

The Disruptive Nature of Personalized Medicine Technologies: Implications for the Health Care System

R.J. Carlson

Resource Center for Health Policy, Department of Health Services, and Department of Pharmacy, School of Public Health, University of Washington, Seattle, Wash., USA

‘... [in the future] cancers will be classified by their mutations, rather than broad categories such as lung cancer or breast cancer’ [1].

Key Words

Disruptive technology • Genomics • Policy

Abstract

Genomics technologies, notwithstanding rising complexity and low productivity to date, once translated to clinical care, promise significantly improved outcomes through cost-effective interventions and prevention. But, along the way, every business model and every stakeholder group will be challenged to adapt to the disruptions that will arise as our health care system seeks to embrace those technologies. This paper identifies many of the key issues and stakeholders to be directly effected, including payers, providers, and suppliers. An even greater challenge faces public policy makers if these technologies are to be optimized. Many of these issues are raised as well. Finally, the point is made that the greatest barriers are not necessarily raised by stakeholders but rather arise from the deepening complexity of the science itself, requiring a long-term, large, and consistent research commitment from both the public and private sectors – a commitment made harder by the indisputable need to reform the current health care system.

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A Context for Disruption

In the 1950s, when the Salk vaccine displaced the crude technology of the Iron Lung, science writers and the popular press loudly proclaimed the arrival of a golden age of modern medicine, a medicine that would systematically eradicate the lengthy and gory list of human maladies. That age proved to be more tin than gold. Human disease and disability were not so easily malleable. This must necessarily chasten any prediction about the future of medicine.

Over the 53 years since Salk announced the discovery of the eponymous vaccine in 1955, the fundamental heuristic of medicine has not notably changed: it remains largely based on a mechanistic model analogized to fixing a car: figure out what part is busted and fix or replace it. My hypothesis for the balance of this discussion is that genomics returns us to the holistic and contextual rather than the mechanical and linear modes. There was some concern in the first few years that genomics, with its re-

This study is based on research led by David Sugerbaker at Brigham and Women’s Hospital in Boston about the unique genetic profile of each cancer in each patient.

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Fax +41 61 306 12 34
E-Mail karger@karger.ch
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1662–4246/09/0123–0180\$26.00/0
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Prof. Rick J. Carlson
Resource Center for Health Policy, Department of Health Services
School of Public Health, University of Washington
Seattle, WA (USA)
Tel. +1 206 545 7294, Fax +1 206 545 7293, E-Mail rickjcarl@aol.com

lentless focus on mechanism, would intensify the prevailing reductionist focus of modern medicine. With the emergence of epigenetics as a model for gene/environment/behavioral interactions, however, the science of genomics is far more consistent with the classical public health model that places the pursuit of human health within a social determinants framework, in which medical care is only one determinant and the lesser one at that. And this is why, in spite of modest achievements so far, eventually the impact of genomics will be truly disruptive to the health care system. Nevertheless, this transformation will be slow and gradual because the underlying scientific and business models will be resistant to change as all guarded paradigms are.

The balance of this paper will address a few of the specific and observable changes in the businesses and practices of medicine expected over roughly the next 10 to 15 years, and then, upon the stakeholders on the health care delivery system, including medical care practice, public health, the bio-pharmaceutical enterprise, and our private employer-based insurance model. I close with a discussion of some of the many slippery bioethical slopes that lie ahead for us to navigate.

Genomics, Pharmacogenomics (PGx), Medicine, and Health Care

In the last year or so, the potential and significance of genomics in medical and in health care has slowly become more apparent. Though the science continues to be challenging and complex, new research tools, especially genome-wide associations, are yielding a number of targets for potential therapies to address the common complex diseases, including cancer, heart disease, diabetes, obesity, and related metabolic conditions. Because, however, it is increasingly clear that the genetic component in these diseases is multigenetic, featuring a proliferating number of genes, it is equally clear that its impact will be measured in decades, not years.

