A new project by the Genetic Alliance is hoping to turn the traditional investigator-led research paradigm on its head, amassing a group of patients who want to participate in research and giving them access to the fruits of their participation and ongoing control over what happens to their data.

The alliance, which represents an array of disease advocacy organizations, hopes the Registries for All (Reg4All) project will accelerate the pace of medical research and enable patients to take a more active role in managing their health (http://www.reg4all.org). The online interactive portal, created by a company called Private Access, surveys patients about their health status and allows them to see how their answers compare with others (http://bit.ly/12DfCMl).

Participants may also submit medical information, such as test results for breast cancer–related BRCA gene variants.

Officially launched in April, the project has won awards for innovation: $15,000 from pharmaceutical firm Boehringer Ingelheim and Ashoka Changemakers, a startup incubator, and $300,000 from pharmaceutical firm Sanofi. And it’s not alone in trying to shake up the way researchers connect with participants in clinical research. An array of research organizations, nonprofits, and patient groups are exploring how similar digital tools may improve the consent process, give patients more information about and control over what happens to their data, and facilitate pooling data for future studies.

Sharon Terry, president and chief executive officer of the Genetic Alliance, explained that traditional means of patient consent do not provide patients with as much flexibility and control over their data as emerging digital models, which keep patients engaged with researchers over the long term.

“We need consent, but we don’t need only consent,” she explained.

**Legalese and Limitations**

Obtaining informed consent from participants in research has long been a cornerstone of the research process. But as research, technology, and patient attitudes have changed, the approach to consent hasn’t necessarily kept pace.

Historically, obtaining patient consent required one-on-one interactions between researchers and participants, but in many cases it has become more of a legal contract, explained Amy L. McGuire, JD, PhD, director of the Center for Medical Ethics and Health Policy at Baylor College of Medicine. The emphasis is often on disclosing the potential risks of participation and ensuring that patients are willingly participating. But this approach has limitations. She explained that patients often don’t understand what the consent documents are trying to communicate, which raises questions about whether they are truly making an informed decision to participate.

Growth in studies based on biobanked materials or genomic data is also creating a new set of challenges for both researchers and research participants.

For example, McGuire explained that in a traditional clinical trial, participants are actively involved in the research process, interacting with their clinicians or investiga-
tors, and they can choose to withdraw from the research. But in genomic research, participants give a sample up front and have little contact with investigators.

"It makes it harder to withdraw," she said.

Researchers may also feel constrained by the current consent paradigm. John Wilbanks, chief commons officer at Sage Bionetworks, which is developing an online interactive consent system, explained that traditionally patients have given consent for participation in a single study at a single institution for a specific purpose. However, researchers are increasingly pooling data, especially genomic data, from multiple sites and studies to create larger data sets that have more statistical power.

"It creates downstream barriers to using the data that make it hard to do aggregation of study data," Wilbanks said.

McGuire noted that biobanks have sometimes resolved this issue by asking participants to give very broad consent for use of their data and tissues, but this limits patients' say in how their information is used. She noted that research participants may have different comfort levels depending on who will be accessing their data.

"Some people distrust what the government will do with the data, and a lot of people feel that if they are contributing samples, they don't necessarily want other people profiting from that," she said.

**Dynamic and Digital**

New models for patient engagement and consent, which are collectively described as patient-centered initiatives, use digital or social media technologies to connect research participants and investigators over time, McGuire noted. This longitudinal relationship and the flexibility of the technologies are creating opportunities for patients to get updates about the outcome of the research they have contributed to and to change their minds about participation in future research.

For example, Reg4All allows users to establish very specific limits on who can see what information about them. For example, Terry explained that individuals could choose to share information about their orthopedic health issues but not psychiatric ones, specify which organizations may access their data and whether their data may be submitted to patient registries, and change their preferences over time. Researchers will also be able to use the system to find potential research participants by searching for individuals who have indicated they are open to such invitations.

Wilbanks and his colleagues have developed another model called Portable Legal Consent (PLC), which allows individuals to donate their genomic data for wide use by others, even those outside the traditional research enterprise. Many people who have sought out genome testing from private companies, such as 23andMe, may not have contact with physicians or researchers at academic medical centers who can connect them with research projects.

"Consumers are now ordering genomic testing, and they need a route into the clinical enterprise," Wilbanks explained.

The idea behind PLC is that participants' consent is not tied to a particular study but rather "is something that patients carry around with them like organ donation status."

The database of genomic information being collected through PLC is available to anyone who wants to use it and agrees to its terms, including not to use the data to harm anyone or to try to identify participants. Users also agree to publish any work based on the data under the National Institutes of Health's open access policy, which requires submitting manuscripts to PubMed Central on acceptance and making the manuscripts public within a year of publication. Wilbanks acknowledged that he and his colleagues have limited means for enforcing these terms of use but added that they are exploring potential strategies for boosting compliance.

Patients will be able to change their consent status for future studies, and methods are being developed to facilitate ongoing contact between researchers and participants, such as by allowing participants to see a list of researchers' publications related to their data.

Jane Kaye, PhD, director of HeLEX, the Centre for Health Law and Emerging Technologies at the University of Oxford in the United Kingdom, and her colleagues published an overview last year of ongoing patient-centered initiatives (Kaye J et al. Nat Rev Genet. 2012;13[5]:371-376). She argues that such initiatives have the potential to boost public confidence in the research enterprise by respecting patients' autonomy and contributions and increasing transparency.

