discovery and trials. This would enable a direct link to patients—and may even be required to comply with drug approval requirements down the line—as biopharmaceutical companies demand more patient data on usage and efficacy as they seek to partner with payors. Nevertheless, claims that mobile technology can currently accelerate research at scale may be premature; there are still significant creases to iron out.

Additional example applications of connected devices in clinical trials

Asthma—One study linked known real-world events such as pollution to increased reports of local asthma episodes.[3] Researchers from the Icahn School of Medicine at Mount Sinai in New York analyzed data from the Asthma Mobile Health Study, a program launched in March 2015. Relying on a specially created iPhone app called Asthma Health, the study data was compared with the results of other asthma patient studies, with researchers noting common metrics between the sets of results, such as peak flow. Scientists were also able to correlate data from patients with external factors, including air quality, and this also appeared to match existing studies. Changes to the level of pollen and heat could also be corroborated in the study, when taking into account the user's location and other device data. Although the study is unlikely to have been 100 percent stable (it was based on self reporting with inevitable variations in robustness of the data), it serves as a good indication of the direction in which wearables are headed.

Epilepsy—A research study on epilepsy using Apple Watch and ResearchKit helped shed light on seizure triggers.[4] During a ten-month survey, participants tracked their seizures via a custom-built app. When participants felt an "aura" for the seizure building, they opened up the app, which then instructed the Apple Watch to record heart rate sensor and accelerometer data, while the iPhone recorded gyroscope data for ten minutes. During this period, the app prompted users to respond for reflex and awareness testing. Following conclusion of the seizure, study participants were surveyed about seizure type, aura, loss of awareness, and possible seizure triggers. The app also tracked prescription medication use and drug side effects, activities that are important in helping people manage their condition.

3 Malcolm Owen, "Asthma study using Apple's ResearchKit proven accurate when compared to existing research," AppleInsider.com, March 13, 2017.
4 Mike Wuerthele, "Apple Watch & ResearchKit epilepsy study concludes, gleans insight on seizure triggers," AppleInsider.com, February 22, 2017.

Patient adherence

Patient adherence in the clinical trials setting is driven by a myriad of factors (Exhibit 2). These include the degree of difficulty the trial protocol poses for individual participants, patients' attitudes toward their condition; individuals' ability to manage their health, how the trial drug makes them feel, and how much support patients have during the process. All of these need to be factored in if the clinical-trial process is to be optimized around the patient. (See the following sidebar for the four key drivers of adherence.)

Exhibit 2

A myriad of influencers have an impact on adherence

1 How difficult the trial protocol is for me	2 My attitudes toward my disease/condition	3 My ability to manage my health	4 How the drug makes me feel	5 How much support I have
▪ Time required ▪ Costs ▪ Dosing regimen and trial requirements ▪ Data collection ▪ Complexity	▪ Personality ▪ Motivation ▪ Acceptance of disease ▪ Emotional state ▪ Competing priorities ▪ Sense of control	▪ Co-morbidities ▪ Health literacy ▪ Adequate insurance coverage ▪ Diet and exercise	▪ Toxicity ▪ Efficacy ▪ Side effects	▪ Family ▪ Friends ▪ Health care professionals ▪ Tools (organizers, reminders, and rewards) ▪ Knowledge

One Fortune 100 biopharmaceutical company introduced a customer support program for people with metastatic breast cancer, designed to improve adherence and the patient experience during clinical trials. This program sets out to ensure patients, families, and healthcare professionals experience value at each interaction, by targeting their social, emotional, and educational needs in addition to the physical and structural requirements of a broader service ecosystem. The solution includes a range of digitally enhanced care services that provides each user with options for personalization, peer and expert support, and medication reminders across multiple platforms.

Key drivers of adherence

Adherence is a major factor in managing costs during clinical trials and dictating successful outcomes. There are a number of factors that can contribute to improving participation and retention rates. We see four key areas for attention:

Access

Convenience: Provide the information and options to facilitate making timely decisions.
Hidden costs: Reduce the burden of participation.

Simplicity

Protocol design: Consider the patient experience when designing trial protocols.
Habits: Build educational and motivational triggers into the treatment routine of the trial.

Motivation

Contributions: Reciprocate the motivation to contribute to science by showing gratitude to patients for their contribution.
Desirability: Clarify how people benefit personally from the trial experience, even if they might be on placebo, to provide motivation. Participation in treatments should focus on feelings of achievement, targeting output and meaning, rather than illness.

Support

Relationships: Build relationships between trial sites and participants to share knowledge and encouragement without compromising the trial.
Collaboration: Enable supportive communities to be built around the trial experience. Peer-to-peer knowledge sharing is indispensable to many health consumers as it sets expectations for what success looks and feels like.

In conclusion, there are a number of opportunities for reimagining clinical trials around patients, to improve experience and outcome, before, during, and after the trial (Exhibit 3). Digital engagement of patients provides us with both a qualitative and quantitative understanding of their situation and behavior, and enables us to become more patient centric in the way we design trials.

Exhibit 3

Opportunities for reimagining clinical trials around patient to improve experience and outcome

Before the trial

- Co-creation in protocol design
- Patient identified key performance indicators (KPIs)
- Patient input in the formulation and use of the molecule itself
- Simulation and service prototyping of the trial experience
- Team based on-boarding to drive better engagement
- Patient identified studies to run

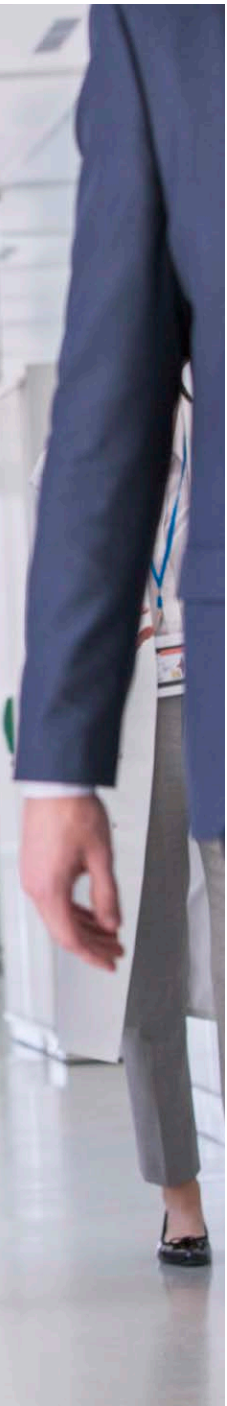
During the trial

- Patient experience measurements used to improve service delivery
- Better adherence data collected to understand true influencers of patient adherence
- Social and emotional support accounted for through trial specific peer communities
- "Wrap-around" services are improved and evidence based
- Tools targeting communication and comprehension ("trial literacy") are offered to support patients throughout the trial experience

After the trial

- Patients are "given back" their data collected during the trial
- Patients are kept informed of the progress of the trial and future comercialization
- Patients are thanked for their participation and contribution
- Patients are engaged as subject-matter experts in the trial experience
- Patients discuss their total experience and connect potential future trial participants through word-of-mouth

Deploying digital engagement technologies to support patients at key stages of their journey allows us to optimize the trial process via a more comprehensive understanding of that journey and ultimately improve participation and adherence.



The journey toward investigator engagement

Edd Fleming and Fareed Melhem

Adopting a partnership mind-set with investigators will ensure better engagement and ultimately enhance clinical trials.

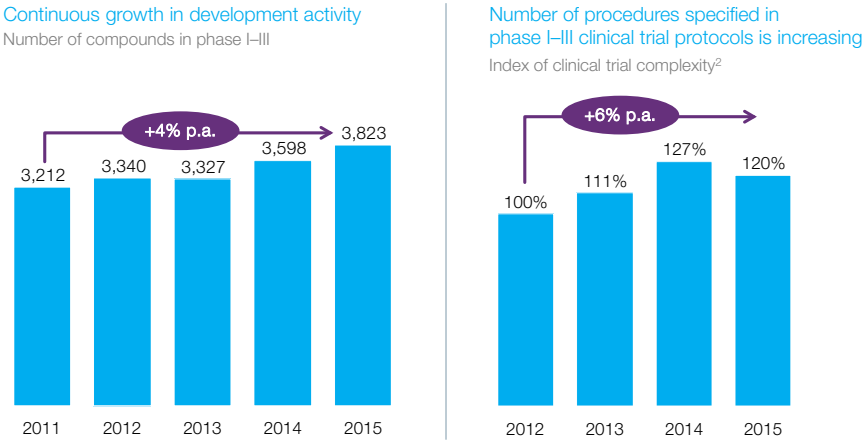
Engaging customers effectively is one of the primary drivers of business success, and biopharmaceutical company R&D should be no exception in this respect. The success of any clinical trial—from protocol design, through enrollment, adherence, and completion—is heavily dependent on engaging two very important groups successfully: trial participants (research subjects) and clinical trial investigators and their staff.

Today investigators and their staff are often treated as service providers are faced with onerous demands from trial sponsors and contract research organizations (CROs). Investigators may often be presented with limited lead times and expectations of a rapid start up, following protracted budget negotiations; frequent amendments to trial design and protocols, and numerous data queries with rapid turnaround expectations. Improving these relations should be a priority for sponsors, especially those in crowded therapeutic areas (TAs) where investigators have a choice of partners.

This is especially important in today's trial landscape, which is becoming increasingly complex. The growth in the number of assets, trials, and countries involved are adding to the trial workload for clinical operations functions and investigators. In addition to growth in development activity, trials are becoming more complex with inclusion/exclusion criteria becoming more detailed and the number of procedures specified in protocols expanding (Exhibit 1).

Exhibit 1

The number of trials is multiplying and they are becoming more complex



1 Trials reported in ClinicalTrials.gov; limited to interventional trials with reported start dates for drug, biologic and genetic interventions.
2 Defined by number of procedures per patient, indexed to 2012 value.
SOURCE: clinicaltrials.gov; Pharmaprojects

Against this backdrop, competition for trial sites is growing, in particular in crowded TAs such as oncology and immunology. As companies become increasingly sophisticated in their approach to site selection and patient recruitment, we expect top sites to receive even more attention. These factors are conspiring to increase pressure on clinical investigators, making it all the more important for biopharmaceutical companies and CROs to upgrade and differentiate in their approach to investigator engagement.

Companies today are at various stages of sophistication in terms of investigator engagement. Nevertheless, there is an opportunity for every trial sponsor to take a more holistic view as competition for sites becomes more and more intense. In this context, digital opens up several new avenues to help us consider the investigator experience in terms of collaboration and communication, trial design, and process simplification.

Understanding investigators: Shifting to a customer-centric mind-set

As discussed above, engaging investigators effectively requires a customer-centric mind-set and detailed understanding of the process. In particular, an empathy-backed approach—taking time to talk to a sample range of investigators and understand their pain points—will facilitate engagement. One effective way do this is in the context of an investigator journey map (see sidebar). This exercise maps the various stages of the investigator's journey throughout the course of the trial from the point of view of the investigator and their staff, logs any potential pain points, and charts investigator sentiment during these events. The focus is not only on the actions but also on the associated feelings and challenges.

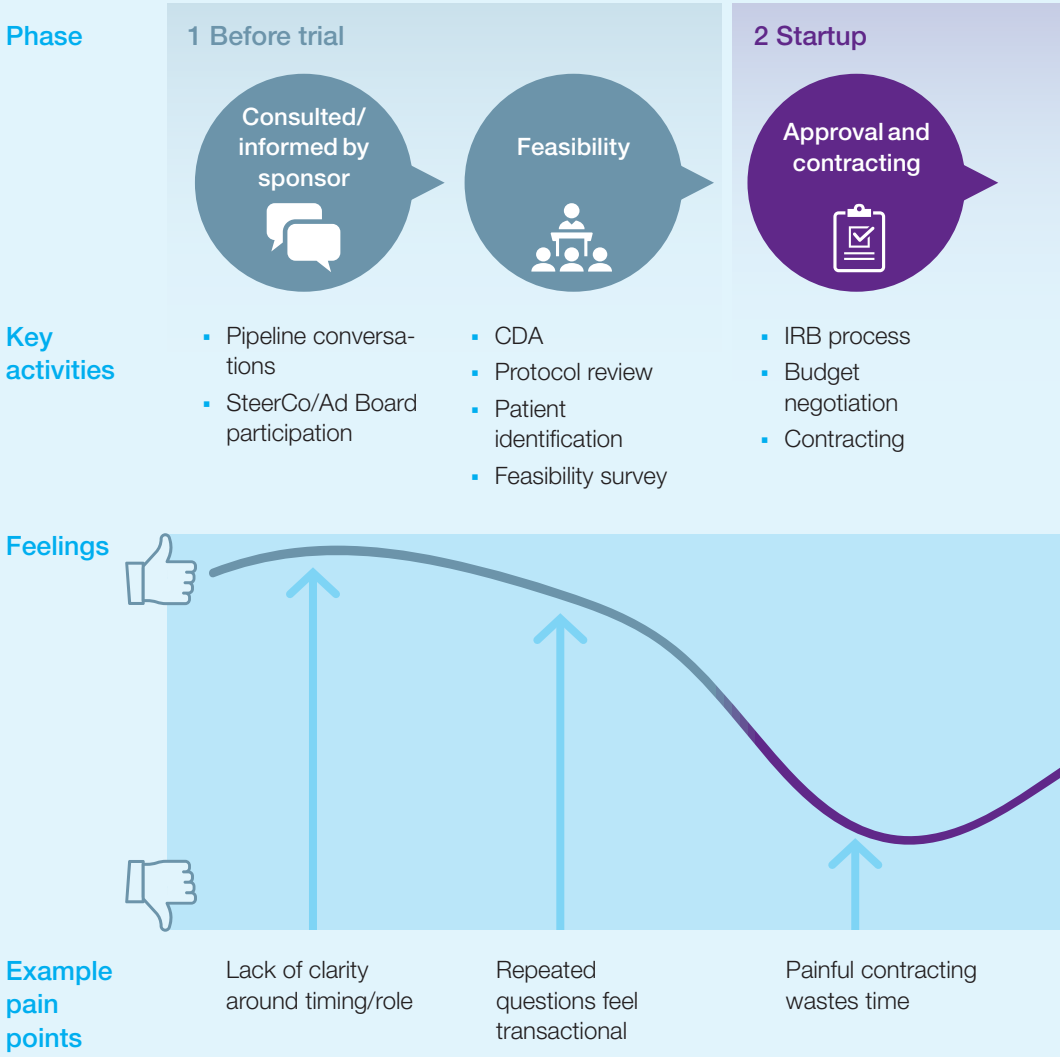
It is also important to acknowledge that investigators have different concerns, and to personalize the journey maps accordingly. For example, the needs of an investigator working at a leading research institution are markedly different from an investigator running their own clinic. Typically, a few representative personas can be defined to act as proxies for the different segments of investigators. These personas allow you to develop empathy for investigators and craft a narrative around their specific needs and pain points.

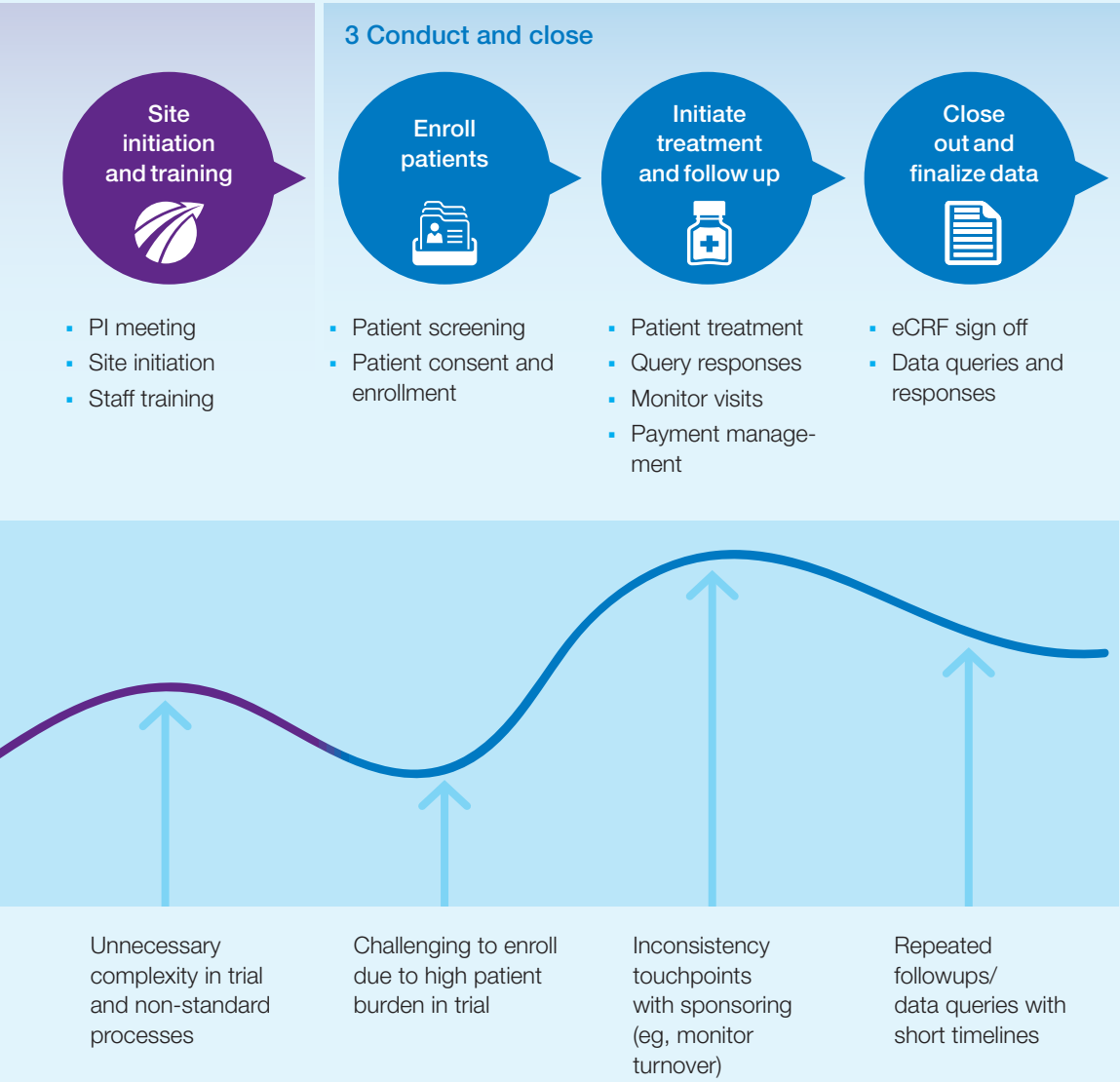
This approach of personas and journey maps enables trial sponsors to identify potential problem points, and address them upfront by designing more investigator-friendly formats. An important part of this process is to consider and include all relevant stakeholders, not just investigators, but coordinators and patients too.