Much of the early promise, some in oncology but primarily rooted in the translation of genomics research into pharmacogenomics (PGx), has focused on responses to medications as mediated by the genetic profile of the patient. The premise of this paper is that, overall, genomics will be profoundly disruptive, not just in medicine and health care, but more generally across society. Demonstrably then, genomics should be viewed through a wider lens than just PGx in order to better profile its disruptive character. That said, PGx, focused as it is on just

one dimension of clinical care, draws its power from the underlying heuristic of genomic medicine and hence can represent a full range of anticipated impacts on medical care and our health care system of the future. Further, addressing the disruptive character of genomics through the more focused lens of PGx is also justified because all genomic technologies share one characteristic that distinguishes a genomics inspired medicine from the mechanistic medical model that still largely prevails, that is the focus on our differences rather than our sameness, specifically those differences which can influence our health status through more empowered health care services. The astute clinician always looks for a differential response to interventions, but with genomics all of the actionable data are about differences, and the realization of these technologies in health care will eventually transform our medicine. When and if that occurs with any force, then it will take considerable political will to reform the health care delivery system to accommodate it.

Personalized Medicine: Why Difference Is More Expensive to Treat than 'Sameness'

Over the next 10 to 20 years genomics in health care practice should take 3 predominant forms:

(1) Personalization: earlier intervention with potent and effective drugs, devices, and treatments targeted by more actionable diagnostics;

(2) Prediction: disease and clinical risk management programs focused on lifestyle calibrations and based on increasingly granular and individualized risk data, and

(3) Prevention: Public Health and preventive clinical initiatives informed by probative epigenetic environment/behavior/gene interactions (for example, to address the causes rather than the symptoms of diabetes and obesity).

This personalized medicine construct – personalization, prediction, and prevention – is beguiling, even not yet tangible. But, if plausible and practical, and if we are successful in scaling back the sheer uncontrolled expansion of overall system costs, we might envision a more robust and cost-effective system of health care, one that could foster targeted, personalized risk-reduction programs and preventive practice by moving systems of care upstream closer to cause. Its gestation, like all disruptive technologies, however, will be long and fraught even under favorable conditions [2]. There are many uncertainties about genomics that arise at the threshold of integration into the delivery system which could limit, even de-

rail, its potential. The most daunting uncertainty is its affordability at a time when what we sell now – a far less targeted medicine – is rapidly becoming unaffordable by governments, employers here in the US, and families and consumers.

This point – the problematic nature of a personalized medicine in times of heightening financial stresses in health care – can be made, simplistically, this way: if all cars and trucks were made out of the same materials, had the exact same tires, and were all painted blue, then the truck supply warehouse would be much smaller, and the technical training and competencies needed by repairmen would be much less demanding. Similarly, if we were functionally standardized (except for obviously important differences such as gender), we would need a smaller medical warehouse, many fewer specialists, and a supply chain infinitesimally smaller even than the one we have now (the scale of our existing supply chain is a function of economics, not medicine). But this is not the complex medicine that would evolve if we are to achieve a system of personalized medicine. Personalized medicine drives differences arising in the complexity of diagnosis and in our variable response to interventions. If we were functionally largely the same, diagnostics would be relatively simple, almost declarative, and diagnostic algorithms very short. Instead, the emerging complexity that genomics is showing us means an ever expanding diagnostic toolkit and a proliferating supply of treatments tailored to match genetic risk profiles, each more granular than the profile preceding. There would be no need for generalists, only ever proliferating categories of specialists. Soon, the truism, ‘when you’ve seen one tumor, you’ve seen one tumor’, will be supplanted by, ‘when you’ve seen one patient, you’ve seen one patient’. Personalized medicine is a powerfully attractive notion, but a personalized medicine will necessarily be a very costly one, unless, as argued later, we can effectively harness its preventative capacities.

Why the Prevailing Model for Private Health Insurance Will Not Work

Our private health insurance model is a hybrid of economic ruthlessness and utilitarian social policy. On one hand, the insurance industry is supposed to perform the social policy role that the public sector can’t or won’t, and that is to ration (this is precisely though implicitly what the 1973 HMO Act intended). In doing so, however, insurance companies have to stay in business by denying and/or constraining access to care. This model distrib-

utes risk across a pooled population through the heavily regulated group insurance contract through which we are made to take care of each other though abstractly, because the benefits we don’t need go to meet the needs of others we don’t know.

