



A \$3 Trillion Challenge to Computational Scientists: Transforming Healthcare Delivery

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Healthcare spending in the US is nearing \$3 trillion per year, but in spite of this expenditure, the US is outpaced by most developed countries in terms of health and quality of life outcomes—for example, it ranks 36th internationally in life expectancy.¹ The share of health spending in its gross domestic product has increased sharply, from 5 percent of GDP in 1960 to more than 17 percent today,² a rate of increase that's widely believed to be unsustainable.³

Policy and regulatory reform have important roles to play in addressing these challenges. Yet one of the largest underexplored avenues is the better use of information derived from the vast amount of health data now being collected in digital format.⁴ I believe that one of the most significant open frontiers for computational scientists is the engineering of human health and healthcare delivery.

Through the National Institutes of Health's "Big Data to Knowledge" program, much recent discussion has focused on the changing nature of biological discovery in the era of Big Data. Other researchers and federal officials have recognized and described the need for an improved health infrastructure in several reports, with a view toward recommendations for federal involvement and support.^{5,6} Yet, others have described the broad role for computing research.⁷ Here, I emphasize the important role that computational scientists can play towards advancing the more translational goal of improving healthcare delivery.

Catalysts for Accelerating Change

Until recently, one of the key bottlenecks for research in care delivery was the lack of data to analyze the health system's workings. Much of the valuable data on symptoms, treatments, services, costs, and individuals' health states were stored as

paper records that weren't amenable to retrospective, automated analyses. The Health Information Technology for Economic and Clinical Health (HITECH) Act, a program that was part of the American Recovery and Reinvestment Act of 2009, incentivized the adoption of Electronic Health Records (EHRs) to encourage the shift from paper to digital records. That program has made more than \$15.5 billion available to hospitals and healthcare professionals conditioned on their meeting certain EHR benchmarks for so-called "meaningful use." It's one of the largest investments in healthcare infrastructure ever made by the federal government.

A survey by the American Hospital Association showed that adoption of EHRs has doubled from 2009 to 2011. Today, much of an individual's health data—demographics, personal and family medical history, current and past treatments, history of allergic reactions, vaccination records, laboratory test results, imaging results, and so on—is stored in an EHR. Various "omics" data, such as genomics and proteomics, will likely soon become part of routinely collected patient data as well.⁸ Administrative information, including billing information, insurance provider, dates and nature of previous visits to the healthcare provider, referrals received, and so on, are already stored electronically.

The proliferation of daily-use electronic devices such as smartphones and fitness monitors has led to an explosion of wellness and activity data, ready to be mined; simultaneously, storage and processing costs have declined dramatically. We've continued to make rapid advances in techniques for big data analysis. Within the next decade, I believe that we'll see an unprecedented innovation in the delivery of care using data. However, to achieve meaningful progress, we'll need to address important computational challenges