"Patient-centered initiatives use technology to engage, consult, and respect people," she said. She and her colleagues are also developing a dynamic consent model for use by patients who agree to participate in one of 3 biobanks at Oxford.

**An Ethical Imperative**

Kaye argues that there is huge potential to use these interactive consent tools to capture data that might otherwise go untapped. For example, patients with rare or chronic diseases may relay to their physicians information that never makes its way to studies.

"Often researchers see getting consent as kind of a regulatory hurdle, rather than being part of an ongoing process of engagement with patients," Kaye said. "Patients have enormous expertise and knowledge about their condition, but right now we aren't tapping it, even though we have the technology to do so."

Engaging patients also demonstrates respect, McGuire said. Individuals are likely to vary in how much contact they want with investigators; some people may not want contact after they have given permission to use their data, while others may want to get regular updates and assurances that their information is being used in ways they are comfortable with.

"But the vast majority of people at least want to be asked," McGuire said. "They feel strongly that it's a sign of respect. They want to be recognized for the contribution they are making."

There is an ethical imperative to respect these contributions by giving patients access to information about how the samples are being used, how many times they are used, what is being discovered, and the benefits of the research. Kaye said. "People have a right to know how their information is being used, rather than being treated as passive providers of information," she said.

To help respect patients' autonomy, she and her colleagues are setting up a communication interface that will allow patients to give dynamic consent. It allows patients to give varying kinds of consent for different studies over time and to be recruited for new research or contacted for new consent when a protocol changes.

Other aspects of respecting patients are ensuring their privacy and being honest about the risks of participating in research or submitting their samples or data to a bank.

Wilbanks said this consideration is particularly important for genomic data, which is "by definition a fingerprint. The risks associated with having one's genomic information exposed aren't entirely clear. Some scenarios for potential harm were laid out in a recent version of PLC—for example, the possibility of one's DNA being synthesized..."
and placed at a crime scene. But Wilbanks noted the risk content is being revised. He said he now worries more about online bullying of individuals whose DNA reveals information about their health.

"The biggest risks are ones we don’t understand yet," he said. "We want to make it extremely clear that the individual bears the risk and society gets the benefit, at least in the short term."

Kaye said the nature of genomic information and the ubiquity of identifying information online make it difficult for researchers to promise participants anonymity. But identifiers can be removed, and researchers can protect patients’ privacy by securing their data.

"People aren’t so concerned about being identified if they know their data are within the safe cocoon of the research enterprise," Kaye said. "I think the days when we could put [genome] sequence data on the Web and ensure that donors would remain anonymous are gone."

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**Task Force: Evidence Is Lacking That Screening for Glaucoma in the General Public Leads to Improved Outcomes**

Mike Mitka, MSJ

Rigorous evidence that screening for primary open-angle glaucoma in asymptomatic adults reduces the risk of blindness or improves quality of life does not exist. So it is not surprising that the latest assessment of this practice by the US Preventive Services Task Force (USPSTF) concludes that current evidence is insufficient to evaluate the balance of benefits and harms of such screening. But ophthalmologists, while acknowledging the limited evidence, say screening is still beneficial.

Glaucoma is a chronic disease and a leading cause of blindness. Open-angle glaucoma, the most common type of the disease, affects more than 2 million individuals in the United States, with almost 2% of adults older than 40 years having the condition. Glaucoma appears to be more prevalent in black and older individuals.

Most individuals who develop glaucoma will not become blind because the disease sometimes progresses very slowly or current treatments adequately control the condition. But in some patients, glaucoma can be asymptomatic until late in the disease process when visual loss and functional impairment are irreversible. So some experts suggest that screening for glaucoma in asymptomatic adults may help raise awareness of the condition in the general population and increase the likelihood that individuals at increased risk seek evaluation for the disease.

**Scant Evidence**

The problem for the USPSTF is that there is scant evidence that actually demonstrates whether general screening for glaucoma works, as the group noted in its recommendation statement issued July 8 (http://bit.ly/189Hton). The task force did find convincing evidence that treatment of increased intraocular pressure (a risk factor for glaucoma) and early glaucoma reduces the number of individuals who otherwise would go on to develop small visual field (field of view) defects that are unnoticeable to patients or to experience a worsening of their visual field defects.

However, the group found inadequate evidence that screening for or treatment of increased intraocular pressure or early asymptomatic glaucoma reduces the number of individuals who will develop impaired vision (any kind of vision loss) or experience a worsened quality of life. The task force concluded that available studies assessing effectiveness of early detection and treatment were not large or long enough to detect differences in rates of visual field loss or clinically relevant outcomes given the slowly progressive nature of the disease. The American Academy of Ophthalmology and American Glaucoma Society have argued that the task force’s criteria for determining rigorous studies are too limiting and exclude studies that do show benefit of early detection and treatment.

"We did not find definitive evidence that treatment in the presymptomatic period made a difference," said Virginia A. Moyer, MD, MPH, task force chair and vice president for maintenance of certification and quality at the American Board of Pediatrics in Chapel Hill, North Carolina.

The measurement of intraocular pressure with a tonometer and other screening methods to predict risk for primary open-angle glaucoma in asymptomatic adults lacks rigorous evidence of benefit or harm, says the US Preventive Services Task Force. Ophthalmologists say screening is still beneficial.