Reinventing Discovery

By Irene M. Wielawski

As the popularity of smart phones has soared, so has enthusiasm for app-based research studies. Scientists see such digital tools as a means to capture biomedical, behavioral, and other data from many more people than traditional research studies can, thereby accelerating medical discovery.

But plunging public trust in commercial technology companies has jolted the field. Security breaches of digitally stored data are now regularly in the news, as are accounts of commercial exploitation of customers’ personal information. Government agencies, meanwhile, have launched probes of the major commercial technology companies.

Scientists can no longer assume public acceptance of app-based research. Improved security and standards for ethical data use are urgent needs if the field is to grow. And there are new concerns as scientists confront dropout rates among app users as high as nine out of 10. Early proponents have also begun to question the degree to which interactive tech can replace human dialog and the relationships that help to sustain traditional research studies.
Shifting Terrain

Earlier this year, the New York Times ran a story about a 14-year-old boy who discovered a security gap in Apple’s popular video chatting software, FaceTime. The design flaw, dubbed “FacePalm” by security experts, left millions of iPhone and iPad users vulnerable to third parties’ secretly listening in and seeing images from their conversations.

Even more alarming was how long it took Apple—which markets itself as the most security conscious of the big tech companies—to respond to efforts by the boy’s mother to alert the company. The newspaper reported that she emailed Apple’s security staff, posted alerts on Facebook and Twitter, and even sent Apple a video of her son’s hack. Only after a news article about the flaw went viral a week later did the company act to protect the privacy of its customers.

The New York Times story by Nicole Perlroth was one in a steady stream of bad press on the tech industry over the last year that has exposed a generally careless attitude toward privacy. It followed disclosures of repeated failures by social media giant Facebook to protect members’ personal information. What initially seemed to be naiveté on the part of Facebook executives—founder and CEO Mark Zuckerberg claimed as much in testimony before Congress in April 2018—has since emerged as a widespread industry practice to profit from the sale of users’ personal data, sometimes without their knowledge or permission.

Public concern has spread beyond Facebook to a wide range of commercial applications preloaded onto smart phones or available for purchase or no-cost download. These include health-related apps, more than 200,000 of which are available from the online stores of Apple and Google. Among them are general health tools for improving fitness, losing weight, monitoring heart rate, tracking moods, and managing pain as well as apps that target specific diseases. In order to work, many of them require users to key in medical information such as diagnoses, medications, and personal health or life goals. Not disclosed, except sometimes in the fine print of an app’s consent document, is the manufacturer’s intention to sell this information. The Wall Street Journal and the Washington Post have reported on several apps which provide such intimate information as users’ ovulatory cycles, sexual activity, and heart irregularities to Facebook, employers, insurance companies, and other business partners.

The continuing media scrutiny suggests Big Tech won’t get out of this self-made mess easily. Already, some policymakers have called for investigations and tougher regulation, citing, among other issues, inadequate privacy safeguards and exploitation of users. And in June, the U.S. Securities and Exchange Commission and the Justice Department opened antitrust investigations, based partly on security concerns, into Apple, Google, Facebook, and Amazon.

Beyond official scrutiny is the long tail of lost public trust, which has been eroding for some time under the onslaught of hacks, identity thefts, robocalls, and criminal scams. Regaining it will require a great deal more thought, investment, and action than the industry’s suddenly ubiquitous ‘we-care-about-your-privacy’ messages.
What does this mean for research?

Among many consequences of this turmoil may be its impact on research-oriented efforts to persuade people to digitally share their biomedical and psycho-social information to advance medical science. Many such projects are underway, fueled by the potential of smart phones to connect researchers with the health data of millions of sick and not-yet-sick people from all walks of life. The belief is that such a robust and demographically diverse data bank could illuminate disease processes and help in the development of better treatments.

Scientists pursuing these goals are understandably dismayed by the news reports; some openly grumble about “the media” scaring off prospective research subjects. But others see in the journalists’ revelations a roadmap for science-oriented tech to strike off in a different direction, guided and girded from the outset by principles of public service.

How to accomplish this is less clear. An oft-cited obstacle is the lack of information about smart phone users coupled with wide variation in researchers’ understanding of how to deploy the technology effectively. And, the societal context of such tech-facilitated relationships has only begun to be explored.

