commentary

Health care in the age of genetic medicine

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Occasionally the emergence of new technology or knowledge propels medicine across a threshold that is so monumental it mandates changes in the structure of health care delivery. In the 20th century, a deep understanding of infectious diseases and cardiovascular risk factors triggered such changes, stimulating action at the governmental and population levels with the creation of organizations such as the Centers for Disease Control and Prevention and departments of public health.

Today, medical science is at another such threshold with the advent of individualized medicine. Driven by advances in genomics, emerging insight into each individual's unique susceptibility to disease promises to transform patient care. However, such advances will also compel a fundamental restructuring of the way medical care is delivered in the United States.

There are many reasons to pursue a rational, just, and workable system of health care for the millions of United States citizens who have no health insurance and for the insured for whom the cost of medical care is a constant threat to financial security.[1] The potential success of genomic medicine provides a series of additional compelling arguments to embrace a system of care that provides universal coverage and broadly pools risk. It is no small irony that the emergence of individualized medicine ultimately mandates a shared approach to health care delivery.

Modern health insurance is based on the tenet that it is possible to accurately predict aggregate risk but much more difficult to predict individual risk. For instance, insurance actuaries can reliably estimate the percentage of a population that will develop breast cancer, but because they are unable to predict precisely *which* individuals will develop it, resources are pooled, enrollees pay similar premiums, and all derive benefit. However, the emergence of individualized medicine, driven primarily by advances in the ability to dissect the individual's genome, undermines this traditional system. By learning to identify an individual's risk, that individual becomes less attractive to insure for the very maladies for which they require coverage. Pending legislation, such as the Genetic Information Non-Discrimination Act[2] will help limit genetic cherry-picking by insurers and is critically important. However, in a fragmented health care system, such potential remedies ultimately run the risk of simply shifting the inequity back to insurers by enabling individuals to select coverage based on their own specific risks. Either way, the foundation of the system is undermined; the solution is for all to pool their risks.

Individualized Medicine and Prevention

One of the promises of individualized medicine is the possibility of engaging in a level of preventive care that far exceeds current abilities. Screening programs are, by their very nature, inefficient because an entire population is subjected to screening while relatively few individuals benefit and some are actually harmed.[3] This inherent inefficiency is expensive for both the individual (in terms of morbidity) and for society (in terms of cost).

With increases in the ability to parse individual risk, screening programs for everything from heart disease to cancer can be more efficiently tailored, resulting in possible savings of time and money and reduced morbidity. However, genetic predispositions being discovered by such means as whole-genome association studies are often modest, typically demonstrating odds ratios of less than 2. Although the emerging ability to assess numerous risks may eventually provide clinically actionable information for the individual, even in the absence of such optimistic scenarios, it is important to remember that screening is essentially a public health endeavor. In this sense, individualized medicine offers the potential for better targeting of populations so screening efforts can be used more efficiently.

However, the current health care delivery system is poorly equipped to incentivize prevention. Most United States citizens who have medical insurance stay with a given carrier for an average of less than 6 years.[4,5] Thus, in the present system individual insurers are unlikely to be paying for an enrollee 10 or 20 years hence and therefore have little real motive to engage in long-term preventive care. A system of universal coverage with broadly shared risk could reap the benefits of individualized medicine at the population level and could provide potent incentives for the long task ahead of further defining genetic and environmental risks for common diseases.

Ubiquitous Mutations

Predictive genetic testing may lead to aggregate cost savings through more efficient targeting of those at risk for disease. But in the current system any such overall advantage comes at the individual's expense. The discovery of increased disease risk typically mandates more intensive surveillance of that individual (usually with high-cost modalities) and subsequent treatment. The emergence of individualized medicine will amplify

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inequities of birth so that those born with a disease-predisposing mutation will bear the brunt of increased costs, whereas those without such predispositions will seek less expensive care. One's attitude might be: "I'll take my savings and run" Setting aside the unsavory ethical implications of such an attitude, it is flawed by one of modern genetics' most piercing insights: every individual has mutations.

