

# Patient-centric healthcare of the future from the prospective of biomedical research and technology

## Abstract

The impact of the healthcare industry on our mere existence is enormous as it defines the quality of our lives from beginning to end. Advances in healthcare are streaming from every constituent of its ecosystem from policy-makers, payees, and payers, to care providers, drug developers and scientists. The information technology nowadays plays an integral role in healthcare infrastructure: not only does it link the data from each component of the ecosystem for a simple communication-coordination purpose, but it is responsible for the information collection, maintenance, safety, analysis and provides tools for making better and more educated decisions in healthcare business with an ultimate goal of improving the patients' lives. The biomedical research also makes significant strides towards developing new options for medical treatments with outcomes that surpass previous results and allow for personalized approach in patient's treatment. While each organization within healthcare has its own mission and goals, they all have to share a common vision, a vision about the Healthcare of the future. Here we share our opinion about potential future of healthcare from the perspective of advances in biomedical research and patients' needs, including other factors and trends within this cross-functional industry.

**Keywords:** health care, patient-centric, biotechnology, biomedical research, drug discovery, cross functional, big data, wearable, population health, clinical trials

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**Abbreviations:** AAAS, American association for the advancement in science; ACA, affordable care act; CCNSC, cancer chemotherapy national service center; CDER, center for drug evaluation and research; CES, consumer electronic show; NSECHN, nano scale science and engineering center for high-rate nano manufacturing; CMS, centers for medicare & medicaid services; CRISPR, clustered regularly interspaced short palindromic repeats; FDA, food and drug administration; HER, electronic health records; HIPAA, health insurance portability and accountability act; IND, investigational new drug; IT, information technology; IVIG, intravenous immunoglobulin; NCHS, national center for health statistics; NIH, national institutes of health; NSF, national science foundation

## Introduction

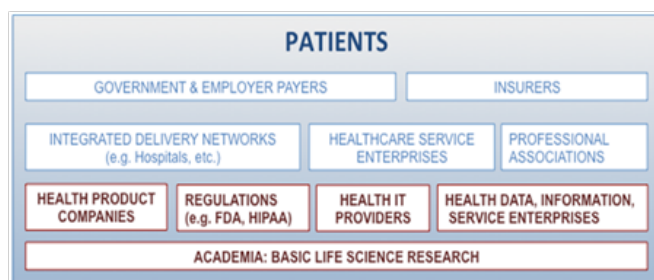
The mission of the healthcare industry is to maintain and improve health via diagnosis, treatment, and prevention of disease, illness, injury, and other physical and mental impairments in human beings.<sup>1</sup> This simple notion emphasizes the enormous impact this industry – healthcare – has on our lives. This review highlights the ever-growing complexity and breadth of the concept of “personalized” medicine from biomedical research and technology perspective, without going into the depth of each topic.

Economists<sup>2</sup> predict several healthcare trends and challenges in the upcoming years including the formation of cross-industry collaborations within the healthcare ecosystem and the growth of interest in the population health management. Moreover, since the human genome was first sequenced in 2000, patients have become ultimately involved in primary clinical data collection at the molecular level. Furthermore, with mobile technology booming, each person with a mobile device becomes a potential creator of individual ‘normal’ baselines for behavioral or clinical data. Both of these phenomena as well as other biomedical research innovations have a powerful impact on the rapidly changing landscape of patient-centric healthcare.

All together these changes will definitely contribute to the growing improvement of healthcare outcomes and will pose greater challenges for executive management and policy-makers in overcoming the technical complexity of the administrative cross-functionality and interdisciplinarity of research.

## Opinion

The ecosystem of the healthcare has several key components.<sup>3</sup> For the purpose of this review we will concentrate on trends in life science research, drug discovery, and information technology, while staying focused on patient needs (Figure 1, components in the crimson font). After all, the major change taking place today in healthcare is that our current physician-centered system is being replaced with one that revolves around the patient.



