

Informatics Opportunities and Challenge

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Over the past few decades, the miracle of modern medicine has been sustained in part by “blockbuster” drugs from the pharmaceutical industry. This approach to drug discovery—one driven by high throughput screening—was successful for a long time in terms of benefits to patients and profits for the pharmaceutical companies, even though a typical drug took around 12 years and more than \$800 million to bring to market. Ultimately, billions of dollars in revenue over several years could be expected, justifying the high cost of discovery and development.

This approach has now been judged to be inadequate in a number of ways. Drugs that work successfully in some individuals can be ineffective or cause serious adverse events in others. In addition, candidate discovery has begun to saturate, and development is becoming more expensive, while established blockbuster drugs are simultaneously losing patent protection and putting billions of dollars of revenue at risk for large pharma companies. Already, new drug approvals are not keeping pace with R&D costs. Over 20 years, from 1983 to 2003, drug R&D costs increased more than eightfold, while the number of approved new chemical entities per year grew by only around 25 percent.

Life sciences companies are now increasingly focused on “personalized medicine” approaches to improve their returns on drug discovery. Driven by an understanding of the molecular genetic basis of disease, personalized drugs and treatments vary based on an individual’s unique genetic profile, or “genotype.” The resulting drugs and treatments are usually targeted toward sub-segments of the population within which they are effective and safe. With this approach, drugs that might ordinarily have failed clinical testing for a number of reasons can treat disease in specific target populations. Many targeted drugs are already on the market or in the pipeline today.

The Importance of Informatics

The new model of personalized medicine will rely heavily on informatics to identify and exploit new insights into the genetic variability of diseases. Within clinical trials, the mandate to incorporate genetic information requires patient recruitment that provides genetic diversity and statistical significance within major genotypes in a trial sample. Hence, in order for the personalized medicine model to be both economical and scalable, pharmaceutical R&D will have to be more closely tied to clinical care delivery. In turn, information that is trapped in silos either on the R&D side or on the clinical side will have to be more effectively combined and cross-referenced. Once approved, targeting appropriate patients for safe and effective use of a drug will also require expanded informatics support. The recent Food and Drug Administration mandates for increased post-market surveillance will drive further integration between clinical trial software and healthcare delivery systems.

There are two significant challenges in creating a seamless integration of clinical and R&D data. First, regulations and policies to protect patient privacy can prevent organizations from freely sharing clinical information with outside research institutions. This constraint can be overcome using de-identification capabilities that are now commonly available in clinical IT applications and middleware products, which allow personally identifiable information to be stripped before sharing with external entities. A second challenge is around data models used in clinical vs. R&D applications. While most clinical data models are designed to be longitudinal (following patient history), most R&D data models are focused on individual drugs, and hence take an episodic view across many patients over a limited time. Hence many clinical informatics efforts expend significant resources first in normalizing clinical data

across data sources, translating to a common terminology, and then focusing on data reuse across clinical and R&D applications.

Large hospital networks are already moving toward consolidation of clinical data, either by implementing a common clinical information system across all network hospitals (which can sometimes become expensive if network hospitals are already using different systems), or integrating existing data sources using a middleware-driven approach. In either case, the objective is to harmonize processes across the organization and to make clinical information more secure and available to a variety of applications (including informatics) in a normalized form. To encourage further integration of clinical and R&D efforts in the near term, the National Institutes of Health has spurred investment at major Academic Medical Centers (AMCs) through its Clinical and Translational Science Awards (CTSA). These incentives are encouraging AMCs to invest in the infrastructure necessary to bridge the gap between R&D silos and clinical practice.

To truly complete this integration, diagnostic labs must also be brought into the framework. The number of genetic tests offered through diagnostic labs is expanding rapidly. Bio-banks are building up repositories of genetically identified tissue samples. These two sources are yielding mountains of new data on genotype-phenotype correlations, which can and must be leveraged in personalized medicine R&D. This new data often does not fit within the designs of older lab information management systems (LIMS). While leading AMCs are in many cases developing their own data models to store and utilize this data, over the long run, open standards-based solutions will be required in order for the industry to truly leverage all available data. Diagnostic images are another important component of clinical data that has long been difficult to manage and hence remains trapped within specialized imaging systems (like PACS). New database technology now makes it possible to work with images directly within databases, thereby making image repositories more robust, scalable, and more accessible across various clinical applications.