“We are so bad right now at using this technology,” said Jason R. Bobe, a researcher at the Mount Sinai School of Medicine in New York and longtime advocate of more open and collaborative relationships among researchers and human subjects. “We know nothing about what users really want from their participation and we haven’t sufficiently explored the ethical, legal, and social aspects of this relationship. We’re really just getting an idea of all the work that’s still ahead in order to do this right.”
Experiments Underway

The best known of the science-oriented efforts is the National Institutes of Health’s All of Us Research Program—part of the government’s Precision Medicine Initiative. Launched by President Obama in 2016 amid high confidence in the public’s willingness to contribute their personal health information, All of Us aims to collect such data from 1 million demographically diverse Americans, using mobile apps as well as traditional research methods.

Other smaller experiments have sought to explore and improve the utility of Internet-based tools for research collaborations. The Robert Wood Johnson Foundation invested in a number of such projects under a program called Reinventing Discovery which awarded grants of 18 to 24 months duration for an array of specific tasks. The purpose, as described in the Foundation’s 2013 program summary, was:

- **Explore** new collaborative models of patients, researchers, practitioners, and funders
- **Investigate** the platforms and tools being created for shared data and open science
- **Demonstrate** the value of the models, platforms, and tools in accelerating medical discovery

That last one was a tall order, given the short duration of the grants. Suffice to say, none of the grantees got anywhere near documenting acceleration of medical discovery. This turned out to be an important finding, given the near giddy enthusiasm at the time about the potential of digital tools to connect scientists to vast swathes of research subjects—and to do so relatively cheaply compared to traditional research studies.
The Promise and Pitfalls of Using Digital Tools in Scientific Research

The cost of research today burdens virtually everyone working to advance medical science but it’s not the only concern. Scientists say they also need more research participants in greater variety to pursue new lines of inquiry. For example, recently discovered sub-categories of cancer—breast, lung, and others—require matched patients and controls to test treatments. Digital tools potentially offer a means to track and collect data from many more people undergoing experimental treatment than traditional studies can.

In traditional studies, subjects typically travel to research centers to have their blood drawn or organ functions measured or to be interviewed about symptoms, drug reactions, and other relevant factors. Trained personnel perform these data collection tasks, while other professionals carry out data analysis and still others are responsible for building relationships with participants. Relationship-building—essentially making people feel good about their role in advancing medical science—is especially important for studies that require a long-term commitment by participants. The 71-year running, multi-generational Framingham Heart Study is a standout example. Based in Framingham, Massachusetts, a city of about 68,000 residents located 23 miles west of Boston, the heart study puts a great deal of effort into sustaining participant relationships via newsletters, email and phone communications, social gatherings, and minute attention to the details of each person’s experience.

Such a labor-intensive infrastructure, not to mention the project’s physical needs—offices, laboratories, convenient parking, comfortable waiting room chairs—is expensive. App-based research is seen by many in the nascent field as not only less expensive but potentially more convenient for scientists and participants.

For example, lifestyle and other questionnaires could simply be routed through the app and completed via the same technology instead of asking study participants to come in for an interview. App sensors could directly transmit physiologic measurements, and back-up data from participants’ electronic health records could easily be uploaded. Finally, being able to interact with scientists entirely from one’s phone might encourage more people to join research studies.

Another appeal: traditional research studies have not been able to achieve demographic diversity; a chronic deficit has been inadequate participation by racial minorities. This uneven representation skews results and leaves many clinical questions unanswered. For example, why is the prevalence of diagnosed diabetes in Hispanic and black Americans more than 60% higher than in whites? Why do Asian Americans have half the incidence of breast cancer compared to all other racial groups? Why are death rates from dementia so much higher for whites (70.8 per 100,000 population) and blacks (65.0) than for Hispanics (46.0), according to data compiled by the U.S. Centers for Disease Control and Prevention’s National Center for Health Statistics.
Because they are popular, smart phones have been seen as a means to harness millions of research subjects and, through sheer numbers, improve participation from heretofore underrepresented demographic groups.

So goes the theory. But it has proved harder than expected to recruit diverse participants and get people to stick with app-based research long enough to test it.

“The participation just falls off a cliff,” said Lara Mangravite, president of Sage Bionetworks, a non-profit research group in Seattle which has developed several research apps as part of a larger effort to build Internet-based data-sharing systems for large-scale biomedical collaborations.