**Figure 1** Healthcare ecosystem.

Many improvements in healthcare have already been implemented to ‘personalize’ medical services. By mid-2016 personalized medicine has been discussed in over 24,000 publications, addressed in 460 clinical trials, has become the focus of 30 patents and 220 conferences. Yet the battle is still “on” with certain financial and data management challenges to be conquered and new trends in development to be embraced. More importantly, the health care industry continuously employs traditional approaches to accomplish its mission without a clear unified vision about its future.

When thinking about an ideal doctor we, as patients, usually think about a doctor (or services) that will support our healthier and longer lives with less medical intervention and with lower costs. We wish to have a doctor, who knows everything about us, and diseases, the one that you can trust with your doubts and concerns, who knows your parents (and their disease history) and a doctor who will take a good care of your children the same friendly way s/he does it for you and your parents. Ideally this doctor will follow you in your trips around the world either (work or leisure) and who will be at your disposal 24/7. Is this even possible? For a human doctor - it is not, but for a digital doctor (say, a “*Family eDr*” digital system)– absolutely. It is only a matter of time–, and collaborative work between members of the healthcare ecosystem, to create a comprehensive IT system. This system will have access to the latest global bio-medical knowledge, personal patient information (from individual genome, microbiome and/or epigenome– to a family disease history and daily exercise/diet monitoring data), and with predictive algorithms about potential treatment outcomes, to keep up with the upcoming changes, all parts of the healthcare ecosystem (including insurers, government and employer payers) will have to develop new policies, regulations and guidelines. Will this proposed patient family-centered eDr system allow for reduced medical costs? Who will be responsible for establishing this type of system? These and other important business questions will have to be answered at the right time in a different document.

Traditionally, *pharmaceutical industry* is one of the biggest contributors towards improved healthcare and personalized medicine via developing new drugs and manufacturing generic ones. While new drug development process is rather lengthy (~12y on average), is risky (~10% will make it on the market), and expensive (over \$300M per commercial drug), - it is the only well-defined way of bringing new remedies to ailing people.<sup>4</sup> There are several types of drugs, including small-molecule drugs (usually derived from chemical synthesis), biopharmaceuticals (e.g. creation of recombinant proteins, vaccines, gene therapy, monoclonal antibodies, IVIG), and cell therapy (e.g. stem-cell therapies).<sup>5</sup> Medicines are also classified by their mode of action, route of administration, biological system affected, or therapeutic effects. This range of approaches to drug development requires robust biomedical research. Here we will highlight four major novel approaches that are currently used for developing new therapies, each of which is patient-specific.

Among most prevailing diseases, cancer is the second leading cause of death right after heart disease, according to the NCHS 2013 reports.<sup>6</sup> No wonder then that the majority of pharmaceutical and biotech companies focuses their efforts on developing drugs against different types of cancer. Since establishment of the CCNSC in 1955, resulted from four World War II-related programs, cancer treatment approach advanced from direct chemotherapy to neo-/adjuvant chemotherapy, irradiation therapy, electro-chemotherapy, and immunotherapy.<sup>7</sup>

Emerging *immuno-oncology* approaches are focused specifically on the patient's immune system.<sup>8</sup> They are designed to target tumor environment by blocking its inhibitory pathways and inhibitory cells–, or enhancing the specificity of antitumor immunity by inducing the expansion of T cells and antibodies directed to well-defined tumor antigens. It was shown that when administered as mono-therapies these novel treatments have a significant impact on the treatment of patients with advanced cancers–, that were previously considered untreatable. There is an exciting expectation that when used in various combinations or in early stages of disease, this immunotherapy may

improve the prognosis for many patients and ultimately transform cancer treatment–, as we know it today into a new era of cancer cure with focus on the patient.