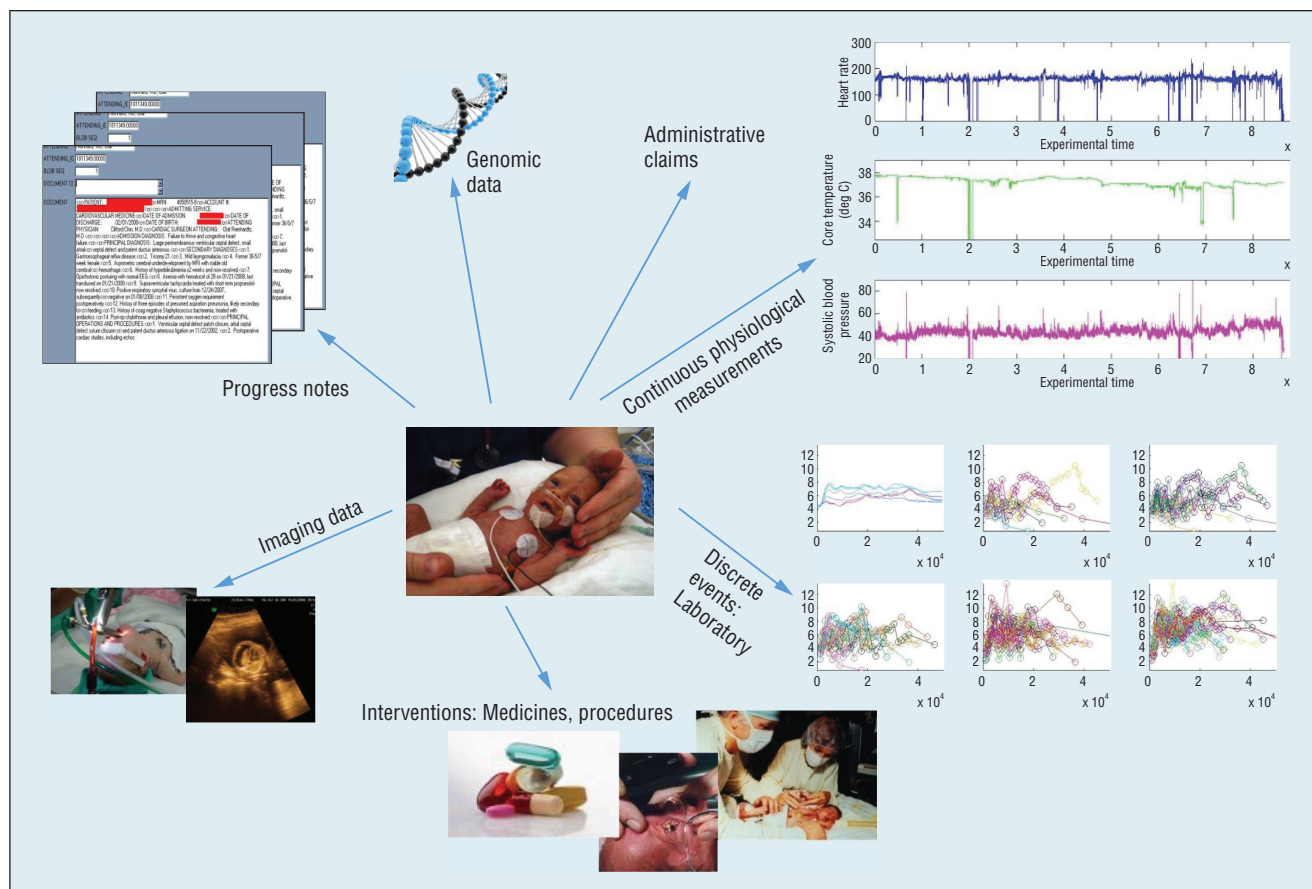


Figure 1. An illustration of the diverse electronic health data (EHD) that are routinely collected, including physiological measurements, laboratory test results, medications administered, imaging test results, progress and discharge reports, genomic profiles, and administrative claims.

for leveraging electronic health data (EHD) and to train “hybrid” scientists who deeply understand both computational sciences and the healthcare delivery ecosystem.

Opportunities for Computational Scientists

The literature on adoption of data-driven tools within the care-delivery loop is beginning to emerge.⁹ In the following, I discuss three example areas for potential impact from data-driven innovations in healthcare delivery; I also provide examples of the associated computational challenges.

Predictive Models for Targeting Care

Nearly a quarter of US healthcare spending is estimated to be unnecessary,

although defining precisely what is unnecessary can be controversial.¹ An avenue for reducing unnecessary spending is to reduce hospital readmissions, where in the Medicare programs almost 1 in 5 patients are readmitted within 30 days. As many as a third of these readmissions are estimated to be preventable,¹ along with almost 40 percent of Emergency Room visits and roughly 10 percent to 17 percent of all inpatient hospitalization costs.¹⁰ Patient outcomes can also be improved by early detection and intervention for acute adverse events such as sepsis and cardiac arrest in hospitalized patients; these conditions significantly worsen outcomes, increasing length of stay and unnecessary spending. For patients with chronic conditions, the observation has been made repeatedly

that only about 5 percent of patients account for about 50 percent of health-care costs.¹ Innovative ways to manage this population are likely to yield substantial savings.¹¹ In each of these areas, predictive models that can identify those individuals who would benefit from early, targeted interventions have the potential to improve outcomes, reduce unnecessary utilization, and drive down spending.

