

HOW TO **Change Medicine**

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The practice of medicine today is obsolete, extremely wasteful, driven by patient crisis and perverse incentives.

New tools in medicine can reboot the future of health care, making it more precise, consumer-driven, and truly preventive. While not intended to be a comprehensive overhaul of all of the maladies of medicine, the 9 steps outlined here address exceptional opportunities for getting us on the right path for the future.

STEP 1. Change the Focus From the Population to the Individual

Today's practice of medicine relies on the wrong concept that the median of patients is the message. Virtually all patients with a given medical condition are prescribed the same drug, even though a significant proportion are not going to respond to it or may require markedly different dosing. Examples of commonly prescribed drugs that are mismatched to patients include clopidogrel (Plavix)—for patients who have a stent placed—and metformin, the first line drug for Type 2 (non-immune mediated) diabetes mellitus. At least 30% of patients do not have the normal genetic capability of metabolizing clopidogrel and will require either tripling of the normal dose or use of an alternative agent that bypasses the glitch in their metabolic pathway. Similarly, at least 20% of patients who receive metformin do not have any response to the drug, but this is typically not diagnosed and another anti-diabetic medication is simply added on to the regimen. With over 370 million diabetics on the planet, one can imagine how many individuals are taking metformin without any effect. While these 2 drugs are just cited as examples, they are fully representative of the more than \$300 billion of prescription drug expenditures for the United States each year.

But the mismatching of drugs is just one dimension of the problem of population-based medicine. Consider our use of mass screening tests. Mammography for all women every year after age 40, colonoscopy for all individuals every 5 years after age 50, and many other expensive mass testing irrespective of the specific characteristics of the individual. Not only are many women adversely affected by mammography because of initial false positive results that result in unnecessary biopsies and emotional hardship, but the majority of women do not have a significant risk of developing breast cancer throughout their lifespan. Yet all are included in the mandate and expense of annual testing at the costs of several billion dollars per year.

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Added to the mismatch of prescriptions and mass screening is the problem of “evidence-based medicine.” While we want definitive evidence for recommending a specific treatment, ideally derived from large scale, randomized, controlled clinical trials, most of what constitutes the daily practice of medicine has little hard evidence. There are often guidelines that have been drawn up from opinion leaders, which could be better known as “eminence based medicine.” When large clinical trials are performed, the actual benefit is typically quite small. Take for

example statins, which are widely prescribed to treat high cholesterol levels and prevent heart attack or stroke. The largest clinical trials of statins (e.g. Lipitor, Crestor) for primary prevention (treatment when there has been no prior arterial disease) have only demonstrated that 1 out of 100 people taking the drug would actually benefit with respect to preventing a heart attack. What about the 99% of people who take the drug for the duration of their lives without benefit except for the improvement of their blood cholesterol level?

Until now we have accepted this profound inefficiency and extraordinarily imprecise sense of who benefits from a treatment or a test, but that has to change. Fortunately, we are right at the cusp of having new tools to affect that change—the ability to define each individual in “high definition” at the biological, physiological and anatomical levels. While we have long appreciated that each human being is unique, it is only now that we can leverage this information to improve medicine.

STEP 2. Embrace Biologic Individuality

Our DNA sequence is the essence of our biological individuality, but the 6 billion bases that comprise our genome represents only one part of each person’s “omics.” Other omics include our full set of proteins (proteome), metabolites (metabolome), the “resident” bacterial flora in our gut, skin and other tissues (microbiome), and the packaging and side-chains of our DNA

(epigenome). Even identical twins do not have the same omic features, even though their DNA sequence is the same—their epigenome differs substantially, no less their microbiome. Now that we have a “bar code” for each individual, why not use this to make medicine more precise?

