**NIH plots million-person megastudy**

Questions abound as researchers discuss personalized medicine project

By Jocelyn Kaiser

Could convince 1 million Americans to wear smart watches that beam their blood pressure, steps walked, and other health information to a central database every hour of every day? Ask them to weigh in on how their genetic data are used by researchers? Those were some of the ideas floated last week at a workshop to flesh out the precision medicine initiative that President Barack Obama proposed last month. To accelerate the development of treatments tailored to individual patients, Obama called for enlisting at least 1 million American volunteers in a long-term study of genes, environment, and health (Science, 6 February p. 601).

It may sound straightforward, but not so, concluded the nearly 90 scientists and industry and patient representatives who met at the National Institutes of Health (NIH). Still, by the end of the 2-day meeting, most of the participants seemed enthusiastically on board, if somewhat daunted by the challenges of designing what could be a project costing a billion dollars or more and lasting a decade or longer.

“This absolutely needs to be done. But we need to crisply articulate the goals and design it to optimize success,” says cardiologist and human geneticist Sekar Kathiresan of Massachusetts General Hospital in Boston. “Otherwise, we are headed down a rabbit hole of spending lots of money, people questioning it left and right, and it being really wasteful.”

The U.S. cohort study, the centerpiece of the precision medicine initiative included in Obama’s 2016 budget proposal, is the brainchild of NIH Director Francis Collins. He first broached the idea in 2004, when he was director of NIH’s genome institute. At the time, other countries, including the United Kingdom and Estonia, were already moving forward with large population studies. But Collins’s plan, deemed impractical and prohibitively expensive, went nowhere.

Now, the situation is different, Collins says, thanks to new technologies that should lower costs. The money-savers include electronic health records, cheaper genome sequencing, and ubiquitous devices such as smartphones and Fitbits that can monitor health.

Still, huge questions loom: Who should be recruited? How can researchers knit together their health data? What should be the study’s overall objectives—to find rare disease genes or to test new treatments and devices?

To save money, as an initial step NIH proposes to recruit participants who are already enrolled in ongoing cohort studies, instead of starting from scratch. For example, the precision medicine initiative could piggyback on the Department of Veterans Affairs’ Million Veteran Program, which is linking veterans’ DNA samples to its 20-year database of health records. Some participants, however, wondered whether this approach really will be cost-effective. Researchers would have to re-contact the participants to ask if they’re willing to participate, and many may decline. Others warned that existing cohort studies may not adequately represent the country’s geographic, ethnic, and socioeconomic diversity.

Participants must be involved in the study’s design and decisions about how individual data will be used, Collins says. But such inclusion will be a challenge, he concedes. Some ideas could come from existing programs, such as PatientsLikeMe, a commercial Web portal that allows patients to share their health data for disease studies.

Another company, 23andMe, has built a genetics research database using information from consenting customers. If older cohort studies had let patients “own” their data, “we could recruit this million person cohort almost instantaneously,” said 23andMe CEO Anne Wojcicki.

Others raised additional questions. For example: Should the study enroll children? Including families would strengthen the study’s power to find genetic links with disease, some noted. But Rory Collins, a leader of UK Biobank, a cohort study of 500,000 adults, recommended a separate pediatric cohort because recruiting children and studying their diseases is a very different enterprise than dealing with adults. “If you try to do everything, you’re likely to fail,” he predicted—a problem that contributed to the recent demise of NIH’s National Children’s Study (Science, 19 December 2014, p. 1441).

There was greater agreement that mobile, “mHealth” technologies that can monitor a person’s health hold promise, for tracking not just physical activity and heart rate, but also measures such as social interactions and toxic exposures—factors that electronic health records have trouble capturing. Some participants were eager to outfit all 1 million participants with a smartphone and smart watch. But others urged caution, noting it’s still not clear how useful such mobile data will be to researchers.

Once it was over, Collins called the workshop “historic”—and concluded that despite the unsettled issues, there are no “big showstoppers.” But NIH has a tight deadline to work out the details. The 2016 fiscal year begins in October, and assuming Congress approves a “down payment” of $130 million (which appears likely), NIH will have just 12 months to issue requests for proposals and spend the money. A working group, led by Yale University human geneticist Richard Lifton and NIH policy chief Kathy Hudson, is charged with coming up with an interim plan by September. Before then, Lifton said, “there is an enormous amount of work that remains to be done.”