The Transformation to Value-based, Personalized Healthcare—Implications for Translational and Clinical Research

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The current paradigms for healthcare provision and pharmaceutical R&D are being challenged by several macroeconomic trends that will drive a convergence of healthcare and life sciences ecosystems. The paradigm shift will transform translational research and put health sciences firmly on the road toward delivering personalized healthcare. Intelligent use of longitudinal healthcare data, and the potential of next-generation gene sequencing as a unifying platform that accelerates drug discoveries and ushers in the biomarker era, will push personalized healthcare forward. Many of the advances have been enabled by the growing power of healthcare information technology. However, although many of the current systems are good at executing and automating the transactional tasks they were designed to perform, they are often siloed and proprietary and lack the facility to integrate, analyze, and visualize data as a whole, across populations and at the individual level. The new healthcare delivery paradigm will require an unprecedented collaborative environment that provides data for an integrated view. This will need an investment in context-specific analytics platforms that leverage the valuable data to support translational research.

Convergence in Healthcare and Life Sciences

Several macroeconomic trends are challenging the current paradigms for healthcare provision and pharmaceutical research and development (R&D). As a result, the traditional axioms will be transformed as healthcare and life sciences ecosystems intersect to deliver a framework for healthcare based on 'value' associated with outcomes for individual patients. The factors influencing this era of change include:

- unprecedented pressures on the life sciences industry;
- an evolving regulatory compliance landscape;
- the increased focus on safety and pharmacovigilance;
- the shift towards value-based reimbursement in healthcare;
- inefficiency in healthcare delivery systems;
- the need for healthcare providers to compete on cost and quality; and
- the increasing adoption of healthcare information technology (IT).

The Pressures on Life Sciences

In the life sciences sector, despite increasing financial investment in pharmaceutical R&D, innovation has reached a plateau. The number of new drugs from R&D pipelines has declined since the high of 2004,[1] leading many to conclude that the 'easy' targets have been discovered. Furthermore, the impact of the patent cliff on the industry has also highlighted the fragility of the blockbuster model, which the industry has recognized as being unsustainable.[2] At the turn of the millennium, the initial mapping of the human genome led to a flood of new science and optimism for accelerated progress in drug discovery. However, a decade later the reality is that, although there have been remarkable advances in our understanding of many diseases, the relevance and complexity of disease-associated targets bring significant challenges in drug discovery as well as the regulatory schemes overseeing the industry. Nevertheless, the real need to improve innovation and R&D productivity is driving a

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fundamental change in medical research that will see a convergence in healthcare and life sciences. By leveraging novel molecular tools and unlocking longitudinal healthcare data from a 'real world' setting to generate understanding about what works in a specific population, the transformation of R&D paradigms will have lasting implications for translational and clinical research. This convergence is particularly acute when viewed through the lens of healthcare data where, increasingly, the biopharmaceutical industry needs access to long-term, observational patient data not only for facilitating translational research and clinical development but also for supporting comparative effectiveness studies, safety studies, and pharmacovigilance.

In recent years, the pharmaceutical industry has contended with increased scrutiny regarding drug safety arising from high-profile product recalls.[3] The subsequent focus on improving pharmacovigilance has also given rise to the need for longitudinal healthcare data to strengthen safety data generated from pre-approval clinical trials. The industry will need to revise the previously accepted wisdom of drug safety in order to gain a greater understanding of the complex interactions of medical interventions in populations in the real-world setting. A further pressure from the life sciences perspective is the shift toward value-based reimbursement and comparative effectiveness; value-based healthcare, comparative effectiveness, along with health technology assessment are all terms that allude to a future in which payers will demand to see the true value of medical technologies before any reimbursement will be granted. As a consequence, an additional demand will be placed on the pharmaceutical industry above safety and efficacy. The need to show evidence of value will place a significant pressure on the life sciences industry. Life sciences companies will need to have access to long-term, observational healthcare data or deliver significant investment to trials that provide comparative effectiveness data.