Translating into concrete tactics

From our work in the area, including numerous conversations with investigators across segments and regions, we have identified a number of opportunities to better support and engage investigators. Digital is a major facilitator of these opportunities, whether this be creating seamless communication platforms, rethinking study design, or reducing investigator burden through analytics.

An investigator journey map logs pain points and charts investigator sentiment




3 Conduct and close
Site initiation and training
Enroll patients
Initiate treatment and follow up
Close out and finalize data
PI meeting
Site initiation
Staff training
Patient screening
Patient consent and enrollment
Patient treatment
Query responses
Monitor visits
Payment management
eCRF sign off
Data queries and responses
Unnecessary complexity in trial and non-standard processes
Challenging to enroll due to high patient burden in trial
Inconsistency touchpoints with sponsoring (eg, monitor turnover)
Repeated followups/ data queries with short timelines

Some key areas for consideration include:

- **Supporting better collaboration and communication.** Investigators tell us they want to feel like partners, not vendors—and this includes collaboration on trial design and ensuring simple and fast two-way communication. In this context, digital communication platforms offer the opportunity for clear points of contact, frequent communication, as well as the ability to solicit feedback from a larger number of investigators. Equally, an effective customer relationship management (CRM) system allows trial sponsors and CROs to understand which investigators are being contacted across the organization and how this is being done.

- **Develop investigator- (and patient-) friendly studies.** As we have seen, it is important to consider the patient and investigator burden in any trial design. We can adopt a number of practical approaches to ensure this happens:
  - Being thoughtful about protocols up front to reduce amendments, which advanced analytics can support by identifying the drivers of slow enrollment and amendments and by developing more robust scenarios before trial start
  - Undertaking live run-throughs of studies with investigators and patients
  - Ensuring broader engagement of different types of investigators to seek their input

Technology that is capable of supporting innovative trial design such as telemonitoring and remote data collection, can reduce the burden on investigators and trial sites.

- **Streamline the administration process by going digital.** Simplification of the process and digitization of supporting paperwork can reduce the investigator (and patient) burden dramatically:
  - **Contracts—**Streamlining via digitization of the documentation, implementation of e-signature, and standardizing contract language

can simplify the contract process, while standardization of pricing can address a common complaint from investigators around the need to renegotiate each trial.

- **Feasibility—**Checking site-level feasibility can be unnecessarily complex and repetitive. Digitalizing and simplifying this process—for instance, by avoiding unnecessary repetition of standard questions to a site that has participated in multiple trials over time—avoids duplication of effort for investigators and busy trial sites.
- **Consent forms—**These can be daunting documents. Simplifying them can make the process of acquiring consent easier and less time-consuming for investigators and subjects alike.

- **Streamline the process of data collection.** Simplifying data requirements, streamlining data capture, and deploying risk-based approaches to monitoring can greatly reduce the data burden on investigators, a key pain point:
  - Electronic data capture and electronic medical record (EMR) integration has already made significant strides, and continuing to deploy it will be a key to ameliorating investigator burden. In addition to these technological solutions, sponsors should also more strongly consider which data is truly necessary to capture. Often, there is an over-collection of data, burdening both patient and investigator.
  - Quality monitoring is a critical aspect of any trial, and ensuring data integrity is important. Yet this activity also places a significant burden on both companies and investigators. Moving toward predictive analytics to focus monitoring visits in places it will matter increases the efficiency of the process significantly. By shifting toward predictive site quality monitoring (that is, next-generation risk-based monitoring) that incorporates and integrates site-level data with machine learning, biopharmaceutical companies can significantly improve their early-warning system and shift resources appropriately. At the same time, it can reduce and simplify data queries. The majority of queries have limited impact, but determining which ones are actually required is challenging. Advanced analytics can help

resolve this problem by developing predictive models to identify important queries and so reduce the overall volume of queries to be followed up. In addition, such analytics can help biopharmaceutical companies be more proactive, so that when queries are needed, there is more lead-time available to investigators, which in turn helps to reduce the burden of rapid data turnaround.

- **Partnership mind-set throughout the organization.** Optimization of investigator engagement is not just about digitizing a collection of processes—it requires a change in mind-set within the organization. It is essential to rethink the internal organization from a partnership perspective. Moving away from viewing investigators simply as service providers to improve the way studies are conceived and designed to ensure the investigator point of view is included. This partnership mind-set needs to flow through the whole organization so that the vision is translated into action at the front line. Practical measures to promote this mind-set could include sponsors taking time to spend a day with an investigator to understand specific pain points and gain a fresh perspective, including an investigator advocate in meetings where trial design and protocols are discussed, and ensuring that senior company leadership have designated a partnership approach as an explicit priority.

Steps to take

How then might we transform our approach? There are a number of practical steps that organizations can take as part of a roadmap to better investigator engagement.

- **Consider the people and places where you need to win (high-competition areas)—**for example, by identifying segments of investigators or sites that you think are critically important, either because of their productivity or their scientific credibility. Consider those aspects that influence relationships with investigators where there are a number of competitive trials going on and they have a choice of which companies they work with. Give these investigators extra support and really focus on relationship building in these instances, because it will be difficult to provide the same level of service to all investigators.

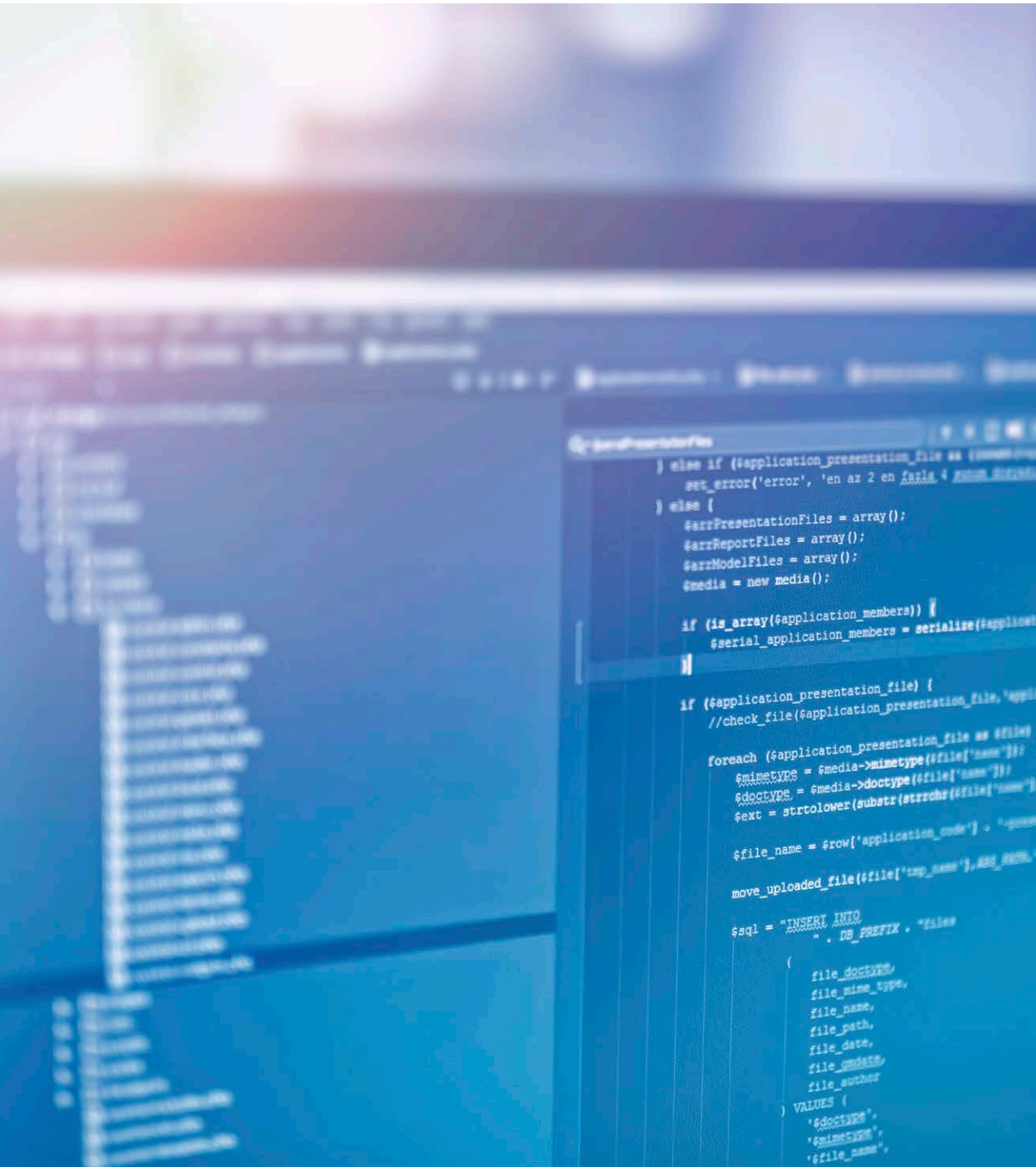
- **Map the investigator journey using an empathy-backed approach** by including investigators in the conversation to understand their concerns and pain points. This is not something that can be done within the walls of the company, nor is it a "fluffy" approach; it needs to be rigorous. To do this, the company must go out and engage investigators in a journey-mapping exercise, and ask them questions from their point of view. This needs to be done in a structured way to drive a deeper level of understanding than could be achieved via a traditional survey.

- **Identify a small set of changes to begin to shift the mind-set—**there are opportunities for both internal and external initiatives. Internally, this could be as simple as having someone play the role of investigator advocate in every study planning meeting to talk about how the trial would work from the investigator point of view, or it could involve a walk-through of the study design to understand what it looks like and how it feels. Externally, initiatives might include an operational feasibility advisory board to help stakeholders work through the practicalities of the trial from the investigator and patient perspective; equally, it might involve development of minimum levels of service such that when an investigator has a query, the company gets back to them within a specific timescale. These types of changes are relatively easy to adopt and roll out on an incremental basis while simultaneously planning more transformational changes.

Conclusion

Improving investigator engagement will continue to become more important as competition for sites and patients increases. Analytics and digital open up important new opportunities to engage investigators individually and streamline and enhance the trial process. By reconsidering the entire process from the perspective of the investigator (and trial participants), it is possible to identify a number of opportunities to better engage stakeholders through the stages of trial design, set up, conduct, and close. Ultimately, these efforts should promote a feeling of partnership that will stand sponsors in good stead and make it more likely that a specific trial receives the attention it deserves. Listening to investigators during the trial process also allows biopharmaceutical companies to capture any additional ideas and improvements to enhance trial design and execution.

Designing a digital transformation at scale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} else {
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$arrReportFiles = array();
$arrModelFiles = array();
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}
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$doctype = $media->doctype($file['name']);
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file_gmdate,
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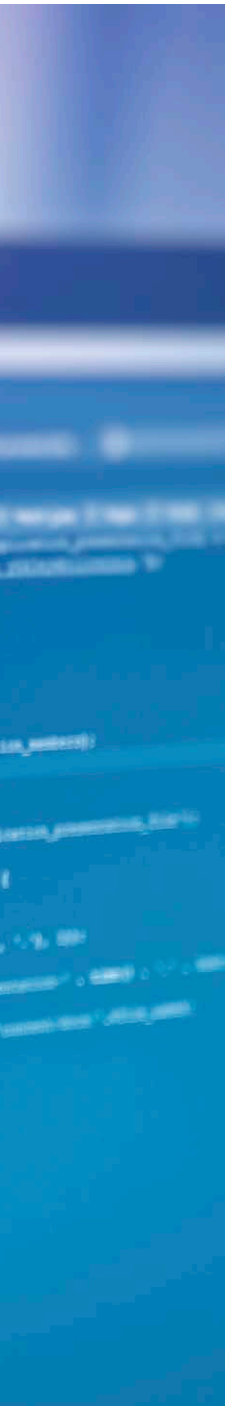


Four keys to successful digital transformation in healthcare

Sastry Chilukuri and Steve Van Kuiken

By taking a comprehensive approach to digitization, healthcare companies can deliver products and services more quickly, boost innovation in the industry, and hold down costs.

Healthcare companies (device manufacturers, payors, and providers, among others) have long relied on technology for such things as tracking R&D efforts and patient information, scheduling payments and services, and launching new care options.

The digitization of products and processes, however, has dramatically changed the game for everyone. Consumers' expectations about healthcare services are increasingly being informed by their experiences with large digital-born companies. With this "customer experience" frame in mind, healthcare companies are seeking to integrate the latest technologies into existing business models and IT architectures to improve services. At the same time, they are grappling with new, nontraditional entrants to the marketplace (such as IBM and Microsoft), as well as ever-present regulatory and risk-related concerns.

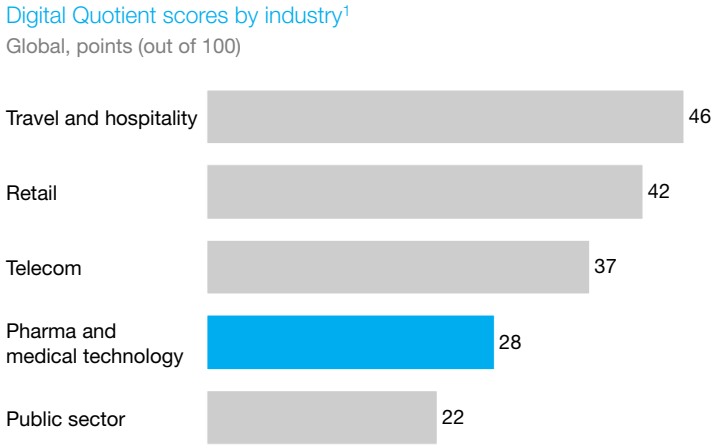
More and more healthcare companies worldwide are finding that digital technologies must be managed not as utilities but as strategic assets. Some are attempting to bridge the gap between legacy and digital IT by undertaking complex systems transformations. One large healthcare-technology company is experimenting with ways to maintain its existing IT architecture while using analytics to securely mine the data it collects for useful business insights. Similarly, a number of large biopharmaceutical companies are exploring the use

of cloud platforms to reduce data storage and processing costs and to boost the speed of their R&D efforts.

Still, most pharmaceutical and medical-technology companies are digital laggards compared with companies in travel, retail, telecommunications, and other sectors (Exhibit 1). Their digital transformation efforts stall for many of the same reasons they do in other sectors—for instance, a limited understanding of the specific ways that implementation of new technologies across complex product and services lines can create business value, a shortage of native digital talent, and insufficient focus on digital topics from senior leadership.

Exhibit 1

Pharmaceutical and medical-device companies lag other industries in their digitization efforts



1 McKinsey's Digital Quotient assessment measures organizations' digital maturity and capabilities against benchmark companies in various industries and geographies. The tool considers companies' digital business strategies, culture, organization, and capabilities in determining scores.

Source: McKinsey analysis

Our experience with companies inside and outside the healthcare ecosystem suggests there are four core principles for succeeding with this kind of all-encompassing change program. Healthcare companies must:

- Identify and prioritize their critical sources of value; they need to identify the products and services they provide that lead to competitive differentiation and that would benefit most from digitization
- Build their service-delivery capabilities—not just in physically integrating and managing new digital technologies but also in implementing new approaches to product development and distribution (for instance, agile and DevOps methodologies)
- Modernize their IT foundations: for example upgrading pools of talent and expertise in the IT organization, moving to digital platforms such as cloud servers and Software as a Service products, managing data as a strategic asset, and improving security protocols for the company's most vital assets
- Ensure that they build and maintain core management competencies, in other words, all the enablers that allow them to pursue a successful digital agenda

In this article we consider the changing healthcare landscape, the emerging opportunities in digitization, and the four core principles healthcare companies can follow to succeed with their digital transformations. Consistent with digital leaders in other industries, the front-runners in digital healthcare have a significant opportunity not just to win in their desired markets but also to change the rules of the game.

Understanding the changing landscape

Healthcare companies today face a different competitive environment than they did a decade ago—in part, because of the degree to which digital tools and technologies are disrupting typical product- and service-development processes, customer interactions, delivery mechanisms, back-office operations, and supplier relationships for large players in the sector.

Indeed, never before have so many technologies with the potential to affect the healthcare industry matured so quickly. Next-generation genomics; big data and advanced analytics; machine learning and automation programs; connected, sensor-enabled devices and wearables; 3-D printing; and robotics—all have the potential to fundamentally change the way healthcare companies develop products and provide services. Technology allows consumers to be more informed about and more engaged in healthcare decisions. At the same time, regulators and policy makers are advocating for the development of open data and technology standards as well as knowledge-sharing initiatives among companies in the industry.

As a result, some of today's healthcare companies are focused on using technology to improve their interactions with patients and ecosystem partners, rein in costs, streamline operations, and better manage changing industry regulations. They acknowledge the shift toward evidence-based medicine and are exploring ways to use big data to customize care programs and make the case for investment in and reimbursement for emerging devices or treatments. A good example of digital reinvention in healthcare is the life sciences giant Johnson & Johnson. This company has undertaken a massive digital transformation of its IT organization, moving the bulk of its processing workload to a hybrid cloud environment and incorporating data lakes, data analytics, and agile development practices into its operations. As a result, the company has been able to bring together different business capabilities such as design thinking, deep clinical knowledge, and a global understanding of healthcare systems in order to create new patient-centered offerings. (See "Healthcare giant shares prescription for digital reinvention," on McKinsey.com.)

