

Personalized Medicine and Stakeholders' Perceptions

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Patients suffer the same form of illness but their responses to therapy may differ greatly. This can be attributed to their genetics or other environmental factors. Personalized Medicine may improve the outcomes of treatment by understanding the individuals, causes of their disease, and the best treatment for their cure.

KEYWORDS: Personalized medicine, and warehousing, Genetics, Pharmogenomics, Data security Clinical data mining.

INTRODUCTION

The Health Information Technology for Economic and Clinical Health (HITECH) Act and the Affordable Care Act (ACA) established several programs intended to accelerate the transformation of the health care delivery system in the United States (U.S.). Some of these programs include the adoption of the Electronic Health Record and its meaningful use, participation in Accountable Care Organization and the use of Clinical Decision Support (CDS) systems to improve point-of-service care. These initiatives are major drivers to enhance clinical data quality and availability (The office of the National Coordinator for Health IT). Currently, there is much data available to health care delivery organizations as a byproduct of the practice of medicine and possibly the adoption of the aforementioned programs. It is the expectation of health care practitioners, health policy makers and care organizations that the accumulation of data will be valuable for the improvement of the U.S. and global health care systems. Three major areas of using data to enhance performance include improving patient care, reducing health care related costs and managing performance (Rhoads & Ferrara, 2012). According to Pogorelc (2013), most hospitals will produce more than 665 terabytes of data by 2015; this rapid data growth in health care organizations presents both an opportunity and a challenge for the health care industry (Pogorelc, 2013). This paper will discuss data warehousing and mining in health care, the opportunities and challenges inherent in the use of medical data and, specifically, the application of these concepts in optimizing personalized medicine.

LITERATURE REVIEW

Data Warehousing and Mining in Healthcare

In recent times, organizations have understood the opportunities inherent in the meaningful use of data from their information systems for better decision making, cost savings, trending and prediction of

outcomes. Hence, there is an increasing need to store vast amounts of data in what is currently known as a “data warehouse”(Pedersen & Jensen). According to Pedersen, the functionality offered by data warehousing has traditionally been used by businesses, in the areas of retail & finance; but this technology is now increasingly being used in more scientific areas(Pedersen & Jensen). Previously, data warehousing was primarily used by corporations to obtain information to guide management and financial decision making. Initially, the use of data warehousing was a bit more complicated as organizations held their data in disparate systems (Inmon, 2007). However, with progress, data warehousing, required the integration of disparate systems for the meaningful use of information.

Data warehousing as a term was first used by Barry Devlin, but became popularized by Bill Inmon who defined it as; “A data warehouse is a subject oriented, integrated, non-volatile and time-variant collection of data in support of management’s decision” (Pedersen & Jensen).

Data in the warehouse is optimized for analysis rather than for data entry. It is therefore used to understand and manage the enterprise both at a strategic and tactical level. Gray and Watson (1998) posited that data warehousing is fundamentally created to provide a dedicated source of data to support decision making applications. The data warehouse can provide a single version of the truth by providing users and applications access to the same source of information (Watson,2002).

