Personalized Health Care: Unlocking the Potential of Genomic and Precision Medicine

by Ralph Snyderman, M.D. and Connor D. Drake, M.P.A.

President Obama's Precision Medicine Initiative has refocused national attention on the ability of genomics and other emerging technologies to provide a better understanding of the relationship between genetics, environment, lifestyles, and the development of disease[1]. This initiative was heralded as a "bold new research effort to revolutionize how to improve health and treat disease"[2]. Yet, in 2000 the sequencing of the human genome was also anticipated to lead to new ways to personalize medicine and to prevent, diagnose, and cure disease. While there have been major advances in diagnosing and treating disease, the goals for personalized medicine to improve health and prevent disease have not yet been achieved[3-5]. Despite the benefits of more targeted disease treatments, the real promise of personalized/precision medicine lies in its ability to prevent disease and improve health as, in addition to the human cost, our nation spends almost 80% of its unaffordable health care expenses on treating complex, chronic diseases which are preventable. Research in precision medicine will certainly provide new capabilities to improve health and minimize disease, but to actually do so, the approach to the practice of medicine must change so it is prepared to use them.

The Limitations of Reductionism in Medicine

Medical care today is derivative of concepts developed over a century ago when science began to be applied to the practice of medicine and identified the causes of many, particularly infectious, diseases. The logical assumption arose that diseases have a root cause and the role of the physician became to "find it and fix it." This concept led to a paradigm of care based on the capability of the physician to identify the disease underlying the patient's chief clinical complaint and, when possible, eliminate the cause. With improving technologies and clinical experience, this reductionist approach to care has improved and resulted in wondrous cures and treatments for many diseases. However, the concept of treating disease by removing its root cause is overly simplistic in dealing with the increasingly common chronic multifactorial diseases that develop over long periods of time. Complex chronic diseases such as obesity, type II diabetes, and cardiovascular disease are but a few examples of many conditions which account for a vast proportion of our nation's health and medical expenses. As medical practice continues to be reactive to the patient's chief complaint rather than also being proactive, care is not designed to effectively adopt new technologies to improve health or predict and prevent disease. To do this, a new approach to care is needed; one that utilizes the best of what works in the current system but is based on what we know about the evolution of disease.

Contemporary Understanding of Disease Development

It is well recognized that health and disease evolve over time as a consequence of the interaction of genes and environmental exposures. Thus, genetic inheritance modified over time by what one does or is exposed to influences their level of health or the development of disease. Knowledge of one's disease risks and the ability to track disease progression can be synergized with strategies to prevent them. This concept is sometimes termed "systems medicine"[6,7]. The understanding of the dynamic interplay of heredity and environment gives rise to a strikingly different approach to care from how medicine is practiced today. Currently, clinicians are trained to start with a patient's chief complaint and, with differential diagnoses, identify the most likely cause of their established illness. This often leads to interventions at a late stage in disease development when symptoms become apparent (Figure 1). An example of the difference between current care and what is possible is illustrated by the approach to the treatment of coronary heart disease, the leading cause of death in the United States. While approximately 735,000 Americans have an acute myocardial infarction (AMI) each year[8], the mortality rate has been reduced significantly. As a consequence of dramatic new approaches to care including rapid administration of recombinant protein thrombolytics, coronary artery stenting and advanced supportive care, the in-house mortality rate for AMI has been reduced from 29% in the 1960s[9] to approximately 6% in 2006[10]. Despite this achievement, many survivors of AMI go on to develop congestive heart failure and while the reduction in AMI mortality is an example of the wonders of modern medicine, there is significant room for improvement. The development of coronary artery disease is strongly influenced by genetics and behavior. Risks can be quantified long before serious disease develops using current tools including family history, Framingham-type risk models, and clinical biomarkers. Genomic studies, while revealing the complexity of the disease, will continue to provide additional predictive insights. Therefore, a focus on care consisting of early risk assessment, appropriate behavior modification, and preventive therapies along with tracking disease progression could provide a powerful preventive approach that is synergistic with capabilities to treat disease if it occurs. Although health care today is becoming more effective and precise in reacting to established disease, it is not yet structured to address the complexity of the multitude of factors contributing to disease development and the need for a proactive, planned approach to assure the most favorable outcomes.

Personalized Health Care

We herein propose and describe Personalized Health Care (PHC) as a broad new clinical delivery model that not only enables a strategic and proactive approach to care[7], but also facilitates the adoption of emerging genomic and other precision medicine technologies and aligns them with the components needed for rational health care. PHC embraces personalization, prevention, prediction, precision, coordination of care, patient engagement, and enables the establishment of a rational reimbursement system. Some of these components have been initiated, but what has been lacking is a model that incorporates them all. This approach is vastly different from the current "find it and fix it" model yet it is readily adaptable to currently available capabilities and resources.

