Clinical Trials, Genetic Testing, and Personalized Medicine

By Barry P. Chaiken, MD, MBA

As medicine marches toward its embrace of personalized medicine and immunotherapy, researchers struggle to obtain meaningful discoveries that can be applied to the ever-expanding number of patient cohorts. The growth in the understanding and use of genetic testing results creates slices of patients that shrink as rapidly as the number of these cohorts grows. Pharmaceutical companies see these subcategories of patients as potentially large sources of revenue, recognizing that effective treatments for cancer and other life-threatening diseases bring little resistance to very profitable pricing models.

As noted in a recent *New York Times* article (Kolata, 2017), immunotherapy drugs that attack a protein known as PD-1 are approved for a variety of cancers, including kidney, bladder, and lung cancer. The article goes on to say,

> "Yet many pharmaceutical companies want their own anti-PD-1. Companies are hoping to combine immunotherapy drugs with other cancer drugs for added effect, and many do not want to have to rely on a competitor's anti-PD-1 drug along with their own secondary drugs.
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> "So in new trials, additional anti-PD-1 drugs are being tested all over again against the same cancers—a me-too business strategy taken to multibillion-dollar extremes."

Currently, pharmaceutical companies are conducting more than 1,000 immunotherapy trials. When adding the number of cancer clinical trials, the total number is many times higher. Identifying patients for these trials often takes longer than conducting the trials themselves. For example, one company took 13 months to identify just 59 cancer patients with tumors that shared a rare genetic mutation.

For patients to be eligible for a clinical trial, they not only must possess the genetic mutation linked to a particular disease, but also must not have been disqualified from participation due to previous confounding treatments. As most patients are treated for their disease in the community rather than at an academic medical center, most would-be candidates never get considered for enrollment in a trial. In addition, without the results from a genetic test identifying the genetic mutation under study, these patients are never brought to the attention of investigators. Due to the $5,000 cost of the genetic test, most patients fail to be tested unless that cost is paid by a pharmaceutical company (or, less likely, by the patient's insurance).

Use EMRs to identify patients

The stratification of patient populations required to conduct meaningful personalized medicine research requires effective definition of a patient cohort and efficient identification of patients that belong to that cohort. While paper medical records proved unwieldy when conducting narrowly focused cohort studies, we largely left the world of paper records behind through our recent embrace of electronic medical records (EMR). The digitization of patient records suggests a wealth of patient information easily accessed through clinical data repositories built from the data collected through EMRs.

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While this might be true within an institution or integrated delivery network using a single EMR running the same software release, aggregation of patient records across different EMRs—or multiple software versions of the same EMR—presents very difficult challenges.

Vendors in the EMR industry possess a rather poor record of effective collaboration. Interoperability continues as the primary challenge organizations face in sharing patient records, both internally and across institutions.

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would benefit from the use of cutting-edge modalities, and researchers would more quickly learn what interventions are most effective.

Test more Americans

Iceland, home of deCODE genetics, Inc., leads the world in genetic testing ("deCODE genetics," n.d.). With over 2,300 of its 330,000+ citizens already fully genetically sequenced and over 100,000 citizens partially sequenced (Palmer, 2015), no other country offers such a rich set of data for researchers to use to devise personalized, genetically driven therapies. In addition, Iceland's detailed genealogical records work to amplify the value of the genetic data by linking genetic information to historical notes (Tirrell, 2017).

While there are several other countries working hard to develop their own population-based genetic repositories, the U.S. approach remains somewhat unclear. Last year, Congress passed and President Obama signed the 21st Century Cures Act, which provides $6.3 billion in funding; of that, $4.8 billion is earmarked for the National Institutes of Health (NIH) over the next decade ("21st Century Cures Act," n.d.). The draft budget released by the current administration proposes a 20% cut in NIH funding, although bipartisan support of the Act and the NIH suggests that such a drastic cut in funding is unlikely.

Although medical leaders espouse the promise of personalized medicine driven by genetic testing, the lack of a coordinated effort to collect genetic information and make it available to researchers presents a significant barrier to meaningful and timely discoveries. With academic tenure positions and industry job promotions linked to data sets, many investigators choose to closely protect their data rather than share it broadly with colleagues. Both life science companies and provider organizations subscribe to this approach, too—after all, sharing data reduces marketplace advantages that can deliver enormous profits and outsized employee bonuses.

Rather than considering patient information, and in particular genetic testing results, as private property to be used for private good, perhaps it is time to think of our population's medical information as private property, owned and controlled by the patient, to be used for public good. To achieve this goal, these first steps are necessary:

1. Robust interoperability across both private and public healthcare facilities, using standards accepted by every health IT vendor
2. Expansion of genetic testing of Americans across all ethnic and socio-economic strata
3. Formation of a public-private partnership to facilitate the building of clinical data repositories populated with EMR-collected patient data for use by researchers in both public and private settings

With more than $3 trillion spent on healthcare in the U.S., any effort to more effectively deploy that expenditure makes sense. The current model of duplicative research efforts using limited, hard-to-identify data sources delivers marginal results to researchers and poor outcomes to patients. With the value of personalized medicine so large, it is time for us to implement effective interoperability and build the robust investigative repositories that will expand our medical knowledge while curing disease and extending life in ways we can now only dream about.

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