By making the shift from a healthcare company to a digital enterprise, industry participants can capitalize on a number of emerging "battleground" opportunities. Among them are the following:

- **Building** direct relationships with consumers to influence treatment outcomes rather than working through institutional intermediaries. One service provider, for example, has linked disparate sources of data so clinicians can more easily analyze personal, clinical, demographic, genomic, and

environmental information to determine which personalized interventions would be appropriate for patients suffering from chronic conditions such as asthma and multiple sclerosis.

- **Finding** new sources of value in different profit pools. For instance, some healthcare companies, particularly new market entrants from the technology sector, are looking for ways to take caregiving out of its traditional hospital setting. Instead, they are developing ways to offer digital diagnostic services, remote health monitoring, and home healthcare.
- **Collaborating** to acquire complementary capabilities. Increasingly, providers and device manufacturers are partnering with other companies in the healthcare ecosystem, including market entrants from the high-tech sector. The latter are masters of consumer marketing, but, in general, they are relatively unfamiliar with regulatory processes in healthcare. Healthcare companies can help fill that expertise gap.
- **Contributing** to burgeoning industry standards and conduct. Healthcare companies at all levels of the service chain have an opportunity to define new rules of engagement. For instance, they could collaborate with the government on standards for open access to patient information or care protocols, thereby democratizing the delivery of healthcare.

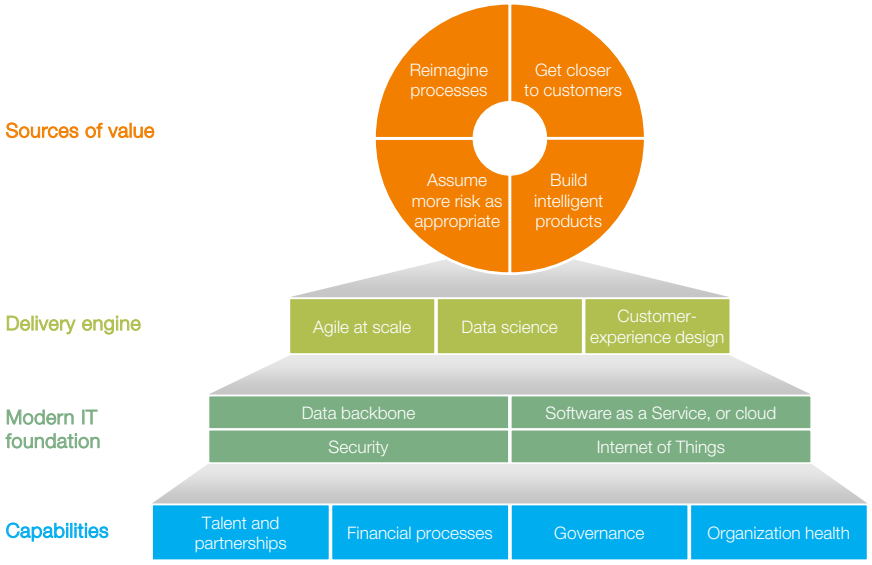
Succeeding with a digital transformation

The healthcare environment is becoming more distributed and complex. To adapt, companies will need to embrace open systems that allow for sophisticated analysis of multiple streams of data and the development of customer-centric services. They must be able to view processes as end-to-end flows rather than discrete hand-offs, embrace more risk (as appropriate), move at higher speeds, and engage in innovative partnerships. All of this is challenging for companies saddled with decades-old legacy systems, processes, and operating models that were optimized for a brick-and-mortar world.

The odds of successfully transitioning to digital systems and ways of working increase when healthcare companies focus on the four important dimensions of their businesses: critical sources of value for the company, the means by which the company delivers products and services, the company's IT architecture, and its talent, finance, and governance processes (Exhibit 2).

Exhibit 2

Digital transformations are more likely to succeed when companies focus on four critical dimensions of their businesses



1. Identify and prioritize critical sources of value

As a first step toward digitization, healthcare companies must clarify where the company provides distinctive value to consumers and stakeholders, and determine how the use of digital technologies could enhance those offerings.

Companies can then determine how best to adjust investments in digital technologies and development approaches to meet the highest priorities. They can also help steer management's attention in the right direction at the right times during the complicated transformation process.

There are several value propositions that companies may wish to target, depending on the company's position in the value chain. A clear source of value emerging for most healthcare companies is an ability to get closer to customers to give them targeted products and services, and engage them in value-based relationships. Some device manufacturers, for instance, may want to create intelligent products—sensor-enabled devices, inhalers, and auto-injectors, for example, that can monitor and manage specific conditions or assist in medical procedures. Biopharmaceutical companies could build digital platforms in order to collect and analyze medical data, conduct synthetic clinical trials, manage market access, and accelerate their research efforts.

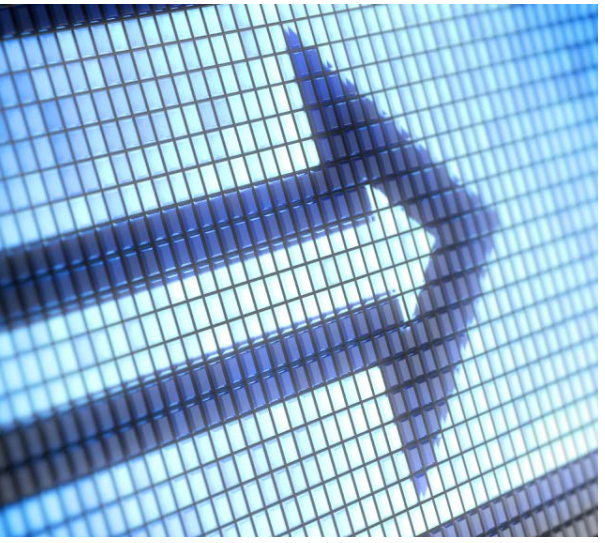
Some healthcare companies may want to explore ways to mitigate risk using previously isolated data sets. For instance, if manufacturers had greater access to cost-of-care figures, patient outcomes, satisfaction scores, and other metrics, they could devise new types of contracts and risk-sharing models with service providers. Consider that in a typical joint-replacement surgery, the implant itself represents just 15 percent of the total cost of care. Forward-looking manufacturers and providers could use shared, collected data to collaborate on ways to optimize the remaining 85 percent of the cost.

And finally, some companies in the healthcare ecosystem may want to use automation, robotics, and Industry 4.0 technologies (such as sensor-based

equipment and the Internet of Things) to break down walls between business units and functions, thereby speeding up processes and decision making and reducing administration costs.

2. Build service-delivery capabilities

Once priorities for digital transformation have been set, healthcare companies will need to focus on the means by which they will offer targeted digital products and services to consumers and stakeholders. In most cases, companies must understand user needs in a detailed way and reimagine their work flow and processes as end-to-end activities that can be automated, virtualized, and personalized employing real-time insights. For example, insights about the supply chain—say the current levels of inventory compared with sales forecasts—could help healthcare companies reduce general and administrative costs and improve customer service. Agile development, data sciences, and customer-experience design can be useful approaches for these companies to explore.



Agile, a software development methodology, has been around for decades, but it is experiencing a renaissance in the digital world. Agile development involves short, fast phases of development, prototyping, reassessment, and adaptation. To make a step in the agile direction, companies will need to modify their organizational structures to be more product oriented, find ways to improve interactions between the business users and IT, redefine roles within the business units and the IT organization, and reconsider their budget and planning models.[1]

1 Santiago Comella-Dorda, Swati Lohiya, and Gerard Speksnijder, "An operating model for company-wide agile development," May 2016, McKinsey.com.

The agile development approach can be combined with capabilities in data sciences and customer-experience design to ramp up the provision of digital services. Co-located businesses, IT operations, and analytics professionals can jointly develop and deploy products and services in a matter of weeks rather than months or years. Indeed, an at-scale digital healthcare organization can have up to 100 agile teams running projects in parallel at any given time. Companies will need to make the case to senior management for the agile approach in an outcomes-driven process. They will also need to think boldly, rather than tag certain projects as agile. Senior leaders in business and IT at one large healthcare manufacturer started with the presumption that all new initiatives would be structured as agile projects, unless proved otherwise.

The results of combining agile operations with data science and customer-experience design can be significant. Some device makers are wrapping digital solutions around their products to create better patient outcomes—allowing for predictive diagnostics and early detection in patients with certain diseases (atrial fibrillation, for instance), or the launch of fully digital surgical units, or remote monitoring of patient care. Meanwhile, some biopharmaceutical companies are using advanced analytics to discover drugs or identify new uses for established ones.

3. Modernize IT foundations

Once digital priorities are identified, and digital delivery models discussed, healthcare companies need to examine their IT infrastructure to determine if it is truly capable of supporting the activities required. Complex legacy technology systems usually become the main sticking point for healthcare companies seeking to go digital. Aging systems have typically been built up in patchwork fashion: new applications and gateways are bolted on to existing ones. The result is spaghetti code and fragmentation, neither of which promotes speed and transparency in IT operations. To support strategic priorities and agile approaches to development, companies will need to modernize their IT foundations.

Companies must build a solid, reliable data backbone to ensure that all data are managed holistically so that users can access data sets quickly and easily. Access should be governed according to a single framework, and data sets should be harmonized according to business use case. In this way, companies can establish a "golden source" of truth for critical information relating to pricing, products, customers, invoices, and contracts.

Healthcare companies should also consider ways to build flexibility into their IT infrastructures by looking at Software as a Service (SaaS) or cloud-based platforms and products. Johnson & Johnson, for instance, is more than halfway toward its goal of migrating 85 percent of its computing workload to a cloud-based platform. The company has been able to manage capacity based on demand, ensure network reliability, and hold costs in check.

Companies should also start incorporating connectivity into their IT architectures—for example, using sensors and other monitoring technologies to generate and manage data collected from medical devices in the field. Some manufacturers have created internal platforms that let them analyze real-world treatment data to prove the efficacy, safety, and value of their offerings. Other device makers have been able to use data collected from devices implanted in patients to predict treatment outcomes or to intervene earlier.

Of course, companies will need rigorous cybersecurity policies and infrastructures to protect the most relevant pieces of information in the corporation. Leaders can take a series of steps to protect these "crown jewels": including identifying and mapping digital assets (data, systems, and applications) across the business value chain; assessing risks for each asset by using surveys and executive workshops; identifying potential attackers and the availability and accessibility of assets to users; locating the weakest points of security and identifying remedies; and finally, creating a set of initiatives to address highest-priority risks and gaps in control.[2]

2 Piotr Kaminski, Chris Rezek, Wolf Richter, and Marc Sorel, "Protecting your critical digital assets: Not all systems and data are created equal," January 2017, McKinsey.com.

4. Strengthen core management capabilities

Any large transformation effort requires that companies strengthen and maintain their capabilities in several core areas. The first is talent and partnerships. In the case of digital transformation, companies must develop a deep bench of internal staffers with expertise in digital technologies and approaches, while also bolstering their ability to acquire top digital talent from outside the organization. They will need to assess existing recruitment and retention capabilities and modify them to incorporate new skill sets, training needs, and employee requirements. Particularly in the field of healthcare and life sciences, a sense of mission and challenging work assignments may be more critical for attracting top talent than money. Companies may also need to look outside the traditional sources of talent to find the right people—hence, the need to develop partnerships with other companies in the healthcare ecosystem and in other relevant industry clusters.

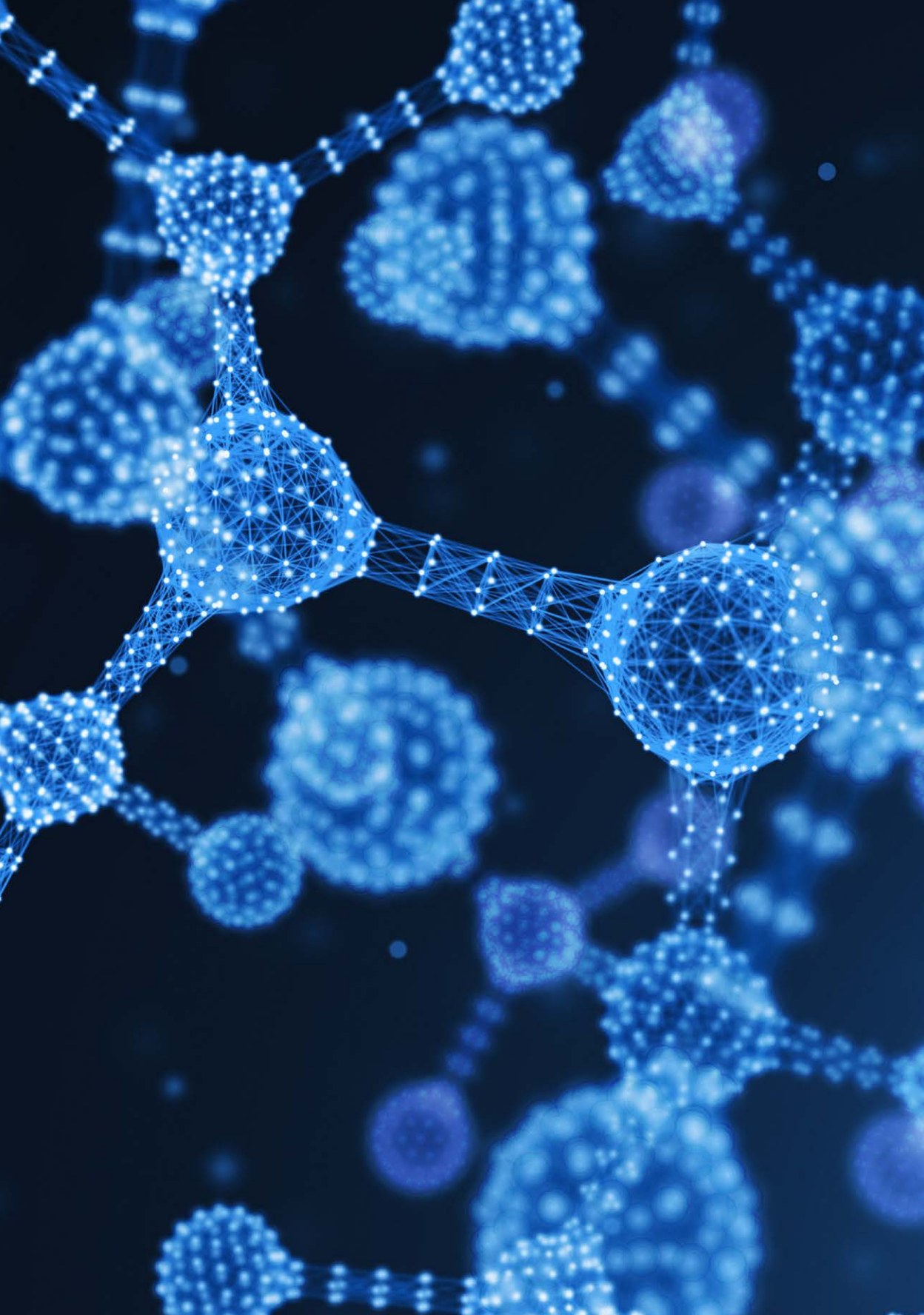
Another core capability is in financial processes. Healthcare players must ensure that investment priorities are communicated clearly, revisited regularly, and updated as needed, and that sufficient capital is available. Some companies have established funds dedicated to digital initiatives, separate from day-to-day budgets. Companies will also need to create a formal governance structure that is inclusive, where internal and external stakeholders alike have an opportunity to weigh in on digital decisions. We have seen healthcare players address this in a number of ways, including convening external advisory boards and creating internal governance councils.

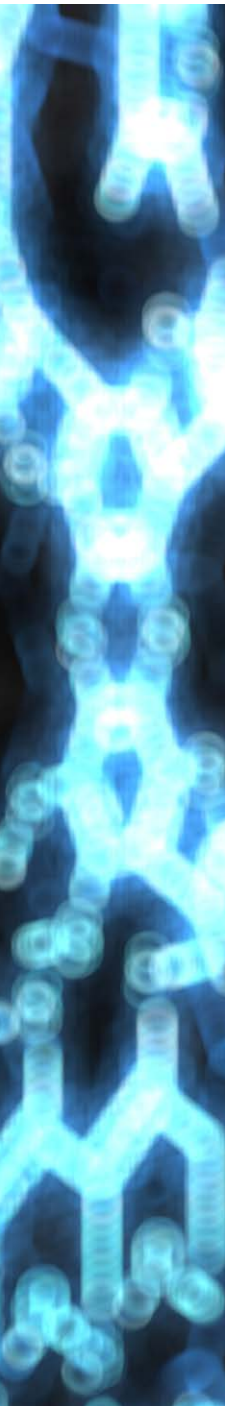
And last, but never least, culture is critical. Our research suggests that 70 percentof large transformation efforts fail because of poor organizational health. Companies must establish a healthy work environment that is open to new ideas and best practices. Senior leaders should keep employees focused on the following questions: Where do we want to go? How ready are we to go there? What must we do to get there? How will we manage the journey? And how do we keep moving forward? In the spirit of agile development, senior

leaders might conduct frequent problem-solving and information-sharing sessions (formal and ad hoc) to help break down barriers between functional and business groups in order to create more transparency and collaboration.

■ ■ ■

Like companies in other sectors, the healthcare industry is being disrupted by digitization—and CEOs and boards are taking notice. It is by now a common story: incumbents face threats from digital natives who are relatively free of legacy constraints and so are able to capture value from nontraditional sources. The winners in digital health, however, are moving quickly to initiate change and capitalize on the battlegrounds cited earlier. They are investing early in promising technologies and risk-sharing relationships with other companies, inside and outside the industry. They are embracing new development and operating models, and relying more on data-driven insights to make critical business decisions. Most importantly, they are reimagining themselves as digital enterprises—adaptive, collaborative organizations that can keep pace with changes in the healthcare marketplace. The four core principles for change that we've outlined can help companies join the ranks of the winners. They can tackle their transformation programs successfully, creating better patient outcomes and more value for all stakeholders.





Reinventing the IT function to enable the R&D digital transformation

Ram Chakravarti and Sastry Chilukuri

A systematic approach to redefining IT strategy and architecture in support of digital R&D will accelerate IT's ability to drive R&D innovation.

