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 is 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.

“This 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, and a blurring of the lines of the physical, digital, and biological spheres.

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, precints, 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.
AKI Increases Long-Term Dementia Risk

By Bridget M. Kuehn

Patients who’ve recovered from acute kidney injury (AKI) have a 3-fold higher risk of developing dementia than hospitalized patients who avoid AKI, according to a study presented at Kidney Week 2018.

Patients who experience AKI may face long-term health complications even if they completely recover. Previous studies have shown that experiencing AKI increases the risk of developing chronic kidney disease (CKD) and cardiovascular disease. But the long-term consequences of AKI for brain health weren’t clear.

“We used to think that almost all cases of AKI would have complete recovery, but now realize that many people have later development of CKD,” said Hamid Rabb, MD, medical director of the Johns Hopkins Kidney Transplant Program in Baltimore. “Clinicians should be aware that AKI could have important kidney as well as non-kidney distant organ long-term effects, and therefore follow patients closely even after seeming resolution of AKI.”

To assess the potential long-term effects on the brain, Jessica Kendrick, MD, associate professor at the University of Colorado School of Medicine, and her colleagues looked at 2082 patients without a history of dementia treated in an integrated health system in Utah between 1999 and 2009. During the study, which followed patients for a median of 5.8 years, 97 patients developed dementia. Those who had AKI were more likely to develop dementia than those who didn’t (7.0% vs 2.3%). The hazard ratio was 3.4 (95% CI 2.14–5.40). The magnitude of the dementia risk was comparable to the risks of other long-term complications, noted Kendrick.

The study was “provocative” and needs to be confirmed by others, Rabb said. He noted it is not surprising that AKI might lead to an increased risk of dementia.

“AKI is well known to cause clinical changes in brain acutely, and some of these could lead to chronic changes,” Rabb said.

Exactly how AKI might contribute to an increased risk of dementia is not clear. Kendrick noted it may be related to endothelial dysfunction after AKI. Now, she and her colleagues are looking at whether AKI may change cerebrovascular dynamics.

Rabb noted that patients with AKI may have other risk factors for dementia, such as diabetes, vascular disease, older age, or hypertension. Additionally, AKI is known to cause dysfunction in distant organs. Rabb suggested it might affect the blood-brain barrier, microglial activation, or protein leakage in the brain, which might contribute to dementia as well. He said it would be interesting to look at the renal function in patients who developed dementia compared with those who didn't, because it is possible they did not completely recover kidney function after AKI.

Kendrick noted it is also not clear how AKI contributes to other long-term complications like CKD or cardiovascular disease.

“It’s an area that really needs to be investigated,” she said.

Kendrick said it is important to research whether changes in the way hospitals care for patients with AKI could help prevent long-term complications, for example, whether more monitoring of kidney function after AKI would help identify patients’ persistently elevated proteinuria.

“Even when people do well and recover, it’s still associated with significant adverse outcomes,” she said. “It would be nice to have something to offer them to hopefully prevent these complications from developing.”

“Acute Kidney Injury is Associated with an Increased Risk of Dementia” (Abstract 3024328).

The general consensus is that end stage renal disease creates a proarrhythmic environment,” Assimon said. To assess the heart risks of SSRIs, Assimon and her colleagues looked at data from the United States Renal Data System on patients on dialysis enrolled in Medicare. They compared the risk of sudden cardiac arrest in the first year of taking citalopram and escitalopram, which have greater QT-prolonging effects, with the risk while taking fluoxetine, fluvoxamine, paroxetine, and sertraline, which have more modest effects on QT intervals. The study included 65,654 patients. Taking citalopram or escitalopram was associated with an increased 1-year risk of sudden cardiac death (adjusted hazard ratio 1.14; 95% CI: 1.05–1.25) compared to the SSRIs with lower QT-prolonging potential. Women, patients age 75 or older, and those with structural heart disease or taking additional QT-prolonging medications were particularly at risk.

“Our results suggest that SSRI therapy selection should be individualized, and clinicians should consider the differential QT-prolonging properties,” Assimon said. For example, they should consider factors like age, gender, existing heart conditions, and concurrent medications when prescribing SSRIs. They may want to consider monitoring patients with ECGs.

Mehrotra also urged caution about potential QT-prolonging drugs, including SSRIs.

“It is important to be careful when using drugs that prolong QTc (whether SSRIs or others) in patients with end-stage renal disease,” he said. “A significant proportion of patients undergoing dialysis have baseline QTc, and a longer QTc does increase risk for sudden cardiac death, the most common cause of death in patients undergoing dialysis.”

He noted that he and his colleagues considered cardiac risk during the design phase of the trial. They chose sertraline because it has been used in large clinical trials of patients with congestive heart failure and coronary artery disease and was not associated with a higher risk of cardiac events.

“This reassured us when selecting the drug,” he said.

“Comparative Efficacy of Therapies for Depression for Patients Undergoing Hemodialysis” Oral abstract 148

“The Comparative Cardiac Safety of Selective Serotonin Reuptake Inhibitors (SSRIs) in the Hemodialysis (HD) Population” Oral abstract 093