FIGURE 1

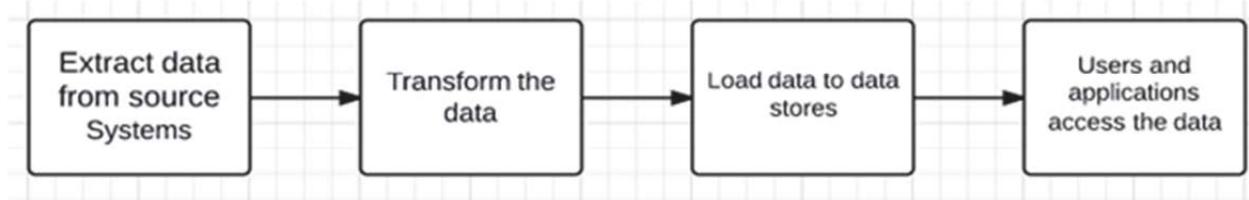
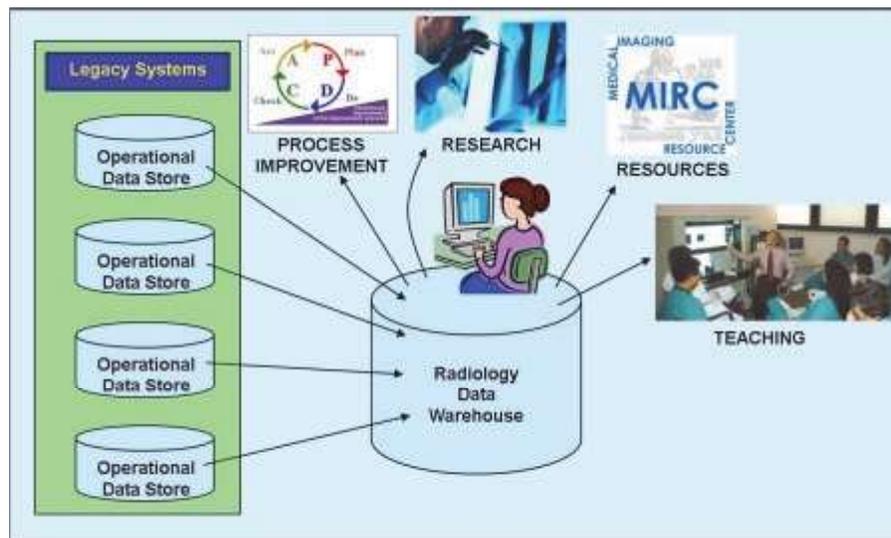


FIGURE 2



Picture source: Recent developments in Data Warehousing (Watson, 2002).

The need for a clinical or healthcare data warehouse is advocated by Gray and Watson (1998) because it can provide the same version of data for various needs. The provision of the same version of

data can save different users the time and resources to write programs to answer questions on different kinds of data. Hence increasing the focus on data analysis rather than data collection and cleansing.

To understand healthcare issues and solutions, unbiased and timely data must be available. Healthcare data are usually stored in diverse formats both logically and physically and it is limited in scope of reports therefore making it ripe for the application of data warehousing technology to integrate these data sources. Data warehousing technology supports more effective healthcare decision-making at both individual and community levels. In addition to administrative uses, different clinical uses of data warehousing have been reported in the last 15 years. For example, data warehousing has been used for recruitment of participants for clinical trials, gene-disease association studies, family health history data patterns, public health applications, and trends in drug use/cost/interactions, infection surveillance and so on. Moreover, it has also been found to be a fundamental tool in the personalization of patient care (Evans, Lloyd, & Pierce). Data warehousing in healthcare is quite challenging because the industry is ripe with often incompatible medical standards & coding schemas. Sensitive data may be obtained from several sources and be delivered in many forms which require added attention to privacy and security issues.

Another major issue is that the health care industry is widely decentralized and largely autonomous (Berndt, Fisher, Hevner, & Studnicki, 2001), which makes issues of data sharing quite challenging. As clinical data warehousing is being adopted rapidly by health care systems, the value of these information systems cannot be harnessed without applying data mining technology. Data mining tools are search tools that originated in statistics, computer science, and other non-biomedical disciplines to find associations among variables that may be useful in making management decisions (Mullins et al., 2006). Data mining is the process of selecting, exploring and modeling large amounts of data. Data mining has been defined variedly. For example, Yoo et al. (2012) defined data mining as “the analysis of (often large) observational data sets to find unsuspected relationships and to summarize the data in novel ways that are both understandable and useful to the data owner” (Yoo et al., 2012). Kaur and Wasan (2006) also defined it as the non-trivial extraction of implicit previously unknown and potentially useful information about data. Data mining enables the generation of scientific hypotheses from large experimental data sets and from biomedical literature by bridging the gap between data availability and the use of knowledge that can be derived from it (Yoo et al., 2012). Often times, the concept of data mining and Knowledge Discovery in Databases (KDD) have been used interchangeably; however, both concepts are quite distinct. According to Fayyad et al. (1996) data mining is one of the steps (Selection, Pre-processing, Transformation, Data mining and Interpretation/Evaluation) of KDD which involves fitting models to or determining patterns from observed data while KDD refers to the overall process of discovering useful knowledge from data such as data cleaning and incorporation of heuristics (Fayyad, Piatetsky-Shapiro, & Smyth, 1996).

