Personalized medicine may do more to treat rather than prevent chronic diseases

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Personalized medicine, which involves tailoring health care to each person's unique genetic makeup, has the potential to transform how we diagnose, prevent and treat disease. After all, no two people are alike. Mapping a person's unique susceptibility to disease and targeting the right treatment has deservedly been welcomed as a new power to heal.

The human genome, a complete set of human DNA, was identified and mapped a decade ago. But genomic science remains in its infancy. According to Francis Collins, the director of the National Institutes of Health, "It is fair to say that the Human Genome Project has not yet directly affected the health care of most individuals."

It's not that there haven't been tremendous breakthroughs. It's just that the gap between science and its ability to benefit most patients remains wide. This is mainly because we don't yet fully understand the complex pathways involved in common chronic diseases.

I am part of a research team that has taken on the ambitious goal of narrowing this gap. New technologies are allowing us to probe DNA, RNA, proteins and gut bacteria in a way that will change our understanding of health and disease. Our hope is to discover novel biological markers that can be used to diagnose and treat common chronic conditions, including Alzheimer's disease, heart disease, diabetes and cancer.

But when it comes to preventing the leading causes of death which include chronic diseases, genomics and precision medicine may not do as much as we hope.

Many diseases aren't due only to genetics

Chronic diseases are only partially heritable. This means that the genes you inherit from your parents aren't entirely responsible for your risk of getting most chronic diseases.

The estimated heritability of heart disease is about 50 percent. It's 64 percent for Type 2 diabetes mellitus, and 58 percent for Alzheimer's disease. Our environment and lifestyle choice are also major factors; they can change or influence how the information coded in our genes is

translated.

Chronic diseases are also "complex." Rather than being controlled by a few genes that are easy to find, they are weakly influenced by hundreds if not thousands of genes, the majority of which still elude scientists. Unlocking the infinite combinations in which these genes interact with each other and with the environment is a daunting task that will take decades, if ever, to achieve.

While unraveling the genomic complexity of chronic disease is important, it shouldn't detract from existing simple solutions. Many of our deadliest chronic diseases are preventable. For instance, among U.S. adults, more than 90 percent of Type 2 diabetes, 80 percent of coronary arterial disease, 70 percent of stroke and 70 percent of colon cancer are potentially avoidable.

Smoking, weight gain, lack of exercise, poor diet and alcohol consumption are all risk factors for these conditions. Based on their profound impact on gene expression, or how instructions within a gene are manifested, addressing these factors will likely remain fundamental in preventing these illnesses.

Will more knowledge be more power?

A major premise behind personalized medicine is that empowering patients and doctors with more knowledge will lead to better decision-making. With some major advances, this has indeed been the case. For instance, variants in genes that control an enzyme that metabolizes drugs can identify individuals who metabolize some drugs too rapidly (not giving them a chance to work), or too slowly (leading to toxicity). This can lead to changes in medication dosing.

When applied to prevention, however, identifying our susceptibility at an

earlier stage has not aided in avoiding chronic diseases. Research challenges the assumption that we will use genetic markers to change our behavior. More knowledge may nudge intent, but that doesn't translate to motivating changes to our lifestyle.

A recent review found that even when people knew their personal genetic risk of disease, they were no more likely to quit smoking, change their diet or exercise. "Expectations that communicating DNA-based risk estimates changes behavior is not supported by existing evidence," the authors conclude.

Increased knowledge may even have the unintended consequence of shifting the focus to personal responsibility while detracting from our joint responsibility for improving public health. Reducing the prevalence of chronic diseases will require changing the political, social and economic environment within which we make choices as well as individual effort.

What about treating chronic diseases?

Perhaps the most awaited hope of the genomic era is that we will be able to develop targeted treatments based on detailed molecular profiling. The implication is that we will be able to subdivide disease into new classifications. Rather than viewing Type 2 diabetes as one disease, for example, we may discover many unique subtypes of diabetes.

This already is happening with some cancers. Patients with melanoma, leukemia or metastatic lung, breast or brain cancers can, in some cases, be offered a "molecular diagnosis" to tailor their treatment and improve their chance of survival.

We have been able to make progress in cancer therapy and drug safety and efficacy because specific gene mutations control a person's response

to these treatments. But for complex, chronic diseases, relatively few personalized targeted treatments exist.

Customizing treatments based on our uniqueness will be a breakthrough, but it also poses a challenge: Without the ability to test targeted treatments on large populations, it will make it infinitely harder to discover and predict their response.

The very reason we group people with the same signs and symptoms into diagnoses is to help predict the average response to treatment. There may be a time when we have one-person trials that custom tailor treatment. However, the anticipation is that the timeline to getting to such trials will be long, the failure rate high and the cost exorbitant.

Research that takes genetic risk of diabetes into account has found greater benefit in targeting prevention efforts to all people with obesity rather than targeting efforts based on genetic risk.

We also have to consider decades of research on chronic diseases that suggest there are inherent limitations to preventing the global prevalence of these diseases with genomic solutions. For most of us, personalized medicine will likely complement rather than replace "one-size-fits-all" medicine.

Where does that leave us? Despite the inherent limitations to the ability of genomic medicine to transform health care, medicine in the future should unquestionably aspire to be "personal." Genomics and molecular biosciences will need to be used holistically – in the context of a person's health, beliefs and attitudes – to fulfill their power to greatly enhance medicine.

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