Citizen Science on Your Smartphone: An ELSI Research Agenda

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Beginning in the 20th century, scientific research came to be dominated by a growing class of credentialed, professional scientists who overwhelmingly displaced the learned amateurs of an earlier time.[1] By the end of the century, however, the exclusive realm of professional scientists conducting research was joined, to a degree, by "citizen scientists." The term originally encompassed non-professionals assisting professional scientists by contributing observations and measurements to ongoing research enterprises. These collaborations were especially common in the environmental sciences, where citizen scientists participated in counting wildlife and measuring environmental conditions.[2] Later, patient groups began to play a more active role in supporting clinical trials and collecting health records from affected individuals.

In the 21st century, the term "citizen scientist" has taken on additional meanings, and now includes non-professionals who conduct scientific experiments of their own design independent from professional scientists. These endeavors have been made possible to a large extent by technological developments, such as online crowdsourcing, big data capture strategies, and computational analytics. They have also been supported by societal changes that reflect a growing do-it-yourself approach to managing one's own affairs and the hacker-scientist mindset of the computer age.[3]

In the field of health research, citizen science (as well as professional science) increasingly will rely on smartphones and similar mobile technologies, which have emerged as collectors of an increasing amount of personal health and wellness information.[4] On a less complex level, fitness trackers, such as Fitbit and Jawbone, sold 70 million units worldwide in 2014.[5] Apple Watch and Motorola's Moto 360, both of which can perform fitness tracking as well as many other functions, continue this trend. On a more sophisticated level, thousands of new health applications (apps) can convert smartphones into electronic stethoscopes, ultrasound machines, diagnostic hearing devices, skin cancer detectors, blood test platforms, and various other medical devices.[6] According to the Food and Drug Administration (FDA), by 2015 there there were anticipated to be 500 million smartphone users with one or more health apps, and by 2018, 50% of the more than 3.4 billion smartphone and tablet users will have downloaded mobile health apps.[7] In 2014, the FDA announced it would start regulating these "mobile medical applications" as medical devices.[8]

To take advantage of these technologies, in March 2015, the first major smartphone-based health research study of Parkinson's disease was announced by Sage Bionetworks, a nonprofit research organization based in Seattle.[9] The research study, called mPower (further discussed below), combined the Apple ResearchKit mobile health application platform with additional software developed by Sage Bionetworks. The study was supported by funding from the Robert Wood Johnson Foundation and the Helmsley Charitable Trust. The participants were recruited online and utilized a novel, highly visual, self-guided consent process. Study

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data were generated by recording the voices of the participants, their posture and stability, their reaction time, and other measures of Parkinson's disease symptoms.

A second Sage Bionetworks-led research project, Share the Journey: Mind, Body, and Wellness after Breast Cancer,[10] also using the Apple ResearchKit, was launched in March 2015. The study recorded survey and phone sensor data on five common side effects of breast cancer treatment: fatigue, changes in mood and cognition, sleep disturbance, and reduction in exercise. The goal was to gain insights that may lead to improved post-treatment quality of life for breast cancer survivors. Participants were recruited from a pool of 60,000 enrollees from several national breast cancer organizations.

Both the Parkinson's disease and breast cancer studies were conducted by professional scientists in collaboration with leading experts in mobile health applications. They used informed consent and external review in accord with prevailing research ethics to guide participation, data collection, and use. Nevertheless, because the research was neither federally funded nor otherwise subject to federal research regulations, there was no legal mandate to comply with research ethics safeguards.

The prospect of newly-emerging, technology-enabled, unregulated citizen science health research poses a substantial challenge for traditional research ethics. Unquestionably, a significant amount of research ethics study is needed to prepare for the inevitable, widespread introduction of citizen science health research. Using the case study of mobile health (mHealth) research, this article provides an ethical, legal, and social implications (ELSI) research agenda for citizen science health research conducted outside conventional research institutions. The issues for detailed analysis include the role of IRBs, recruitment, inclusion and exclusion criteria, informed consent, confidentiality and security, vulnerable participants, incidental findings, and publication and data sharing.