In health care practice, data mining has been used to reduce adverse drug effects and also to suggest cheaper and safer alternatives. Areas where data mining techniques have been applied successfully in healthcare management include but are not limited to: Executive Information System for health care; forecasting treatment costs and demand of resources; anticipating patient's future behavior given their history; Public Health Informatics; e-governance structures in health care; health insurance, etc. (Kaur & Wasan, 2006). An emerging field of healthcare where data warehousing and mining is of absolute importance is personalized medicine. Personalized medicine is a new trend of patient care whereby patients are treated not only based on presenting symptoms, but also on the causes of the disease, its rates of progression, and how their body will react towards prescribed medications and diets. The data mining techniques can be used to garner a better understanding of the etiology of a disease, its particular structure, and how to design personalized therapies (Sackman & Kuchenreuther, 2014). Thus, Data warehousing may be used as a central research repository for personalized medicine with respective services for collecting, sharing, and further elaborating annotated anonymized clinical data and other research relevant data from diverse heterogeneous sources (Schera, Weiler, Neri, Kiefer, & Graf, 2014).

Personalized Medicine

Over the past six decades, much evidence has emerged indicating that a substantial portion of variability in drug response is genetically determined; with age, nutrition, health status, environmental exposure, epigenetic factors, and concurrent therapy playing important contributory roles (Alyass, Turcotte, & Meyre, 2015). To achieve individual drug therapy with a reasonably predictive outcome, one must further account for different patterns of drug response among geographically and ethnically distinct populations (Vogenberg, Isaacson Barash, & Pursel, 2010). The observation in variability of drug response in the early 1950s, led to the evolution of *pharmacogenetics* which is a confluence of genetics, biochemistry, and pharmacology. According to Vogenberg et al., advances in molecular medicine spawned the newer field of pharmacogenomics which seeks to understand all of the molecular underpinnings of drug response. Vogenberg posit that personalized medicine came about as a result of the commercialization of the aforementioned research application.

According to the United States Food and Drug Administration, the term “personalized medicine” is described as “*providing the right patient with the right drug at the right doses at the right time*”. They also described it as tailoring of medical treatment to the individual characteristics, needs, and preferences of a patient during all stages of care, including prevention, diagnosis, treatment, and follow-up. With the scientific breakthroughs and technological advancements in recent times, personalized healthcare has the capacity to detect the onset of disease at its earliest stages, pre-empt the progression of disease, and at the same time increase efficiency of health care systems by improving the quality, accessibility, and affordability (Alyass et al., 2015; Personalized Medicine, 2014). The National Institute of Health also defined personalized medicine as “an emerging practice of medicine that uses an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease. Knowledge of a patient's genetic profile can help doctors select the proper medication or therapy and administer it using the proper dose or regimen (Shoenbill, Fost, Tachinardi, & Mendonca, 2014).” The National Cancer Institute however, defines personalized medicine as “a form of medicine that uses information about a person's genes, proteins, and environment to prevent, diagnose, and treat disease (Offit, 2011). In cancer cases it uses specific information about a person's tumor to help diagnose, plan treatment, find out how well treatment is working or make prognosis (Josko, 2014). The most prominent examples of modern personalized medicine are genomic tests designed to guide treatment choices such as testing for human epidermal growth factor receptor type 2 (HER2, also referred to as HER2/neu) to select patients with breast cancer who will benefit from trastuzumab and of testing for the *KRAS* mutation to determine who is likely to benefit from therapies inhibiting the epidermal growth factor receptor (Garber & Tunis, 2009).