For example, let’s say there is a drug with a very serious side effect like carbamazepine (Tegretol), which can cause a fatal autoimmune skin reaction known as Stevens-Johnson syndrome. But only 1 in 1000 people who get this drug will get the life-threatening side effect. Now we have found the gene variant that can be tested before anyone receives this commonly prescribed drug that would pre-empt the chance of the side effect. Shouldn’t everyone getting a new prescription of Tegretol have the genetic test? In Taiwan, that is how this medication is managed today. But, unfortunately, this is not the case in the United States—no one is tested. Instead, we are tolerating a version of Russian roulette by not applying vital genomic data to prevent a rare but potentially fatal side effect.

With this example, shouldn’t we find out the genetic basis of all serious side effects of medications so that we can avoid them, especially knowing there are hundreds of thousands of individuals who are hospitalized each year with medication-induced illnesses? By the same token, shouldn’t we use genetics to identify which patients will benefit from a treatment, such as statins or clopidogrel or metformin, three of the most commonly used drugs today?

Moreover, if we knew what conditions people were susceptible to during their lifetime, wouldn't that be the path to tailored prevention? If we knew certain women have an exceptionally low risk of breast cancer, wouldn't we avoid screening them altogether or at least change the periodicity of screening to once a decade instead of once a year? Ditto for other forms of colon cancer and most late-onset diseases.

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While on the topic of cancer, how can we continue to prescribe toxic, often ineffective, and expensive biologic agents as a function of a particular diagnosis, such as colon cancer? When we sequence the tumor DNA and compare it with the native, germ-line DNA it is now eminently feasible to determine the so-called “driver” mutations. With this information, cancer therapy can be much more precisely guided to the individual's root cause of cancer, rather than by a general diagnosis. For instance, we already know that a mutation in a gene such as BRAF may be responsible for malignant melanoma in some patients, but also for developing thyroid cancer in other individuals. It's not the type of cancer that matters; it's the mutation!

STEP 3. Accelerate and Adopt Remote Physiologic Monitoring

Biosensors are rapidly being developed that can remotely, continuously, wirelessly monitor virtually any physiologic metric in real-time. Let's run through a few examples for sensors that are available today. Continuous glucose monitoring, with a blood glucose reading every 5 minutes, is available today but its use among insulin-dependent diabetics is far less than 10%. Use of the sensor helps individuals learn precisely what foods and what size portions lead to jumps in blood sugar, how exercise favorably affects their glucose level, and whether symptoms they experience during the night are correlated with very low or high blood sugars.

A band-aid sensor placed on the chest for a number of days can detect heart rhythm, and the data are archived and mailed in for analysis. A smart phone can be adapted with a case that has sensors for heart rhythm and used as an event recorder for individuals who develop episodic lightheadedness, dizziness, or palpitations. These devices will soon render the cumbersome Holter monitor, invented in 1946 and still widely used today, obsolete. In a short time ahead, all vital signs, including blood pressure, blood oxygen saturation, respiratory rate, body temperature, and heart rhythm will be captured via sensors. Other biosensors that are already in use include continuous eye pressure for prevention of glaucoma and the ability to measure brain waves.

So far these sensors, coupled with data processing systems to make them practical for medical applications, have had little incorporation in clinical practice. But the need to adapt simpler and less expensive solutions is abundantly clear. For example, why would we need a hospital sleep laboratory to diagnose a sleep disorder, which typically costs \$3000 per night, when we could get all the data in from the patient in his or her home at a markedly reduced cost? And how could anyone have a normal “physiological” sleep pattern in a hospital sleep laboratory anyway? Moreover, the ability to capture data that we previously could not access, such as blood pressures and glucose measurements in the middle of the night, or in the midst of an emotional upset, provides a new opportunity to understand an individual’s physiology.

But the far-reaching impact of having all these sensors available in our hyper-connected world is that we could perform remote monitoring and pre-empt the need for hospitalization for most patients except those requiring an intensive care unit. Sensors can be developed to pick up the earliest physiologic signs of an asthma attack or congestive heart failure, well before an individual has manifest any symptoms. There appears to be extraordinary potential with this technology, known as “mHealth” or “mobile” health, and accelerating the development and rigorous testing of the sensor systems vis-à-vis existent methods (e.g. hospital sleep lab data directly compared with home sensor data).