Another novel approach in drug development, *gene editing*, is based on CRISPR/Cas9, which are segments of prokaryotic DNA containing short repetitions of base sequences. The use of CRISPR for editing genes was named by the AAAS as breakthrough of the year in 2014.<sup>9,10</sup> This novel precise gene-editing technology has been prized as having an enormous potential for drug development industry by offering new ways for identifying CRISPR targets, designing CRISPR assay cascades, developing CRISPR disease models and even as CRISPR therapeutics. With such wide application across industry this powerful technology will certainly have a major impact, on the future of personalized medicine and healthcare overall.

*Reprogrammable cell therapy* was named the second in top 10 world-changing ideas 2014, right after CRISPR. /Cas9. SQZ Biotech, for example, is developing novel methods for engineering cell functions to use the power of a patient's own cells to fight disease more effectively across a broad range of indications. Scientists at SQZ Biotech use a Cell Squeeze chip with micro fluidic channels that rapidly deform the target cells to induce temporary disruption of the cell's membrane.<sup>11</sup> The delivery material can then enter the cell through the membrane disruptions before they reseal. This technology provides a robust platform for engineering a diversity of cell functions for a range of therapeutic applications.

One other trend in modern personalized medicine is the application of *companion diagnostics*<sup>12,13</sup> for the safe and effective use of corresponding drug or biological product. Companion diagnostic usually refers to a medical device, which provides physician and patient with immediate readout and essential information during drug treatment about treatment benefits or serious side effects or risks. Companion diagnostics can help clinicians with identification of patient cohorts that most likely will benefit from a particular therapeutic product or will be at increased risk for serious side effects as a result of treatment with a particular therapeutic product. The ability to closely monitor a patient's responds to treatment offers a unique method for medical treatment adjustment with improved safety and efficacy, with cost and time effectiveness.

Every new drug or treatment approach has to be approved by the FDA based on developed guidelines, indications, and clinical trial results. The Center for Drug Evaluation and Research (CDER) at FDA ensures that drugs marketed in US are safe and effective. As an example, to help companies identify the need for companion diagnostics at an earlier stage in the drug development process and to plan for co-development of the drug and companion diagnostic test, the FDA issued “Guidance for Industry: *In Vitro* Companion Diagnostic Devices”.<sup>14</sup> Another example concerns CRISPR technology: in December 2015, the FDA authorized the world's first human clinical trial for an *in vivo* genome editing, a Phase 1/2 open-label, dose-escalation study on up to nine male adults with severe hemophilia B. The study will examine the gene therapy's safety, tolerability and potential efficacy.

The overall scope and size of national biomedical or behavioral research studies on human participants is enormous. According to the official clinical trials government site<sup>15</sup> there are total of 216,408 listed clinical studies performed today in all 50 states and in 193 countries. The 174,302 interventional studies include 49,638 behavioral studies (28%), 18,861 surgical procedures (10%), and 108,141 studies with drugs or biologics (62%). These studies are designed to generate

data on safety and efficacy for the drugs/treatments and to ensure the scientific validity and reproducibility of the results. Remarkably, only 10% of all drugs started in human clinical trials are approved.

*Patient-centric healthcare of the future* cannot evolve without novel clinical devices, tools for diagnostics and screening, and without tools that are used in studies on human genomics, proteomics or metabolomics. Modern scientific community exploits a number of commonly used equipment for their daily research, such as sequencing machines (Solid, 454, MiSeq, GA2, Ion Torrent, and Proton) for high-throughput genome sequencing, microarray chips (Gene Chip/Affymetrix, 3D-gene/Toray, Bead Chip/Illumina) for gene expression profiling, and mass spectrometers (SCIEX, Beckman, Waters, Thermo Fisher) for peptide analysis, metabolite profiling and identification. Existing instruments certainly differ by data resolution and sensitivity, quality of readout and its format, and the choice of equipment is usually based on specifics of their application in research or diagnostics. Data integration from different platforms remains one of the biggest challenges for uncovering translational meaning of human systems biology and functional genomics.