However, many practical considerations must be addressed in developing effective predictive models from EHD. First, data sources vastly differ with regard to their noise properties, quality, and measurement frequencies; we need approaches that can integrate such heterogeneous data. Second, much of the relevant health information is contained within unstructured data sources such

as continuous temporal measurements, images, or text (see Figure 1), and the choice of how to extract informative representations from such data is likely to be most critical in a predictive model's success. For example, by analyzing the patterns of patient movement between multiple hospital departments, Ben Reis and his colleagues showed that you can predict a patient's risk of a future diagnosis of domestic abuse.¹² In another example, using machine learning techniques, my colleagues and I discovered subtle signatures in physiological data, that were indicative of deterioration;¹³ we then showed that by integrating early physiological responses one can predict downstream morbidity in infant.¹⁴ Both of these examples exploited novel representations of routinely collected data.

Third, models that provide “actionable” information such as which factors impact an individual's risk, which measurements to consider next, or which treatments to apply are more amenable to adoption. Fourth, the extent of confounding and “missingness” in EHR data render existing approaches to missing data inapplicable. Right censoring due to drop outs is discussed extensively in the clinical literature; in EHR data, another significant source of biased missingness results from confounding due to medical interventions.¹⁵ Application of predictive models without accounting for this bias can lead to erroneous conclusions.¹⁵ Thus, we need principled ways of addressing such biases^{15,16} that are endemic to this data. Fifth, predictive models that can incorporate institutional and end-user preferences such as cost or pain of measurement can improve adoption. Finally, more than 40 percent of preventable deaths are related to lifestyle choices and other patient behaviors outside of their interactions with the healthcare system.¹⁷ Thus, approaches that can turn data captured “in the wild” by

personal devices (activity and heart rate monitors, cell phone sensors, and apps) into actionable measurements for informing care delivery hold tremendous promise. Methodology for addressing these challenges—and for developing effective predictive models from longitudinal EHD—is still in the early stages.

Individualizing Treatment Recommendations

The current evidence base for guiding an individual's treatment is insufficient in several ways. First, clinical practice guidelines (CPGs) overemphasize simplicity so that they can be easily implemented by healthcare providers without computerized decision support. Second, the majority of our practice guidelines are currently derived from randomized controlled trials (RCTs) for single disease treatments, which can exclude patients with other comorbidities. Consequently, the knowledge needed to provide appropriate therapy to multimorbid, high-risk patients, who also consume the lion's share of healthcare spending, are largely lacking.¹⁸

Third, our current evidence base provides information useful in diagnosing and treating the “average” patient. For many diseases, the extent of heterogeneity between patients can be substantial. As a concrete example, Figure 2 presents data from an ongoing study of patients with Scleroderma, a systemic autoimmune disorder that affects multiple major organ systems. The ways in which this disease presents itself vary greatly between patients: in any given individual, deterioration can take place in only a subset of their organs. Figure 2a shows clinical data from a large-scale Scleroderma database tracking patients over 15 years; predicted forced vital capacity (pFVC), total skin score (TSS), and right ventricular systolic pressure (RVSP) measure disease severity for three different organ systems—the

lung, skin, and vasculature, respectively. Using clustering, we can discover subgroups of patients with similar trajectories of progression for each of the organ severity measures. Figures 2b, 2c, and 2d show three subgroups for each of the three severity scores. Clearly, the disease course across patients varies dramatically; for example, in Figure 2a, subgroup 4 shows stable progression, while subgroup 16 shows active disease and very rapid decline. Conversely, in Figure 2c, subgroup 8 shows decline in the vasculature at a nonuniform rate.