Reforming Healthcare

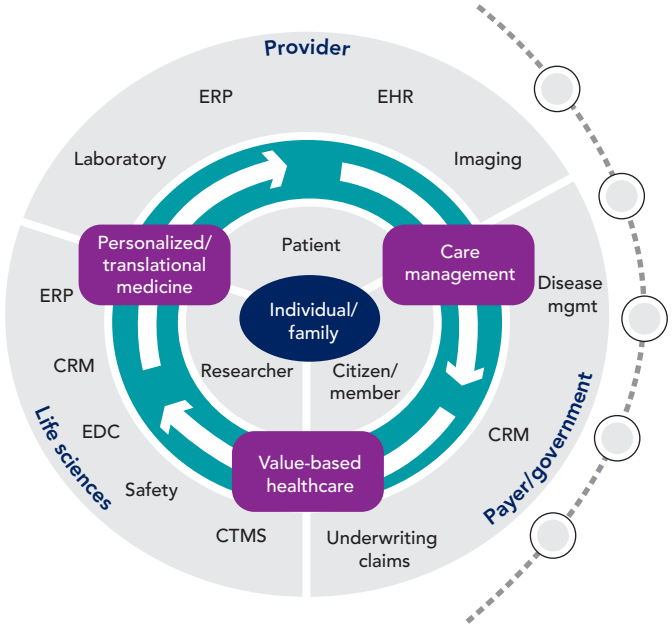
The macroeconomic pressures driving convergence have also been well documented in the delivery and reimbursement of healthcare. There is an increasing awareness of the need to eliminate 'waste' in the provision of healthcare. Many medical interventions do not work in the intended patient populations. Indeed, established drugs for cardiovascular diseases, such as angiotensin converting enzyme (ACE) inhibitors and beta-blockers, are only effective in 10–30% of their target population.[4] This results in physicians trying multiple interventions before discovering which one works in a particular patient creating waste and suboptimal quality care across the system. Although this trial-and-error approach to medicine continues, it is also coming under increased scrutiny because of the accumulation of inefficiency in the system and the unsustainable level of healthcare spend of many countries. Depending on the disease area, the Personalized Medicine Coalition estimates that the cost of ineffective healthcare interventions can range from $390 million to 8.8 billion.[5] Also worth noting, according to a UK NHS study over a six-month period, an estimated 3–7% of hospital admissions were related to ineffective medical therapies.[6] This adds to a compelling argument in favor of capturing more longitudinal data to create a better understanding of what is effective and what does not work in a patient population. This knowledge, together with the increasing influence of biomarkers, which have the potential to become the major currency of translational medicine, will eventually lead to better healthcare management and outcomes by ensuring that the right medicine or intervention is given at the right dose and goes to the right patient—the ultimate goal of value-based, personalized healthcare.

The decreasing margins observed in healthcare systems also present challenges. In the US, reimbursement from the Medicare/Medicaid healthcare scheme is decreasing. In a changing healthcare landscape, where care management and delivery needs to focus on cost and quality, this creates an enormous challenge for healthcare providers including hospitals and physician networks. Moving forward, the need to find new sources of revenue is driving the formation of novel partnerships between the life sciences industry and healthcare providers who are seeking ethical new partnerships that respect patient privacy to subsidize their investments in healthcare IT platforms. Furthermore, advances in science are creating additional economic and cultural pressures on healthcare. Genomics, molecular profiling, and direct-to-consumer genetics testing will create an abundance of data for which current healthcare systems are unprepared. Many of the electronic medical record (EMR) systems currently in place or being implemented were not designed with this new technology and/or data in mind. In fact, most EMRs were not designed to easily cope with new data types, particularly complex ones such as the new molecular profiling technologies that will increasingly become part of clinical care as they become more affordable and more accurate. As if these pressures were not enough, there are major healthcare-reform policies, proposed or under way, in many developed nations, as countries look to curb rising costs. In the US, the 2009 stimulus bill, or American Recovery and Reinvestment Act (ARRA), allocated $1.1 billion for comparative effectiveness research. Moreover, the stimulus bill contained the Technology for Economic and Clinical Health (HITECH) Act, which allocated $23 billion to accelerate the adoption of healthcare IT; more specifically the adoption, implementation, and maintenance of Health Insurance Portability and Accountability (HIPPA)-compliant EMRs to improve healthcare quality and reduce costs.

Transformation through Enabling Information Technology

Healthcare and life sciences experts are increasingly turning toward sophisticated IT and information-management platforms to cope with many of the challenges previously outlined. This has resulted in the implementation of core transactional systems in healthcare and life sciences in an attempt to automate processes electronically. From the life sciences perspective, the majority of clinical trials are now being conducted electronically. Thus, information can be captured more efficiently in a meaningful way and on a much larger scale. This electronic foundation enables the life sciences industry to ask these higher-order questions within and across studies. From the healthcare viewpoint, the increasing adoption of EMRs will lay the foundation for electronic information that will enable healthcare providers and the life sciences industry to gain meaningful insights into medical interventions in practice. However, these core transactional systems are just a starting point for the industry. Additional investments must be made to create an integrated information and analytics infrastructure to manage the secondary use of data across disparate transactional systems that will improve understanding of what works, for whom, why, in what context, and at what cost.