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Parkinson's Disease mPower Study: Aims, Methods, and Early Lessons

Sage Bionetworks launched the Parkinson's disease mPower study to explore how better to manage the symptoms of Parkinson's disease (PD) through a participant-centered, app-based clinical study. PD is characterized by neuro-motor defects that affect gait, posture, voice, and manual dexterity. Although there is a long gradual decline in function as the disease progresses, patients often report significant fluctuations in short-term severity of the disease for reasons that are not well understood. The study aims to understand why some people with PD have different symptoms than other people with PD, why a person's symptoms and side effects can vary over time, and what can be done to help manage these differences in symptoms day to day.

The mPower study application runs on iPhones, and was built as part of the first wave of Apple ResearchKit mobile clinical studies. The app prompts enrollees to complete surveys and perform tasks that activate phone sensors to collect and track health and symptoms of PD progression like dexterity, balance, or gait. The study uses microphone, accelerometer, touch-screen, and other sensors to measure participant fluctuations more consistently over time and explore correlations with environmental factors such as sleep and exercise. These data are then combined with surveys common to studying PD, allowing correlation of symptoms as measured by the sensors to patient-reported outcomes.

Participants enroll in the mPower study using an IRB-approved,[11] visual e-consent process combined with a study "quiz" that must be completed without error. The visual consent is an "interface" layer atop the legal document that expresses essential clinical concepts using design methods successful in software, including icons and text labels. The consent process draws on the Participant-Centric Consent toolkit, developed by Sage Bionetworks through a yearlong multi-stakeholder partnership with the Electronic Data Methods Forum. The study is open to American residents over the age of 18, and more than 17,000 participants enrolled in the first six months of the study.

During the development of the study application, the gap between contemporary mobile application

developers and the requirements of clinical study was clear. Very few developers had ever heard the phrase "Institutional Review Board" or understood the ethics tradition in clinical studies. Because contemporary software development methodologies often build on short, rapid iterations of features and interfaces, they can be at odds with the slow pace of protocol amendment. Developing the app thus required consistent and regular contact between Sage Bionetworks' governance team and the technology team.

Regulatory Framework

Studies such as mPower raise numerous ELSI issues, and the first step in analyzing them is to determine if current federal research regulations apply. In short, because the three main sources of regulation — the Common Rule, the FDA research regulations, and the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule — only apply in limited circumstances, citizen science research is largely unregulated.

The Federal Policy for the Protection of Human Subjects (Common Rule) applies "to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research."[12] In addition, the Common Rule applies to all research, regardless of funding source, undertaken by entities that have signed a Federal-wide Assurance with the Department of Health and Human Services.[13] Therefore, virtually all American academic and health care institutions are covered for all of their research involving human participants. However, research undertaken by independent entities or individuals, including citizen scientists, is not subject to the Common Rule.

The FDA has issued research regulations that generally mirror the Common Rule.[14] They apply to research involving investigational drugs or medical devices using human participants.[15] Any research intended to support a submission to the FDA for approval of drugs or devices must comply with the FDA regulations. Consequently, the FDA regulations apply to privately funded research undertaken by pharmaceutical and medical device companies and their research partners. Nevertheless, research not undertaken to support an application to the FDA is not subject to the regulations.