Even research apps dedicated to the specific health problems of the people downloading them show use patterns virtually identical to commercial products such as diet or exercise-trackers like the popular Fitbit. At first, people are enthusiastic, checking their step counts several times a day and exploring other options within the app. But, according to Sage’s Mangravite, the enthusiasm is short-lived. Within weeks—sometimes, only days—Sage researchers measured precipitous drops in use by all but a fraction of the people who initially signed onto their apps.

The dropout rates documented by the Sage team match the experience of other research app investigators, among them, Brennan M. R. Spiegel, director of health services research for Cedars-Sinai Health System in Los Angeles and a professor of medicine and public health at the University of California, Los Angeles.

Spiegel has spent more than a decade in the e-medicine arena trying to figure out how to get patients to stick with app-facilitated experiments and therapies. “There’s a big drop off, quickly,” he said. “We’ve learned that most people don’t use the apps, or they decide they don’t want to.” Those who do tend to be quantified-self personalities—they like measuring and tracking data about themselves. They also tend to be younger people with few co-morbidities, according to Spiegel.

One experiment undertaken by Spiegel and colleagues sought to get patients who use fitness apps like Fitbit to share this data with their doctors. Of 66,105 demographically diverse people invited through CS-link, a patient portal used by Cedars-Sinai and affiliated hospitals, only 499 (0.8%) agreed to participate. Most of them were young, male, and white. Spiegel’s team published these findings in late 2016. The backlash from app promoters was swift—and startlingly virulent—despite similar use and retention patterns documented by other research groups.

“There was immediate criticism from the tech community that we’d failed to properly advertise or market our study and that we hadn’t explained it well to the patients,” Spiegel said. “We certainly had. They knew exactly what we were asking of them.”

The small numbers and narrow demographic band attracted by Spiegel’s and other app-based research experiments particularly challenge the assumption that smart phones alone are the means to harness large groups of research subjects and improve diversity.
An Emerging View of Research Apps: One Tool Among Many

The Framingham Heart Study is working on an app to make it easier for participants and researchers to communicate and share some data back and forth. People who agree to use the app can also choose to receive a blood pressure cuff and Apple watch to facilitate weekly biometric reports.

But study staff emphasize that participation is optional, with the app presented simply as an additional communication tool, not as a substitute for the personal interactions on which the long-running study is grounded.

Framingham participants, all of them volunteers, typically come to the research center every six to eight years for physicals, lab tests, and interviews lasting about 4 hours per person. Most live in Massachusetts or greater New England, but some participants travel from more distant parts of the country and even from abroad. Their commitment to the research is underpinned by relationship nuances that heart study leaders acknowledge would be hard to duplicate in an app algorithm.

“We have a very dedicated staff that has been here a long time,” said Emilia J. Benjamin, Framingham’s senior investigator and a professor of medicine and epidemiology at the Boston University School of Medicine. “They recognize people’s voices on the phone, even when they’re calling from Europe or some other faraway place. They call them by name, ask about their families. Sometimes when our participants see their own doctors and mention that they’re part of the Framingham Heart Study, the doctor’s reaction is, ‘Wow!’ The City of Framingham also is very supportive—we’re often invited to community events. All of this is very positive feedback that makes people feel they are valued, that their research contribution is important.”

Joanne M. Murabito, Framingham’s co-principal investigator and a professor of medicine at the Boston University School of Medicine, leads the app venture. She started in 2016 with a pilot project of 200 people to test the level of follow-through on remote sign-up for the app via an email invitation sent to volunteers. Her comparison group was invited to the research center to learn about the app and how to use its sensors, answer surveys, and connect devices like the blood pressure cuff to their phones. A staff member facilitated these enrollment and training meetings. Depending upon the measurement sought—blood pressure, general activity, heart rate, for examples—participation averaged 25% higher among those who received on-site assistance.

Murabito and Benjamin acknowledge their advantage over start-up research projects based entirely on app or other digital interactions. The heart study has literally decades of relationship building with participants, their children and, now, grandchildren to support the new venture. “It certainly helps that our younger participants saw their parents participating so that it’s actually part of the family culture to be part of this,” Benjamin said.