Role of R&D IT

We are witnessing an unprecedented simultaneous maturing of multiple breakthrough technologies such as genomics, big data and advanced analytics, sensors and wearables, robotics and artificial intelligence (AI), and 3-D printing. This promises to transform biopharmaceutical R&D and has significant implications for the IT function.

While the IT function has traditionally played an important role in enabling operations—overseeing clinical trials, coordinating clinical supplies and payments, supporting pharmacovigilance (PV) and safety surveillance, managing regulatory submissions—it now faces an urgent need to reinvent itself and take on a strategic role in enabling innovation and the broader digital transformation. However, for many organizations there are several challenges to be overcome: aging IT infrastructure, talent gaps, inconsistent adoption of modern practices such as cloud and agile, and an imbalance in spend. All conspire to hinder the capture of the digital transformation's full potential.

Designing a fit-for-purpose R&D IT strategy

Consistent with the themes outlined in the "Four keys to successful digital transformations in healthcare,"[1] we believe a systematic approach can be adopted to reinvent the R&D IT organization to address strategic imperatives such as applying breakthrough science to accelerate pipelines and delivery, bringing products to market faster, and fostering innovative collaboration across top talent.

Identify and prioritize the sources of value in R&D

Understanding and prioritizing the highest sources of value in R&D is crucial. Going digital enables us to reach insights faster, demonstrate efficacy more efficiently by eliminating failures faster, and reduce the overall cost of operations. We can do this by getting closer to the customer, building intelligent products, assuming more risk as appropriate, and reimagining processes. While many of the high value use-cases have been detailed in other parts of the book, other potential use cases are summarized below.

Getting closer to customers—This is particularly applicable to the "development" phase of R&D where leading biopharmaceutical companies are actively exploring innovative, more customer-centric approaches that have potentially transformative implications for patient recruitment and retention, optimizing drug delivery, regulatory interactions, as well as site and investigator experience.

Building intelligent products—It is not too futuristic to envision an ecosystem of intelligent medical products where every pill comes with an embedded sensor, every medical product is accompanied by companion applications to improve outcomes, digital diagnostics (such as for depression or obesity) are commonplace, and where there are drugs targeting specific patient sub-populations which evolve even further with precision medicine to offer individual patients the greatest chance of treatment success. Intelligent medical products may incorporate wearables and sensor-enabled devices

1 Sastry Chilukuri and Steve Van Kuiken, "Four keys to successful digital transformations in healthcare," Digital McKinsey, April 2017.

such as Bluetooth-enabled smart inhalers, portable medical breathalyzers, and auto-injectors that support medical procedures. Similarly, biopharmaceutical companies may seek to explore wearables for patient recruitment (which is already being done in non-interventional studies), as well as for monitoring and drug delivery in a clinical trial setting. However, wearables on their own provide limited impact unless the associated applications and programs anchored on the intelligent medical product truly address a real pain point (such as health outcomes or convenience) and deliver real value to the stakeholder(s) involved.

Assuming more risk as appropriate—Across the industry, leading companies are harnessing the power of data and analytics to improve decision making in the context of risk. Applied to R&D organizations, this approach can transform the drug discovery and development process. Companies can use advanced analytics to achieve higher-order insights in a number of key areas: exploit real-world evidence (RWE) for regulatory approval, build payor perspectives early into clinical trials to design for reimbursement, and innovate how clinical trials are operated and run. Initiatives being pursued by some leading biopharmaceutical companies involve exploring the power of artificial intelligence and cognitive computing to streamline drug discovery, with reduced risks. Another example is integrating new sources of data—such as electronic medical records (EMR) and social media—as a means to improve signal-detection capabilities within an integrated approach to benefits, risk, and signal management, and with the overall goal of improving patient safety. Perhaps the best example of assuming more risk in an appropriate way involves risk-based-monitoring (RBM) of clinical trial sites where there is targeted manual intervention based on the risk profiles of different sites. Done right, RBM offers high potential to reduce the cost of clinical trials, while improving time-to-market of new medical products. With a vast array of

previously unavailable information at hand, the difference between leaders and followers could well be their risk appetite; when managed effectively this can lead to better medical products faster.

Reimagining processes— There are significant productivity gains to be realized by reimagining and redesigning R&D processes to take advantage of both task-level and end-to-end process automation. Some examples include automating regulatory submissions, end-to-end PV automation, automating investigator payments processes, and auto-population of key clinical trial documents.

Once the sources of value have been defined, the next step is to identify specific capabilities within these opportunity areas that can benefit the most from digitization. While each organization's pain points vary, there is merit in understanding the digitization potential of specific capabilities within R&D (Exhibit 1), to help with both short-term and long-term prioritization of enabling initiatives. The path to unlocking value in R&D for these capabilities requires defining use cases for digitizing these capabilities, estimating the value and cost to implement each use case, and prioritizing and implementing the digital use cases based on value and feasibility.

Exhibit 1

Capabilities in R&D function

High potential for digitization

Research capabilities

Research		
Discovery	Pre-clinical operations	Translational science
Disease-state understanding	Pharmacokinetics/ Pharmacodynamics (PK/PD)	Biomarker identification and qualification
Lead identification	Dosing	Genomic and phenotype studies
Ligand binding and structural biology	Galenics	De-risking entry into humans
Lead optimization	Study management	
IP registration and access	Comparative toxicogenomics	
Discovery operations	Toxicity animal studies	
Proteomics	Pathology	
Computational biology	Pre-clinical modeling and analytics	

Development capabilities

Development				
Clinical operations	Regulatory affairs	Pharmaco-vigilance	Medical affairs	Product lifecycle management
Planning & setup	R&D document management	Signal management	Medical communications	Governance, risk, and compliance
Trial management	Dossier and submission mgmt.	Aggregate reporting	Medical strategy	
Data management	End-to-end label tracking	Case processing	Medical science liaison (MSL)	
Trial design tools	Regulatory intelligence	Safety data intake & MedDRA coding	Continuing medical education	
Study document management	Health authority interactions	Medical safety	Medical publication	
Trial supply and randomization	Regulatory archiving	Risk management	Quality management	
Transparency and trial disclosure	Translation	Compliance	Commercial support	
	Compliance and training	Alliance management		

Build service-delivery capabilities

Even as technology trends continue to enable new business and operating models, IT has struggled to deliver against business imperatives with traditional approaches (nearly 70 percent of software projects cannot be delivered fast enough to satisfy business leaders).[2] Further, business functions use only a fraction of the features developed (more than 60 percent of features developed are rarely if ever used).[3] Successful organizations optimize their portfolio to prioritize and rapidly execute on the highest-value initiatives—these organizations typically use the agile methodology to address the shortcomings of traditional IT development, and deliver value rapidly and iteratively. Agile is a set of engineering and project management practices designed to address some of the most common issues in software development. The agile way of working requires everyone working "shoulder to shoulder" in the same room, gathering requirements through discussions and visual design. Business and customers see the output on a weekly basis and "course correct." The benefits of the agile way of working are compelling—it results in faster delivery of better-quality solutions with increased cost efficiency and enhanced employee satisfaction. Agile also requires a major change in the business–IT partnership, mandating formal business product ownership and significant business involvement during implementation. Given R&D requirements, GxP-compliant agile methodology can generate value quickly, especially if complemented by lean and optimized IT delivery processes (inclusive of redesigned testing, validation, and quality assurance). However, implementing agile in large-scale organizations is not without complexities.

2 Forrester Research.
3 The Standish Group International.

There are five enablers for successfully shifting to an agile delivery model at scale:

- Tailor agile to fit the unique requirements of each organization.
- Invest in engineering talent and foundational technical practices (for example, continuous integration, test-driven development, refactoring, and code review).
- Scale incrementally to establish the required mind-sets and capabilities.
- Plan for and invest in significant capability building.
- Use reliable and consistent cascading standard metrics.

Across industries, the ability to exploit data has enabled leaders to leapfrog competition. R&D organizations now have the means to use vast amounts of external data (for example RWE, Internet of Things) that they can integrate with internal data to generate previously unavailable insights to drive decisions. To effectively harness the power of this information, organizations need to significantly raise the bar on data sciences and other data-centric capabilities. This requires a strong commitment from leadership to create, operationalize, and scale data-centric capabilities. There are six criteria to do this successfully:

1. **Talent—**The importance of having a critical mass of in-house data science talent that can mine information using advanced methods cannot be overstated. Other important roles are the business integration roles—the "translators" who can bridge analytics, R&D IT, and business decision makers. R&D IT also needs to scale capabilities across data engineering, data architecture, and data analysis.
2. **Get the data foundation right—**Invest in a robust foundation comprising the IT infrastructure for the data backbone, data engineering, a flexible information model, and data quality improvement. The next section ("Construct a modern foundation") addresses this in greater detail.

3. **Create 1–2 "anchor" customers to build momentum**—Data transformation needs to be a business-driven effort focused on addressing business opportunities, prioritized on their sources of value.

4. **Scaling requires self-funding**—Successful data transformations balance practical business impact with ongoing investments (for instance, in the data backbone).

5. **It is about more than building predictive models**—Predictive modeling is just the beginning; often, changing processes and driving frontline adoption is a bigger barrier to impact. Understanding the business context behind the data is as important.

6. **Leadership**—There are real barriers to impact (data quality, adoption, legacy IT systems) that require creativity and sustained leadership to overcome and reach impact from the analytic solutions—this is about getting started and staying committed.

Using empathy to put customers, clients, and end users at the center of the problem-solving equation is the foundation of design thinking. Many companies are committing to improve user experience—this can be extended to IT organizations to deliver superior solutions to R&D stakeholders. We have seen examples where designers have co-created visual patient pathways and patient stories to deliver a superior patient experience. Embedding the design-driven culture in R&D IT will take time, but can be accelerated by understanding what truly motivates R&D customers, having designers work with the right people in the organization, continuously reviewing metrics to accelerate IT processes, and changing actions in a constant test-and-learn cycle. This is particularly applicable in drug development where redesigning the customer journey from the perspective of—and with the involvement of—patients, physician investigators, care givers, regulators, and other external partners will be truly transformative for R&D organizations.

Construct a modern foundation

A modern digital foundation in healthcare cannot be created without both core IT components and truly transformational digital enhancement. Core IT

includes data backbone, Software as a Service (for core systems), information security, Internet of Things (IoT), and a truly transformative digital enablement: advanced analytics and artificial intelligence, automation, cognitive search, knowledge management.

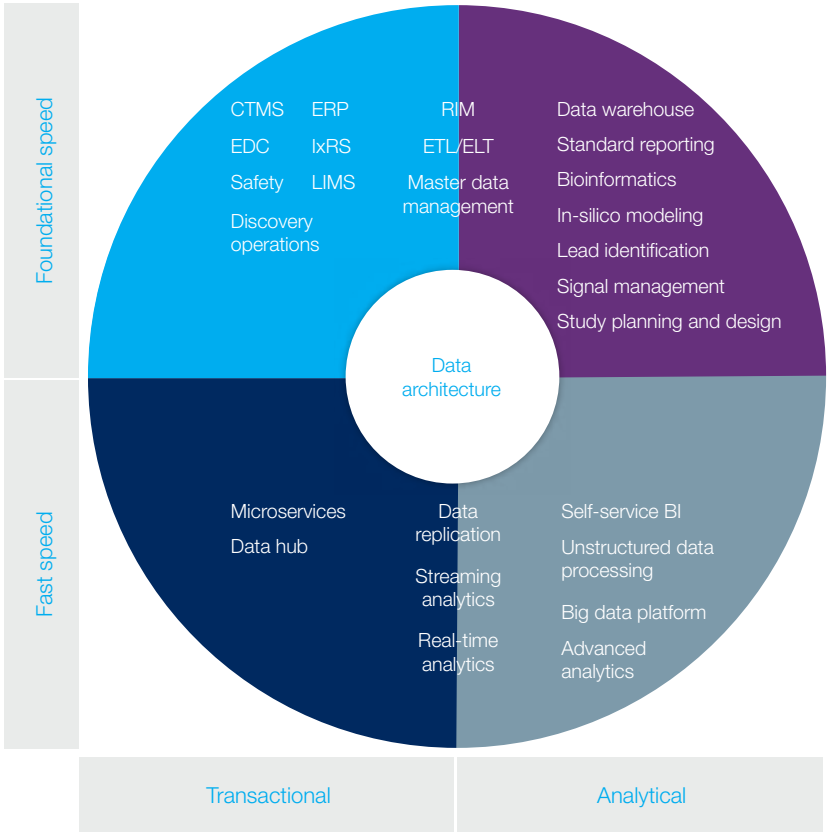
Data backbone— Four business benefits results from a robust data architecture: improved business transparency, greater business agility, generation of new insights, and reduced cost of IT and operations. The data architecture should support integrated data, supporting technologies (such as data lakes), as well as new technologies (for example, in-memory and streaming analytics) and "value-generating" features (for instance, real-time data ingestion). The blueprint for the architecture should be informed and driven by business opportunities and pain points; importantly, it should be holistic to capture end-to-end implications. The data backbone strategy should address two key areas: first, core information assets; and second, the data architecture building blocks and other innovative data technologies.

1. **Core information assets—** The data backbone needs to support real-world data, including genomic and phenotypic data from biobanks, in addition to internal structured data as well as the vast amounts of unstructured content that researchers and scientists need access to for drug discovery and development. Defining a canonical information model for R&D will streamline the effort in identifying core data sets for use cases and mapping them to the required technology capabilities and source systems. Classifying R&D technology capabilities in terms of meeting transactional or analytical needs and, whether they support foundational or fast-speed needs provides clarity in defining the right set of building blocks for each use case (Exhibit 2).

Exhibit 2

Understanding R&D data architecture needs…

NOT EXHAUSTIVE

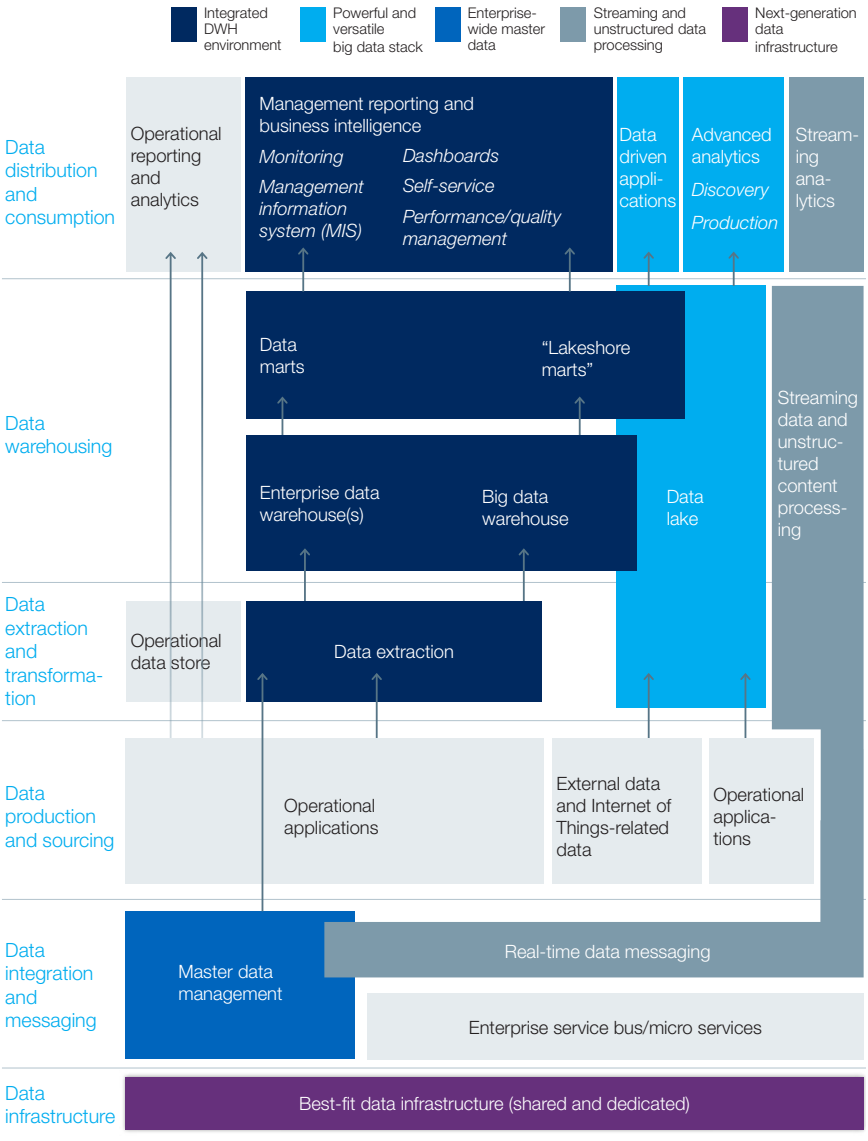


Note: BI = business intelligence, CTMS = Clinical trial management system, EDC = electronic data capture system, ELT = extract load transform, ERP = event-related potential data, ETL = extraction transform load, IXRS = interactive voice/web response system, LIMS = laboratory information management system, RIM = regulatory information management

2. **Architecture building blocks—**The building blocks of the architecture include a powerful and versatile big data stack, enterprise-wide master data, an integrated data warehouse environment for storage and retrieval of structured data, streaming data processing and analytics, and next-generation infrastructure and data tools (Exhibit 3).