While overall OMICS-technology continues to evolve and is primarily being used for *research purposes*, the technology for genetic screening has already become a standard and is offered as services for both healthy individuals and patients alike. For example, one of the leading companies in personalized genetic screening, 23andMe, offers over 60 reports for its customers including genetic carrier status reports for educated family planning, ancestry reports for confirming family history, wellness reports that help to choose the best diet and exercise, programs and trait reports with a subset of genetic markers describing customer's unique genetic makeup.<sup>16</sup>

Current tools for *proteomics*, on the other hand, cannot yet provide an ultimate solution for a thorough exploration of the proteome let alone its clinical application for diagnostic screening. Proteome is a more complex biological system. The functional role of many identified proteins is not yet known. (e.g. lung cancer) is not yet known and a solid clinical validation is still lacking. Proteomic technologies in research are mainly based on two-dimensional gel electrophoresis (2D-PAGE and/or 2D-DIGE) and isotope labeling methods (ICAT, iTRAQ, SILAC), followed by mass spectrometry analysis. Although proteomic approaches<sup>17</sup> improving rapidly, clinically relevant hypotheses are hard to generate from those intricate data. Nonetheless, some physicians already practice blood tests for tumor protein markers to detect breast cancer activity in the patient's body. It is also reported that a 6-protein panel<sup>18</sup> could be used as a potential biomarker for early detection of lung cancer in bronchial brushings. Unfortunately, the complexity of the accurate cancer diagnostic is amplified by the fact that cancer is a multifactorial disease. It will require a great deal of time and effort to define cancer-associated proteome modifications and to translate them into practical clinical applications.

*Biomedical engineering* improves human health through cross-disciplinary activities that integrate engineering sciences with biomedical sciences and clinical practice. Considerable progress have been recently made by bioengineers towards development of novel tools, approaches and assays. For example, it is known that over forty percent of the new chemical entities are poorly soluble in water and cannot be taken orally, while intravenously administered micellar formulations are highly toxic and invasive. To address this challenge, bioengineers at the NSF Nano scale Science and Engineering Center (NSECHN) use nanotechnology to develop oral preparation of poorly soluble drugs by forming drug-loaded polymeric micelles into orally acceptable 3D nanorods.<sup>19</sup>

Another potentially desirable example of the bioengineering approach for healthcare improvement is use of microscale sensors and systems for tissue engineering and regenerative medicine.<sup>20</sup> The 3D scaffold constructs with human cells are being designed as an alternative to animal studies or for obtaining in-vitro readout of patient responses to drug treatments. These micro fluidic bioreactors, or "organs on a chip" systems, are being generated with integrated miniature physical and biochemical sensors to provide information about physical parameters such as pH, osmolality, temperature, etc., as well as the metabolic activity of cultured cells. In addition to their application in drug development, some miniature sensors can be used for monitoring wounds. Specifically, flexible sensors can be used for chronic wounds monitoring of diabetic patients to prevent infection or further complications.<sup>21</sup>

The most important component of future healthcare is *Information Technology*, including management of patient's private information from omics to clinics. Recent explosion of wearable personal devices adds another layer of complexity to this challenge. Evolution of information technology for mobile devices towards consumer wearables took off in the first decade of the 21<sup>st</sup> century with incorporation of the Bluetooth microphone into a pair of earrings.<sup>22</sup> This innovation paved the way to many more other ideas and the consumer market today flooded with a variety of wearable health devices. The ten top commercially available wearable devices for healthcare were identified in 2016 at CES – the global consumer electronics and technology tradeshow.<sup>23</sup> Clinical or therapeutic applications of these devices range from measuring blood pressure, glucose monitoring, and eyesight performance to futuristic biometric shirts with sensors woven into the fabric for measuring heart rate, pace, breathing rate and volume, steps taken, calories burned, and sleep patterns.