STEP 4. Using Medical Imaging Appropriately

Unlike little adoption of wireless sensors in medicine to date, we have just the opposite problem with the use of medical imaging. Nuclear scanning and CT scans are so promiscuously ordered in the United States that it is thought 2% of cancers may relate to the overuse of ionized radiation. In 2010, there were over 80 million CT scans in the U.S. and that number is still growing more than 10% per year. Over 20 million nuclear scanning procedures were done in the past year, and about half of them were for the heart that exposed each individual to about 40mSV, or the equivalent of 2000 chest X-rays. And many patients with heart disease have a nuclear scan as part of their annual follow-up. At a time when the public is concerned about backscatter X-ray imaging at airports, there are serious problems with overuse of ionizing radiation.

Even though ultrasound and magnetic resonance imaging (MRI) are free of the concerns of ionizing radiation, they too are grossly overused. There are over 20 million echocardiograms ordered each year, and probably at least half of them are unnecessary. The threshold for ordering an MRI has gotten down to the presence of back or joint pain. Not only do these advanced imaging tests pose an enormous financial burden, but there is also an increased likelihood of backing into to incidental findings, which then require additional evaluation, such as a “spot” in the lung that requires a biopsy.

There are new types of medical imaging that provide an excellent way to reduce costs and improve efficiency and convenience for patients. The prototype is the miniature, handheld, high-resolution ultrasound device that can be incorporated to the physical examination. As a cardiologist who has relied on listening to heart sounds for almost 3 decades, I have not had to use my stethoscope for 2 years to listen to heart sounds by virtue of now being able to see everything—each of the 4 chambers of the heart, their size, the heart muscle function, the status of the valves, the sac around the heart—all in just a minute or two. This is vastly more informative than listening to “lub-dub.” I can review the findings in real time with the patient, which typically does not occur when the patient is referred to an ultrasound laboratory. Moreover, I can pre-empt the need for the majority of ultrasound studies by this rapid screening integrated with the exam.

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Why is such a device potentially transformative? It can bring together experts in interpreting the video loops so long as someone can acquire the images. For example, an emergency room doctor can place the transducer on the patient, email the study to a cardiologist or radiologist and get

immediate interpretation. Similarly, a paramedic in the field evaluating a patient in an accident can send the images to a trauma team to determine whether an operating room should be readied. By avoiding X-rays, by wirelessly connecting health care professionals, and with rapid acquisition of high quality images, there is considerable potential to provide improved care. The only reason pocket ultrasound has not caught on yet in the United States is that there is not a reimbursement code for it; in other countries it has gained marked popularity.

STEP 5. Using Personal Electronic Health Records and Health Information Systems

While the uptake of electronic medical records has been painfully slow and ridiculously expensive, every person deserves the right to have all of their medical information, from birth to the present moment, readily accessible. It is striking that the paternalistic medical profession is still debating such questions as to whether patients should have access to their laboratory data or whether patients should have access to their office notes. Meanwhile, health systems like Kaiser Permanente and the Veterans Administration are pacesetters here, maintaining first-rate electronic health records for all their patients and sophisticated health information systems.

An investment of \$40 billion was made by the United States as part of the Affordable Care Act of 2010 (ACA) legislation for health care reform. But the way a large proportion of the funding is being doled out to the medical community is tagged to “meaningful use.” The threshold for achieving this is remarkably low, so this large investment is unlikely to have substantive impact for a number of years.

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A dominant obstacle for electronic records to move forward is the “tower of Babel” issue with so many different vendors and lack of any inter-operability. A way to circumvent this would be to mandate one universal form of personal electronic health record for all—which would be issued at birth or at the initiation of the program for each individual—and have every cumulative bit of medical data, imaging, radiation exposure from medical testing, genomics, and physiologic monitoring captured. Clearly such an ambitious program would need to be piloted, but we need a much more aggressive and rapid means forward. The solution is a patient-based electronic record, not one that is solely hospital or health system centric. Until now, most emphasis has been placed on the latter, which needs to change.