Still, there’s much to be worked out. Currently in testing is whether a survey generated every three months by the app is too much to ask of participants. Data entry “burden” has been reported as a factor discouraging use. Another unknown is the best time of day to send messages needing attention. Murabito is experimenting with Wednesdays or Saturdays, 7 AM or 7 PM, to measure the rate of response. She is also testing the response rate to messages with different tonalities, for example, comparing the business-like: “We appreciate your involvement in the eFHS. Please … measure your blood pressure weekly” with the more familiar: “Mr. [last name], way to go! We received another blood pressure from you last week. Thank you!”
The People Problem: Recruitment and Retention

Why is recruitment so tough? And why do people drop out so quickly? Research app developers initially focused on technical challenges encountered by participants such as difficulties in navigating the app or confusion about how and to whom their information was being sent. But there is growing recognition of real-world factors in play, such as boredom, irritation, and competition from urgent or more appealing tasks. How much can researchers impose on participants’ time, say with a questionnaire, and still obtain reliable data? And to what degree are privacy and security concerns making initially willing participants change their minds? These are among the many unknowns about users bedeviling the field, say those confronting dropout rates as high as nine out of 10.

A study by Kit Huckvale and colleagues published in the Journal of the American Medical Association (JAMA) found that 29 of 36 commercially available smart phone apps for depression and smoking cessation transmitted users’ personal data to Google and Facebook for advertising and marketing purposes. Only 12 of the apps accurately disclosed in their privacy policies that they were doing so, while 11 of the apps tested didn’t even have privacy policies.

Even among developers of apps for scientific studies, there are no consensus standards, and the researchers using them sometimes lack the skills and protocols necessary to protect participants. They may borrow jargon from commercial apps like “de-identify” and “anonymize” and promise to use only “aggregate data” without understanding how to make good on such promises.

“Claims of de-identification are a positive image to present, easy to misrepresent, and rarely questioned in the research context,” said Jason Bobe, who discovered this deficit while working on an online portal for researchers to access data from the Harvard Personal Genome Project (PGP).

Established in 2005, PGP collects and stores DNA and cell lines from volunteers who contribute this and other biological information for use by researchers worldwide. Because it functions as an open science data bank, meaning it is publicly accessible, PGP takes pains to inform participants of the risks of sharing such personal health information digitally, including the potentially adverse impact on the “employment, insurance, and financial well-being or social interactions” of data donors and their immediate families. The project’s 24-page consent form is extraordinarily thorough; would-be volunteers can’t even give consent until they pass a test to determine their competence to understand these and other risks. And the project asserts the right to verify users’ identities periodically to guard against false data.

At the time, Bobe was PGP’s executive director and well-versed in both genetics and web-based information science. Not so, he was to learn, were the researchers lining up to use his Open Humans Research Portal to download and analyze the data contributed by PGP volunteers.
Trial, Error, Rethink, Try Again: The Sage Experience

Sage Bionetworks had one of the app development projects funded by the Robert Wood Johnson Foundation. The funding encompassed three goals. The first was technical: Build an app that research subjects could easily navigate and that researchers could customize to their information needs. The other two assignments were more conceptual. The first was to figure out a way to embed an informed consent process—the means by which people give permission to be studied by scientists—that met ethical standards for human experimentation. The second was to sustain participation. This last would prove to be the most difficult, owing to a remarkable lack of knowledge about people’s actual relationships with their smart phones, computers, and other Internet-based tools, including the degree to which they trust these devices.

At the time, roughly 2012-2013, the Sage team was focused on projects related to the human genome, a massive data trove offering many avenues for research. But if a gene abnormality were identified, what would it say about the people living with it? “We had all this genomic information on people but no idea how healthy they were at any given point,” recalls Mike Kellen, Sage’s chief technical officer. Nor, arguably, did their doctors know since even people with serious chronic illness such as diabetes or heart failure or Parkinson’s disease can go weeks, even months between medical appointments and tests.

The idea of collecting information on people’s ongoing state of health was tantalizing—and it suddenly seemed possible, thanks to the popularity and technological versatility of smart phones. Some 81% of Americans own smart phones today, according to a Pew Research Center survey, up from 35% in 2011. Sage’s grant application in 2015 took note of this upward trend in presenting app-based research as a win-win for patients and scientists alike: “The recent emergence of the smartphone as a ubiquitous feature of modern life has created an opportunity to collect data directly from individuals in their everyday lives outside the clinic, and dramatically reduce the costs of data collections,” the proposal said, referencing the limitations of traditional research studies in both the number of human subjects from which to extrapolate medical insights and the expense of mounting and sustaining these experiments. “While the cost of collecting many biomedical data types has been rapidly decreasing, the costs of enrolling individuals and managing their care during the course of a study are increasing. Increasingly more expensive trials are required to produce results with decreasing clinical impact.”