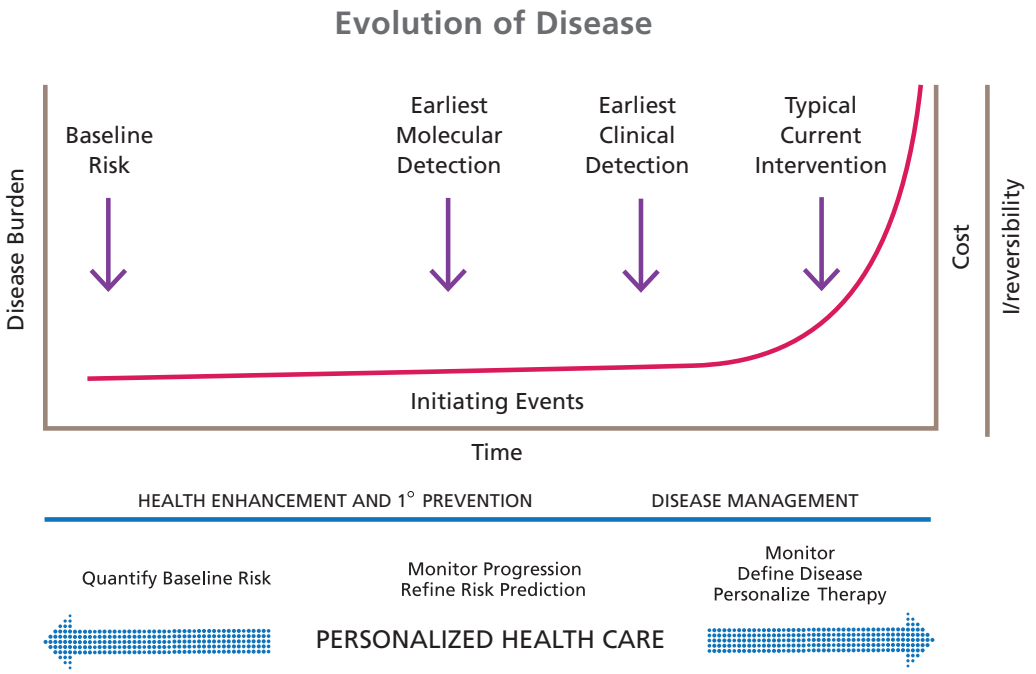

FIGURE 1: Inflection curve illustrating the development of disease over time. Depending on genetic and environmental factors, disease pathology may advance subclinically until a clinical event makes its presence apparent. Available and emerging technologies allow for earlier detection and quantification of risk, monitoring of progression of disease, and implementation of preventive interventions before a decrease in reversibility and an increase in adverse outcomes and costs occur.

PHC is founded on the understanding that the evolution of health or disease is dynamic and based on genetic inheritance and environmental exposure over one's lifetime[7]. As a result of recent medical advances, health status, disease susceptibilities, and disease progression can be quantified and tracked with increasing precision. PHC leverages these advancements through integration with a flexible clinical approach to care that helps prevent, mitigate, and treat disease as early and effectively as possible (Figure 1). Linking the clinical workflow to an electronic health record facilitates collection and analysis of data.

The components of PHC are:

- Evaluation of the patient's current health status.
- Assessment and quantification of their health risk(s).
- Enhancement of the patient's engagement.
- Development of a therapeutic plan with shared patient/clinician goals to meet plan objectives.
- Development of tracking metrics.
- Creation of a personalized health plan to implement the therapeutic plan, monitor goals, and coordinate care[3, 7].

Personalized Health Care in Practice

The PHC operating model is illustrated by its application to an initial primary care visit. Prior to seeing their clinician, the patient is given material to conduct a health self-assessment and to quantify their readiness for engagement in their care. If available, a health coach, nurse, or other member of the care team can assist the patient in creating goals for their health based on their values and priorities to guide the visit with their provider. The visit with the clinician begins with the evaluation of the patient's current health status and a health risk assessment through medical history, physical examination, family history, diagnostic tests, and health risk assessment tools including genomic evaluation where appropriate. As genomic predictive data become validated, they can provide insight into risks for a range of diseases and enhance mechanistic capabilities. Genomic and other precision diagnostics allow clinicians to sharpen the identification of the most important proximate and long-term health risks and develop plans to mitigate them. If a disease is identified, when possible, it is defined mechanistically and treated precisely using predictive diagnostics to anticipate its course and target therapies (Figure 2). The clinician's assessment is discussed with the patient and shared patient/clinician goals to meet therapeutic needs are created collaboratively.

A personalized health plan documents the goals to be achieved, their timing, and the metrics to track progress via biomarkers and clinically appropriate tracking tools. The personalized health plan includes an as needed formal follow-up in which the health care team can monitor the patient's progress through relevant clinical metrics via telephone, social media, instant messaging, wearable health technology, mobile applications, or additional visits if necessary.