STEP 6. Educate Physicians on New Technologies

An interesting paradox that demonstrates the desperate need for physician education is that 90% of doctors surveyed do not feel comfortable using genetic data to guide their patient's prescriptions—whereas 90% of patients trust their physicians with their genetic information. There is hardly a curriculum in American medical schools that delves into the genomics of complex, polygenic diseases or the latest advances in pharmacogenomics. Wireless medicine barely shows up. Beyond that, in order to change a curriculum for a medical school it typically takes multiple years for approvals at many levels. Moreover, just targeting more up-to-date medical school education does not address the needs of the 700,000 physicians who are out in practice. How can we get this vital educational initiative jump-started?

The historical model for educating physicians in practice is through continuing medical education programs that predominantly occur at regional or national meetings or via the Internet. However, these programs are more utilitarian, and typically require travel and significant expense. Most of these are supported or sponsored by the life science industry. This traditional means of educating physicians would clearly not work for rebooting medicine.

Salman Khan has created the most attractive model for re-inventing education with the [Khan Academy](#), which presently attracts more than 4 million unique users per month for over 2600

informative videos. The subjects range from calculus, biology, banking, and art history—why not genomics, biosensors, imaging and all things medical? The videos are short, lucid, inexpensive to produce and immensely popular, capitalizing on a few outstanding educators. 90% of them are produced with just one-take, 99% with two-takes. This would likely be the most rapid and practical way to reach all physicians, and on-line credentialing process could be created to assure that the course materials were reviewed and key information gleaned. The trouble with this idea is that there is no interested party or sponsor to educate physicians. One would think that professional organizations like the American Medical Association would take the initiative, but there is no sign that this is occurring or likely to. Meanwhile, the field of digital medicine is moving ahead at warp speed and busy, practicing physicians are being left behind.

STEP 7. Incentivize Frugal Innovation

Throughout the history of medical technology and innovation, new devices, diagnostics and drugs have been associated with marked increases in cost. With health care expenditures in the United States at \$2.7 trillion and rapidly rising, this will no longer be tolerated. The future of medical innovation is tied to improving outcomes for patients at lower costs. This defies precedent that is usually set by what the market will bear. For example, when the highly innovative procedure of replacing the aortic valve of the heart through a catheter was introduced in 2011, instead of

requiring open-heart surgery, the cost for the valve was nearly \$40,000. Essentially, the price was derived from what surgery would cost rather than with the concept that patients would benefit in two ways—avoiding open-heart surgery with its attendant risks, and a much less expensive alternative.

We need a system that rewards all stakeholders for frugal innovation. That includes the inventors and innovators from the life science industry along with the government agencies of the Food and Drug Administration (FDA) and the Centers for Medicare and Medicaid Services.

Any diagnostic and treatment with a genuine potential of substantially improving patient outcomes and lowering costs should be given a fast track, streamlined review process and, if appropriate, the setting up of reimbursement schedules. Just as we prioritize orphan drug applications for rare diseases, a parallel process could be set up to incentivize frugal innovation. Of course, there would have to be follow through that the projected cost matches up with the actual cost. Furthermore, the traditional review process at the FDA, which ignores the cost-effectiveness side of the application, needs to be modernized like many other countries throughout the world. The FDA also needs to set up a conditional approval program that accelerates the commercialization of such innovations and closely monitors the test or intervention following general release. We can no longer tolerate the inordinate delays and overwhelming evidence of safety via prospective clinical trials before larger exposure to patients in the real world. The appropriate risk to

benefit tradeoffs can be established such that the real world data are systematically gathered and scrutinized, to gain a more realistic assessment of the innovation.