At about the same time, analyst Doug Laney from META group (now Gartner) for the first time addressed large data phenomenon by defining data growth as 3V-dimensional: data volume, data velocity, and data variety.<sup>24,25</sup> Since then the 3V model for describing Big Data is being used for all datasets that are so large and complex that traditional processing is ineffective.<sup>26</sup> Despite many technical challenges that Big Data brings (storage, transfer, querying, maintenance, curation, analysis, etc.), it also offers tremendous advantages to both science and businesses. It has a capacity to reveal patterns, trends, and associations for making informed strategic decisions, building predictive models, and moving businesses the next level of success.

Patient clinical information in the form of *Electronic Health Records* (EHR), as well as the clinically beneficial derivatives from technological platforms described above (drug development, omics, bioengineering, wearables, medical devices), a mass substantial amount of data per patient. Clearly, Healthcare industry data fall well under Big Data description with all its challenges and benefits. Remarkably, hospitals and other healthcare providers are already trying to change the way they generate and use clinical information. As a start, they are looking for methodologies that allow IT and hospitals work together as partners by using proven agile development and deployment methods, while sustaining reliable and secure data infrastructure, to address quick changes in processes and data. For healthcare providers, says Andy De, "...today's analytics and insights could make the difference in tomorrow's clinical outcomes. The need to understand healthcare data and to draw insights and correlations from it continues to grow".<sup>27</sup>

Let us not forget about the highly regulated environment of the Healthcare, designed to protect patient's rights. Since 1960 Federal and State governments have passed a number of laws that protect patients



from discrimination by employers on almost any grounds including age, disability, pregnancy, gender, race, national origin, religious or sexual harassment, and sexual orientation.<sup>28</sup> Going forward, it will be important to protect new types of patient's information such as genetic disease markers, against discriminations based on predicted disability or disease (cancer, neurological, others). Another challenge in the patient-centric healthcare of the future is aging population. The eldercare is projected to be the fastest-growing employment sector within healthcare industry. By the year 2030, the number of people reaching retirement will double.<sup>29-31</sup> These people will be in need of a wide range of professional health and social service expertise, specialty surgeries (including beauty/youth enhancements and joint replacements), and heart disease control. With improved healthcare outcomes and increased lifespan expectancy, many baby-boomers may continue to work. This will have a strong impact on the overall landscape of workforces resulting in new types of jobs creation, adjustments for on-job performance expectations and enforcement of age/disability discrimination laws. But this topic is for altogether another discussion.

The affordable Care Act (ACA or "Obamacare"), the most significant innovation in healthcare system, was signed into law by President Barack Obama in 2010.<sup>32</sup> Since its implementation, many medical service providers feel financial pressure. Healthcare CEO's are concerned about the financial position of their hospitals, new CMS mandates and rulings, patient satisfaction and quality scores, population health managements, and personnel shortages. The assessment of risk tolerance associated with new strategies has shown the decreased reimbursement risk from CMS's value-based programs, an explosion of value-based contracts for the commercial sector, and a new risk of non-reputable representation on Social Media.<sup>33</sup> On the positive side, however, new CMS regulations allow physicians to provide additional services (e.g. remote chronic care management-, and telemedicine). Innovations and improvements, whether at the level of research, treatment, or administration-, should always be respected as positive changes within existing organizations or systems. The Healthcare ecosystem, albeit patient-centric, is a business organization with its growth potential and financial projections, depending on a clearly depend on clearly defined vision and mission.

## Conclusion

In this manuscript (review/opinion), we have demonstrated the complexity, continuous progress and interdependency of the modern Healthcare ecosystem. To build the Healthcare of the Future, each sector of this system from basic research, to drug discovery, healthcare providers, payers and payees will have to share information centered around a specific patient and his or her family on different levels (molecular, environmental, behavioral, ancestral, clinical, legal, etc.). It is clear that in order for the comprehensive and streamlined implementation of the Future Healthcare to take place, all constituents of the ecosystem will have to collaborate consistently towards common mission, vision and goals. What a fascinating journey lies ahead of us!

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## Conflicts of interest

Author declares that there is no conflict of interest.

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