Despite the inapplicability of its research regulations to citizen science, the FDA will play a major role in the regulation of mHealth research. The FDA has announced that it will regulate "mobile medical applications" by applying the same "risk-based approach" it uses to "assure the safety and effectiveness for all medical devices."[16] The FDA plans to regulate apps that are intended to be used as an accessory to a regulated medical device or that transform a mobile platform into a regulated medical device.[17] The FDA will not regulate apps that, for example, provide patients with simple tools to organize and track their health information, provide easy access to information related to health conditions or treatments, or help patients communicate with their health care providers.[18] Also excluded are apps that allow a user to collect and track heart rate, weight, and similar information.[19]

The main source for protecting the privacy of health research participants is the HIPAA Privacy Rule.[20] The Privacy Rule applies to three classes of covered entities (health providers, health plans, and health clearinghouses) and their business associates (an individual or entity that assists covered entities with functions such as claims processing, utilization review, quality assurance, legal services, management, and financial services).[21] The Privacy Rule requires that any research uses and disclosures of individually identifiable health information must have a HIPAA-compliant written authorization signed by the individual.[22] Research undertaken by a HIPAA-covered entity, such as an academic medical center, is subject to the Privacy Rule. On the other hand, research undertaken by an individual or entity that is not a HIPAA-covered entity, such as a citizen scientist, is not required to follow federal privacy rules. Unregulated researchers have no legal obligation to prevent hackers from accessing the sensitive health information of research participants or to notify individuals in the event of a security breach, and they are not prohibited from selling individually-identifiable health information to marketers.

In the future, even individuals whose health information is maintained by a HIPAA covered entity may not be protected from nonconsensual research uses of their information. The 21st Century Cures Act, currently pending in Congress, provides that health data research would be defined as part of "health care operations" or "public health." The effect would be that any HIPAA-covered entity or business associate would be able to access all individually identifiable health records for health data research without the need for an authorization.[23]

A few states have enacted laws regulating research with human participants or protecting health privacy. Such laws would be valuable in extending protections to research not covered by the Common Rule. In general, however, these laws do not provide significant protections or remedies in the event of breaches of research or privacy standards.[24] California,[25] Maryland,[26] New York,[27] and Virginia[28] are notable exceptions because they require informed consent or other elements of research ethics for all research with human participants conducted in the state, regardless of funding.[29]

Traditional Elements of Research Ethics

In the absence of federal regulatory coverage for citizen science mHealth research, the key question is whether any type of regulation or self-regulation is necessary or desirable to safeguard the welfare of research participants. In this section, we consider fundamental elements of research with human subjects and identify a research agenda for each of these elements in the context of citizen science mHealth research.

Oversight by Institutional Review Boards

The regulatory requirement for IRB review reflects a broad consensus in the international research ethics community that research on human participants should be subject to oversight by an independent ethics panel.[30] However, this model presupposes that investigators and participants are distinct from one another, and that participants may lack the understanding to evaluate the risks and benefits of participation and the autonomy to act in their own best interests. This paternalistic perspective is implicitly rejected by the citizen science model, which emphasizes the ability of research participants to interact with investigators as equals in the research process.

Because of this dynamic, it would seem that not many citizen science investigators would voluntarily submit to IRB oversight. This assumption is supported by the emphasis on efficiency and scalability in mobile research settings, where oversight by an IRB is likely to be viewed as a barrier to efficient and responsive research. Taking these factors into account, it will be important to examine how citizen scientists perceive the tradeoffs involved in external ethics review, as well as to consider existing policies that exclude non-federally funded research from oversight. Furthermore, the question arises whether, in the absence of explicit research oversight, other models of independent research review are feasible and desirable.

Recruitment and Inducements for Participation

Oversight by IRBs has traditionally involved careful scrutiny of recruitment practices and the financial and other incentives offered for participation. This scrutiny derives from the concern that coercive practices, such as large financial inducements or recruitment messages that encourage — or at least fail to dispel — the therapeutic misconception, threaten participant autonomy.[31] By blurring the lines of power and responsibility in research, citizen science significantly increases the complexity of these issues. Another concern is that recruitment by citizen scientists, especially individuals afflicted with the same illness, could be coercive in ways that traditional research recruitment is not.