The proposal mirrored the client orientation of Big Tech, which largely caters to business partners willing to pay for the personal information of app users—their locations, shopping patterns, interests, contacts, politics, and so on. For early developers of research apps, the clients decidedly were scientists. Besides on-line access to user-donated biomedical data, these customers would need management tools to, for example, create and send out surveys or extract from large data pools only the information useful to their studies. For a study on diabetes, it might be blood glucose levels while a Parkinson’s disease study might focus on neuro-muscular function and drug effects.

“We’ve repeatedly encountered researchers describing highly identifiable data as “de-identified,” Bobe wrote in an October 2015 report to the Robert Wood Johnson Foundation, which funded the portal work. “For example, one researcher described data containing personal email addresses as ‘de-identified’ merely because names had been removed. Some organizations describe the mere removal of an individual’s name as ‘de-identification,’ despite retaining other highly identifying elements (e.g. birthdate, profile photo, personal biography).”
To this end, Sage proposed a web-based “dashboard” using Apple’s Research Kit software to help researchers configure their studies, schedule app activities, and interact with participants. “As part of this tool, we would give researchers the ability to create and manage subpopulations of their user base that could receive different sets of activities, or be exposed to different consent mechanisms,” Sage’s grant application stated. “This capability will allow researchers to compare the data and usability of different versions of a module and is critical to establishing a process of continual testing and refinement of modules.” On the user side, Sage proposed to develop chat rooms within the apps for people to talk with one another, dashboard tools for participants to explore their own and comparative population data, and possible web-based seminars with the researchers. The expressed goal of these features was to give research subjects something of value—so-called return of results—that would sustain their engagement with the experiment.

Sage already had several research apps in development, the most sophisticated of which, mPower, targeted Parkinson’s disease. An incurable and degenerative brain disorder, Parkinson’s disease mostly affects older people, causing tremors and stiffness and, in time, difficulties with walking, balance, and speech. The mPower app came with sensors to capture subtle changes in gait, dexterity, and voice. By correlating these measurements with, for example, the type, dosage, and timing of a patient’s medication, scientists might gain new insight into drug effects and devise better treatments.

To fully automate the app as a research device required embedding an interactive informed consent module that satisfied ethical standards for disclosure of risks and benefits to participants in medical experiments. Christine Suver, Sage’s governance director, oversaw much of that work. Because there would be no trained staff to guide the conversation or answer questions, as in traditional studies, the consent module had to document participants’ understanding of what they were getting into.

“We aimed for a fifth to eighth grade reading level,” Suver said. They also added “read more” hyperlinks intended to clear up confusion or provide additional detail. Early testing, however, showed that few participants opted to “read more” after the summary tutorial. The finding pointed to a problem of conditioning among smart phone users by the typical consent documents that accompany commercial products such as games, search apps, and phone-based shopping and financial tools. There’s no aim in these for a fifth to eighth grade reading level. Indeed, the intensely legalistic language of commercial consents, many of them running in tiny print over multiple screens, seems intended more to discourage than to promote understanding. Consumers commonly click “yes” or “agree” without reading—and most commercial apps make it possible to do so.

Such click-through consent, however, would not qualify as “informed” under research protocols. The anemic response to the “read more” option led Sage’s governance team to rewrite the summaries to make sure all the main points were covered. It was a first of many app tweaks in response to user behavior and feedback. The Sage team then added a second safeguard to meet ethical standards for informed consent: a comprehension test consisting of five questions that prospective research subjects had to answer correctly in order to move on to the next consent topic. The results, according to Sage’s Mangravite, were “sobering.”

“Fifty percent of the people who signed up for the app couldn’t get through [the consent process] in an hour—it was really too complicated,” Mangravite said. “We were conservative because you don’t want people getting involved in this unless they are well-informed,” she added, but the complexity of the consent process presented a barrier to enrollment before users even reached the part that aimed to keep them engaged in the study.
What’s the Solution?

People familiar with the participation problem express doubt about a purely technology-based solution. There’s more in play than convenience of use or smart phone savvy, according to Marjorie A. Speers, executive director of Clinical Research Pathways, a public charity in Atlanta, Georgia, that works to expand access and inclusion of racial and ethnic minorities in clinical research. Among many influential factors—education, language skills, socio-economic status—are people’s historic experience with health care and medical research. African Americans, for example, have a long history of exploitation by research scientists, an example being the notorious [Tuskegee syphilis study](https://www.nps.org/learn/historical/tuskegee-syphilis-study) in which black men were denied life-saving penicillin.