Each individual carries (eventually identifiable) genomic risks for something. With an ever growing ability to link genotype to risk, all individuals will likely discover that their risk for some future malady is increased; every person has preexisting conditions. This inevitable bad news for individuals is actually good news for the common lot and represents a compelling inducement to share risk: because all are flawed at the level of the genome, all people need each other.

The Emergence of Pharmacogenomics

The promise of pharmacogenomics is that specific subgroups of patients will be identified who are more or less likely to receive benefit from a given agent, improving on the current practice of broad, somewhat random prescribing of a medication to everyone with a given disorder. Thus, successful application of pharmacogenomics will inevitably fragment the markets for pharmaceuticals. Under the current balkanized system of health care financing, this situation will burden patients, insurers and the pharmaceutical industry with challenges that will increase in direct proportion to the field's success. Because each individual's insurance plan cannot be expected to have the broad formularies necessary to reap the practical benefits of pharmacogenomics, patients may be insured by plans that will not provide reimbursement for a drug that could result in significantly improved care. This situation is undesirable from the perspective of the patient and insurer alike and argues strongly for pooling both risk and resources so patients have access to an increasingly individualized formulary while insurers are spared endless petitions by patients for off-formulary drugs.

Harnessing the potential of pharmacogenomics offers the possibility of significant economic benefits. A recent estimate[6] suggests that formally integrating genetic testing into routine warfarin therapy in the United States could prevent 85,000 serious bleeding events and 17,000 strokes annually with a cost savings of more than $1 billion per year. Unless broad access to the right drug at the right dose for the right patient is ensured, insurers profits will suffer along with patients because of avoidable complications and sub-therapeutic treatment.

The emergence of pharmacogenomics is understandably not seen as an unalloyed good from the perspective of the pharmaceutical industry. Fragmentation of markets, wherein only an identifiable subset of patients will benefit from a given agent, necessarily decreases the market of potential consumers of that drug. However, by unifying the health care delivery system and expanding access to all individuals, the increased number of patients who will require and have access to even a "niche" drug may help offset the downsides of individualized medicine for this vital industry. Moreover, by eliminating fragmentation in the health care system and thereby enabling pharmacogenomics to reach its full potential, drugs that previously failed to come to market may well be found to be safe and effective for those individuals with the appropriate genetic makeup.

Irrational Rationing

Healthcare in the United States is currently "rationed" in an irrational and unjust manner based on circumstances of birth and income. The emergence of individualized medicine could make matters worse. Despite hopes to the contrary, genetically based medicine may actually increase health care costs, in part by finding previously unknown risks in large numbers of individuals who will require clinical intervention, usually in the form of high-technology surveillance. This situation will add to widespread demands for universal coverage as more individuals stand to benefit from genetically targeted care. On the other hand, individualized medicine has the potential to reduce the aggregate cost of health care by enabling better preventive strategies. If such cost savings materialize, they will be primarily population-based and thus most readily realized within a health care system that is not fragmented. Whether individualized medicine will result in cost-savings or not remains an open question; what can be predicted is that either outcome will provide potent stimuli for universal care and shared risk.

A Genetic Underclass

Embracing individualized medicine without a corresponding commitment to broadly shared risk runs the risk of creating a genetically defined underclass which, because of inheriting more than a fair share of disease-susceptibility genes, is unable to afford adequate care. This new genetically defined underclass could transcend all social strata and, except for a tiny number of individuals with truly exceptional resources, the cost of medical care will be beyond this group's reach. To prevent a blossoming of irrational rationing and the emergence of a biologically defined group precluded from obtaining proper care, it will be necessary to share risks and pool resources to ensure that, regardless of genetic makeup, a humane and basic level of medical care will be available to all.

The Philosophical and Moral Imperative

Although universal health care will hardly be a panacea for all the complex problems that affect health care delivery in the United States, there are compelling practical reasons to pursue it. The emergence of individualized medicine forcefully adds to this imperative. But this burgeoning genetic knowledge also has a profound moral dimension. The young science of medical genetics starkly illuminates the common lot, revealing in the most vivid way possible that all people are in the same boat. Every individual shares his/her genome with his or her fellow citizens and all are somehow genetically "flawed." As

professionals who will wield the potent new tool of genomic medicine, physicians must insist that the boat is shared by all and is just.

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