Participants in citizen science research rarely receive financial incentives, and instead are usually induced to participate by the offer of access to research data, including their own records. Although this arrangement is generally framed as increasing rather than decreasing autonomy, it still introduces a significant risk that a participant's decision to enroll in research will be motivated by the therapeutic misconception as to their own health or misapprehending the likelihood of near-term scientific discoveries that could benefit others.[32] An examination of this novel situation related to recruitment and inducements for participation should be an important priority in the research agenda on citizen science.

Inclusion, Exclusion, and the Input/Output Problem

Increasing participation in health research among populations that have been traditionally underrepresented is an important goal because the benefits of health research will disproportionately help those patients whose ancestry and social environments are similar to research participants. This has been referred to as the "input/output problem."[33] Mobile devices may prove to be an important tool for achieving greater diversity among participants in health research because, according to the Pew Research Center, mobile devices provide access to the Internet for many minorities and low-income Americans with no alternative.[34] It remains unclear, however, whether access to mobile devices will translate into increased research participation, particularly when the research is conducted within a citizen science framework.

Empirical studies on research participation have highlighted that trust in researchers and research institutions are important prerequisites for research participation.[35] In order for mobile devices to increase research participation among underrepresented groups, the individuals and organizations leading the research will need to build trust with potential participants. Empirical research on these perceptions of traditional research institutions and citizen science-driven research will support an analysis of the potential for mobile device-based research to mitigate the input/output problem.

Informed Consent

Informed consent, the touchstone of modern research ethics, contains two important elements: (1) the obligation of researchers to inform potential research participants about known risks and benefits, as well as other relevant information; and (2) the autonomy of individuals to decide whether to participate, with additional protections for individuals with diminished autonomy (e.g., children, individuals with cognitive impairments).

Despite its centrality to research ethics (or perhaps because of it), informed consent has become the focal point for critics who contend that informed consent is too burdensome on important health research and fails to protect the interests of research participants in the way it was envisioned.[36] The September 2015 Notice of Proposed Rulemaking proposed to amend the Common Rule in several respects, such as by adding exclusions and expanding exemptions. The result is that more research conducted by traditional researchers will be unregulated. In addition, the proposal calls for the use of "broad consent" for research using specimens and data in unspecified future research.[37]

It is against this backdrop that citizen science mHealth research will emerge, with the possibility that unregulated researchers might significantly modify informed consent or dispense with it entirely. Therefore, the ELSI research agenda for citizen science mHealth research should consider a wide range of informed consent-related issues, including the necessity and viability of informed consent for citizen science research,

the appropriate applicability of informed consent, the feasibility and validity of online informed consent, and possible new methods for addressing the informational and agreement elements of informed consent.

Confidentiality and Security

Health care providers have legal and ethical duties to safeguard the health information of their patients, disclosing the information only with the consent of the patient or when compelled by law.[38] Similarly, regulated health researchers have legal and ethical duties to safeguard the health information of their research participants in accordance with the agreed upon research protocol, only disclosing information according to the prior agreement or when compelled by law.[39] This raises the issue of what, if any, confidentiality obligations should apply to citizen science health research. It is possible that the frequently anonymous nature of mHealth research might *better* protect confidential health information, but this needs further examination. Finally, it is important to consider how assurances of confidentiality made by citizen science researchers can be enforced or breaches redressed.

Security is invariably implicated when health information, including clinical records, is transmitted electronically. It is unclear whether the same standards for security apply to citizen science health research as to regulated health research and what level of security is reasonable for mHealth research. The sensitivity of the health information, its identifiability, the ability of researchers to protect the information, the use of encryption, and other factors may be very important. Also, security considerations are likely to interface with measures to verify the subject's eligibility to participate. These and other issues should be an essential part of the citizen science, mHealth research agenda.

Children and Other Vulnerable Subjects

Vulnerable research participants, including children and intellectually impaired adults, raise a particularly thorny set of issues for mHealth research.[40] In face-to-face research contexts, investigators are able to evaluate the competence of the individuals to consent or assent to participate in research and, when necessary, to identify the competent adult legally authorized to give permission in their stead. Making such assessments through a mobile device can be quite difficult, however. In addition, experts, including the American Academy of Pediatrics, recommend that media use by children, including the use of mobile devices, should be monitored by parents.[41] Investigators utilizing mobile devices to interact with pediatric research participants should typically follow this standard, but have no reasonable way to confirm that parents are monitoring their interactions with participants. These challenges and an array of others involving children and other vulnerable subjects require careful examination.