“The relationship between the researcher and the participant is key—it’s what keeps a person engaged in traditional research,” Speers said. “It’s a challenge with the apps because the relationship is essentially with an electronic device. That said, we are missing an opportunity if we don’t take advantage of technological advances. The problem from the research perspective is that we don’t have sufficient information on what patients want, what they think would be helpful. We are basically working on assumptions.”
A Different Approach

The early work of Sage Bionetworks and other research app pioneers sheds light on how the field can differentiate itself from commercial apps and satisfy user preferences. One idea is to pull back from the idea of apps as stand-alone research platforms and reposition them as simply one tool of engagement among many, thereby giving research participants leeway and choice. The Framingham Heart Study is taking this approach with an app intended to facilitate communication among participants and researchers during the multi-year intervals between cardiovascular workups. Study staff emphasize that app use is optional and not a substitute for personal interactions.

This careful attention to user preferences and tolerances marks a new way of thinking among scientists interested not simply in the volume of research participants but in the quality and usefulness of the information they provide and in their long-term commitment. Abhishek Pratap, a researcher at the University of Washington and a member of Sage’s digital health team, is among the advocates of this user-oriented approach, believing it will yield greater value over time compared to the mass data uploads that initially fueled enthusiasm for app-based research.

“The ‘in the wild’ data is very attractive to researchers; they have a sense that they can ask for any information they dream up and also that it is a cheap solution compared to a traditionally structured research study,” Pratap said. “We got all excited about this in my research group, seeing the technology as a way to harvest a treasure trove of population data. But what we didn’t think about is that population is made up of individuals—it’s you and me. When you think this way, you begin to understand why 80% to 90% leave the apps in seven days.”

Pratap, who thinks somewhat obsessively about the interface between apps and audiences, believes an early mistake was underestimating the public’s sophistication about “what on a phone is worth their time and effort”—a sophistication that has only grown more acute. Think about it: Who answers calls anymore from strangers or robots? What percentage of inbox messages get swiped off to trash without being opened? Who even notices the ads and political messages on news site feeds? What is the return rate on the “How did we do?” customer surveys that pop up in peoples’ phones as soon as they disembark from a plane or leave a bank or complete an on-line purchase? How many people in the target audience for research studies have had to deal with identity theft, fraud, and other harms due to hacks of digitally stored information?

In other words, the population isn’t a blank slate when it comes to technology intrusions and cyber insecurity. The degree of awareness varies as does the sophistication with which people guard their personal information. The demographic mix desired by scientists—racially diverse, male, female, young, old, college graduates and people who didn’t finish high school—adds more variants and consequent challenges to app design.
The Sage research group, for example, realized quickly that it had erred in building its Parkinson’s mPower app chiefly to serve researchers’ needs. Among the promises to participants was that they would have access to their own data and educational material about ongoing research. But the original app did not make it easy for them to find this information.

“We had to build a dashboard to help participants easily manage their research information and navigate their way through the study,” said Sage CEO Mangravite.

Additional lessons came from participant interactions with the app’s informed consent document. In a study, Megan Doerr and her Sage co-authors reported confusion with comment boxes related to consent questions. Some participants used them to pose questions or offer suggestions as one might with an online customer service survey. Other comments laid bare the complex psychology of living with serious illness, suggesting a pitfall for researchers depending entirely upon app interactions to cement long-term engagement.

"After going through that last series of questions though I’m going [to] quit this program. I don’t like going through all those symptoms that I don’t have yet. I don’t want to think about what may be coming," one person wrote.

The sentiment is familiar to anyone who has grappled with serious or incurable illness—and to clinicians who treat such patients. Megan L. Ranney, an emergency medicine physician and director of the Emergency Digital Health Innovation program at Brown University in Providence, Rhode Island, was particularly struck by the plight of depressed teenagers brought to the emergency room after being injured in a fight, some of whom were also found to be suicidal. She wondered if a phone app could be developed to help them recognize mood changes and keep them from acting on depressive or aggressive thoughts.