PHC is a vast departure from the traditional reactive, disease-oriented, and generally uncoordinated chief-complaint-driven approach to care. In addition to PHC's strategic focus on proximate and long-term health risks and tracking the progression of disease, shared decision-making empowers the patient to be an engaged member of their care team. PHC enables patients to participate in their health care decision-making through the creation of a personalized health plan wherein care is coordinated to match their specific goals and needs. Patient activation, or the knowledge, skills, and confidence to manage one's own health care, has been shown to be a major predictor of good health outcomes including a lower probability of having an emergency department visit, being obese, and smoking. Developing approaches to care that activate or empower the patient is essential to

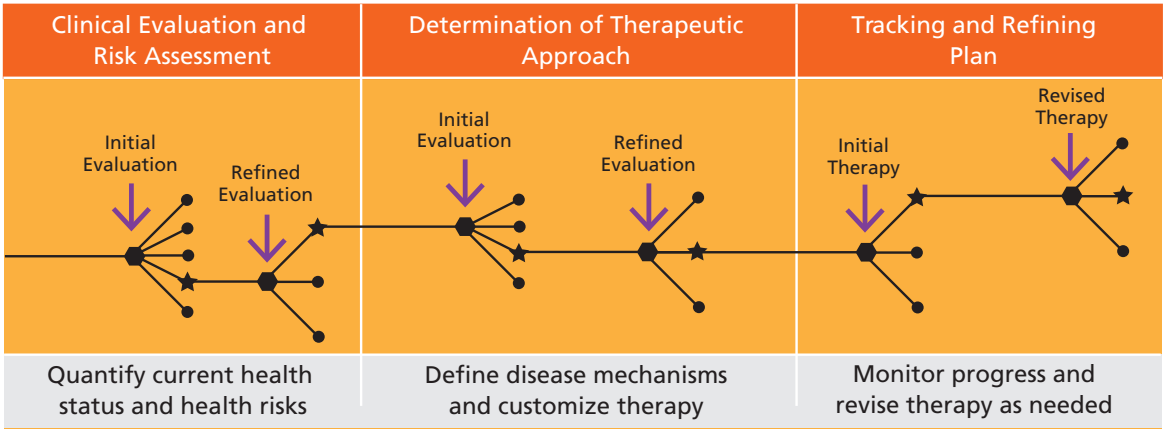

FIGURE 2: Decision tree simulating clinical evaluation and risk assessment leading to a therapeutic plan and follow-up. The clinician is faced with diagnostic and therapeutic decisions based on various data inputs. Predictive and diagnostic tools aid in the precision of diagnostic and therapeutic decisions including selection of targeted therapies.

Precision Tools

- Health risk assessments
- Clinical risk models
- Genomics and other predictors
- Patient activation measures

- Biomarkers
- Genomic analysis and gene expression
- Proteomic and metabolomic analyses
- Single cell network profiling
- Companion diagnostics
- Drug metabolism tests

- Biomarkers
- Disease activity tests
- Adverse event predictors

KEY

- Decision to be made
- Alternate choices
- Decision made

any strategy for health promotion and disease management[11]. To do so, creating a health care experience that is patient-centered by having patients more actively involved is a key first step. PHC fosters this type of engagement by recognizing that a patient's involvement in their care is an integral part of any plan to manage a complex chronic condition. The personalized health plan is not just personalized because it uses precision technologies, it is personalized because it incorporates the patient's perspective and facilitates their maximum engagement in their care.

One key advantage of PHC is that its clinical workflow facilitates the early adoption of precision technologies as they arise. For example, as the understanding of genomic and environmental information enhances risk prediction, it can be incorporated into the process. Similarly, when companion diagnostics and targeted therapies are relevant, they are incorporated into the therapeutic plan. The collection of data across clinical decision points in episodes of care is a key feature of this approach and facilitates the evaluation of process and outcomes. By using statistical modeling techniques, it also allows better predictive tools to be developed, improved, and validated[12]. Thus, PHC creates a continuous learning cycle with the added benefit of informing rational reimbursement by identifying processes, therapies, and specific interventions that are linked to favorable outcomes and worthy of incentivizing. PHC's concepts have been recognized in the Veterans Health Administration (VHA), the largest integrated health care system in the United States, who in 2013 chose personalized, proactive, patient-driven care as one of its major strategic goals[13]. It has conducted primary care pilots of personalized health planning in major VHA hospital systems. These pilots indicated that this approach can indeed be integrated within primary care clinics to provide health care tailored to the individual[14]. Additional pilots at Duke and at the Durham VA Hospital are underway. The rudiments of PHC, described herein, are adaptable to any integrated provider system, patient-centered medical home, or employer-sponsored wellness program.

Conclusion

In order to speed effective clinical use of the myriad of capabilities emerging from genomic and other research, new approaches to health care delivery are needed. We propose PHC as one such model. PHC is rooted in dynamic concepts of systems biology and creates a flexible clinical approach for health promotion, disease prevention, and precision therapy. It provides emerging predictive and precision technologies with a clinical workflow that embraces them. This approach recognizes the centrality of patients' engagement and their role in health care decision-making in order to facilitate the best outcomes. While this process embraces new science and technologies, it synergizes them with a more holistic approach that is patient-centered and collaborative. PHC thus unifies proactivity with a precise and personalized approach that engages the patient in a flexible, coordinated delivery process constructed to continually improve care. It provides transparency for best practices and outcomes thereby providing information for rational reimbursement. We suggest PHC as an important step toward unifying the forces needed for a rational health care delivery system by providing a clinical platform for the adoption of promising advances provided by the explosion of genomic information, the Precision Medicine Initiative, and other innovations in health care.

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