Personalized medicine works by making use of information from genomes and their derivatives (RNA, proteins, and metabolites) to guide medical decision making. Such medical decisions should be done while people are still healthy or at the earliest stages of the disease, and therefore be considered as preventive healthcare (Ginsburg & Willard, 2009). Such kind of preventive healthcare is now very affordable. The cost of sequencing a human genome has dropped to \$1000 compared to \$ 400 million that was last decade (Collins, 2015). There has been demonstrated and documented evidence of success for several conditions and treatments, the question now is: will personalized medicine be able to achieve its acclaimed widespread benefits?

Benefits of Personalized Medicine

- **Disease susceptibility:** Pharmacogenetics has made genetic linkage studies in families with hereditary breast and ovarian cancer syndromes as well as families with hereditary colon cancer possible. It has led to the identification of several important loci that are used for screening, disease risk counseling, and preventive treatment programs. For instance, women who carry mutations in either *BRCA1* or *BRCA2* (*human genes that produce tumor suppressor proteins- these proteins help repair damaged DNA and, therefore, play a role in ensuring the stability of the cell's genetic material. When either of these genes is mutated, or altered, such that its protein product either is not made or does not function correctly, DNA damage may not be repaired properly. As a result, cells*

are more likely to develop additional genetic alterations that can lead to cancer) have a high risk for breast and ovarian cancer, and it is now recommended that women in such families have the opportunity to undergo genetic testing to make decisions about surveillance or even surgical approaches to mitigating a high risk of developing breast cancer. Similarly, people in families with a strong history of colon cancer can undergo testing for genes such as MLH1 and MSH2 that may identify individuals who have a risk as high as 60% for colon cancer. Early and regular screening colonoscopy in these individuals (as opposed to the recommendation for the general population to begin screening at a particular age) may enable the early detection of colon cancer (Ginsburg & Willard, 2009).

- **Reduction in adverse drug reactions:** Personalized medicine has been shown to reduce the adverse effect of certain drugs by being able to interpret genetic information of individuals to determine the likelihood of positive response to a particular treatment option. A typical case is that of *panitimumab*, a drug for the treatment of colon cancer, it has shown to be effective only in the absence of KRAS mutation in tumor. Also, the drug *maraviroc* is only beneficial for HIV patients with certain strains (CCR5) of HIV disease. These examples, among others, demonstrate how genomic information may lead to tailored treatments with fewer adverse effects and a positive impact on personal health and well-being (Najafzadeh, Davis, Joshi, & Marra, 2013).

Issues and problems

Personalized medicine promises so many opportunities in the improvement of health care, from cost savings to prevention and reduction of adverse drug reactions. In the midst of all these promises, there are many challenges that need to be addressed in order to fully harness the tremendous benefits of personalized medicine. These obstacles range from obstacles in public policy which include uncertain regulatory requirements, insufficient insurance reimbursement for diagnostic tests linked to pre-emptive care, incomplete legal protections to prevent genetic discrimination, the lack of a comprehensive healthcare information technology system, and a lack of integration of this knowledge into the medical education system; thereby making it difficult for physicians to incorporate personalized medicine diagnostics or pharmacogenomics into their practices (Personalized Medicine, 2014).

Davis et al. offers a slightly different perspective to the challenges of personalized medicine through an investigation carried out in 2009 on the challenges of and promises of personalized medicine; their findings highlighted the three following major obstacles that have held back the advancement of personalized medicine:

- Scientific challenges (for example, poor understanding of molecular mechanisms or a lack of molecular markers associated with some diseases);
- Economic challenges (that is, incentives that are poorly aligned between stakeholders);
- Operational issues - electronic tracking of diagnostic information, privacy concerns, reimbursement coding issues and provider and patient education). Although scientific challenges remain, it now seems that the economic challenges and operational issues present the most significant obstacles to the further development of personalized medicine. In many cases, operational issues can largely be resolved within a particular stakeholder group (Davis et al., 2009) (Davis et al, 2009).