To build the app, Ranney inverted the top down development process typical of commercial products. “I start the design by doing rigorous and thoughtful interviews with patients —high income, low income, immigrants, high education, low education,” Ranney explained. “You want to explore their inner motivations and to understand how tech interfaces with their lives. Then you do a mock-up, basically a minimum viable product, and you let them test it and then you bring them back for another interview to work out the bugs.”

In developing the app, called iDOVE, for depressed teens, Ranney said she went so far as to test whether the voice in the app’s messaging software was more effective if the syntax mimicked a nurse or ‘talked’ like a peer. Among many things she’s learned by this minute investigation of how to connect with users and retain their interest is that the apps must have the capacity to be adjusted as preferences change.
“It’s not like you’re one and done,” Ranney said. “Assuming you can just passively collect data from people and not consider anything else going on in their lives simply doesn’t work. You need to be able to monitor use and step in to modify the app as needed. Of course, you can’t meet every individual’s needs, but the users have to feel heard.”

This user-centered design process was applied at the other end of the age spectrum in an experiment to create a digital health advisor to aid the frail elderly and people with multiple chronic illnesses in their daily tasks. The researchers identified a need for digital tools that comprehensively address these patients’ emotional and functional issues rather than piecemeal, with an app for each illness, and that integrate the tool with trusted caregivers such as the user’s doctor. Writing in *Health Affairs*, the research team of Eric C. Schneider and Lovisa Gustafsson of the Commonwealth Fund and Onil Bhattacharyya of the University of Toronto noted that the “value proposition of a digital tool is not just the collection of its features, but also the way in which it is integrated by a patient and their care team into the workflow.”

**Building Trust**

Is there any such thing as data security in the digital world? The question is a popular one among app developers, including some in the scientific realm. It’s meant to be rhetorical and dismissive—the verbal equivalent of a shrug—with only one possible answer: of course not.

In fact, there are established methods to protect user privacy and deter unauthorized use of their data—encryption, firewalls, multi-layered surveillance and identity verification systems, and, in the medical realm, privacy safeguards mandated by the 1996 *Health Insurance Portability and Accountability Act* (HIPAA). The deterrent is the cost of building such protections into the architecture of smart phone apps and their corresponding research networks.

Such data controls would also limit options to make money from users’ personal information by selling it to medical industry companies or other business partners. And, while Facebook has repeatedly been hammered for slow response to identified security and privacy loopholes, the problem is bigger than one company’s practices, experts say, noting that the quality of security and privacy safeguards ranges widely among companies and research groups soliciting people’s personal health information over smart phone apps.

“One of the insights is that it is very unlikely that people are going to trust third party applications,” said Commonwealth’s Schneider. “They are looking for someone or an organization to trust. Essentially, it’s the halo effect from an already existing relationship but it falls to that organization to recommend and supply these digital apps and protect the user. The relationship can be completely undone by a single data breach.”
In 2013, RWJF authorized $5 million for the Reinventing Discovery grant program. It was set up to explore new collaborative models of patients, researchers, practitioners, and funders; and, the platforms and tools being created for shared data and open science, and to demonstrate the value of the models, platforms, and tools in accelerating medical discovery.

Ten grants were awarded under the program. Below is a brief summary of the grants.

**MASSACHUSETTS INSTITUTE OF TECHNOLOGY SCHOOL OF ENGINEERING**
*Developing a ‘science of collaboration’ to sustain biomedical and health care innovation.*

This project sought to lay the foundation for a new discipline, the “science of collaboration,” to help drive the value and sustainability of biomedical and health care innovation.

**SAGE BIOPHARMACOLOGY**
*Developing a Web-based open-source platform to leverage patient and citizen involvement to provide biomedical research with insights and energy.*

This project developed Bridge, a collaborative-science platform that incorporates open data, patient wisdom, and public involvement into biomedical research.

**INTERNATIONAL AIDS VACCINE INITIATIVE**
*Establishing the Human Vaccines Project as a paradigm for accelerating vaccine development against major global diseases.*

This project helped establish the Human Vaccines Project, an immunology-based clinical research initiative to address key questions impeding vaccine development for multiple global diseases, with the goal of more effectively generating vaccine-induced immune responses.

**PERSONALGENOMES.ORG**
*Building a portal to improve researcher utility in accessing the Harvard Personal Genome Project.*

This project helped create PersonalGenomes.org’s Open Humans Research Portal to enable and structure collaborations between external researchers and Open Humans participants.