Incidental Findings and Return of Research Results

Substantial recent scholarship has been devoted to the issue of whether researchers, especially those engaged in genetic or genomic research, are required, permitted, or prohibited from disclosing incidental findings to research participants.[42] Several factors are frequently mentioned in the literature as important, including the strength of the genetic association, the severity of the condition, and the clinical actionability.[43] To the extent that researchers have obligations to disclose incidental findings, they flow from the researcher's ethical precepts and the trust inherent in the researcher-participant relationship.[44]

It is difficult to imagine that unregulated, citizen science health research containing few of the characteristics of the researcher-participant relationship would give rise to comparable ethical obligations to disclose incidental findings. Nevertheless, if a consent document is used that provides for disclosure, there may be an ethical duty to disclose incidental findings. As there is little precedent for disclosure in citizen science research, even if the researchers were inclined to disclose incidental findings and the participants wanted to receive them, it is not clear how an incidental finding notification process would take place. The ELSI research agenda for this issue should include careful consideration of the bases for and the contours of a duty to offer incidental findings to research participants.

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Publication and Data Sharing

Researchers contemplating disclosure of the results of health research can be influenced by two countervailing pressures. One pressure, the interest in being the first to discover a particular finding, sometimes leads

to the premature announcement of results, even before the finding has been replicated or published in a peer-reviewed journal. "Science by press conference" is the disparaging term applied to such practices.[45]

The opposite pressure on researchers is to suppress findings, sometimes referred to as "hoarding," which may be based on intellectual property considerations or the interest in being the sole researcher to conduct follow-up studies. The NIH has adopted detailed regulations requiring NIH-funded researchers to provide public access to data and publications,[46] but these rules do not apply to independent, citizen scientists.

It is not known what pressures may affect citizen science researchers engaged in mHealth research, but it is likely that they will be affected, at least to some extent, by these concerns. It would be ironic if the advent of citizen science would result in *less* sharing of discoveries with the public because there are no data sharing obligations. The ELSI research agenda should consider a broad range of issues surrounding public availability of findings, data sharing, publication requirements, and the effect on scholarly journals of citizen science health research.

Conclusion

Citizen science research is a term that lacks a precise definition. In general, the term has been used to describe research activities in which individuals who are not professional researchers in a particular field actively participate in a research project in partnership with traditional researchers or on their own. This article has considered only a subset of the expanding domain of citizen science health research, and the subset discussed in this article has two defining characteristics.

First, we considered only health research undertaken independently by citizen scientists. The lack of involvement by academic, health science, or pharmaceutical or medical device company researchers means that this type of citizen science health research is not subject to the federal research regulations. Citizen science research involves new roles, boundaries, and relationships for researchers and research participants. It also raises important questions about how, if at all, traditional elements of research regulation, such as external review and informed consent, ought to apply to citizen science research. Deciding what elements of the research regulations ought to apply even to unregulated research requires reconsideration of the basic assumptions on which research ethics have been based and their applicability to new circumstances.

Second, we used the new developments in mobile medical technology as a case study in analyzing citizen science health research. As already demonstrated by recent mHealth research projects, it is now possible to enroll thousands of research participants online in a matter of days and to conduct highly powered mHealth studies in weeks rather than years. Unresolved issues concerning privacy, return of results, data sharing, and scientific publication, among others, still await careful analysis and explication.

As with other types of new biomedical research in the post-genome era, embedded, collaborative, mixed-methods ELSI research can play an important role in framing essential issues and helping to ensure that the design, conduct, and consequences of this new research are scientifically and ethically defensible.

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