Improving our ability to better identify and target interventions to subgroups that stand to gain the most will reduce waste and side effects from overtreatment. Existing clustering algorithms are not robust to the degree of measurement process variability and noise observed in EHD. The results shown in Figure 2 were obtained by using a novel algorithm that clusters patients into groups based on clinically relevant measures of “similarity.”

Many open challenges in subgroup discovery remain, including accounting for confounding due to treatment effects. Moreover, Scleroderma is only one example in a family of 80 different autoimmune disorders, many of which are similarly heterogeneous in their presentation; therefore, the challenge of individualizing treatments is enormous, as is its potential impact. An even more ambitious but desirable goal is to develop computational approaches that can learn and adapt treatment and preventative care recommendations to an individual's preferences.¹⁹

Reducing the Cost of Developing New Therapies and Practice Guidelines

The cost of developing and testing new drugs and treatment strategies is a significant barrier to rapid

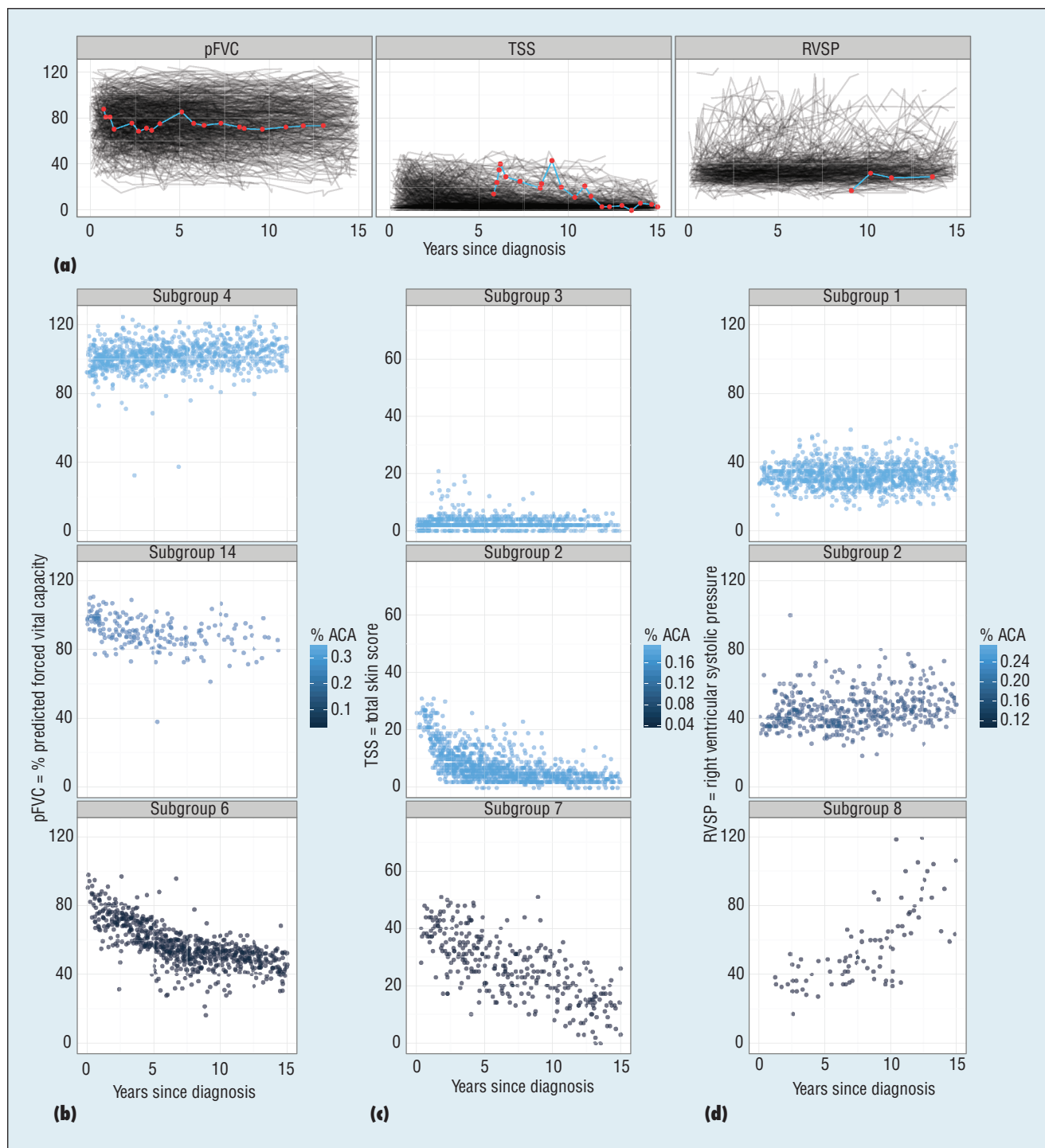


Figure 2. Clinical data from a large-scale Scleroderma database tracking patients over 15 years. (a) Tracking predicted forced vital capacity (pFVC), total skin score (TSS), and right ventricular systolic pressure (RVSP) to measure disease severity for the respective lung, skin, and vasculature organ systems. Three subgroups are shown for each of the three organ severity scores: (b) pFVC, (c) TSS, and (d) RVSP.

innovation in healthcare delivery: the typical approach of conducting RCTs is extremely resource intensive. Methodological approaches for augmenting

data generated from RCTs with (cheaply available) observational EHD are likely to provide impactful opportunities for accelerating the development

of new therapies and practice guidelines. However, the “messiness” of observational data presents many computational challenges; chief among these

is the lack of the ability to randomize individuals between interventions.²⁰ This leads to a concern that those who receive a particular intervention are likely different from those who don't in ways that could confound the effects. Although some approaches such as propensity score matching have been introduced to address this problem, adapting them to draw robust inferences from the massive, noisy EHD setting remains an open challenge.²⁰