There are at least 3 problems with this model as genomics further evolves. First, in this era of urgent transparency, as our steadily more detailed genetic profiles are more widely developed and disseminated, the social risk-spreading function of group insurance is very problematic because we will increasingly know who else needs what and why, and then question why we should pay for others who got a bad roll of the dice? The recently enacted Genetic Information Non Discrimination Act (GINA) offers protections to individuals from discrimination by employers and insurers, but doesn’t reach the perspectives and attitudes of individuals about their fellow citizens. Take this scenario: family A has 2 children with juvenile diabetes, who require a great deal of medical attention – and their diabetes is, in part, genetic in origin. Family B, next door, and let’s say enrolled in the same health plan, also has 2 juveniles at home, in apparent good health, except that they have both tested genetically for a substantially greater likelihood of suffering from adult-onset diabetes. So, in one case, family A uses far more medical care than the 2nd right now, but pays the same premium. Family B is subsidizing the 1st, but now also faces a downstream loss of insurance if the family has to move for a new job or for other reasons, or, at a minimum, substantially higher premium costs because of those pre-existing conditions, assuming that one of the children actually gets diabetes – GINA only protects against the use of genetic data in underwriting, not against the denial of coverage and/or steep premium increases as to the condition itself, once present. In other words, GINA only protects against putative genetic risk, not extant risks, genetic or otherwise, associated with health conditions already manifest. In the system we have today, when risk is only a financial metric, the most obvious ‘hot potato’ in our entire business system is holding onto risk for too long; so there is little incentive to collect and analyze risk data constructively because the business imperative is to shed risk, carefully and mindfully, but ‘shed’ it, nonetheless.

There is also the reality of behavior in response to moral hazard wherein those seeking insurance with known genetic risk are subsidized by those with demonstrably superior health status – raising the costs of insurance for everyone. As a result, those with little demonstrable risk are likely to prudently seek much lower cost

coverage with high deductibles to relieve them of the cost tides that raises everybody's costs, thereby exposing those remaining in the group coverage pool to even higher costs.

A 3rd problem is that current policy assumes that insurance companies actually insure, which of course they really don't, except when one of us is hit by a truck, an unexpected, conventionally 'insurable' risk. Insurers know what their aggregate risk is; if they didn't they'd fail as businesses, and they have profiled that risk by patient types and characteristics so they can manage their business risk exposure. To be sure, carriers 'pool' risks in the group insurance contract coverage – this doesn't mean that they don't know quite precisely what those risks are – and underwrite against in setting group rates (and occasionally disenrolling whole groups to better manage that aggregate risk).

In a genomics medicine instead, granular risk data could be used to design service packages tied to risk and risk-rated in cost. Naturally, the policy implications of a stratified premium structure are considerable, but the challenge in addressing such social policy implications is a political, not a scientific question. Put differently, genomics is very likely to create actionable data at both the individual and public health level. But our public policy makers fail us if we want to take advantage of the data if they proscribe its use, because insurers will have little, if any, incentive to either collect and/or use genetic data to tailor treatments to known risks. If we wished to leverage the expected actionability of genetic data, providers must learn how to use it constructively, and insurance companies could be freed to shape products to demonstrable need – you aren't insuring when you know more about risk than you don't! Genomics, over time, will throw off streams of risk-related data more precise and targeted as time passes, even as it will always continue to be nearly all probabilistic. Public policy could facilitate the constructive uses of these data by shaping financial and access reforms to the genomics medicine that is arriving, not the far less personalized medical model we are leaving.

Why Looking for Quality through Standardization Does Not Work if 'Differences' Are What Is Important

Over the last 50–60 years, a singular objective in health care services has been their standardization. Proponents of quality assurance, or more saliently, evidence-based medicine (EBM), have been painstakingly seeking to

standardize more and more of the inputs of modern medical practice, at the very time when genomics research offers the clinicians almost unimaginable variability in the patients they see. Standardization for quality assurance, however, must operate on both sides of the patient care equation. In outcomes measurement, standardizing only the input will be reliable only to the degree to which the output finds a patient population that is biologically sufficiently the same. There's the rub: to be effective, a personalized medicine must build on our ever more definitive differences, defying standardization for the very long haul, if ever. Measuring quality in health care under a genomics model is crudely analogous to measuring automobile fuel efficiency when every automobile is assembled from a wide array of materially different but functionally interchangeable parts, performs differently on every trip, and changes in performance with the moods and capacities of every driver.