Exhibit 3

Data backbone reference architecture



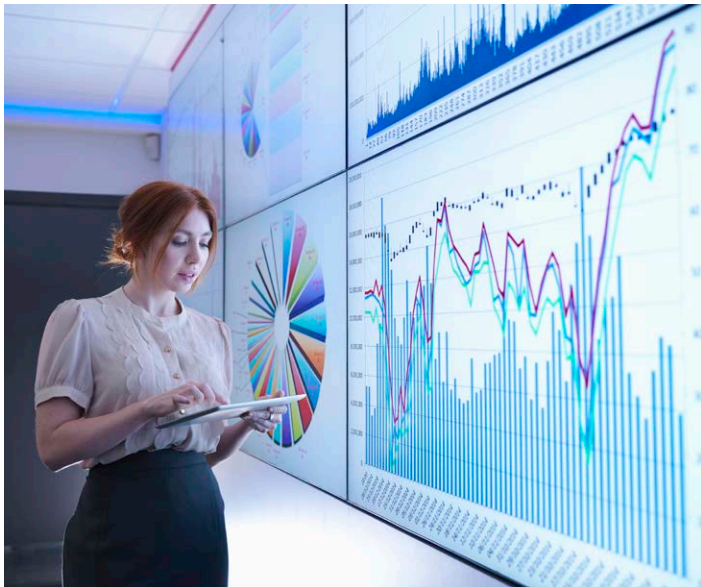
Software as a Service—There is a strong need to coordinate R&D activities globally within a dynamic environment using large amounts of data to ensure cost efficiency. The core systems strategy must be based on the need to standardize (rather than differentiate) across R&D functions. For those areas requiring standardization, it would benefit R&D organizations to double down on SaaS commercial-off-the-shelf (COTS) solutions. SaaS solutions offer multiple benefits such as automatic upgrades, user-friendly interfaces, pay-as-you-go models, and easy scalability. In the R&D space, leading SaaS providers offer significant functionality across clinical development, regulatory affairs, and safety. Alternatively, organizations should strive for purpose-built solutions where they desire competitive differentiation (for example, adaptive trial design, and faster trial execution).

Information security—This is predicated on best-in-class identity management, fine-grained access controls empowered by well-defined security policies, and overarching governance to protect access to sensitive information. Information security must address protection for both data at rest and data in transit. Further, the R&D information security strategy must ensure that regulatory and privacy mandates such as the Health Insurance Portability and Accountability Act of 1996 (HIPAA) are complied with, especially as biopharmaceutical companies scale up usage of external data (for example, genomic, phenotypic, social media). R&D IT leaders must also be prepared to address emerging new regulations, such as the recent General Data Protection Regulation (GDPR) in Europe.

Internet of Things (IoT)—The IoT continues to grow as a technological disruption, and promises to reshape healthcare over the next decade. The value-creation potential of IoT in the human setting is primarily in ingestibles and wearables linked to monitoring and maintaining human health, wellness, and productivity (such as, wearable fitness devices). IoT has the potential to generate more than $500 billion in wellness benefits. However, there are three major barriers that need to be addressed: technology maturity, pace of clinical trials, and cultural adoption. Five types of enablers will drive IoT adoption: software and hardware technology, interoperability, security and privacy, business organization and culture, and public policy. Further, five design principles should guide the architecture definition of the IoT platform:

1. **Provide live functionality**—There needs to be a provision for low latency with real-time data flows (input, throughput, and delivery), as well as data processing across the whole platform to support live services and data collection.
2. **Ensure scalability**—It is important to establish architecture that is capable of growing seamlessly, one that is horizontally scalable in the context of an exponentially increasing user base and data without the need for architecture changes.
3. **Enable multi-tenancy**—Establish a single architecture capable of serving multiple tenants to support proprietary data storage and service creation as well as third-party access by container concept.
4. **Support connection of devices and back-ends**—Provide a platform interface supporting backend-to-backend as well as device-to-backend connectivity ensuring that functions are agnostic of connection.
5. **Allow sharing of common data**—Allow sharing of common data among tenants via a joint data repository (beyond private tenant containers), such as for creation of crowdsourced services.

Advanced analytics and AI—Biopharmaceutical R&D offers enormous potential to draw inferences and recognize patterns in large volumes of patient histories, medical images, epidemiological statistics, and other data. Advanced analytics and artificial intelligence (AI) can enable several differentiated use cases along the end-to-end research and development processes. Analytics use cases in research include (but are not limited to) in-silico modeling, pharmacokinetic/pharmacodynamic (PK/PD) modeling and simulation, pathway analytics, and identification of unmet patient needs. Analytics use



cases in development include (but are not limited to) streamlined trial planning, quicker trial execution, statistical analysis for integration of medical and real-world data, and potential adverse-event detection. Differentiated analytics capabilities encompass descriptive (hindsight—what happened?), diagnostic (insight—what happened and why?), predictive (foresight—what will happen, when, and why?), prescriptive (what will be the likely outcome?), and cognitive (self-learning) analytics capabilities, methods, and tools at scale.

Automation—Automation at scale can be a major differentiator for biopharmaceutical R&D organizations. This is still maturing across industries as organizations aspire to harness the power of robotics and cognitive agents. Process automation across the R&D value chain can be the difference in attaining a leadership position in the industry.

Cognitive search—Organizations have not fully harnessed the power of big data—nearly 90 percent of all information available is unstructured content, yet the investment focus in many healthcare companies is still on structured data management. Cognitive search, tagged as the next generation of enterprise search, is based on natural language processing (NLP) and machine learning algorithms. These technologies can empower the R&D community to search, analyze, and gain valuable insights from large and diverse silos of structured and unstructured data, both internal and external to the organization. With the right set of cognitive search and analysis technologies, the time taken for scientists to discover, explore, aggregate, and understand information can be significantly reduced. While some healthcare companies have used these technologies, in research, they are yet to achieve mainstream adoption in drug development, where there is opportunity to reduce the effort to parse and interpret the unstructured content generated in clinical trials.

Knowledge management—R&D organizations aspire to create, capture, and share knowledge across the medical product lifecycle. However, many biopharmaceutical R&D organizations lack a systematic way of capturing knowledge from experience, which results in loss of knowledge, reinventing the wheel, and non-productive work. Effective use of technology for knowledge management to share the collective wisdom of R&D stakeholders and

learnings from prior experiences is key to growing and creating value in drug development. A mature knowledge-management competency offers the following benefits:

- Enables R&D organizations to systematically and proactively identify the topics in demand and with limited knowledge; provides a mechanism for social interactions internally and with external experts to foster ideation.
- Eases the creation and capture of knowledge, ensuring faster codification, along with the right visualization.
- Helps R&D organizations curate, organize, and share their knowledge assets to efficiently connect all employees with the best knowledge.

A modern digital foundation for R&D is illustrated in the reference architecture outlined in Exhibits 4 and 5. Note that the reference architecture should address not just the modern foundation but also the legacy IT core still required to support the remaining R&D functions. Such a model will deliver value without overwhelming R&D IT organizations by enabling the rapid delivery of new in-demand digital capabilities (for instance, driving patient insights with real-world data), while opportunistically reducing the legacy technology debt over time.

Exhibit 4

Research—conceptual digital reference architecture

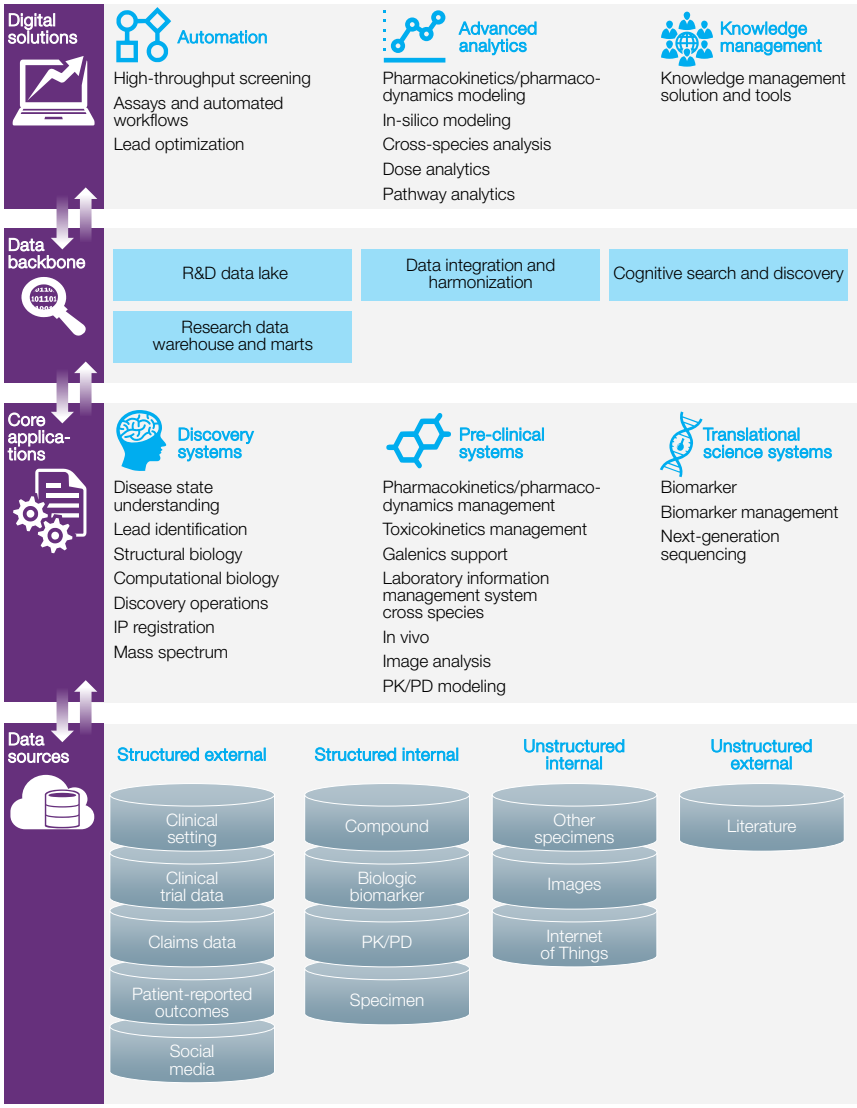
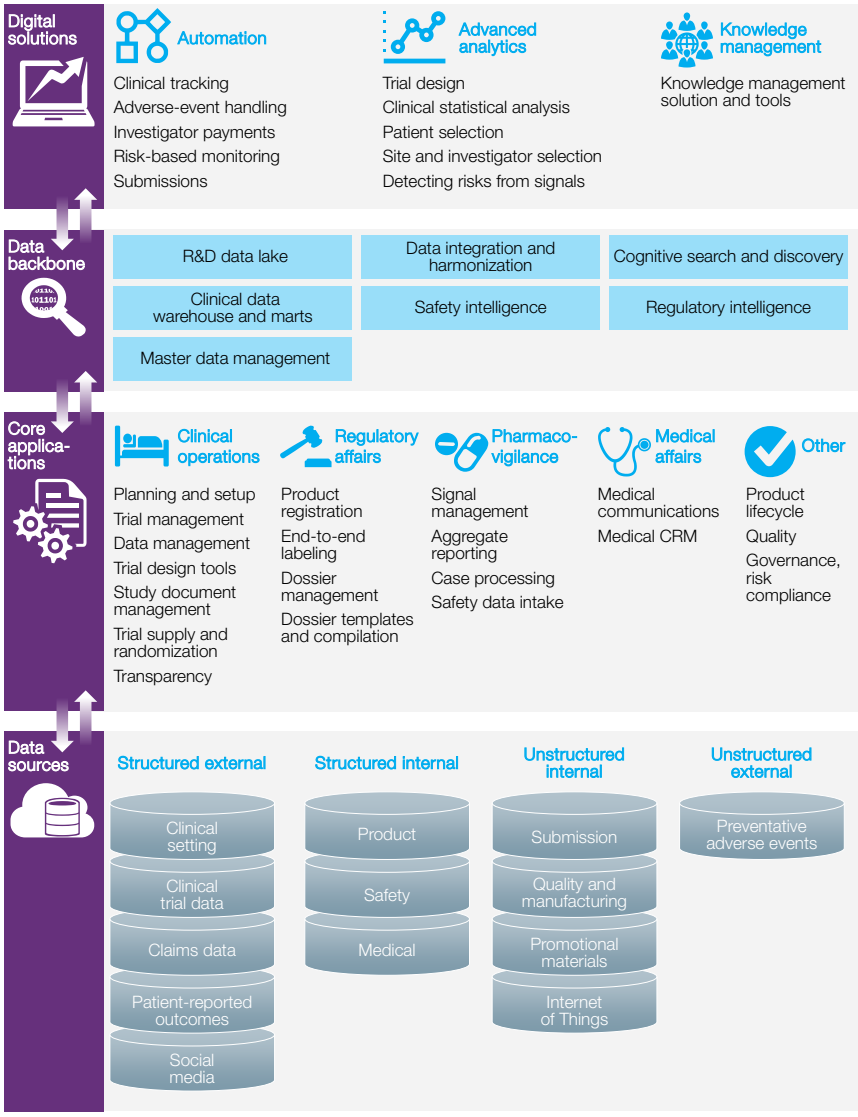


Exhibit 5

Development—conceptual digital reference architecture



Strengthen R&D IT core management capabilities

R&D IT has to address capability development in multiple dimensions such as talent and partnerships, financial processes, and culture. From a talent and partnerships standpoint, the organization must develop a deep bench of internal staff who not only understand digital technologies but also biopharmaceutical company R&D processes and functions. Additionally, R&D IT leadership must get creative to acquire and retain top digital talent from outside the organization. Strategic partnerships with IT vendors and service providers can help meet short-term resource demands.

Greater value and quality of service can be realized when the structure of the IT organization mirrors that of the R&D functions. This business-IT interaction can be optimized through the introduction of dedicated roles that can represent the "voice of the customer" within R&D. The design of this future-state IT organization should consider the following elements:

- **Business relationship management (BRM) organization**—This is a stakeholder-focused team interfacing with business to drive business strategy and apply innovative technology solutions to R&D. BRM partners with the R&D stakeholders to provide the "voice of the customer."
- **Product line ownership**—Common product lines across R&D can support BRMs to deliver digital solutions efficiently at scale across the R&D organization (for example, lab innovation and workflow).
- **Data and analytics (D&A) competency center**—This acts as a single point of focus to prioritize analytics use cases to drive maximum impact for the organization. Designing the data-management organization will require the organization to consider six key decisions based on the vision of the transformation. These comprise degree of centralization, organization integration, internal organization, ownership, skills and talent, and degree of outsourcing. This center of excellence should allow for business-led and IT-enabled data governance. The key strategic roles to consider are chief data officer, data owners, and data committees.
- **Automation factory**—Redesigning R&D processes to improve productivity with automation will require automation as a core capability to be established within the organization. Leaders in other sectors have adopted an

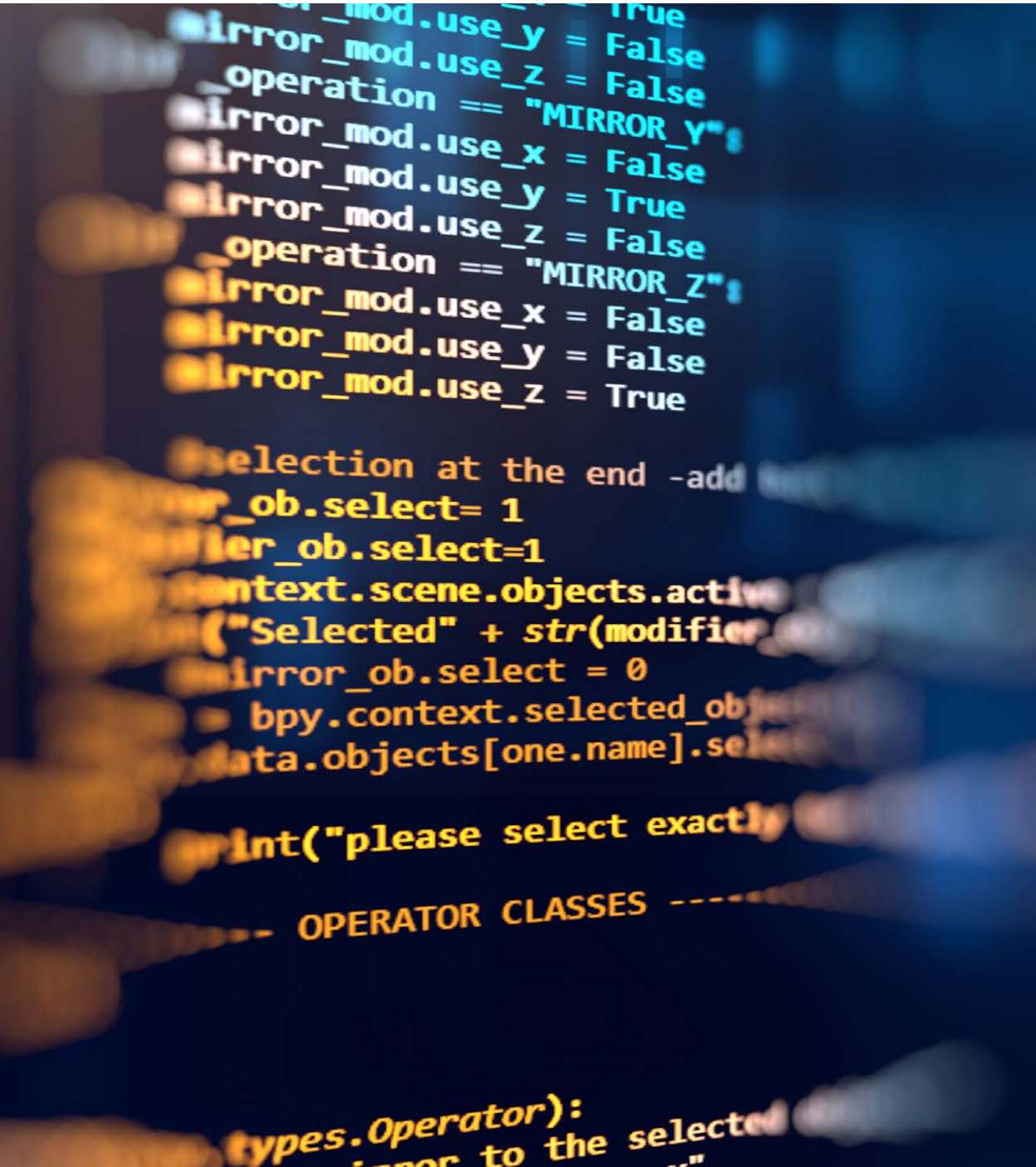
automation factory model to set up large automation and artificial intelligence (AI) labs, which biopharmaceutical R&D organizations can emulate, to capture the full potential from automation.