Ethical Issues: Unlike many other diagnostic tests, genomic sequencing for personalized medicine allows the identification of individual and related family members. Thus, concerns regarding data security, confidentiality and privacy are raised and access to genomic patient data must be restricted to the use in clinical practice (De Lecea & Rossbach, 2012). In the meantime, the data collected by biological specimen such as patterns of RNA and DNA, individual's cell populations, protein and metabolites are very sensitive data which makes the security a high priority for the institutions who keep such records (Mathias, Lipori, Moldawer, & Efron, 2016). For patients or individuals to be willing to take advantage of personalized medicine, they need to make sure that their privacy is protected to a great extent. Certain ethical questions arise on the extent to which genetic information of an individual should be used for

personalized medicine services. Collecting personal information and sharing it with other family members who share the same genetics, increases the likelihood of learning a lot of personal information of other relatives. Furthermore, this kind of data, even after you remove the identifiers, can provide enough information to identify someone. Therefore, their privacy can be at risk. Another major issue that may arise from personalized medicine is that insurance companies may require genetic testing to pay for targeted treatment even though it might be against a patients' choice; secondly, insurance companies might not agree to pay for a particular treatment or drug because it is not a known treatment for a particular disease but can be used for a unique individual (Josko, 2014) .

Practitioners' perceptions

According to Raghavan and Vassy (Raghavan & Vassy, 2014), there are many issues or factors affecting physicians' rate of the adoption of personalized medicine. Most important is the highly variable knowledge and comfort with genetic concepts and their specific applications to clinical medicine. For example, in a survey of US physicians including generalists and specialists, Selkirk *et al.* found that 79% and 69% of primary-care and non-primary-care physicians, respectively, report that "lack of knowledge about genomic medicine" is a barrier to its incorporation in practice. In another study, Haga *et al.* found that, while only 43% of respondents to a survey of US primary care physicians reported inadequate knowledge of genomic testing, feeling well-informed about genomic testing was a very strong predictor of genomic test utilization (an odds ratio of 4.6 of ordering a genomic profile for a patient)(Selkirk, Weissman, Anderson, & Hulick, 2013). Also in a recent focus group conducted by Najafzadeh et al (2013) in Canada, 36% of 28 physician participants self-reported unfamiliarity with the concept of personalized medicine. The physicians expressed different opinions on the actual meaning of personalized medicine: some physicians indicated that the term referred to tailoring treatment based on physician's knowledge about patient-specific information (e.g., health record, co-morbidities, hereditary, familial risks, etc.) while others emphasized on the role of genetic information in personalized medicine. A few physicians speculated that personalized medicine referred to improved treatments for socio-economically advantaged patients.

Patient perception

In a study by De Marco et al(De Marco et al., 2010), patients' attitudes towards personalized medicine, genetic testing, and race-based prescribing and whether they differed between white and African American participants) were examined. The findings of the study suggest that personalized medicine and genetic testing, though not well understood by lay persons, were considered positive advances in medicine. However, participants also voiced a range of concerns. For example, participants felt that, while promising, the use of genetic testing to personalized medicine might be too expensive to be accessible to the general public. The African American group discussed more about medical mistrust by marginalized populations which may affect the acceptability of personalized medicine when it becomes widely available.

A welcome development in this technology was that African Americans viewed personalized medicine and genetic testing as positive developments that could reduce the trial-and-error nature of prescribing and the possibility of side effects. In particular, patients need to understand the purpose of genetic testing and how it can be used together with other clinical information to determine the best treatment. Health professionals will need to draw from many disciplines such as psychology, anthropology, and advertising to create social marketing campaigns that address the numerous barriers to acceptance and utilization. Even in the face of overall positive views of personalized medicine, some participants were wary of participating in any sort of medical testing, believing that they might be exploited or that the privacy of test results could be compromised. One way to address this concern is to provide patients with information about the Genetic Information Nondiscrimination Act (GINA), legislation signed into law in 2008 to protect patients from discrimination by their health insurers and employers based on their genetic information. An approach similar to the dissemination of information during health care visits on the Health Insurance Portability.