Figure 1: Personalized Healthcare Will Require Further Integration and Interoperability



CRM = customer relationship management; CTMS = clinical trial management system; EDC = electronic data capture; ERP = enterprise resource planning.
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Health Sciences Convergence and Impact on Drug Discovery

Personalized healthcare promises to address not just cost and quality challenges by reducing inefficiency but also to improve outcomes and innovation by driving more preventative and targeted interventions. To realize the goal of personalized healthcare, translational insight needs to be gained from the vast and growing body of clinical data. As healthcare and life sciences systems intersect, the impact on translational research will be significant. Although translational medicine is often broadly defined as 'bench-to-bedside', in reality the process is much more circular and the term 'bedside-to-bench' is just as relevant. One way to think about translational research is in the context of the learning healthcare system that has been championed by the Institute of Medicine.[7] Within this framework, every single patient encounter should and can become a 'learning' event if the data about that encounter is captured electronically in a format where it can be used to understand what worked and why for that particular patient. With the right IT infrastructure in place, the same data-management systems will evolve into clinical decision support systems at the point of care. However, the reality of the current healthcare setting recognizes that organizations working in the research space operate with a number of core transactional systems that are often siloed and proprietary. While these systems are good at executing and automating the tasks they were designed to perform, many systems lack the facility to integrate, analyze, and visualize data as a whole across populations and at the individual level. Indeed, many current healthcare IT systems are missing a means to integrate clinical, operational, research and financial data. The new healthcare delivery paradigm will require an unprecedented collaborative environment that provides data for an integrated view (see *Figure 1*). Therefore, bringing these data sets together in a centralized model should remain a priority for the healthcare and life sciences industries.

The Value of Data Sources—Converging Intelligence

Increasingly, new data sources offer a potential wealth of information for translational research. Indeed, many organizations have established biobanks: large repositories of human biological samples linked to clinical data. However, the current focus has been on storing these samples, and greater investment, in terms of IT, is needed to leverage the molecular data from biobanks for translational research and the development of biomarkers. Although their value cannot be underestimated, the new data sources should not be prioritized at the expense of existing phenotypic data that are currently locked away in silos. The growing body of data being generated in healthcare systems has been restricted to the mundane, such as transactional data, and basic patient demographic information. The true value of the data has not yet been realized. Coupled with enterprise health analytics and integrated information management systems, the existing data can be unlocked from core transactional systems to support translational research and clinical decision support at the bedside. Essentially, in the rush to generate new data types the need to improve the management and analysis of existing data should not be overlooked.

Bringing 'Omics' Data to the Health Sciences Ecosystem

As mentioned above, translational research will rely on a whole host of data sources to identify and exploit new insights into the genetic variability of disease. There have been major advances in genomics, proteomics, genetics, and metabolomics but fundamental challenges still exist regarding the translation of the information generated by these technologies within a clinical context. The industry needs the capability to integrate the different omics data points with long-term, observational outcome data in order to facilitate and accelerate translational research—enabling scientists and clinicians to operate effectively within a clinical framework. Arguably, the industry has done a reasonable job at managing the analytical pipelines around molecular data alone, but we have not realized the full potential of this technology because we have not done as good a job of correlating it with clinical outcomes.

Next-generation sequencing is expected to influence translational research significantly. The technology allows for more-stable measurements in terms of genetic variation and single-nucleotide polymorphisms (SNP) in the genome, correlating their impact on efficacy and safety of medical interventions. When omics technologies are examined in more depth it becomes clear that next-generation sequencing has the potential to transform the different omics platforms into a single platform—sequencing the genome, measuring gene expression, and SNPs to enable genetic analysis in one place. This will enable a systems biology approach that helps improve understanding of important biological systems. Whole-genome sequencing will assist the transition towards personalized medicine. From an IT perspective, the paradigm of translational research will need to be supported by the integration of the omics data with high-quality clinical data. Moreover, robust, interoperable informatics requires an investment in analytics platforms that would serve to satisfy the translational needs of clinicians in addition to researchers. Currently, in the field of bioinformatics, the bioinformaticians, biomedical informaticians, and the biostatisticians hold the analytical keys to translational research but a point has to be reached where scientists and clinicians become more self-sufficient

regarding the analysis and visualization of this type of data. This will require next generation translational medicine platforms that enable non-power users to leverage these analytical tools.