How to get the transformation started

R&D IT strategy must align with and support the overarching digitally enabled R&D strategy. Organizations must address the following questions to define a transformative R&D IT strategy:

1. What is the vision and strategic intent of the digitally enabled R&D transformation?
2. What are the digitally enabled high-value business use cases?
3. What is the set of technology capabilities required to support each digitally enabled business use case?
4. What is the ideal target state R&D IT required to effectively support the digitally enabled R&D transformation?
5. What is the current state of the R&D IT organization, operating model, architecture, talent, foundational capabilities, and delivery disciplines?
6. What are the biggest gaps between the current and future state of the R&D IT organization?
7. What are major barriers to successfully attaining the target state (for example, limited ability to attract and retain top talent)?
8. What have competitors and industry leaders from other sectors done to succeed in digital transformations?
9. What are the quick wins and the most critical priorities to deliver against business imperatives?
10. What are the strategic partnerships that we need to pursue?
11. What would a pragmatic integrated roadmap look like (that is, one based on prioritizing and sequencing initiatives based on dependencies, value, and time to value)?
12. What is our immediate plan to mobilize and deliver quick wins while building critical capabilities for long-term success?

The authors wish to thank Jenn Boldt and Maria Fernandez for their contributions to this article.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R&D process redesign: Improving productivity through automation

Ram Chakravarti, Sastry Chilukuri, Maria Fernandez, and Anton Mihic

R&D automation has the potential to generate exceptional value, and should be treated as a core capability of the organization. Agile techniques enable us to design and scale new processes at speed.

Automation—the global disruptor

Digital disruption, driven by the simultaneous maturing of advanced technologies such as big data, artificial intelligence (AI), cloud, and mobile, is dislocating the role of the knowledge worker and unleashing a new wave of productivity and innovation across industries. McKinsey research reveals that in 60 percent of jobs, almost a third of the actions can be automated using proven technology. This represents an enormous opportunity and industry leaders are starting to recognize its potential. In financial services for example, banks have reduced mortgage approval times from 16 days to 8 hours. Similarly, the automotive industry has transformed complex rule-based procurement processes to reduce cycle time by 66 percent and enable richer and more frequent negotiations. In consumer marketing, real-time, closed-loop automated models have freed up analysts' time to focus on insights, yielding over 7 percent increase in revenue. Pharmaceutical companies, however are still entrenched in large-scale, expensive, labor-

intensive processes, and the value potential is dramatic. Technology companies such as Facebook generate five times more EBITDA per employee than the average top five biopharmaceutical company.

The biopharmaceutical R&D opportunity

As we analyze the automation opportunity in biopharmaceutical companies, we believe R&D represents one of the most attractive functions given both high cost base as well as the missed opportunity to redeploy talent toward accelerating innovation. R&D in a typical company represents about 25 percent of cost and 20–25 percent of employees.[1] Areas such as clinical, regulatory, and pharmacovigilance (PV) are structured, process intensive, and ripe for automation. Indeed, our research and experience suggests a 25–40 percent productivity boost is achievable, representing up to $25 billion to $30 billion in value for the industry.

This value is tied to a few important use cases that we believe can reduce overall drug development costs, while improving time to market for new medical products (Exhibit 1).

Approaches to capturing the automation opportunity

In our work across industries redesigning processes and digitizing customer journeys, we have anchored around two potential approaches toward automation: task-level automation and end-to-end reimagination. Depending on the business objective, either approach can be optimal.

Task-level automation uses automated scripts/algorithms to substitute manual, transactional activities. Techniques include:

- **Robotic process automation**—repetitive, predictable steps that are fairly standardized and stable over time
- **Deep insights machine-learning-enabled decision making**—complex pattern recognition required where relationships among the data not readily apparent

1 Annual reports of top 20 biopharmaceutical companies.

Exhibit 1

Automation opportunities across the clinical, regulatory, and safety functions

Use cases

Clinical

- Identify and qualify study site
- Establish vendor agreement
- Verify study data, compliance, and progress (data monitoring, study success metrics, data monitoring committee, interim analysis)
- Close study site, lock database, analyze study data, close out study

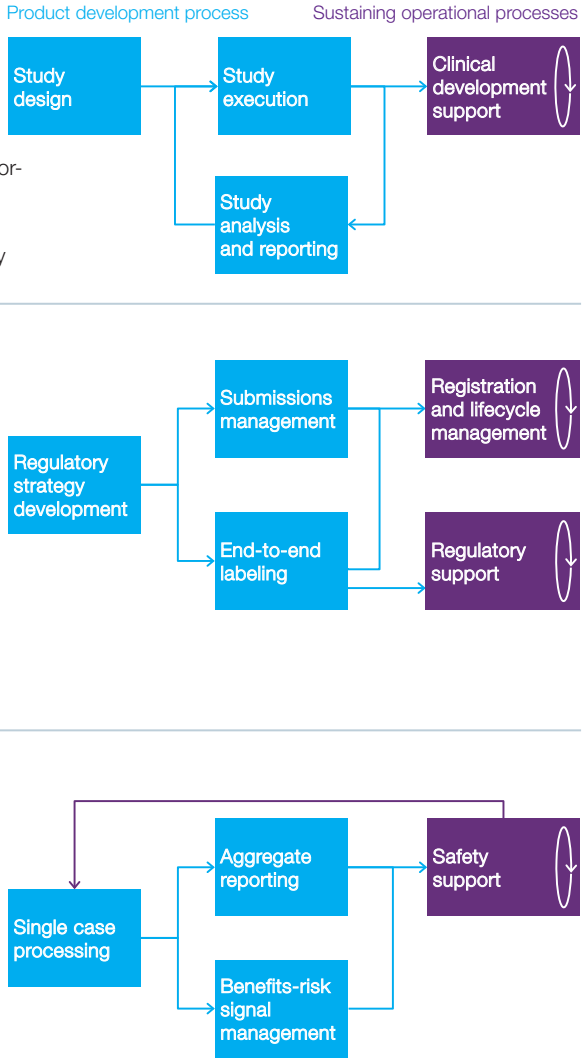
Regulatory

- Define regulatory strategy and intelligence capture
- Harmonize dossier planning and tracking
- Standardize content development and creation
- Track and plan company core data sheets (CCDS) for labeling
- Approve and revise label changes
- Track product registrations
- Manage product life cycle

Safety

- Automate end-to-end PV reporting
- Standardize intake and triage of cases
- Report adverse events to regulatory bodies
- Integrate benefits, risk, and signal management

Conceptual process map



- **Natural language processing (NLP)-enabled automation**—processing text that is based on structured, accessible data where the prose follows a predictable format

End-to-end process reimagination involves deploying technologies to fully/mostly automate the end-to-end process using zero-based design and smart workflow. End-to-end process reimagination can be enabled by:

- **Smart workflow automation**—Automation of end-to-end processes with workflows minimizing handoffs between people, robots, and other systems to reduce waiting time and bottlenecks
- **Cognitive agents**—Scaling simple but time-consuming tasks with multiple start points and varying formats and questions

Agile approach—a new methodology for delivery

In conjunction with identifying the appropriate automation technique, agile methodologies can be employed to rapidly prioritize use cases, and accelerate delivery. The agile methodology is a set of process and engineering practices executed by an integrated business and IT team working collaboratively. The agile team relentlessly focuses on the highest-priority challenges, and on quickly delivering the solution to mitigate the challenges. A viable automation solution can be delivered in as little as 8–12 weeks using the agile approach, as opposed to 6–12 months or longer with traditional approaches to automation. Success with the agile approach requires a significant change in how business and IT work together. Some of the keys to success include co-location and constant communication among

stakeholders, experimentation with a "test-fail-learn-improve" approach in two-week sprints to deliver incremental features, autonomy in decision making, continuous testing, integration and delivery, and perhaps most importantly a mindset of being comfortable with changing scope and requirements.

Agile guiding principles

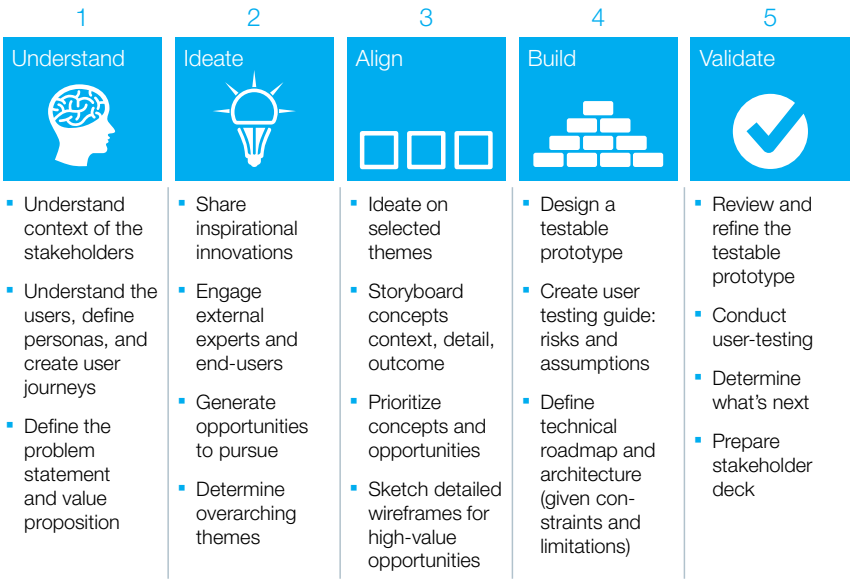
- Identify and solve for the most pressing business need, not shared needs or the entire universe of needs.
- Design around user experience and customer journeys, not goals or endpoints that the R&D organization typically uses.
- Support close involvement between business and technology from vision to delivery, and adjust processes and systems in tandem.
- Use initial waves to address processes with high transaction costs and opportunity to improve outcome, process quality, and experience. This will require teams to define the minimum viable product—the most pared-down version of the required solution that remains functional—not the perfect, optimal product.
- Iteratively build on the basics of agile process development work and clarify the rationale and goal of decisions along the way.

In order to truly understand user needs and define minimum viable product (MVP), we have successfully used the concept sprint approach. A concept sprint is an adaptation of the design sprint method created by Google Ventures to build service concepts. It is a combination of design, technology, and business to make an idea tangible and make it ready for fine tuning and development. The concept sprint turns a challenge into an idea, represented in a rough prototype. This enables the stakeholders to rapidly create an outline for the initial version of a solution.

Concept sprints are particularly useful in validating hypotheses and accelerating ideas, so that potential solutions can be identified without a significant drain in time and resources. There are five phases in the concept sprint: understand, ideate, align, build, and validate (Exhibit 2). The concept sprint is most effective in R&D automation when used to identify one or two primary pain points, and then define a minimally viable solution to rapidly address the pain point(s). For example, we were able to identify specific automation levers to improve time-to-market products by 15 percent, in an end-to-end product lifecycle management process.

Exhibit 2

Five phases of a concept sprint



Setting up and scaling for successful implementation

Going beyond successful pilots to implementing at scale across R&D and to capture the full potential will require establishing automation as a core capability within the organization. Leaders in other industries have successfully created large automation and artificial intelligence (AI) labs. In our experience introducing this capability and establishing an operating model that works requires a sequence of seven components from defining the initial objective and scope through to making a roadmap of prioritized use cases (See sidebar "Automation and AI lab target operating model").

Automation and AI lab target operating model

In order to successfully set up a lab it is important to consider these seven factors:

1. **Objective**
   - What is the objective (mission, vision) of the lab?
   - What KPIs are used by the lab?
2. **Organization and governance**
   - Who does the lab report to and how is it financed?
   - What model for the lab do we choose (CoE owns both methodology and development resources versus CoE owns only methodology, with users being trained on automation)?
   - Has the lab mainly own resources, or is it mainly a virtual lab where key people spend "20 percent" of their time?
3. **Service/product portfolio**
   - What services or products does the lab exactly offer (for example, program management, consultancy, opportunity assessment, own development competency)?
   - How is the work divided between lab and departments?
4. **Mind-set and communication**
   - How do we ensure that our employees are not hesitant about embracing automation?
   - How do we create an "eliminate-optimize-automate" mind-set?
   - How do we actively encourage engagement and communication between the wider organization and the lab?
5. **Skills and sourcing**
   - What skills do we need in the lab (such as developers, data scientist)? Which of these skills should be insourced and outsourced?
   - How can we hire the world's best experts? What partnerships do we need to forge?
   - How do we need to reskill the rest of the organization? What certification programs and training are required?
6. **Technology framework**
   - What vendors or technologies should we work with?
   - What is the process to regularly react to changes in the tech landscape to achieve technology flexibility?
   - How do we modernize the IT foundation—that is, the data backbone, security, Software as a Service/cloud, IoT?
7. **Roadmap of prioritized use cases:**
   - What are the priority automation use cases?
   - What does the target state look like? What is the as-is situation?
   - What is the roadmap (for different services)? How is this regularly updated?
   - What is the optimal approach to implement a use case? (This is detailed in the next section.)

Are you ready for process redesign?

We believe our approach has the potential to generate exceptional value especially in biopharmaceutical and medical product development organizations, by reducing the time currently devoted to manual, repetitive, and transactional tasks. Additionally, adopting the agile way of working and establishing a digital automation lab can rapidly scale this capability across R&D. Getting started on this journey requires clarity on four questions:

- What are the priority use cases that could deliver highest value to your organization?
- What are the most appropriate automation techniques to address each priority use case?
- How can you institutionalize the agile way of working to rapidly deliver value?
- What is your optimal organization model to scale automation in your enterprise?

The authors wish to thank Mike Joyce and Ralf Raschke for their contribution to this article.

Building a data science capability

Sastry Chilukuri, Konstantinos Georgatzis, Balaji Iyengar, Jonathan Jenkins, and Eoin Leydon

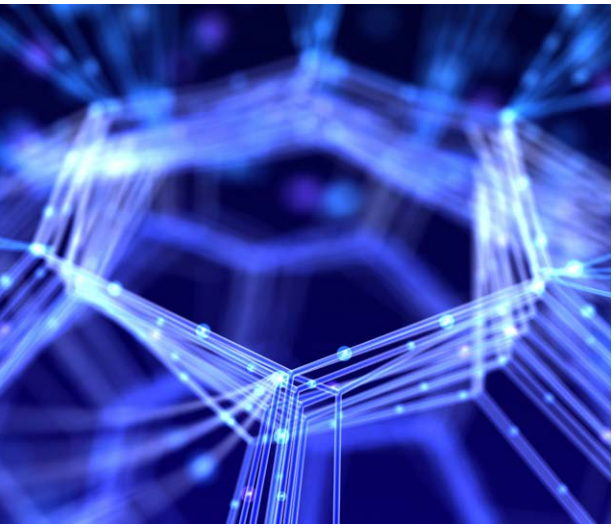
Innovating the business model will allow R&D to identify, capture, and scale the benefits derived from introducing advanced data science techniques.

Digital can enable biopharmaceutical companies to deliver products and services more quickly and boost innovation within the industry, while simultaneously holding down costs—but organizations need to create a comprehensive vision for this transformation and build essential capabilities.

A critical element is the application of innovative data science techniques to extract new insights from a mass of structured or unstructured data—which is the focus of this article.

Let's take clinical operations as an example. At its core, this function is about data: the process of generating high-quality data through clinical trials to demonstrate the efficacy of a drug and to ensure its safety. Traditionally we have achieved these objectives through the judgement and experience of seasoned leaders and large regional organizations. Today's data science technology—including advanced data analytics—extends the possibilities by enabling us to utilize wider data sets (including operational data, real-world data, and technical data to accelerate trials) reduce costs, and streamline the organization. Use cases include site selection, patient recruitment, trial management, country footprint optimization, and quality monitoring.

A framework for innovation



However, embracing this innovation requires us to introduce fundamental changes to the way we work. One promising approach is to employ a 4i framework to innovate the business model (Exhibit 1). This approach comprises a series of steps related to understanding the vision, our ability to unpack the strategy, plus a willingness to challenge performance with analytics. It allows us to identify, prioritize, implement, and embed at scale the necessary components of a data science approach.

1. **Intelligence**—This initial phase assesses the specific performance potential from a given collection of datasets. It sets the scope; enables us to size value and feasibility, and to select promising opportunities.

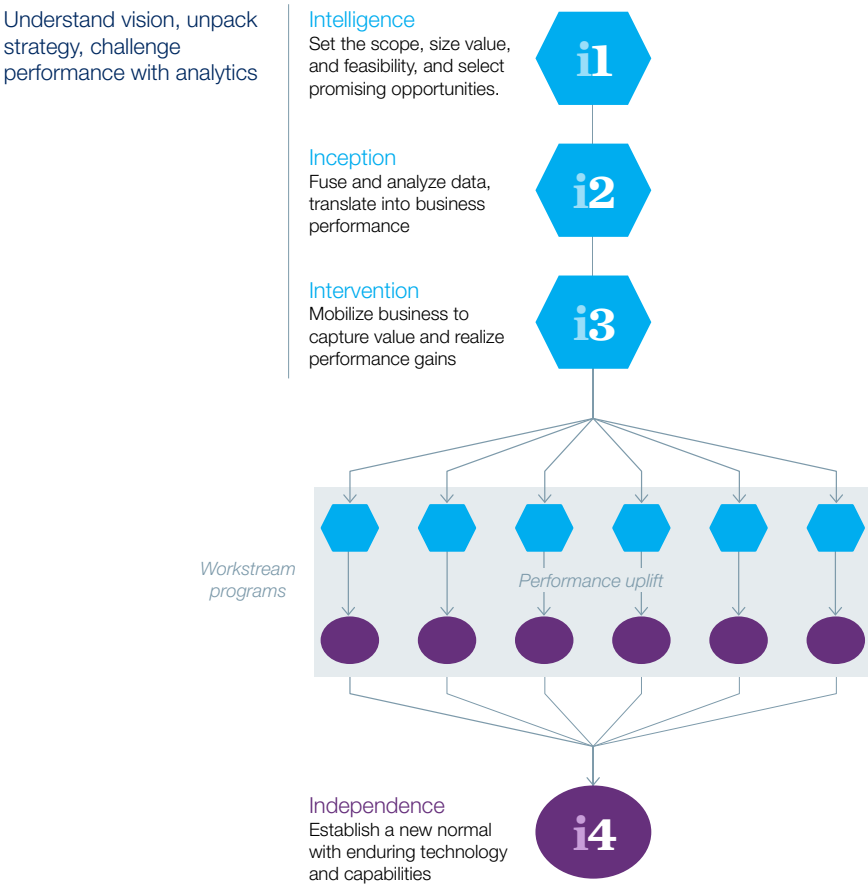
2. **Inception**—This substantial phase translates raw data into business performance, by fusing and analyzing the data.