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There are already some prime examples of frugal innovation that help illustrate how the field can be transformed. As a cardiologist, my practice has been radically changed with the use of a smartphone sensor (a case that attaches to the phone) and app that captures the real-time electrocardiogram (ECG). This allows me to get the heart rhythm and core ECG components on my phone for free rather than having to order a formal ECG. Another device is a handheld genotyping chip, which gives the result back for a patient's gene-drug interaction in minutes at a cost of just a few dollars. Accordingly, we are starting to see new technologies that leverage the existing digital infrastructure that can actually gut costs out of healthcare. Next up would be to eradicate the need for hospital sleep laboratories, and many more to come. But they will come much faster if the system is set up to reward them.

STEP 8. End the Fee-for-Service Medical Care

The elephant in the room for health care costs is the “medicine by the yard” model of the more procedures, the more reimbursement. Obviously that model for the United States, ranked the 37th country in the world for relevant health care outcomes, is not working. Physicians are hard working, dedicated professionals who go through a considerable dwell time to get educated and fully trained—typically 7-10 years after graduating college. They need to be properly compensated for their expertise and efforts, but incentivizing doctors to do more tests, procedures and operations is not the right way forward. Establishing an appropriate salaried system for all physicians would be a game-changer in medicine, fully alleviating the motivation, even at the subconscious level, of doing unnecessary tests or interventions.

This proposal would not affect out-of-pocket health care, such as cosmetic surgery. One of the first responses to the idea would be how could this possibly be accomplished? I believe that a new system could indeed be created that would be acceptable for most physicians, and certainly by all patients, if there was an overwhelming commitment to do so. The current governmental strategy as part of the ACA bill is to nurture accountable care organizations, which render coordinated health care in a cost-effective manner. But like the ACA's electronic health record initiative, this will take many years and is unlikely to reduce the pervasiveness of the fee for service model in American medicine.

STEP 9. Let Consumers Drive the Health Care Revolution

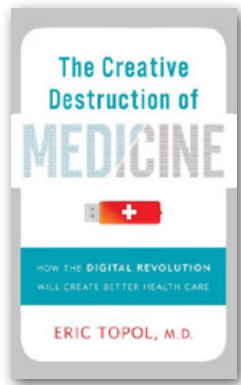
Here is the most important part of the rebooting of medicine. It is time for a jailbreak; it is time for the rise of the consumers to drive the future of medicine. It is their DNA, their medical data, their cell phones, and their own health at stake. We need to see the end of medical paternalism, the “doctor knows best” attitude that has long characterized the interactions between physicians and patients. Exemplifying the problem, the American Medical Association has been lobbying the FDA to prevent consumers from accessing their DNA data unless a physician mediates it. What could be further away from the democratization of medicine?

The era of social networking, one of the most impressive and unanticipated forces to arise from the digital infrastructure, has given rise to the Arab Spring and facilitated the Occupy Wall Street protests through the United States, the first such public demonstrations since the Vietnam era 30 years ago. With over 800 million registrants on Facebook alone, and over 250 million tweets per day, we are hyper-connected like never before. Online health communities like [PatientsLikeMe](#) are commanding more respect from patients for guidance than the traditional doctor-patient relationship.

For all the changes that are outlined here, it is quite unlikely they will be actualized without consumers as the driving force. The access to their own data and information—whether it be DNA sequence or biosensor remote monitoring—will soon be unprecedented and surely each individual has more at stake about his or her health than the busy physician who is looking after hundreds to thousands of patients. Not that the relationship with physicians should be undermined in any way; it should be upgraded and highly valued. But the change will come from the truly empowered, beyond informed, consumer who has access to all the relevant data and is now fully participatory. This transcends the era of internet access to health information that started in the late 1990's, since now each individual should be able to access all of their biologic, physiologic, and anatomical data that was largely unobtainable before. And the earlier in life the better, in order to foster the critically needed emphasis on prevention of diseases—which has been essentially ignored until now.

This is the most exciting time in the history of medicine. If we can make some radical changes to accommodate the enormous opportunities, there will be better health at lower costs for many generations to come. 📖

Info



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