As diagnostics and therapeutics become more closely tied in the personalized medicine world, the

resulting informatics needs are becoming more pervasive within healthcare organizations. The results of a typical genetic diagnostic test often require delicate interpretation and patient counseling before selecting the appropriate course of action. In this rapidly evolving field, it is difficult for physician education and training to keep up with new developments, even within individual practice areas. Hence, the ability to deliver relevant, personalized, up-to-date content within a physician's workflow will become increasingly important to prevent errors and enhance physician decision support. Physicians and nurses will expect care protocols to change more frequently and in more subtle ways, and will look to standardized informatics tools to guide their decision making. These changes in the practice of medicine will also require healthcare delivery organizations to invest in education, incentives, and change management processes to facilitate clinicians and others to move to these new modes of care.

Change Required on Multiple Levels

There are three levels of informatics capabilities that healthcare organizations need to develop as they move toward personalized medicine. First, "In-Silo Informatics" capabilities, which focus on individual clinical specialties, like oncology, cardiology, neurology, and so on. These capabilities integrate relevant clinical data within a specialty with internal and external sources of relevant content to constantly improve the evidence base for the specialty area and to guide specific care protocols. This is also the level at which most collaboration occurs between AMCs and life sciences companies, within the context of a specific disease. As one might expect, these capabilities are of greatest immediate value to clinicians, researchers, and departmental leadership.

Second, "cross-silo informatics" capabilities are required for disease management and to track outcomes across the continuum of care. These cross-silo (and even cross-institutional) capabilities will become even more essential as the utilization of home-based care grows, and as the next generation of medical devices using telematics begin to deliver near real-time data on patient conditions to remote monitoring systems. In clinical practice, these capabilities are most

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valuable for primary care, emergency care, and chronic disease management. They are also applicable to infection control, public health, and other broader medical goals. Hence, while in-silo informatics capabilities are directed at the department level, cross-silo capabilities are more geared toward chief medical officers, senior hospital leadership, and external agencies (such as public health).

Finally, “Performance and Cost Informatics” is required to understand the cost-benefit of personalized treatments. With targeted treatments serving smaller target patient populations, current “pay-for-service” reimbursement models may prove to be ineffective. Understanding the true long-term costs and benefits of personalized treatments will require informatics capabilities that span clinical and financial (billing) systems within hospitals. It is not clear how reimbursement models will need to change to provide the right incentives for personalized medicine practices. Given the fragmentation of the U.S. healthcare system, we may see more innovation in more centralized environments where the government retains most of the cost as well as the responsibility for improving the health of targeted populations.

Most hospitals already have operations infrastructure such as ERP, in addition to clinical systems. Many of these include informatics capabilities for financial consolidation, planning, and performance management. For personalized medicine, hospitals will increasingly need to analyze and demonstrate the cost-benefit of various treatments. This will require an informatics platform that spans both ERP/financial and clinical systems. The added cost of genetic testing, patient education/counseling, and potentially expensive personalized drugs will require a higher level of justification. Hence, in many ways, performance and cost informatics is relevant not only to providers, but also to payers and life sciences companies, even though the primary data needed to support it will lie within provider organizations.

Within life sciences companies, clinical R&D data are similarly fragmented across many silos. As they engage with AMCs to develop new personalized drugs and treatments, life sciences companies would be well served to implement a standards-based platform

that enables both internal and external data sources to be integrated. Such a platform can provide “vertical” informatics capabilities around specific drugs (from discovery, through clinical trials, and beyond to post-market surveillance) and also “horizontal” informatics capabilities required for R&D portfolio management across the drug pipeline. As described above, much of the data required to support informatics around costs and outcomes lies within provider organizations. Hence, the architecture for data integration for life sciences companies must support internal R&D data models, as well as standards-based data models within provider organizations.

Personalized drugs will require rapid, cost-effective development approaches that will be perfected over the next few decades. However, we can already observe a few key drivers of this change. First, the evidence base for the safety and efficacy of new drugs will be more diverse and cover a longer time frame than current drugs; second, cost pressures are driving clinical trials to ever expanding corners of the world; and third, portfolio management will become increasingly complex as niche markets become more important and reimbursement models catch up with personalized treatments. These drivers point to the need for a flexible informatics environment that can scale geographically, and interface securely with external entities.

Even in the best of scenarios, broad informatics capabilities as described above will take many years to implement across healthcare and life sciences organizations. As described above, the different levels of informatics capabilities will benefit various stakeholders across clinical care, clinical research, life sciences R&D, payers, and public health organizations. These stakeholders must first act individually to implement the capabilities that serve their needs first, while participating in collaborative initiatives where possible to move towards common industry architectures. In these early days for personalized medicine, AMCs and life sciences companies are faced with many such opportunities for collaboration. With a proper planning framework, adherence to open standards, and some forward-looking investments, organizations can ensure that their incremental efforts over time will yield a valuable and flexible informatics platform.

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