3. **Intervention**—This phase seeks to deliver the changes required to deliver the performance gains identified during the previous phase; it mobilizes the business to capture value and realize those performance gains.

4. **Independence**—This final phase encompasses the set of projects that will establish the "new normal"—the enduring technology, processes, skills, and culture that will enable the organization to fully own the transformed analytics capability going forward.

Exhibit 1

The 4i framework captures value through advanced analytics



Here, we explore in greater depth how an organization might use this 4i framework to remodel itself to move away from the existing status quo and embed these innovations at scale.

1. Intelligence

As discussed above, the initial step is to identify where there is opportunity for analytics. This involves considering where the latent data has the potential to improve decision making, then prioritizing opportunities, based on value, feasibility, and fit with the organization's strategic priorities. For example, in clinical operations, we frequently find that site selection is identified as a great starting point for the application of advanced analytics because enhancements in this area typically generates high value (10–15% acceleration in trial enrollment) and can be implemented relatively quickly.

2. Inception

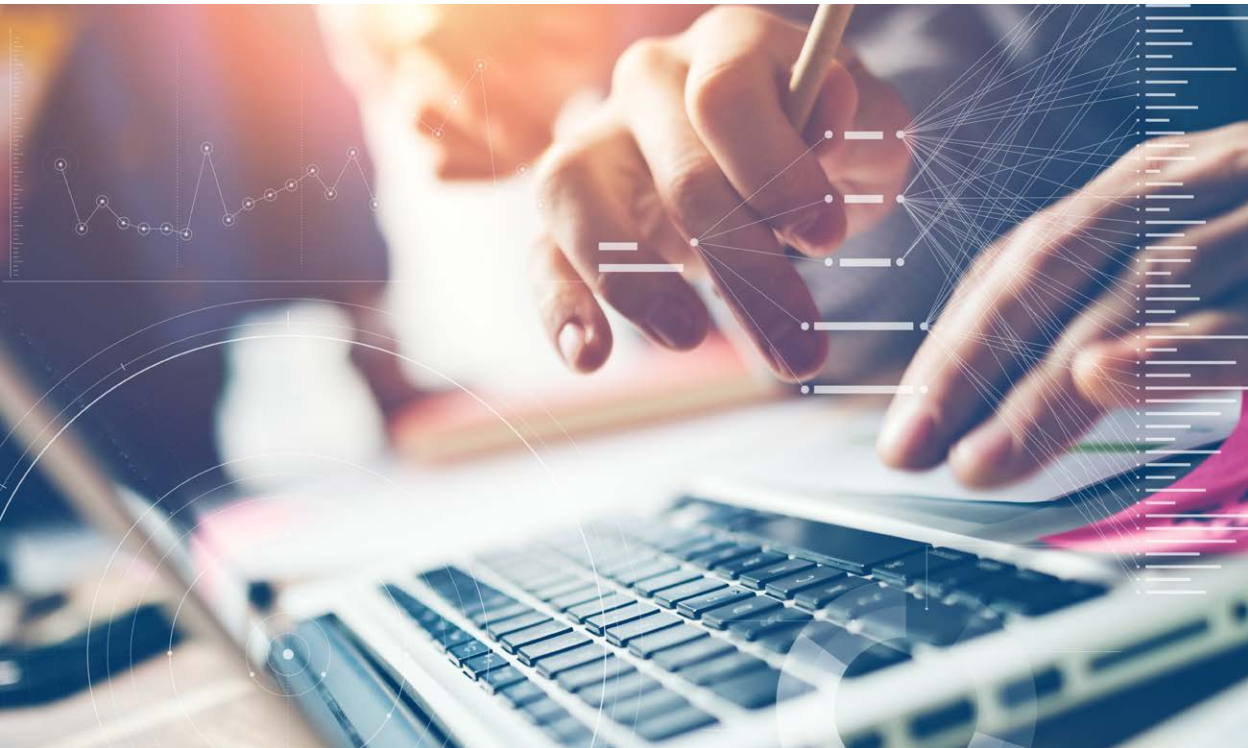
The Inception phase brings together data from diverse sources and involves building different types of analytical models to identify where there is opportunity for value. In this context, data integration and advanced analytical techniques are the key innovation drivers. An explosion in the volume and variety of data collected—operational, quality, finance, communications—along with the advent of new methods of translating unstructured data into machine-readable formats (for example, natural language processing, fuzzy matching, and image processing) has opened up new areas of opportunity. Making sense of this vast data pool has proved possible due to advances in analytic techniques such as diagnostic, predictive, prescriptive, and cognitive analytics. These advances mean we are now capable of finding patterns within the data that generate actionable and impactful insights.

Greater volume and variety of data

Today, there is a much greater volume and variety of data available to support decisions than ever before, and more is being created all the time. In addition, data is also becoming more accessible, and new capabilities to link data sets are now available. For example, in clinical operations:

- **More data is being produced.** Clinical Trial Management Systems (CTMS) software has been in operation for over a decade; this provides a rich data set, incorporating day-by-day trial events. Human resources have increasingly deep data describing and quantifying the trial management team experience and qualifications. Operational data from either internal CTMS software or Contract Research Organizations (CROs) when the trials are outsourced, details drug supply chains, availability, and constraints. Quality systems hold multifaceted data on monitoring visits, audits, and inspections. Cost data has become more complex and holds great promise to improve financial planning and investment decisions, but is also challenging for the application of analytics.

  On the one hand these data sets are extremely rich—to the level of costs per visit at individual sites—and so offer huge potential for live analytics to track expected budget accuracy. On the other hand, they are generally structured based on national and regional reporting regulations—not with big data analytics in mind—and therefore often need detailed work to apply analytical techniques to generate the insights.



External data sources on clinical operations and related contextual information are increasingly mature. Cross-company datasets cover an increasing proportion of trial, site, and investigators' performance, while at the same time, claims data, diagnoses, prescription patterns, and other sources of real-world evidence (RWE) provide a source of deep contextual information.

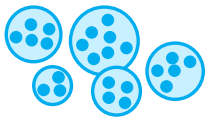
Additionally, these external datasets for investigators, patients, trials, and sites may contain different and sometimes conflicting features (attributes) for the same entity based on the data collection agreements and sampling channels. The extraction, transformation, and loading (ETL) processes must be designed in a robust manner to manage these conflicts and duplication, such that the analytics processes generate reliable results.

- **Improved ability to access data.** Previously inaccessible data are increasingly being digitized, such as protocol data. This enables linking of patient inclusion and exclusion criteria, details of sub-studies and study cohorts into datasets, as well as details of all procedures included in the study. Connecting these with site feasibility reports often creates a powerful addition to datasets designed to support analytics for optimizing clinical trials. In addition, previously inaccessible unstructured data is increasingly available for operational decisions. Email communication and calendars can be connected to other data sources to provide insights on the importance of different types of team collaboration. Written reports, such as site monitoring visit reports are now accessible for analytics, using natural language processing to generate structured data (Exhibit 2). Further possibilities to extend data sets for analytics are extensive. New sources of patient-created data, sensor data, imaging data, and trial process events may be combined with existing datasets to construct rich new datasets for analytic purposes.

Exhibit 2

Natural language processing can be applied to address unstructured data in site visit monitoring reports

Reports clustered, based on occurrence and proximity of words and phrases

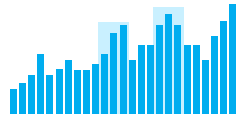


Natural language processing builds on expert input, identifying word groupings associated with categories and refining categories

Creates structure within free text, identifying themes and categories

Results from natural language processing structured in the data cube enable combining with other data for explanatory and predictive analytics

Enables discovery of more complex patterns, interactions and non-linear effects



Concrete, non-intuitive insights, risk of monitoring issues increase when a site has screen failure rate >25%; improved predictions of extent of risk and type of risk

Note: Output illustrates theme-word vectors from early cycles of the algorithm. White text indicates keywords set by domain experts; black text indicates newly discovered keyword
Source: Blei, D. M., Ng, A. Y., Jordan, M. I., "Latent Dirichlet Allocation," *Journal of Machine Learning Research*, 3 pp 99–1,022, 2003

- **Greater ease of linking data sets.** Combining datasets and preparing them for analytics is significantly easier than before. Successful implementations incorporate a common data model (CDM)—for example, Clinical Data Interchange Standards Consortium (CDISC) standards—to manage the different features, conflicts, and duplications. Using a range of fuzzy matching and more recent techniques such as locality-sensitive hashing (LSH), the great majority of entities may be integrated effectively in a timely manner.

  This means that, rather than waiting for multiyear data transformation programs where data is integrated to incorporate advanced analytics at the enterprise or division-wide level, more focused efforts to integrate data for specific use cases are often more impactful. This enables value to be derived from analytics rapidly and incrementally.

Analytic techniques

Analytics enables us to transform business performance through a number of approaches.

- **Diagnostic analytics**, using explanatory models, allow us to identify patterns in data sets, explore past performance, and uncover greater understanding of the factors that have been driving performance (successes and failures) by mining historical data. This approach helps us understand what we need to change in order to improve performance.
- **Predictive analytics** models allow us to forecast what is likely to happen based on large and diverse datasets. This enables us to make predictions on future events (in terms of probabilities) to understand what is likely to happen if we change any of the drivers in a process.
- **Prescriptive analytics** unlock a range of optimization opportunities, using different scenarios, goals, and constraints. These go beyond predicting future scenarios to explore the reasons for different outcomes. Techniques such as Local Interpretable Model Agnostic Explanations (LIME), which identify the key drivers that contribute to the prediction for each test case, have worked well for site selection optimization.[1] A continuous process of data analysis enables organizations to understand how to improve performance by flagging the implications of each decision option, including how to take advantage of future opportunities and mitigate risks. The accuracy of such predictions is honed as more and more data is processed; inputs can be a mix of structured and unstructured datasets.
- **Cognitive analytics** models help find real-time answers from large diverse datasets. These can be used to provide instant access to the most relevant insights. For example, a clinical trial monitor may use these models to quickly comb through site audit reports, investigator notes, patient history, and other documents to find highly relevant information to improve certain aspects of a trial or understand the drivers for that trial site's predictions.

1 Ribeiro M.T., Singh S., Guestrin C., "'Why Should I Trust You?': Explaining the Predictions of Any Classifier," in ACM SIGKDD International Conference on Knowledge Discovery and Data Mining (KDD), 2016.

- **Explanatory models** including statistical analysis and economic models can help identify the business drivers of performance. This enables the identification of interventions that will be most impactful in optimizing performance.
- **Predictive models** could have rich applications. In clinical operations, for example, understanding the likely performance of each potential site for the particular trial before that trial starts, knowing when a trial is likely to finish, and knowing which sites are likely to have quality issues. (The sidebar on the next page illustrates an approach to using advanced analytics for site selection.)

3. Intervention

Interventions deliver the changes required to capture the performance gains identified during the Inception phase. This may be through live applications of analytics or through non-digital interventions that emerge via insights from analytics during the inception phase.

When deploying analytics, we can approach the situation in three ways:

- **One-time analysis—**Conducted on a one-off basis (and potentially refreshed periodically), this identifies where further high-value insights can be found. This is particularly suited to explanatory analysis, where day-by-day changes will not substantially change results.
- **Batch analysis—**This is suited to situations where it is helpful to conduct analysis on a regular basis—even daily—but where real-time analytics is not required.
- **Real-time analysis—**This applies algorithms in response to events in order to raise alerts such as identifying when a machine needs a change of settings or repair to avoid a fault. This is only relevant where there are fast-changing considerations, which require a rapid response. Real-time analytics can also be conducted upon user request, for example to assess the implications of different scenarios.

Site selection example

In order to forecast future site performance, we find using separate estimates for performance metrics—which characterize a site's enrollment behavior, such as time from site initiation to first patient visit and screening rate per week—enables greater interpretability. Moreover, we have found that popular industry metrics produce counter-intuitive results. For example, the impact of site congestion is complex and varies by indication. For some therapeutic areas, having another trial active at the site actually accelerates enrollment, but adding over three trials slows enrollment. For others, high congestion slows enrollment, but decreases default risk.

To facilitate the task of forecasting a site's future performance, a number of features that capture a site's defining characteristics need to be computed (feature engineering) and used as input into our models. For instance, this rich set of features might comprise a combination of domain expertise and automatic feature-generation methods driven by information-theoretic criteria, an algorithm applied to maximize learning from historical data: for example, distribution of numeric features, grouping of categoric features, time-series lags.

In one example on which we have worked recently, we initially evaluated conventional unsupervised learning methods such as content-based recommendation (CBR) and collaborative filtering (CF) techniques[2] for generating recommendations. However, we decided that these methods might not generate satisfactory predictions for specific therapeutic areas due to the low volume of data compared with canonical domains for these methodologies such as movie or product recommendations to consumers.

Accordingly, we selected a multilayered prediction architecture that included predicting industry standard metrics, estimating the prediction intervals, and optimizing to reduce elapsed time (Exhibit A). A variety of machine learning models—such as Random Forests (RFs), Support Vector Machines, Regularized Linear Regression models—were then evaluated in terms of their predictive performance. RFs were selected based on their increased (on average) capability for forecasting site performance based on the defined performance metrics. A variant of RFs tailored for the task of quantile regression, known as Quantile Regression Forests (QRFs),[3] was subsequently used in order to quantify the uncertainty around the predictions of the different performance metrics per site. The outputs from these QRFs can then drive various optimization models (Exhibit B).

Optimization offers a rich set of applications such as in the site-selection example, the outputs from the QRFs were used as the input to a framework of Monte Carlo simulations: this enables one to forecast the expected enrollment time for any given trial and site, along with the uncertainty associated with the time prediction. Based on these simulations, a "greedy optimization algorithm" can be used to automatically select a list of candidate sites that would most effectively meet a trial's objectives (for instance, fastest-possible enrollment time), within the constraints set (for example, maximum cost per patient and proportion of patients per geography).

2 Michael D. Ekstrand, John T. Riedl, and Joseph A. Konstan, "Collaborative Filtering Recommender Systems," *Foundations and Trends in Human-Computer Interaction*, Vol 4, 2011.

3 Nicolai Meinshausen, "Quantile Regression Forests," *Journal of Machine Learning Research*, Vol 7, pp 983–999, 2006.

Once trials are active, Bayesian hierarchical models then enable further effective predictions. These involve combining the prior data from TA-specific models with day-to-day inputs on screening, patient randomization, and other in-trial data.

Exhibit A

Using advanced analytics for site selection

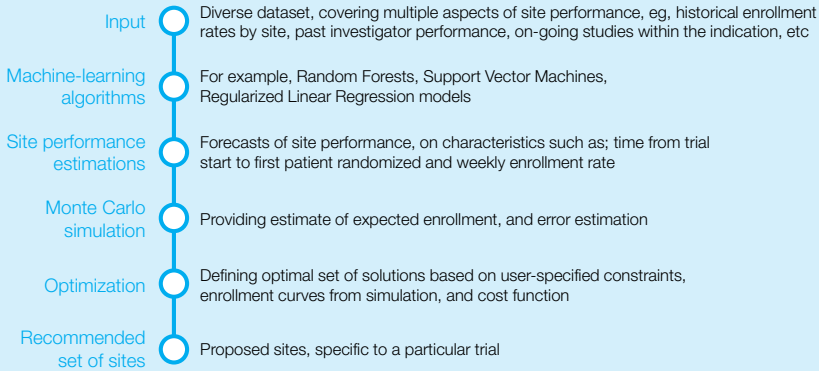
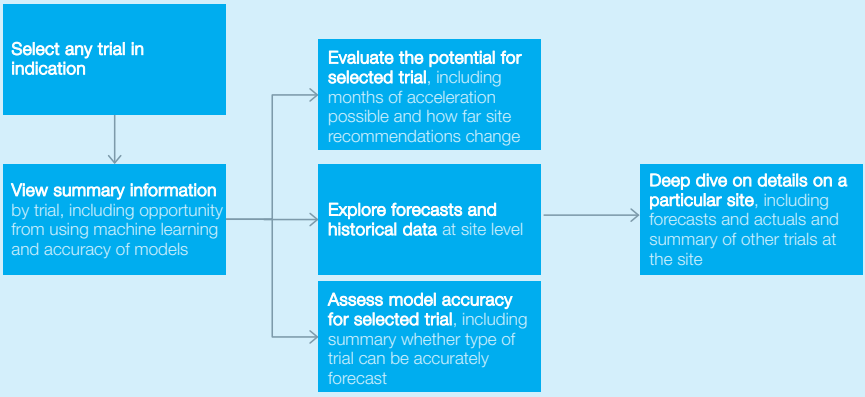


Exhibit B

Example outputs from modeling on-site selection



4. Independence

During the Independence phase we seek to transfer the skills and technology to enable the organization to fully own the transformed analytics capability going forward. It creates a new way of working, which embeds the new capabilities and technology, and has been made possible by advances in computing and cloud infrastructure, but will also require effective change management. A number of areas to consider are:

- **Technology to enable analytics—**The advent of scalable cloud technologies and distributed programming frameworks has slashed the time and cost of setting up an environment to host massively linked data and apply the necessary computing horsepower to crunch through complex algorithms. Cloud computing enables faster, cheaper, scalable, and more-flexible development of analytics. This opens up new possibilities to access live insights from complex analysis to inform real-time decision making, and give immediate feedback on the likely implications of different decisions.

- **Faster, cheaper, and scalable analytics—**Cloud computing offers the advantages of rapid environment set up, lower capital costs, and only paying for computing power used on a minute-by-minute basis. This enables us to perform complex analytics with large data sets, without the heavy cost burden that could ultimately be prohibitive. Technologies designed to support massively parallel processing—such as Apache Spark™ and Scala—allow us to increase computing power to perform at high intensity, as and when required. At the same time, algorithms such as MapReduce process large data sets efficiently, allowing us to tackle massive datasets.