**CURES WITHIN REACH**
*Launching an open-access online platform to support treatment for underserved patients through repurposing drugs, devices, and nutraceuticals.*

This grant supported Rediscovery Research, a collaborative, open approach to rapidly discovering medical solutions for patients who suffer from diseases that currently have no effective treatment.

**GENETIC ALLIANCE, INC.**
*Creating a ‘white label’ version of the Platform for Engaging Everyone Responsibly for sharing health information on a person’s own terms, Phase 1 and Phase 2.*

Under two grants, the Genetic Alliance developed a white-label, customizable version of its registry platform (PEER-Platform for Engaging Everyone Responsibly) that their more than 1,200-member disease organizations can use to enable individuals to share their health data as they so choose.

**WOODROW WILSON CENTER FOR INTERNATIONAL SCHOLARS**
*Facilitating interaction between the emerging ‘makers in biology’ ecosystem and formal regulatory institutions to ensure safe, responsible innovation.*

This grant helped the Woodrow Wilson International Center for Scholars bring practitioners from community labs and crowd-funding platforms together with regulatory agencies to develop and vet codes of conduct that address liability, ethics, and other governance issues.

**HARVARD MEDICAL SCHOOL**
*Developing tools and systems for the efficient collection and sharing of phenotypic data for human health research.*

This project developed tools and systems that enable people to collect their phenotypic data and actively contribute it to data resources and share it with specific research efforts and studies.

**LOUISIANA PUBLIC HEALTH INSTITUTE**
*Facilitating engagement of underrepresented patient communities in biomedical research.*

This project developed evidence-based practices and targeted messaging to foster inclusive engagement with underrepresented patient communities; identified barriers to participation of a more diverse patient population in biomedical research; and co-developed solutions to increase that population’s participation as partners and patients.
Where to From Here?

Since 2015, the dropout rate among participants has been documented as a barrier to app-based medical research. In 2019 it continues to be, challenging the premise that smart phones alone can efficiently and economically yield the number and variety of research participants needed to achieve scientific goals.

Against a backdrop of growing public concern about digital information security, research app developers and the scientists who use them would do well to heed the Russian proverb embraced by Ronald Reagan during nuclear disarmament negotiations with Mikhail Gorbachev: *Doveryai, no proveryai*, Trust but verify. Failing to do so, as did several app developers who *embedded* a commercially purchased analytics tool that exposed users’ personal health information, puts participant trust—and research goals—at risk. Another common mistake, experts say, is relying solely on university or other inhouse security systems to protect sensitive research data. Security standards and protocols for handling such data along with training for research personnel are sorely needed.

Another need: funding for research on smart phone users, generally, and research dropouts, specifically, to power the field with data rather than assumptions. Even scientists relying on the “halo effect” of trusted agents such as doctors or hospitals to round up research participants routinely consign those who decline to enroll or quickly exit to the “Limitations” section of a published study. Case in point was a study published this year in JAMA Ophthalmology which offered text reminders for glaucoma patients to take their eye drops. “We did not collect data on the reasons behind why one-third of the individuals approached were unwilling to use the reminders, and this deserves further investigation,” the researchers *wrote*.

Ranney would like to see research collaboratives with a wider range of participants than in the current app development model, which relies heavily on software engineers. “You want researchers, engineers, and clinicians working together with the end user experience as the primary focus,” she said. “The patient, the research participant, cannot be a second thought.”

Pretap and Bobe concur, especially with the need to include clinicians since many participants in medical research logically assume their doctors will be looped in on any relevant findings. This suggests a future for research apps as integral elements of participants’ electronic medical records, safeguarded by HIPAA security protocols.

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Irene M. Wielawski is an independent journalist, specializing in U.S. health policy and health care delivery innovation. Previously, she was a staff medical writer at daily newspapers, including *The Los Angeles Times*, where she served on the investigations team. Her independent work ([irenewielawski.com](http://irenewielawski.com)) has appeared in the *New York Times, Modern Healthcare, JAMA network journals, and Health Affairs*. Wielawski is the recipient of two team Pulitzer prizes and was a Pulitzer finalist for specialized reporting on medicine, among other awards.

The Robert Wood Johnson Foundation commissioned this report by Wielawski to understand challenges and promising paths forward for engaging people in research studies using mobile apps and other digital devices. The views expressed here do not necessarily reflect the views of the Foundation.