Defining and Characterizing Patient Populations for Personalized Healthcare

To achieve the translational insights, it will be necessary to conduct clinical trials with more-defined population sets. Patient populations that are better defined and characterized with the aid of validated biomarkers will, in turn, help to optimize the clinical research process for that intended population and, as a result, will reduce the cost and complexity of administering targeted clinical trials. However, one of the fundamental factors standing in the way of substratifying patient subsets is access to well-annotated longitudinal patient population clinical data. Currently, this is viewed as a critical rate-limiting step to realizing the promise of personalized medicine; the data are crucial to characterizing specific patient populations. Consider the data that are generated in the management of a chronic disease such as diabetes. By aggregating longitudinal patient data across the diabetic care continuum, potentially meaningful insights could be generated that would be useful for improving the stratification and personalization of care within subsets of diabetic patients. Layering in the molecular information on top of those data increases the ability to become more granular and targeted, which enables even greater stratification. From a clinical development perspective the stratification of subsets of diabetic patients provides the opportunities for improving the effectiveness of clinical trials. Indeed, with the right information management tools in place the current paradigm of defining a protocol for a clinical trial and then recruiting patients, can be turned on its head and clinical trial protocols can instead be defined based on patients in 'real world' settings. This will result in the tailoring of clinical trials to define and characterize patient populations, resulting in better clinical trial outcomes at a lower cost. The concept of adaptive clinical trials is early evidence of this trend. Within this framework, selecting patients based on a set of clinical attributes, and also an omics attribute, produces a defined clinical profile that acts as the foundation for the clinical trial. This creates the opportunity to focus the clinical trial on the specific patient group that is most likely to respond and reduces the uncertainty attached to the current clinical trial process and the uncertainty surrounding the investment that has gone into the development of the drug under investigation.

Opportunities for Improved Performance

A confluence of social, demographic, economic, and technological trends is shifting the dynamics of translational medicine and offers the promise of realizing a future of value-based, personalized healthcare where innovation continues to be rewarded while simultaneously addressing the cost/quality challenges in our healthcare systems. As a result, ecosystems that encourage innovation in translational research, with supportive elements such as the electronic capture of patient data and repositories of long-term, outcome data are being established worldwide. Although these changes are creating opportunities for companies—and entire nations—the ability to adapt to this rapidly evolving environment is also dependent on a number of decisive factors.

One required change is for translational medicine to reach a wider audience. Currently, in the healthcare provider sector, translational medicine is an activity that is performed by technically sophisticated academic medical centers in which performance indicators are used as a consistent set of measures. Translational medicine institutes conduct the bulk of this research and therefore have tremendous expertise in this field. However, translational research, in terms of understanding the genotype and phenotype, and biomarker relationships, need to be made available to the average clinician in a non-academic setting—getting the results back into the clinical setting. This enables clinical decisions to be made at the point of care as opposed to it being a research activity or information that is delivered to impact the daily workflow of a clinician. In the current environment of substantive healthcare reforms there is also the danger of an over-emphasis on value-for-money or on technology focus, like reducing the cost of mapping the genome to $1,000. It is important to maintain focus on connecting the identified genotypic changes with phenotype in a meaningful way and presenting this complex information in such a way that a clinician, faced with a patient at the point of care, will feel confident in making a different decision as a result of having this genetic information to hand.

Concluding Remarks

The primary focal point for translational medicine concerns the translation of the current research discoveries into clinical practice. It is clinical-grade genomics rather than just simply research. That is the mindset that needs to change to accelerate personalized healthcare, which in turn will address not just the cost/quality challenges by eliminating waste but also improve outcomes by driving more preventative and targeted interventions. The reality is that translational medicine is being driven by the convergence of healthcare and life sciences data, and the predicted rise of clinically-relevant biomarkers. Importantly, the technology is already available to facilitate the integration of the healthcare and life sciences ecosystems. However, an investment in context-specific analytics platforms will be needed to transform the transactional data that have already been generated from clinical care and clinical trials into actionable information to accelerate discoveries to practice. Today, translational medicine is a research question. Tomorrow it becomes a clinical decision support question in a personalized healthcare environment that rewards and reimburses for value. ■

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