Another computational strategy for reducing the cost of developing new therapies is via novel adaptive clinical trial designs. These experimental designs use principled statistical approaches to modify randomization patterns during the study in response to earlier results, thereby improving trial efficiency without compromising predictive power.²¹ Many important questions arise in the adaptive case, including how to estimate sample sizes, how to incorporate personalized characteristics (biomarkers, risk categories, prior condition), and how to design the adaptive procedure itself.

To address many of these computational challenges, a deep understanding of statistical and computational sciences is necessary, but alone, they might be insufficient to formulate relevant solutions for improving delivery. First and foremost, it will be valuable for computational scientists to develop deeper relationships and collaborations with healthcare delivery systems, such as hospitals and clinics, and health researchers. Second, tremendous progress has been made in the field of health informatics,²² also called biomedical informatics, in areas including standards for interoperable data exchange and tools for information extraction and data de-identification. It will be useful for computational scientists to become familiar with these

tools.²³ Finally, to become more effective as a “computational healthcare” scientist, it will be important to gain an appreciation of the science and practice of healthcare, as well as the culture and milieu of the environment in which healthcare is delivered.

In many industries over the last decade, a pattern has repeated itself: first, a new source of data becomes digital. Then standards begin to develop around data access, and researchers start to dive in. Then, if there's a problem that data can shed light on, an explosion of creativity occurs as new methods and tools are developed to understand and utilize the data. In many such cases, entirely new industries have formed (for example, instantaneous information access, online personalized retail, and most recently, autonomous driving). Healthcare is still in the early phase of this cycle, and there are endless opportunities for computational scientists to contribute. We can see what's coming, and we can hardly wait. ■

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