Why It Is Important to Give Consumers the Information and Tools They Need to Navigate the New Genomics Medicine

The following quotes taken from 2 recently published commentaries illustrate the fundamental divide on clinical perceptions of genetic testing for consumers:

'Done well, examining one's genome can be an extra medical surveillance practice that has some preventive value and is complementary to traditional forms of health surveillance and patient care. As such, commercial genomic services can advance the aims of personalized medicine by providing a truly individualized approach to defining health-promoting behaviors. Rather than choose to ignore or over-regulate consumer genomics, we should work constructively with commercial providers to develop standards and practices suitable to their role as the front end of what could be a continuum of personalized health awareness and care' [3].

'... What's the right thing to do? With the exception of quitting smoking, the truth is: no one knows. Our ability to read the genome is well ahead of our ability to know whether medical intervention based on such a reading does more good than harm. But we can be sure that haphazard genetic testing will needlessly make well people worry about becoming sick. We need more research, not pricey genomic scans. Until then, save your money, and spare your health ...' [4].

Conceptually, there are 3 levels for all data, including genetic data: information, knowledge, and wisdom. Today, we are in the early stages of 'information'; we have lots of raw data, really an overload, but few discernable patterns and far more data than can be usefully under-

stood today as 'knowledge' translatable into medical care practice. In this sense, there are arguable risks in providing raw data to consumers, for legitimate fears of misunderstanding, misinterpretation, fatalism, and even over-reaction, such as '... well, I seem to be OK, let's keep burning candles at both ends.' The argument for largely unfettered access by consumers to their own genetic profiles, as unrefined as the technology to generate those profiles may be, moves at 3 levels itself: 1st, simple common sense data exist or can be generated by me paying for it, about me, and I have a 'right' to it, if I'm willing to pay for it. The 2nd argument is practical: such data may facilitate more precise targeting of interventions to mitigate, reduce, and/or eliminate risks by payers and providers alike, and then, arguably much more effectively motivate behavioral change. The 3rd argument is based on a simple but unappreciated truth – ignored out of reflexive paternalism – that consumers don't have useful and constructive perspectives and knowledge about their own health. This is why web sites such as 'patientslikeme', and personal genomics companies like deCODEme, 23andMe, and Navigenics, which create opportunities for lateral information sharing by patients with similar conditions, represent such powerful and challenging developments.

Finally, appropriate uses of genetic risk data should be consistent with the health care reform initiatives sure to arise over the next few years after the new Congress is installed in 2009. An essential plank in any particular reform initiative will necessarily be investing consumers with the means, incentives, tools, and most of all, the information upon which to navigate the health care system, actively participate in their care, and modify their behaviors for both health and financial reasons – what might be called 'flattening the hierarchy through the democratization of health information'. Genetic information

might eventually become the predominant means and content for the exchange of information between provider and provider, provider and consumer, and individual to individual through social networks. In short, tied to the larger goal of health care system reform, we must find ways to invest consumers and patients with the tools to far more actively participate in their own care. So we must democratize health care information as a means of shifting useful measures of self-responsibility to the consumer, as we exit the eras of medical paternalism.

Summary

There are 3 grand challenges to the 'constructive' disruptive nature of genomics: 1st, if there is a good reason to doubt the otherwise clear disruptive impacts of genomics, it does not lie in its presumed applicability to fuel the emergence of a leaner, more cost-effective system of care, but rather that the science will prove to be so complex that we will never master it because of the inexhaustible resources it would take to do so; in other words, the complexity of the science will outlast any measure of political will and the attendant economic resources necessary to bring it to fruition. The 2nd, related to the 1st, is that our inability or unwillingness to manage and control the soaring costs of medical care as it is, will strip us of the resources we would need in order to continue to invest in the science and innovation needed to produce a more mature science to personalize care. And the last, related to the 2nd, is that commercial interests and the ever powerful influence of those interests in the Congress will undermine the growth of a more predictive, preventive, and personalized medicine. After all, it is much harder to make money selling prevention than cure.

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