Precision Health Data May Help Curb Declining US Health Outcomes

By Brian Gonzalez

In the "new future" of medicine, data from patients, such as genetics, integrative physiology, digital phenotyping, and the environment, will be collected and tracked, then made readily available to clinicians, according to Robert M. Califf, professor of cardiology at Duke University School of Medicine and founding director of the Duke Clinical Research Institute. By the time a patient enters an exam room, the clinician will already have a "total background" on the patient that can inform treatment with a data trove that goes beyond the patient's self-description.

Dr. Califf, who describes himself as a data science politician, gave a state-of-the-art lecture on "Improving Health Outcomes in the Era of Data Ubiquity" at Kidney Week 2018. Dr. Califf was the Commissioner of Food and Drugs (FDA) in 2016–2017 and Deputy Commissioner for Medical Products and Tobacco from February 2015 until his appointment as Commissioner in February 2016. Dr. Califf is also employed by Verily Life Sciences, a division of Alphabet (the parent company of Google).

Dr. Califf laid out the current tailspin in US health outcomes:

- Life expectancy has declined for the third straight year.
- Geography and income continue to determine health outcomes and life expectancy.
- Premature deaths have increased 3% since 2015.
- Drug deaths have increased 7% in the past year.
- Cardiovascular deaths have increased 2% since 2015.

Additionally, midlife mortality from "deaths of despair," including drugs, alcohol, and suicide decreased or increased only slightly from 1989 to 2014 for white non-Hispanics across several developed countries including Germany, France, Sweden, Canada, the United Kingdom, and Australia. In contrast, midlife mortality from these causes for white non-Hispanics in the United States increased from approximately 35 to 80 per 100,000 deaths during this time period.

As life expectancy continues to decline in the United States, healthcare expenditures are near double those of similar high-income nations. Dr. Califf noted that these developed countries differ from the US in that most consider healthcare an actual right, a topic of debate in the US, and that most have a primary care system that functions well.

Tackling declining health outcomes and high expenditures

These declining health outcomes with high expenditures can be turned around in the US, Dr. Califf said, through what he calls "the fourth industrial revolution of the digital revolution": the fusion of technologies and a blurring of the lines of the physical, digital, and biological spheres.

With the combination of the human touch, clinical care, and quantitative capability built into our system, we will be in a much better place, he said.

"[T]his could be really, really good or really, really bad depending on how we adapt our human systems to deal with this technological revolution," he said, noting that "it will take a lot of human effort and culturally using the information to change what we do and measure the effect of that change."

Dr Califf advocated the need to integrate prediction science, social policies, incorporation of knowledge centrally, and economic considerations in order to find out how best to apply new therapies.

One way to do this would be to integrate all slices of the problem within a new system, such as Project Baseline, a partnership between Verily Life Systems, Duke University, Stanford University, and Google. Its ambitious aim is to measure the human condition and health outcomes and provide real-time information to data scientists, clinicians, policymakers, economists, students, and others.

The project consists of two phases for participants:
- An initial 2-day period of biometric testing to measure clinical labs, genomics, epigenomics, transcriptomics, immunophenotyping, microbiome, proteomics, metabolomics.
- Continuous measurement over time with gadgets like sleep sensors, wearables like smartwatches, and interactive cell phone technology that allows testers to ask participants about their health immediately instead of having them come to a clinic and recall how they felt in the past.

In addition to this fabric of constant observation that will measure the human condition, we are moving into an era where randomization will become the "routine business of understanding how treatments should work," Dr. Califf said. An example is PCORnet, which brings together patients, health systems, and payers to answer pragmatic questions. With this coordinated effort, patient groups could use data curated by health systems to answer their health questions and to further clinical trials. Currently, 25 large health systems in the US are part of this group, as well as HealthCore and Humana payers. Another example is the NIH Health Care Systems Research Collaboratory, which started in 2012 with the goal of developing methods and capacity for pragmatic or "real-world" clinical trials in the sense of generalizable findings, sustainable intervention, and efficient-cost trial conduct.

The hope is that a single individual's precision health data, when combined with data from households, neighborhoods, precincts, and states will then be used for analysis of actionable public health reforms to better address the tailspin of negative health outcomes in the US. ◾

Studies Provide Comparative Data on Antidepressant Safety and Efficacy

By Bridget M. Kuehn

Sertraline may be more effective than cognitive behavioral therapy (CBT) for treating depression in patients on dialysis, according to a study at Kidney Week 2018. Another study found elevated heart risks with selective serotonin reuptake inhibitors (SSRIs) with greater QT-prolonging effects.

Almost one-quarter of patients on dialysis have depression, but many don't receive treatment, said Rajnish Mehrotra, MD, professor of medicine at the University of Washington in Seattle. One obstacle has been the dearth of data on depression treatment in patients on dialysis, who are typically excluded from clinical trials of antidepressants in the general population, noted Magdalene Assimon, PharmD, PhD, a postdoctoral fellow at the University of North Carolina Kidney Center in Chapel Hill. There have been few studies specifically exploring the comparative efficacy or safety of antidepressant therapies in patients on dialysis.

"We extrapolate both efficacy and safety evidence [from trials in other populations], which may or may not apply to patients on dialysis because of their unique situation with drug pharmacokinetics and their cardiovascular burden," Assimon said.

But the two studies presented at Kidney Week 2018 may help begin to close the knowledge gap.

CBT versus sertraline

During the High Impact Trials session, Mehrotra presented results of a multicenter randomized trial that began with depression screening for 2569 patients in 41 dialysis facilities across 3 metropolitan areas. The 636 patients with Beck Depression Inventory (BDI) scores greater than or equal to 15 were randomized to receive either a motivational interview about depression treatment or a brief encounter with a research staff member who alerted patients to their depression and asked if they would like to participate in a treatment study. The study found no significant difference in treatment initiation between those two groups (66% vs. 64%, respectively).

"It is possible that we pre-selected individuals [who] were interested in getting treatment anyway, and that is why we were not able to show a difference between people randomized to engagement versus control," Mehrotra said.

The 120 patients who decided to initiate therapy were then randomized to CBT or the SSRI sertraline. Patients receiving CBT were given the option of having a therapy session during dialysis or a separate private session. Both groups saw a decline in depression symptoms, but sertraline resulted in a greater decrease in depression symptoms as measured by the Quick Inventory of Depressive Symptoms (QIDS-C)—1.84 compared with CBT. Patients on sertraline also had more improvement on measures of disability, energy/vitality, life satisfaction, and sleep.

"In patients undergoing hemodialysis with major depressive disorder, depressive symptoms improved both with individual CBT and sertraline, but improvement was greater with sertraline," Mehrotra said.

However, sertraline was associated with a higher frequency of adverse events, he noted. Patients who received sertraline were more likely to be hospitalized and had threefold more mild and moderate adverse events than those receiving CBT. Mehrotra said he hopes the results help guide clini-