Future of personalized medicine

Genomic information also can predict illness in healthy individuals. In the near future physicians, can look forward to a medical landscape in which the pairing of affordable, efficient DNA sequencing and electronic health records could be used to inform a lifetime of health care strategies. Combined with the use of mobile health technology to assist in real-time monitoring of factors such as diet, exercise, blood pressure, heart rate, and blood chemistries, this approach could lead to more precise ways of preventing and managing chronic diseases (Collins, 2015). Personalized medicine is a chance to revolutionize health care, but this will require a team effort by innovators, entrepreneurs, regulators, payers and policymakers.

A future platform of personalized medicine includes many stakeholders which are not limited to healthcare industry only (see Table 1). This platform should not include only hospitals and the treatment they provide, but should also include drug development efforts (in the early stages); integration of electronic health care system (which includes travel information, emergency rooms etc.); responsiveness towards therapies, in specific disease states; cost – effective treatment data (Jakka & Rossbach, 2013); changing policies related to the ownership of medical information and the patient’s role in making future medical decisions; redefining the reimbursements and pricing policies; and creating organizational structures and programs that support such a platform.

The new platform of Personalized Medicine should address the issue of the rise of healthcare diagnostic tests which are almost 7 times more prevalent in the last 15 years and changing the reimbursement model to a Value-Based pricing model. The new pricing model will help to increase the adoption rates of personalized medicine, increase the reimbursement for tests related to such treatments and overall will increase the quality of patient care with a lower overall cost (Johnson, 2016).

**TABLE 1
A SUGGESTED PLATFORM OF PERSONALIZED MEDICINE**

| The Platform of Personalized Medicine | | | | | |
|--|------------|------------|------------|------------|----------------|
| Medical | Legal | Economic | Ethical | Social | Organizational |
| Properties | Properties | Properties | Properties | Properties | Properties |

The future research in this topic will be towards providing directions and suggestions on what each area properties should include and expanding this suggested platform with other necessary areas which help on creating and sustaining the concept of Personalized Medicine.

Conclusion

The future of healthcare in the United States and beyond looks very promising with the advent of personalized medicine. Personalized medicine has the potential to reduce the cost and pain associated with trial and error/one-size fits all approach of the current health care systems. Moreover, it can introduce new treatment protocols of using molecular elements that signal the risk of disease at the genetic level. THROUGH early detection, prevention, and accurate risk assessments and efficiencies in care delivery, it promises to address current inefficiencies in health care delivery thereby having a significant impact on the economies of nations. For personalized medicine to deliver on its promises, it will be heavily dependent on efficient data mining tools and techniques because of large collection of molecular data from patients and the use of enormous amount of data from EHRs.

According to Chris Edwards on using data for personalized cancer treatment, “one of the problems of personalized medicine is obtaining enough data to work out how different treatments fare under different conditions, getting a database of 10,000 to 20,000 patients with 50 to 100 common tumor types, amounting to at least one million patients. “The future of personalized medicine will be based on a combination of personal data which include genomic information as well as longitudinal documentation

of all possible molecular components. It is therefore pertinent that efficient data collection, storage and mining tools are developed and applied in order to speed up mining of realms of clinical data for meaningful use in personalized medicine and also not forgetting data security which is a major issue in dealing with patients' genomic information in personalized medicine. In order to optimally reap the benefits of personalized medicine, there should be a supportive public policy environment that would address each of the issues raised, and provide incentives to reinforce emerging business models that accelerate the co-development of drugs and diagnostic tests. There should also be strategic alliance amongst the different disciplines involved in promoting personalized medicine which includes patients, scientists and drug companies. Last but very important, there should be sufficient non competing resources and a strong, sustained commitment of time, energy, and ingenuity from the scientific, medical, and patient communities for the full potential of personalized medicine to be realized(Collins, 2015).

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