- **Augmented analytics—**Recent developments include the proliferation of a variety of data types that are both structured and unstructured. Structured data typically include number, strings, date/timestamps that have been stored in relational databases that are often row based and designed to process transactions. Flexible analytics require fast access to columns, which have driven the development of columnar relational databases that are designed primarily for analytics. Unstructured data such as documents, images, and process events are typically stored in noSQL databases and

utilized for feature extraction. These features may then be integrated with structured data for the analytic algorithms.

- **Live analytics—**Often, running one-off or batch-oriented analytics may be all that is required in order to understand what drives performance, or to support strategic decision making. However, in other situations, access to up-to-date analytics is important. For example, visibility across the organization of the expected completion date of any trial—at any moment in time, based on all information currently available—improves targeting of early interventions. Likewise, being able to view forecast site performance for all potential sites, for any given specific trial, can significantly improve and accelerate site selection. Recent developments include analytic algorithms that are designed specifically to handle streaming data in real-time.

What this means for you

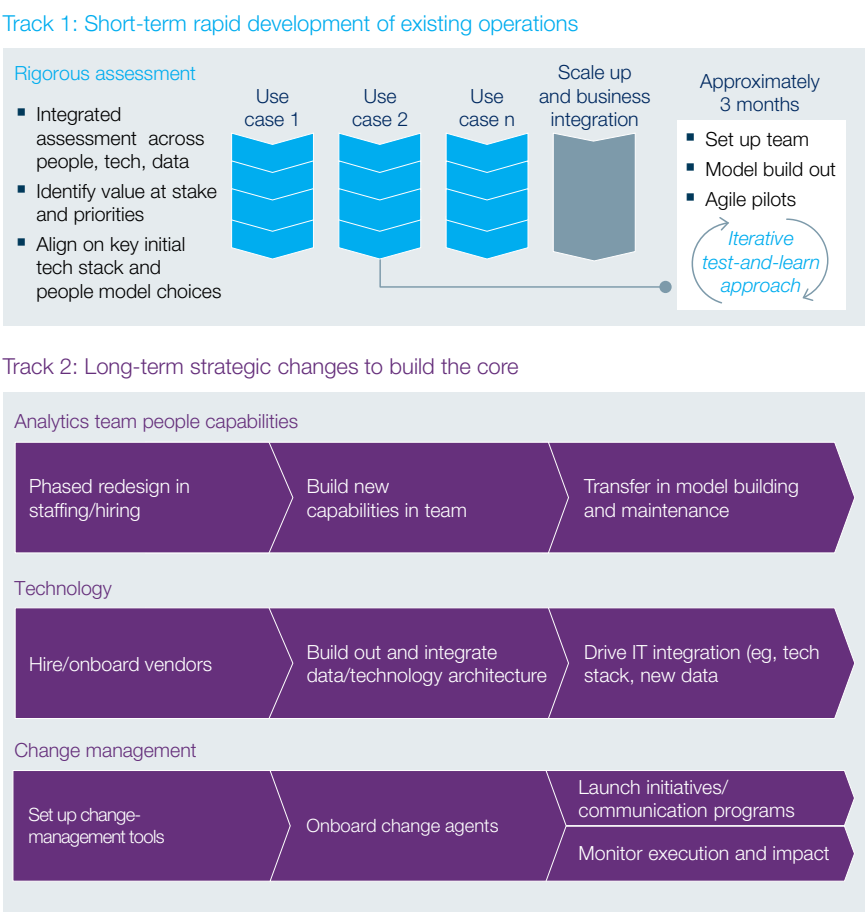
So how do we make sense of this large volume and variety of data and analytical approaches? This requires a clear strategy (Exhibit 3) that can be split into two tracks. The first involves rapid development of existing operations to make best use of existing data to improve performance in the short term (approximately three months). The second track (what really matters) are the longer-term strategic changes to how the data is collected and managed. Integrating the diverse data sets into a data hub typically requires a two- to four-year timescale.

To enable the short-term performance improvement (track 1) the following challenges need to be overcome:

- Bringing unstructured data into play by using Natural Language Processing (NLP) to make it machine readable
- Linking data between silos—this integration doesn't need to be 100 percent; even 80 percent effectiveness can create insights
- Linking data from historically separate organizations combined through mergers

Exhibit 3

Transforming performance through analytics requires clear strategy enabled by people capabilities and technology



Then, in the longer term (track 2), the data and analytics strategy can minimize novel data creation, through storage and management, which makes the whole process more efficient. Here are a few suggestions for how to manage this process.

- **Start from a clear understanding of where analytics could bring value and an assessment of existing data assets, technology, and capabilities.** This enables prioritization of immediate opportunities and identification of where to invest in infrastructure and capabilities.
- **Do not wait for the perfect data.** Capture value from the data you have and drive priorities for improving data based on opportunities identified. However, be very aggressive in collecting—additional data typically generate better predictions compared with testing improved algorithms or analytical techniques on limited datasets.
- **Go beyond business intelligence by combining human intelligence with machine learning—enabling but not replacing human intelligence.** R&D is complex and when there is not enough data, even the best algorithms will often reach conclusions inferior to those made by highly skilled individuals. That said, when front-line teams are able to make more-informed decisions, they can consistently reach more accurate results than experts without the data. For example, screening rates may be lower for studies than models predict because sub-studies may not be in the datasets being used. In other cases, there may be a protocol amendment about to be made that would change the exclusion criteria, and algorithms might require adapting or a different interpretation. Therefore, part of any successful analytics deployment designed to improve performance should include developing a group of "translators,""ambassadors," or "evangelists" from within the business, who are well equipped to use analytics to their best advantage.
- **Redesign processes using analytics.** Include clear objectives regarding where analytics outputs may be used in workflows and incorporate user-centric design to redefine processes and tools that embed the potential of

analytics-driven decisions. Additionally, deploy deep-learning techniques to create, update, and maintain "live" machine-learning models, which evolve over time; new data can assist in reducing prediction errors and reduce the range of prediction intervals.

- **Incrementally build a workforce for analytics.** Successful application of analytics at scale requires new skill sets, from translators to engineers to data scientists. As use cases applying analytics to different business problems are implemented, identify how to build or buy these skillsets.
- **Incrementally build technological capabilities.** Avoid large upfront investment in technology; aim to deliver value early with low IT investment. Selecting a handful of use cases, applying analytics to priority business issues, typically does not require large investment up-front but waiting to create a "data lake" and then piloting a use case can be very expensive. Therefore, identify an approach that avoids multiplication of unconnected or difficult-to-integrate tools. Ideally, address business priorities in a sequence that allows you to build on data structured and algorithms created in previous work.
- **Prioritize change management.** Explicitly assess what will drive performance change, including communicating, role modeling, incentives, what will be tracked, and the process to ensure impact is delivered.

We believe data science/advanced analytics capability is essential to capture value at scale. The 4i framework provides a useful guide to deploy this at scale in the R&D organization.

Glossary

Clinical Data Interchange Standards Consortium (CDISC) is an open, multidisciplinary, non-profit standards-developing organization. It was formed in 1997 to develop global standards and innovations to streamline medical research and ensure a link with healthcare.

Collaborative Filtering (CF)—A method for making predictions based on latent patterns discovered via techniques that leverage "collaboration" among multiple trials and sites.

Latent Dirichlet Allocation—A statistical model for discovering similar, abstract topics in a collection of documents. Latent Dirichlet Allocation is an example of a topic model.

Local Interpretable Model Agnostic Explanations (LIME)—A technique to explain predictions of black-box machine-learning algorithms by approximating them locally with interpretable (white-box) models.

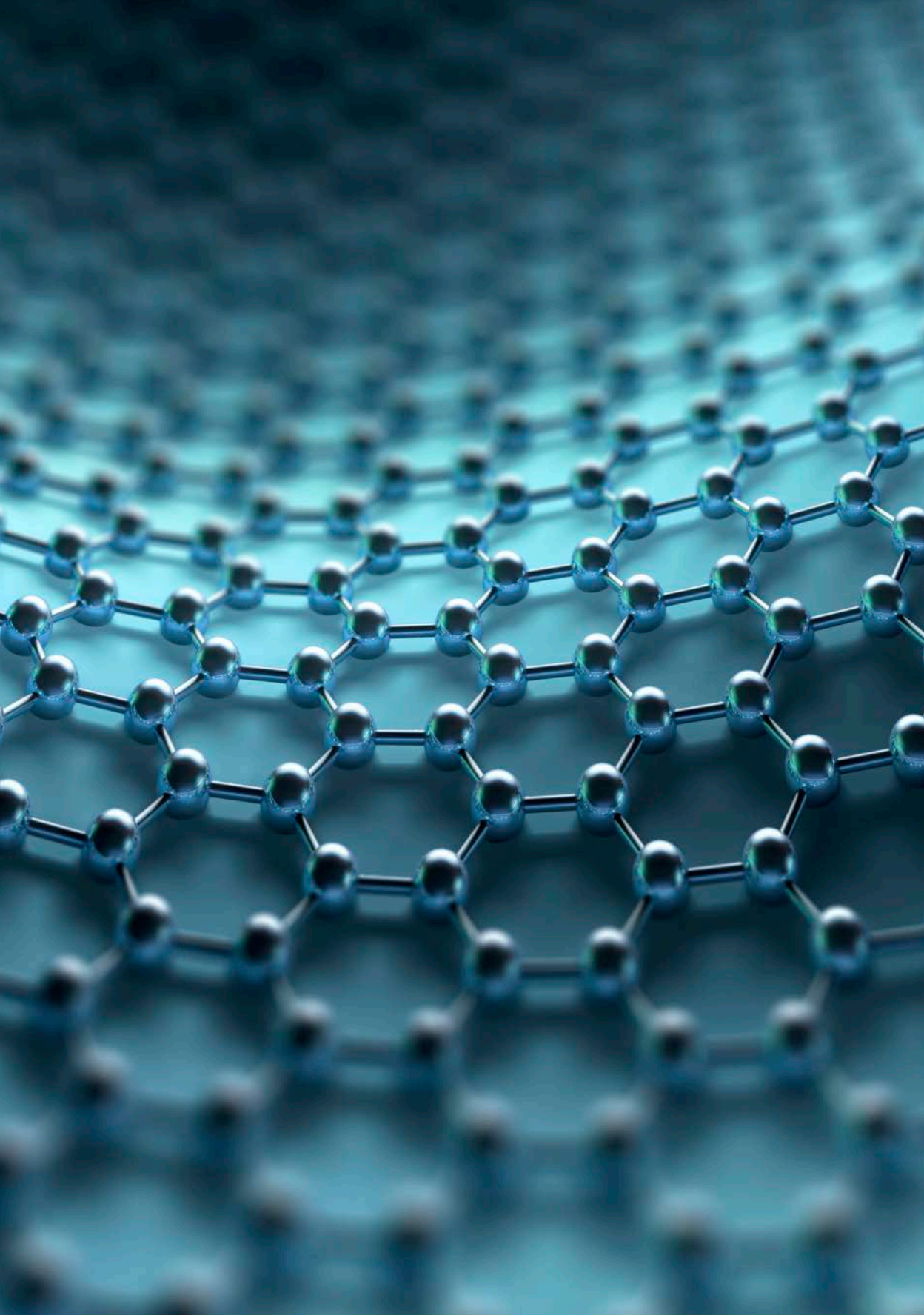
Locality Sensitive Hashing (LSH)—An efficient method for grouping similar points in space into buckets based on some distance measure.

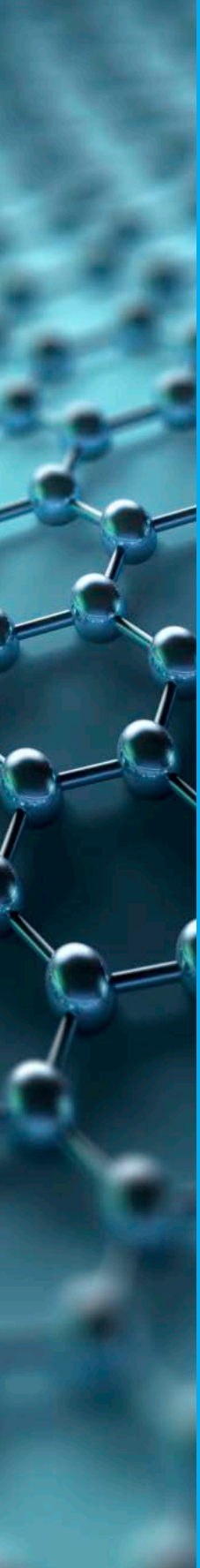
Random Forest (RF)—A collection of decision trees, whose output is the majority vote or mean prediction across individual trees for classification and regression respectively.

Regularized Linear Regression—A method that introduces a penalty term (regularization) for the size of the weights in standard linear regression to avoid overfitting and improve interpretability.

Quantile Regression Forest (QRF)—A method for calculating prediction intervals in Random Forests.

Support Vector Machine (SVM)—A machine-learning algorithm that can be used for classification or regression. It is based on transforming the inputs and then finding an optimal boundary among outputs based on these transformations.





Contacts and references

Authors

We welcome your thoughts and reactions to the topics and ideas in this book. Please contact our practice leadership listed or any of the authors individually.

Nilay Bhatnagar is an Associate in the Sydney Office
Nilay_Bhatnagar@mckinsey.com

Jamie Cattell is a Partner in the Tokyo Office
Jamie_Cattell@mckinsey.com

Olivia Cavlan is a Partner in the London Office
Olivia_Cavlan@mckinsey.com

Ram Chakravarti is an Expert Associate Partner in the New Jersey Office
Ram_Chakravarti@mckinsey.com

Arnaub Chatterjee is a Senior Expert in the North American Knowledge Center
Arnaub_Chatterjee@mckinsey.com

Kate Chavez is an Practice Manager in the New Jersey Office
Kate_Chavez@mckinsey.com

Montana Cherney is a VP of Design at Veryday, New York Office
Montana_Cherney@mckinsey.com

Sastry Chilukuri is a Partner in the New Jersey Office
Sastry_Chilukuri@mckinsey.com

Santiago Comella-Dorda is a Partner in the Boston Office
Santiago_Comella-Dorda@mckinsey.com

Leeland Ekstrom is a McKinsey alumnus

Maria Fernandez is an Engagement Manager in the New Jersey Office
Maria_Fernandez@mckinsey.com

Edd Fleming, MD is a Senior Partner in the Silicon Valley Office
Edd_Fleming@mckinsey.com

Jonathan Jenkins is an Expert Associate Partner in the London Office
Jonathan_Jenkins@mckinsey.com

Mike Joyce is an Engagement Manager in the Washington DC Office
Mike_Joyce@mckinsey.com

Michael Levy is a McKinsey alumnus

Eoin Leydon is an Expert Associate Partner in the London Office
Eoin_Leydon@mckinsey.com

Swati Lohiya is a Knowledge Expert in the London Office
Swati_Lohiya@mckinsey.com

Fareed Melhem is a Associate Partner in the Seattle Office
Fareed_Melhem@mckinsey.com

Thomas Osborne is a McKinsey alumnus

Ivan Ostojic, PhD is an Associate Partner in the Zurich Office
Ivan_Ostojic@mckinsey.com

Brandon Parry is a Partner in the Washington DC Office
Brandon_Parry@mckinsey.com

Michael Pencina, PhD, Director of Biostatistics, DCRI Faculty Associate Director, Professor of Biostatistics & Informatics, Duke University School of Medicine

Eric Peterson, MD, MPH, Executive Director of the Duke Clinical Research Institute, Professor of Medicine, Duke University School of Medicine

Saif Rathore , MD, PhD, MPH, is a Medical Director in the Chicago Office
Saif_Rathore @mckinsey.com

Leslie Ruckman is a Senior Designer at Veryday, New York Office
Leslie_Ruckman@mckinsey.com

Michael Steinmann is a Partner in the Zurich Office
Michael_Steinmann@mckinsey.com

Brindan Suresh, MD, is a Partner in the London Office
Brindan_Suresh@mckinsey.com

Vijay Vaidya, MD is an Associate Partner in the Southern California Office
Vijay_Vaidya@mckinsey.com

Kevin Webster, PhD is an Associate Partner in the San Francisco Office
Kevin_Webster@mckinsey.com

Ann Westra, MD is a Knowledge Expert in the Minneapolis Office
Ann_Westra@mckinsey.com

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Brussels
Avenue Louise 480 - B 23
1050 Brussels
Belgium
Voice: +32 (2) 6454211

Chicago
300 East Randolph Street
Suite 3100
Chicago, IL 60601
United States
Voice: +1 (312) 551-3500

Delhi
Plot No. 4 Echelon Institutional Area
Sector 32
Gurgaon Haryana 122001
India
Voice: +91 (124) 6611000

Dubai
Level 4 Building 4
Dubai International Financial Centre
PO Box 33538
Dubai
United Arab Emirates
Voice: +971 (4) 389 9000

Hamburg
Am Sandtorkai 77
Hamburg 20457
Germany
Voice: +49 (40) 361210

Johannesburg
Sandown Mews East
88 Stella Street
Sandown Gauteng 2196
South Africa
Voice: +27 (11) 506 8000

London
No. 1 Jermyn Street
London SW1Y 4UH
United Kingdom
Voice: +44 (20) 78398040

New Jersey
1 Deforest Avenue
Suite 300
Summit, NJ 07901
United States
Voice: +1 (973) 549-6600

New York
55 East 52nd Street
21st Floor
New York, NY 10022
United States
Voice: +1 (212) 446-7000

Shanghai
17F Platinum
No. 233
Tai Cang Road
Shanghai 200020
China People's Republic of
Voice: +86 (21) 63858888

Silicon Valley
3075A Hansen Way
Palo Alto, CA 94304
United States
Voice: +1 (650) 494-6262

Sydney
Level 35
88 Phillip Street
Sydney, New South Wales 2000
Australia
Voice: +61 (2) 82731600

Tel Aviv
Ackerstein Towers
11 Hamanofim Street
Herzliya Pituach 46725
Israel
Voice: +972 (9) 9718500

Tokyo
Ark Hills Sengokuyama Mori Towr
9-10 Roppongi 1-chome
Minato-ku Tokyo 106-0032
Japan
Voice: +81 (3) 55622100

Zurich
Bleicherweg 30
Zürich CH-8002
Switzerland
Voice: +41 (44) 876 8000

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